

Sixth Edition



Larry P. Tilley
Francis W. K. Smith, Jr.

BLACKWELL'S FIVE-MINUTE VETERINARY CONSULT: CANINE AND FELINE



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CANINE AND FELINE
SIXTH EDITION**

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CANINE AND FELINE

SIXTH EDITION

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To my wife Jeri, my son Kyle, and grandson Tucker
To my late mother Dorothy, who instilled values in my brother Steve and myself that have
helped us throughout life
To family and animals who represent the purity of life.

Larry P. Tilley

To my wife, May, my son, Ben, and my daughter, Jade, who are a constant source of inspiration, love and joy. To my late father, Frank, who was my perfect role model. To Kaylee (dog) and Centie (cat) who remind me each day to make time to play.

Francis W.K. Smith, Jr.

PREFACE

Keeping abreast of advances in veterinary internal medicine is extremely difficult, especially for the busy general practitioner. To keep current with all the veterinary journals while practicing medicine is impossible. The veterinarian in practice can be overwhelmed by all of the findings and conclusions of thousands of studies conducted by veterinary specialists. *Blackwell's Five-Minute Veterinary Consult* is designed to provide the busy veterinary practitioner and student of veterinary medicine with concise practical reviews of almost all the diseases and clinical problems in dogs and cats. Our goal in creating this textbook was also to provide up-to-date information in an easy-to-use format. Emphasis is placed on diagnosis and treatment of problems and diseases likely to be seen by veterinarians.

Our fondest dream was realized when the first five editions of this book were chosen as a comprehensive reference source for canine and feline medicine by veterinary students, practicing veterinarians, and board-certified specialists. The format has proven easy to use and very popular with busy practitioners. The scope of the book and the number of consulting editors and authors have been expanded. We have also increased the number of authors from outside North America, to provide the best advice in the world. The number of topics has been increased, and every topic has been updated to provide you with the most current information possible in a textbook. The appendixes have also been expanded to include more useful tables, and the Drug Formulary has been updated and expanded. New medications have also been added.

Several good veterinary internal medicine textbooks are available. The uniqueness and value of *Blackwell's Five-Minute Veterinary Consult* as a quick reference is the consistency of presentation, the breadth of coverage, the contribution of large numbers of experts, and the timely preparation of the manuscript. The format of every topic is identical, making it easy to find information. An extensive list of topic headings ensures complete coverage of each topic.

As the title implies, one objective of this book is to make information quickly available. To this end, we have organized topics alphabetically from A to Z. Most topics can be found without using the index. A table of contents broken out by organ system and a detailed index are provided. Large volumes of useful information are summarized in charts in the appendixes. Also included in the appendixes are an extensive and detailed drug formulary, toxicology tables, endocrine testing protocols, normal laboratory values, new genetic epilepsy classification table, pain management tables, information page with important resources for veterinarians, and conversion tables.

We are delighted and privileged to have had the assistance of numerous experts in veterinary internal medicine from around the world. More than 300 veterinary specialists contributed to this text, allowing each chapter to be written by an expert on the subject. In addition to providing outstanding information, this large pool of experts allowed us to publish this major text in a timely manner.

Many large textbooks take several years to write, making some of the information outdated by the time the book is published. We are indebted to the many contributors and consulting editors whose hard work allowed us to write, edit, and publish this work in 2 years, with most chapters completed within a year of publication. Our goal is to revise the text every 3 years, so that the contents will always be current.

Blackwell's Five-Minute Veterinary Consult : Canine and Feline, Sixth Edition is available in a variety of digital formats. Visit www.wiley.com/go/5MVC for more information. This edition also includes client education handouts based on the content of *Blackwell's Five-Minute Veterinary Consult*. The complimentary client education handouts are available on a companion website at www.fiveminutevet.com/canineandfeline featuring more than 352 Client Handouts for you to customize and use in practice. These handouts can be edited to reflect your practice preferences and then printed on your letterhead to distribute to your clients.

The book will also be published as an e-book as a downloadable ePub/ePDF. Now veterinarians can quickly access information about necessary clinical skills and new developments in diagnosis and treatment on their computers or mobile versions. Our *Blackwell's Five-Minute Veterinary Consult* website, mobile applications offer fast, affordable access to much of the accumulated wisdom in veterinary medicine by use of a simple search-and-retrieval process. This interactive computer technology brings to the clinic examination room and doctor's office an easy-to-use "dynamic textbook" that will markedly improve the quality of continuing education and clinical practice.

The sixth edition of this textbook constitutes an important, up-to-date medical reference source for your practice and clinical education. We strived to make it complete yet practical and easy to use. Our dreams are realized if this text helps you to quickly locate and use the "momentarily important" information that is essential to the practice of high-quality veterinary medicine. We would appreciate your input so that we can make future editions even more useful. If you would like to see any changes in content or format, additions, or deletions, please let us know. Send comments to the following:

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We would also like to acknowledge and thank our families for their support of this project and the sacrifices they made to allow us the time to complete the book.

In addition to thanking veterinarians who have referred patients to us, we would like to express our gratitude to each of the veterinary students, interns, and residents whom we have had the privilege of teaching. Their curiosity and intellectual stimulation have enabled us to grow and have prompted us to undertake the task of writing this book.

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This book is accompanied by a companion website:

www.fiveminutevet.com/canineandfeline

The website includes:

- Videos
- Images
- Client Education Handouts
- Additional references and internet resources

The password for the companion website: bwc837gx4d

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ABORTION, SPONTANEOUS (EARLY PREGNANCY LOSS)—CATS



BASICS

DEFINITION

- Spontaneous abortion—natural expulsion of fetus(es) prior to the point at which they can sustain life outside the uterus.
- Early pregnancy loss—generalized term for any loss of conceptus including early embryonic death and resorption.

PATOPHYSIOLOGY

- Infectious causes result in pregnancy loss directly by affecting the embryo, fetus, or fetal membranes, or indirectly by creating debilitating systemic disease in the queen.
- Non-infectious causes of pregnancy loss result from any factor other than infection that leads to the death or premature expulsion of the conceptus (e.g., uterine disease, inadequate maternal nutrition, endocrine dysfunction, toxicity, genetic defects).

SYSTEMS AFFECTED

- Endocrine
- Reproductive
- Other systems—any debilitating illness can result in pregnancy loss.

GENETICS

Genetic defects are more prevalent in highly inbred individuals; heritability of susceptibility to FIPV thought to be very high.

INCIDENCE/PREVALENCE

Unknown—pregnancy frequently not confirmed, owners may not recognize late pregnancy loss if the queen is fastidious; early embryonic death is difficult to document.

SIGNALMENT

Species

Cat

Breed Predilections

Purebred cats—higher incidence of non-infectious abortion; inbreeding increases risk of genetic disease. Predisposition to developing FIP increased in some breeds including Bengal, Birman, and Himalayan.

Mean Age and Range

Infectious abortion seen in all ages; non-infectious abortion seen more commonly in young and aged queens.

SIGNS

General Comments

Early embryonic death and resorption frequently have no clinical symptoms; any combination of historical and physical examination findings may occur, with some queens displaying no symptoms.

Historical Findings

Failure to deliver litter at expected time, return to estrus sooner than expected, decrease in abdominal diameter and weight loss, discovery of fetal material, behavior change, anorexia, vomiting, diarrhea.

Physical Examination Findings

Purulent, mucoid, watery, or sanguineous vaginal discharge; dehydration, fever, abdominal straining, abdominal discomfort.

CAUSES

Infectious

- Bacterial—organisms implicated in causing abortion via ascending infection include *Escherichia coli*, *Staphylococcus* spp., *Streptococcus* spp., *Chlamydia* spp., *Pasteurella* spp., *Klebsiella* spp., *Pseudomonas* spp., *Salmonella* spp., *Mycoplasma* spp., and *Ureaplasma* spp.
- Protozoal—*Toxoplasma gondii*
- Viral—FHV-1, FIV, FIP, FeLV, FPLV.

Non-infectious

- Uterine—cystic endometrial hyperplasia, pyometra, chronic endometritis, anatomical abnormalities of the uterus, mechanical trauma to uterus or fetus.
- Ovarian—early termination of corpora lutea function causes a decline in serum progesterone concentrations resulting in early parturition/abortion. Primary hypoluteoidism is rare but secondary hypoluteoidism may result from certain drugs, prolonged stress and uterine inflammation.
- Fetal—chromosomal abnormalities resulting in abnormal or arrested development and embryonic or fetal death.
- Systemic—malnutrition or nutritional disorders such as taurine deficiency; vitamin A deficiency or toxicity; severe non-reproductive illness; exogenous drug administration: estrogens, glucocorticoids, PGF_{2α}, and dopamine agonists (cabergoline, bromocriptine) will disrupt normal corpora lutea function; fetotoxic or teratogenic drugs: chemotherapeutic agents, antifungal agents, some antibiotics (trimethoprim-sulfonamides, tetracyclines, gentamicin); modified live vaccines.

RISK FACTORS

- Previous history of pregnancy loss
- Concurrent systemic disease
- Recent trauma
- Purebred cat with high degree of inbreeding
- Very young or old queen
- Previous use of progestins to suppress estrus
- Malnourishment
- Homemade and raw diets
- Overcrowded or unsanitary environment



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Early pregnancy loss—failure to conceive, disorder of sexual development, anovulatory cycle
- Vulvar discharge—pyometra, mucometra, uterine stump pyometra; vaginitis, metritis, cystitis; impending parturition or dystocia; neoplasia or trauma of urinary bladder, urethra, vagina, or uterus;
- Estrus—very little discharge typically seen
- Abdominal straining or discomfort: urethral obstruction; intestinal foreign body;

peritonitis; trauma; impending parturition or dystocia

CBC/BIOCHEMISTRY/URINALYSIS

- May be normal.
- Inflammatory leukogram or stress leukogram depending on systemic disease response.
- Hemoconcentration and azotemia with dehydration.

OTHER LABORATORY TESTS

Infectious Causes

- Cytology and bacterial culture of vaginal discharge, fetus, fetal membranes, or uterine contents (aerobic, anaerobic, and mycoplasma).
- FeLV—test for antigens in queens using ELISA or IFA.
- FHV-1—IFA or PCR from corneal or conjunctival swabs, viral isolation from conjunctival, nasal, or pharyngeal swabs.
- FIP—submit fetal tissue for histopathology and immunohistochemistry.
- FIV—ELISA: confirm positive results with Western blot.
- FPLV—viral isolation from fetuses submitted for necropsy; document seroconversion in the queen.

Non-infectious Causes

- To rule out anovulatory cycle, confirm progesterone rise > 1.5 ng/mL one week following mating.
- Hypoluteoidism—serum progesterone level < 1.0 ng/mL prior to abortion indicates luteal failure but does not determine whether the luteal failure was primary or secondary.
- Disorder of sexual development can be evaluated with description of external genitalia, karyotype, and histopathology of reproductive tract.

IMAGING

- Abdominal ultrasound in early gestation (21–25 days post-breeding) to confirm pregnancy and screen for evidence of resorption. Later pregnancy, evaluate health and viability of fetus(es) and associated fluid and membranes; abnormal uterine fluid accumulation and non-reproductive disease.
- Radiograph—evaluates relative size, number, and position of fetal skeletons; can also be used to screen for fetal monsters, fetal malpresentation, and non-reproductive disease.

DIAGNOSTIC PROCEDURES

- Genetic defects—necropsy aborted fetus(es); submit samples from aborted and stillborn fetus for karyotyping.
- Nutrition—submit sample of diet for nutritional analysis: of particular importance when queen is fed a homemade and/or raw diet.
- Pedigree analysis to evaluate inbreeding coefficient
- Evaluate cattery for vaccination protocols, feeding regime, general sanitation procedures, and quarantine procedures for pregnant queens and new arrivals.
- Submit reproductive tract (uterus, ovaries, uterine tubes) and aborted, stillborn, mummified fetus(es) and fetal membranes (fresh, refrigerated, on wet ice) for evaluation of anatomic and pathologic changes, gross

(CONTINUED) ABORTION, SPONTANEOUS (EARLY PREGNANCY LOSS)—CATS

necropsy, histopathology, cultures, and viral isolation.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Outpatient management: typically no medical management required for non-infectious stable queens; primary hypoluteoidism—can be managed on an outpatient basis with tocolytic drugs in combination with tocodynamometry.
- Surgical management: OHE for queens with severe illness due to pyometra or metritis.

ACTIVITY

- Isolation for queens with infectious disease.
- No activity restrictions for most non-infectious pregnancy losses.
- Restrict activity as indicated for pregnancy loss due to trauma.

DIET

Feed commercially available diet labeled for use in pregnancy. Correct diets with inappropriate taurine or vitamin A concentrations. Avoid feeding raw meats or allowing queens to hunt during pregnancy to reduce risk for ingestion of pathogenic bacteria and *T. gondii*.

CLIENT EDUCATION

- Infectious diseases—verify client is following good vaccination protocols and disease surveillance measures and is utilizing quarantine facilities for pregnant queens and new arrivals.
- Breeding management—discuss normal reproductive behavior and good breeding management; advise clients to keep detailed records related to reproductive performance, pedigree analysis, and social behavior of queens within the cattery.
- Nutrition—discuss routine diet recommendations for breeding queens; advise homemade diets undergo nutritional analysis.
- Genetic disease—increase in inbred individuals; many reproductive traits are heritable.
- Discuss risk of zoonotic disease from *Toxoplasma gondii*.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Will depend on etiology.
- Amoxicillin-clavulanic acid 13.75 mg/kg PO q12h or enrofloxacin 5 mg/kg/day PO based on bacterial culture results.
- Tocolytic therapy to prevent uterine contractions and help maintain pregnancy: Terbutaline 0.03–1.0 mg PO as needed based on tocodynamometry; 0.03 mg/kg PO q8h if tocodynamometry not available.
- Hypoluteoidism: progesterone in oil—2.0–3.0 mg/kg IM as needed based on

serum progesterone concentration and tocodynamometry.

CONTRAINDICATIONS

- Terbutaline—cardiac or respiratory disease, pyometra, infectious disease, hypertension.
- Progesterone in oil—diabetes, pyometra, infectious disease, CEH.

PRECAUTIONS

• Use of tocolytics to maintain pregnancy requires accurate documentation of breeding dates to know when treatment should be discontinued; tocolytics used most successfully in combination with tocodynamometry to establish desired dosing interval based on increasing preterm uterine activity.

• Terbutaline can cause hypertension leading to increased hemorrhage from the placental sites during parturition or at the time of c-section.

POSSIBLE INTERACTIONS

- Progesterone administration during pregnancy is associated with masculinization of female fetuses; do not administer in the first half of pregnancy and use with informed consent thereafter.
- Use of tocolytics to maintain pregnancy is associated with increased risk of dystocia, failure of normal placental separation at parturition, lack of mammary gland development and milk production, and poor maternal behavior for the first few days postpartum.

**FOLLOW-UP****PATIENT MONITORING**

- Serial ultrasound evaluation q 5–7 days to evaluate fetal viability for queens receiving tocolytics.

PREVENTION/AVOIDANCE

- Institute infectious disease prevention, control, and surveillance plan.
- Replace infertile queens with more reproductively fit individuals.
- Avoid exposure to abortifacient, teratogenic, or fetotoxic drugs.

POSSIBLE COMPLICATIONS

- Depends on etiology.
- Metritis, endometritis, uterine rupture, sepsis, shock.
- Diabetes, CEH, masculinization of female fetuses with progesterone treatment.

EXPECTED COURSE AND PROGNOSIS

- Infectious disease—normal pregnancy, repeated abortion, or infertility possible with viral disease.
- Poor prognosis for normal pregnancy in queens with severe CEH.
- Fair prognosis for successful pregnancy with treatment for primary hypoluteoidism; significant monitoring required for good outcome.
- Pregnancy loss due to genetic abnormalities likely to recur if queen is bred to tom with similar pedigree.

**MISCELLANEOUS****AGE-RELATED FACTORS**

- Queens > 6 years old have higher incidence of infertility.
- Pregnancy loss seen most frequently in very young and old queens.

ZOONOTIC POTENTIAL*Toxoplasma gondii***SEE ALSO**

- Breeding, Timing • Sexual Development Disorders

ABBREVIATIONS

- CEH = cystic endometrial hyperplasia
- ELISA = enzyme-linked immunosorbent assay
- FeLV = feline leukemia virus
- FHV-1 = feline herpesvirus 1
- FIPV = feline infectious peritonitis virus
- FIV = feline immunodeficiency virus
- FPLV = feline panleukopenia virus
- IFA = indirect fluorescent antibody
- OHE = ovario-hysterectomy
- PGF_{2α} = prostaglandin F_{2α}

INTERNET RESOURCES

- www.therijournal.com
- www.whelpwise.com

Suggested Reading

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**Client Education Handout
available online**

ABORTION, SPONTANEOUS (EARLY PREGNANCY LOSS)—DOGS



BASICS

DEFINITION

Loss of a fetus because of resorption in early stages or expulsion in later stages of pregnancy.

PATHOPHYSIOLOGY

- Direct causes—congenital abnormality, infectious disease, trauma.
- Indirect causes—infectious placentitis, abnormal ovarian function, abnormal uterine environment.

SYSTEMS AFFECTED

- Reproductive. • Any dysfunction of a major body system can adversely affect pregnancy.

GENETICS

- No genetic basis for most causes of abortion.
- Lymphocytic hypothyroidism—single-gene recessive trait in borzois.

INCIDENCE/PREVALENCE

- True incidence unknown. • Resorption estimated between 11–13%, some estimates up to 30% of at least one resorption.
- Incidence of stillbirth reported as 2.2–4.4%; increases with dystocia up to 22.3%.

SIGNALMENT

Species

Dog

Breed Predilections

- Familial lymphocytic hypothyroidism reported in borzoi—prolonged interestrus interval, poor conception rates, abortion midgestation, stillbirths. • Many breeds considered at risk for familial hypothyroidism (see Hypothyroidism).

Mean Age and Range

- Infectious causes, pharmacologic agents causing abortion, fetal defects—seen in all ages. • Cystic endometrial hyperplasia—usually > 6 years old.

Predominant Sex

Intact bitches

SIGNS

Historical Findings

- Failure to whelp on time. • Expulsion of recognizable fetuses or placental tissues.
- Decrease in abdominal size; weight loss.
- Anorexia. • Vomiting, diarrhea.
- Behavioral changes.

Physical Examination Findings

- Sanguineous or purulent vulvar discharge.
- Disappearance of vesicles or fetuses previously documented by palpation, ultrasonography, or radiography.
- Abdominal straining, discomfort.
- Depression. • Dehydration. • Fever in some patients.

CAUSES

Infectious

- *Brucella canis*. • Canine herpesvirus.
- *Toxoplasma gondii*, *Neospora caninum*.

- *Mycoplasma* and *Ureaplasma*.
- Miscellaneous bacteria—*E. coli*, *Streptococcus*, *Campylobacter*, *Salmonella*.
- Miscellaneous viruses—distemper virus, parvovirus, adenovirus.

Uterine

- Cystic endometrial hyperplasia and pyometra. • Trauma—acute and chronic.
- Neoplasia. • Embryotoxic drugs.
- Chemotherapeutic agents. • Estrogens.
- Glucocorticoids—high dosages.

Ovarian

- Prostaglandins—lysis of corpora lutea.
- Dopamine agonists—lysis of corpora lutea via suppression of prolactin; bromocryptine, cabergoline. • Hypoluteoidism—abnormal luteal function in the absence of fetal, uterine, or placental disease; progesterone concentrations < 1–2 ng/mL, most often seen at 40–45 days gestation.

Hormonal Dysfunction

- Hypothyroidism; new data shows this is less common than previously thought.
- Hyperadrenocorticism. • Environmental factors—endocrine disrupting contaminants have been documented in human and wildlife instances of fetal loss.

Fetal Defects

- Lethal chromosomal abnormality. • Lethal organ defects.

RISK FACTORS

- Exposure of the brood bitch to carrier animals • Old age • Hereditary factors



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Differentiate infectious from non-infectious causes—*B. canis* of immediate and zoonotic concern. • Differentiate resorption from infertility—helped by early diagnosis of pregnancy. • History of drug use during pregnancy—particularly during the first trimester, or use of drugs (e.g., dexamethasone, prostaglandins, ketoconazole, griseofulvin, doxycycline, tetracycline, dantralene, among others) known to cause fetal death. • Vulvar discharges during diestrus—may mimic abortion; evaluate discharge and origin to differentiate uterine from distal reproductive tract disease.
- Necropsy of aborted fetus, stillborn puppies, and placenta(s)—enhances chances of a definitive diagnosis, refrigerate but do not freeze prior to submission. • History of systemic or endocrine disease—may indicate problems with the maternal environment.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal. • Systemic disease, uterine infection, viral infection, or endocrine abnormalities—may produce changes in CBC, biochemistries, or urinalysis.

OTHER LABORATORY TESTS

- Serologic testing—*B. canis*, canine herpesvirus, and *Toxoplasma*, *Neospora*; collect serum as soon as possible after abortion; repeat testing for raising titers for canine herpesvirus, *Toxoplasma*, *Neospora*. • Slide test for *B. canis*—very sensitive; negative results reliable; prevalence of false positives as high as 60% (D-Tec CB®, Synbiotics Corp., (800)733-5500); • PCR for *B. canis* now available; • Definitive diagnosis made via culture. • Tube agglutination test for *B. canis*—gives titers; titers > 1:200 considered positive; titers from 1:50–1:200 considered suspicious. • Agar gel immunodiffusion test for *B. canis*—effectively differentiates between false positives and true positives in agglutination tests; detects cytoplasmic and cell surface antigens (Cornell University Animal Health Diagnostic Laboratory, (607)253-3900). • Baseline T₄ serum concentration (when no infectious agents are identified)—hypothyroidism is a common endocrine disease and has been suggested as a cause for fetal wastage; role in pregnancy loss unclear; subnormal T₄ concentrations indicate need for further testing (see Hypothyroidism). • Serum progesterone concentration (when no infectious agents are identified)—hypoluteoidism may cause fetal wastage; dogs depend on ovarian progesterone production throughout gestation (minimum of 2 ng/mL required to maintain pregnancy); collect sample and determine as soon as possible after abortion; in subsequent pregnancies, start weekly monitoring at week 3, which may be before pregnancy can be documented with ultrasound; start biweekly sampling around the gestational age of previous loss. Pregnancy loss typically occurs during the seventh week of gestation (see Premature Labor). • Vaginal culture—*B. canis* with positive serologic test; *Mycoplasma*, *Ureaplasma*, other bacterial agents; all except *B. canis* can be normal flora, therefore diagnosis difficult from vaginal cultures alone; *Salmonella* associated with systemic illness in the bitch.

IMAGING

- Radiography—identifies fetal structures after 45 days of gestation; earlier, can determine uterine enlargement but cannot assess uterine contents.
- Ultrasonography—identifies uterine size and contents; assesses fluid and its consistency; assesses fetal remains or fetal viability by noting heartbeats (normal, > 200 bpm; stress, < 150 or > 280 bpm).

DIAGNOSTIC PROCEDURES

- Vaginoscopy—identify source of vulvar discharges and vaginal lesions; use a scope of sufficient length (16–20 cm) to examine the entire length of the vagina. • Cytologic examination and bacterial culture—vagina may reveal an inflammatory process (e.g., uterine infection); technique for culture: use a

(CONTINUED) ABORTION, SPONTANEOUS (EARLY PREGNANCY LOSS)—DOGS

guarded swab culture instrument to ensure an anterior sample (distal reproductive tract is normally heavily contaminated with bacteria), or collection of secretions via transcervical catheterization.

PATHOLOGIC FINDINGS

Histopathologic examination and culture of fetal and placental tissue—may reveal infectious organisms; tissue culture, particularly of stomach contents, to identify infectious bacterial organisms.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Most bitches should be confined and isolated pending diagnosis.
- Hospitalization of infectious patients preferred.
- *B. canis*—highly infective to dogs; shed in high numbers during abortion; suspected cases should be isolated.
- Outpatient medical management—medically stable patients with non-infectious causes of pregnancy loss, endocrinopathies, or endometrial disease.
- Partial abortion—may attempt to salvage the live fetuses; administer antibiotics if a bacterial component is identified.

NURSING CARE

Dehydration—use replacement fluids, supplemented with electrolytes if imbalances are identified by serum biochemistries.

ACTIVITY

Partial abortion—cage rest generally recommended, although the positive effect on reducing further abortion is unknown.

DIET

No special dietary considerations for uncomplicated cases

CLIENT EDUCATION

- Critical for *B. canis*—if confirmed, euthanasia recommended due to lack of successful treatment and to prevent spread of infection; may try OHE and long-term antibiotics; discuss surveillance program for kennel situations: monthly serology for all individuals, culling any positive animals, until three consecutive negative tests are obtained; discuss zoonotic potential.
- Primary uterine disease—OHE is indicated in patients with no breeding value; cystic endometrial hyperplasia is an irreversible change.
- Infertility or pregnancy loss—may recur in subsequent estrous cycles despite successful immediate treatment.
- Prostaglandin treatment—discuss side effects (see Abortion, Termination of Pregnancy).
- Infectious diseases—establish surveillance and control measures.

SURGICAL CONSIDERATIONS

OHE—preferred for stable patients with no breeding value.

**MEDICATIONS****DRUG(S) OF CHOICE**

- PGF_{2α} (Lutalyse, dinoprost tromethamine)—uterine evacuation after abortion; 0.05–0.1 mg/kg SC q8–24h; cloprostenol (Estrumate, cloprostenol)—1–5 µg/kg SC q24h; not approved for use in dogs, but adequate documentation legitimizes its use; use only if all living fetuses have been expelled.
- Antibiotics—for bacterial disease; initially institute broad-spectrum agent; specific agent depends on culture and sensitivity testing of vaginal tissue or necropsy of fetus.
- Progesterone (Regu-Mate) at 0.088 mg/kg (1 mL/25 kg PO q24h); progesterone in oil at 2 mg/kg IM q48–72h; progesterone (Prometrium®; 10 mg/kg PO q24h, adjust daily dosage based on serum progesterone)—for documented hypoluteodism only to maintain pregnancy, must have accurate due date to know when to discontinue therapy— inadvertently prolonging gestation will result in fetal death.

CONTRAINdications

Progesterone supplementation—contraindicated in dogs with endometrial or mammary gland disease.

PRECAUTIONS

PGF_{2α}—metabolized in the lung; side effects are related to smooth muscle contraction, are dose-related, and diminish with each injection; panting, salivation, vomiting, and defecation common; dosing critical (LD₅₀ for dinoprost—5 mg/kg).

ALTERNATIVE DRUG(S)

Oxytocin—1 U/5 kg SC q6–24h for uterine evacuation; should only be considered in cases where uterine evacuation is desired solely through uterine contraction.

**FOLLOW-UP****PATIENT MONITORING**

- Partial abortion—monitor viability of remaining fetuses with ultrasonography; monitor systemic health of the dam for remainder of pregnancy.
- Vulvar discharges—daily; for decreasing amount, odor, and inflammatory component; for consistency (increasing mucoid content is prognostically good).
- PGF_{2α}—continued for 5 days or until most of the discharge ceases (range 3–15 days).
- *B. canis*—monitor after neutering and antibiotic therapy; yearly serologic testing to identify recrudescence.
- Hypothyroidism—treat appropriately; neutering recommended (hereditary nature); see Hypothyroidism.

PREVENTION/AVOIDANCE

- Brucellosis and other infectious agents—surveillance programs to prevent introduction to kennel.
- OHE—for bitches with no breeding value.
- Use of modified-live vaccines (e.g., some distemper, parvovirus, etc., vaccines).

POSSIBLE COMPLICATIONS

- Untreated pyometra—septicemia, toxemia, death.
- Brucellosis—discospondylitis, endophthalmitis, recurrent uveitis.

EXPECTED COURSE AND PROGNOSIS

- Pyometra—recurrence rate during subsequent cycle is high (up to 70%) unless pregnancy is established.
- CEH—recovery of fertility unlikely; pyometra common complication.
- Hormonal dysfunction—often manageable; familial aspects should be considered.
- Brucellosis—guarded; extremely difficult to successfully eliminate infection even if combined with neutering.

**MISCELLANEOUS****AGE-RELATED FACTORS**

Older bitches more likely to have CEH

ZOONOTIC POTENTIAL

B. canis—can be transmitted to humans, especially when handling the aborting bitch and expelled tissues; massive numbers of organisms expelled during abortion. Pathologists should be warned when *B. canis* is suspected. People that are immunocompromised are at greatest risk for infection.

SEE ALSO

- Brucellosis
- Hypothyroidism
- Infertility, Female—Dogs
- Premature Labor
- Pyometra

ABBREVIATIONS

- CEH = cystic endometrial hyperplasia
- OHE = ovariohysterectomy
- PGF_{2α} = prostaglandin F_{2α}

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Client Education Handout
available online

ABORTION, TERMINATION OF PREGNANCY



BASICS

DEFINITION

Termination of an unwanted pregnancy. May be accomplished by drugs that alter embryo transport in the oviduct impeding establishment of a pregnancy, and/or cause luteal regression, terminating an established pregnancy. Due to their possible side effects (CEH, aplastic anemia and bone marrow suppression), drugs that impair embryonic transit through the oviduct (estrogens) are not commonly used or recommended.

PATHOPHYSIOLOGY

After fertilization the embryo travels the oviduct in a timely manner before entering the uterus. Impaired embryo transport through the oviduct leads to embryonic degeneration and implantation abnormalities. In the dog and cat, pregnancy maintenance is dependent on progesterone production from the corpora lutea. In dogs and cats, maintenance of the corpora lutea during the second half of gestation is also supported by prolactin. Drugs that cause luteal regression, antagonize PRL, and/or compete with progesterone receptors will terminate pregnancy.

SYSTEMS AFFECTED

- Cardiovascular • Digestive • Neurologic (caused by drugs used for treatment)
- Reproductive • Respiratory

GENETICS

N/A

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat

Breed Predilections

N/A

Mean Age and Range

Postpubertal bitch and queen

Predominant Sex

Pregnant bitch or queen

SIGNS

- Depends on stage of gestation: ° None
- ° Vaginal discharge ° Fetal expulsion

CAUSES

- Impaired oviductal transport • Luteal regression • Progesterone receptor antagonism

RISK FACTORS

N/A



DIAGNOSIS

- Confirm pregnancy first, less than 40% of mated bitches become pregnant:
 - Abdominal palpation (bitch: 31–33 days after LH surge; queen: 21–25 days after breeding).
 - Transabdominal ultrasound (bitch: > 25 days after LH surge; queen: > 16 days after breeding).
 - Abdominal radiographs (bitch: > 45 days after LH surge; queen: > 38 days after breeding).
 - Serum relaxin concentration in the bitch (> 28 days after LH surge) (Witness® Relaxin, Synbiotics/ Zoetis Corp., <http://synbiotics.com/index.html>; (800)733-5500).
- Ascertain that a breeding took place; a tie in the bitch and coital “after-reaction” in the queen.

DIFFERENTIAL DIAGNOSIS

- Hydrometra • Mucometra • Hematometra
- Pyometra • Pseudopregnancy

CBC/BIOCHEMISTRY/URINALYSIS

- Within normal limits during first half of pregnancy in healthy patients.
- Decrease in PCV during second half of pregnancy in bitches and queens is normal.
- Recommended as screening test prior to treatment in patients with suspected underlying disease.

OTHER LABORATORY TESTS

- Vaginal cytology—determines stage of estrous cycle and presence of sperm (absence does not rule out a previous breeding). Methods to increase detection of sperm: infuse and recover 5–10 mL of saline from anterior vagina using standard AI pipette, centrifuge, examine pellet; collect routine cytology and allow swab to sit in 1–2 mL of saline, express fluid, centrifuge, examine pellet.
- Serum progesterone concentration determines if the female is in diestrus and monitors luteal regression during treatment.

IMAGING

- Transabdominal ultrasound (method of choice): diagnose pregnancy and monitor uterine evacuation during treatment.
- Abdominal radiographs.

PATHOLOGIC FINDINGS

N/A



TREATMENT

APPROPRIATE HEALTH CARE

- Physical examination before initiation of treatment.
- Monitor 30–60 minutes after treatment for side effects (vomiting, defecation, hypersalivation, hyperpnea, micturition, tachycardia).
- Pregnancy status in early diestrus is unknown; ultrasound confirmation of pregnancy is not possible until ~4 weeks after breeding.
- Treatment on day 6–10 of diestrus—may have reduced

efficacy compared to midgestation but can be less distasteful to client (less discharge and recognizable fetuses are not passed).

- PGF_{2α} and bromocriptine given in combination—improves efficacy of either drug given alone.

NURSING CARE

N/A

ACTIVITY

Normal

DIET

Avoid feeding prior to each treatment and for 1–2 hours after treatments (reduces nausea and vomiting).

CLIENT EDUCATION

- Discuss patient's reproductive future with owner. If no litters are desired, then OHE is the best option.
- Discuss with the client the potential side effects of the treatment options; reach a mutual agreement on the treatment plan.

SURGICAL CONSIDERATIONS

OHE is recommended for patients with no reproductive value or when owners do not desire future litters.



MEDICATIONS

DRUG(S) OF CHOICE

- Confirmation of pregnancy before initiating any of the treatment protocols suggested below is recommended. Lengths of treatment suggested may vary; treatments should be continued until abortion is complete.

- PGF_{2α}: causes luteal regression with subsequent decline in progesterone concentration, cervical relaxation, and uterine contractions; bitches and cats low dose protocol: 10 µg/kg SC q6h for 7–10 days or until pregnancy terminated (in the bitch), then 25 µg/kg q6h for 1–2 days; then 50 µg/kg q6h for 3–4 days (the queen is more resistant to the luteolytic effects of PGF_{2α} than bitches—often higher doses for longer periods are required); bitch standard dose protocol: 100 µg/kg SC q8h for 2 days, then 200 µg/kg SC q8h until pregnancy termination; queens: 0.5–1 mg/kg SC q12h every other day > day 40, or 2 mg/cat IM q24h for 5 days > day 33.

- Cloprostenol (prostaglandin analogue): bitches: 2.5 µg/kg SC q8 or q12h every 48 hours until pregnancy termination (~6 days after start of treatment).

- Dexamethasone: mode of action is unknown; bitches: 0.2 mg/kg PO q8–12h for 5 days, then decreasing from 0.16 to 0.02 mg/kg over the last five days; treatment failures not uncommon.

- Cabergoline (PRL antagonist): causes luteal regression; bitches: 1.65 µg/kg SC q24h for 5 days or 5 µg/kg PO q24h for 5 days > day 40; queens: 1.65 µg/kg SC for

(CONTINUED)

ABORTION, TERMINATION OF PREGNANCY

- 5 days > day 30 or 5 µg/kg PO q24h for 5 days > day 35.
- Bromocriptine (PRL antagonist): causes luteal regression; bitches: 50–100 µg/kg q12h IM or PO for 4–7 days > day 35 (50% effective); vomiting common side effect, reduce dose and give with meal.
 - Cloprostenol and cabergoline combination: bitches: cabergoline 5 µg/kg PO q24h for 10 days plus cloprostenol 2.5 µg/kg SC at start of treatment or 1 µg/kg SC at start of treatment and at day 5 of treatment; treatment should be initiated > 28 days post-LH surge; queen: cabergoline 5 µg/kg PO q24h plus cloprostenol 5 µg/kg SC q48h (> 30 days after breeding) until abortion is complete (~ 9 days).
 - Cloprostenol and bromocriptine combination: bitches; bromocriptine 30 µg/kg q8h PO for 10 days plus cloprostenol 2.5 µg/kg SC or 1 µg/kg SC at start of treatment and at day 5 of treatment; treatment should be initiated > 28 days post-LH surge.

CONTRAINDICATIONS

- PGF_{2α} and analogues: animals with respiratory disease (bronchoconstriction); do not administer intravenously.
- Cabergoline and bromocriptine: avoid administration in animals hypersensitive to ergot alkaloids; use with caution in patients with significantly impaired liver function.
- Estrogens may cause cystic endometrial hyperplasia, pyometra, and bone marrow suppression leading to pancytopenia.

PRECAUTIONS

- PGF_{2α} and analogues: side effects are dose-dependent and include vomiting, defecation, dyspnea, tachycardia, salivation, restlessness, and anxiety; side effects subside within 60 minutes; the severity of effects can be attenuated with premedication (> 15 minutes) with a combination of atropine (0.025 mg/kg); use extreme caution in dogs and cats with preexisting cardiopulmonary, liver, and renal diseases.
- Dexamethasone: polydipsia, polyuria, and polyphagia are reported side effects. Long-term administration has been associated with hyperadrenocorticism.
- Cabergoline and bromocriptine: should be administered with caution in patients with impaired liver function. Side effects may include vomiting and anorexia; prolonged use (> 2 weeks) may cause coat color changes.

POSSIBLE INTERACTIONS

- PGF_{2α} and analogues: effect may be reduced by concomitant administration of progestins; use may enhance effects of oxytocin.
- Cabergoline and bromocriptine: cabergoline effects may be reduced with concomitant treatment with dopamine (D₂) antagonists; avoid concomitant treatment with hypotensive drugs.

ALTERNATIVE DRUG(S)

- The following drugs are recommended for use in bitches but not available in the United States:
 - Mifepristone (RU486; progestin and glucocorticoid receptor antagonist): 2.5 mg/kg PO q12h for 4–5 days > day 32 of pregnancy (dog); no side effects have been reported.
 - Aglepristone (progestin and glucocorticoid receptors antagonists): 10 mg/kg SC q24h for 2 days > 32 days post-LH surge (dog); pregnancy is terminated in 4–7 days; mild reaction at injection site have been reported; mild vaginal discharge may be observed.
 - Aglepristone and cloprostenol combination: aglepristone (10 mg/kg SC) combined with cloprostenol (1 µg/kg SC) q24h for 2 days > 25 days pregnancy; pregnancy is terminated within 6 days. Side effects after treatment include vomiting and diarrhea. Vaginal discharge may be observed.
 - Aglepristone (10 mg/kg SC, q24h for 2 days) with intravaginal misoprostol (200–400 µg, depending on body size) daily until abortion complete; abortion complete within 7 days. Vomiting, diarrhea, polydipsia, anorexia not observed with this regimen.
 - GnRH antagonists (Acyline; blocks GnRH receptors at the pituitary gland, causing a decline in gonadotropins concentration): a single treatment with 110–330 µg/kg SC is recommended (dog); pregnancy is terminated within 6–10 days after treatment; prepartum-like behavior has been observed; abortion may be followed by serosanguineous vaginal discharge for 2–3 days; not yet available in the US (currently in Phase I clinical trials for prostate cancer in men).

**FOLLOW-UP****PATIENT MONITORING**

In animals treated with luteolytic drugs (prostaglandins and PRL antagonists), progesterone assays and transabdominal ultrasound examinations should be performed to monitor decrease of serum progesterone concentration and complete evacuation of uterine contents. In patients treated with progesterone receptor antagonist drugs, transabdominal ultrasound examinations are recommended to monitor complete evacuation of the uterus.

PREVENTION/AVOIDANCE

- OHE for bitches and queens not intended for breeding.
- Estrus suppression or confinement of bitches and queens intended for breeding during a later cycle to avoid mismating.

POSSIBLE COMPLICATIONS

Pregnancy termination may not be achieved after one treatment protocol and continuation or change in treatment protocol may be necessary.

EXPECTED COURSE AND PROGNOSIS

- The interestrous interval in bitches treated with prostaglandins and PRL inhibitors may be shortened (~1 month). Queens may resume estrous behavior 7–10 days after pregnancy termination.
- Subsequent estrus fertility is not affected.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYNS

Induced abortion

SEE ALSO

Breeding, Timing

ABBREVIATIONS

- CEH = cystic endometrial hyperplasia
- GnRH = gonadotropin-releasing hormone
- LH = luteinizing hormone
- OHE = ovariohysterectomy
- PCV = packed cell volume
- PGF_{2α} = prostaglandin F_{2α}
- PRL = prolactin

Suggested Reading

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**Client Education Handout
available online**

ABSCESSTION



BASICS

DEFINITION

An abscess is a localized collection of purulent exudate contained within a cavity.

PATHOPHYSIOLOGY

- Bacteria are often inoculated under the skin via a puncture wound; the wound surface then seals.
- When bacteria and/or foreign objects persist in the tissue, purulent exudate forms and collects.
- Accumulation of purulent exudates—if not quickly resorbed or discharged to an external surface, stimulates formation of a fibrous capsule; may eventually lead to abscess rupture.
- Prolonged delay of evacuation—formation of a fibrous abscess wall; to heal, the cavity must be filled with granulation tissue from which the causative agent may not be totally eliminated; may lead to chronic or intermittent discharge of exudate from a draining sinus tract.

SYSTEMS AFFECTED

- Skin/Exocrine—percutaneous (cats > dogs); anal sac (dogs > cats)
- Reproductive—prostate gland (dogs > cats); mammary gland
- Ophthalmic—periocular tissues
- Hepatobiliary—liver parenchyma
- Gastrointestinal—pancreas (dogs > cats)

GENETICS

N/A

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Cat and dog

Breed Predilections

N/A

Mean Age and Range

N/A

Predominant Sex

Mammary glands (female); prostate gland (male)

SIGNS

General Comments

- Determined by organ system and/or tissue affected.
- Associated with a combination of inflammation (pain, swelling, redness, heat, and loss of function), tissue destruction, and/or organ system dysfunction caused by accumulation of exudates.

Historical Findings

- Often presented for nonspecific signs such as lethargy and anorexia.

- History of traumatic insult or previous infection.
- A rapidly appearing painful swelling with or without discharge, if affected area is visible.

Physical Examination Findings

- Determined by the organ system or tissue affected.
- Classic signs of inflammation (heat, pain, swelling, and loss of function) are associated with specific anatomic location of the abscess.
- Inflammation and discharge from a fistulous tract may be visible if the abscess is superficial and has ruptured to an external surface.
- A variably sized, painful mass of fluctuant to firm consistency attached to surrounding tissues may be palpable.
- Fever if abscess is not ruptured and draining.
- Sepsis occasionally, especially if abscess ruptures internally.

CAUSES

- Foreign objects.
- Pyogenic bacteria—*Staphylococcus* spp.; *Escherichia coli*; β -hemolytic *Streptococcus* spp.; *Pseudomonas*; *Mycoplasma* and *Mycoplasma*-like organisms (L-forms); *Pasteurella multocida*; *Corynebacterium*; *Actinomyces* spp.; *Nocardia*; *Bartonella*.
- Obligate anaerobes—*Bacteroides* spp.; *Clostridium* spp.; *Peptostreptococcus*; *Fusobacterium*.

RISK FACTORS

- Anal sac—impaction; anal sacculitis.
- Brain—otitis interna sinusitis oral infection.
- Liver—omphalophlebitis sepsis.
- Lung—foreign object aspiration bacterial pneumonia.
- Mammary gland—mastitis.
- Periorbital—dental disease; chewing of wood or other plant material.
- Percutaneous—fighting, trauma, or surgery.
- Prostate gland—bacterial prostatitis.
- Immunosuppression—FeLV/FIV infection, immunosuppressive chemotherapy, acquired or inherited immune system dysfunctions, underlying predisposing disease (e.g., diabetes mellitus, chronic renal failure, hyperadrenocorticism).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Mass Lesions

- Cyst—less or only transiently painful; slower growing.
- Fibrous scar tissue—firm; non-painful.
- Granuloma—less painful; slower growing; generally firmer without fluctuant center.
- Hematoma/seroma—variable pain (depends on cause); non-encapsulated; rapid initial growth but slow increase once full size is attained; unattached to surrounding tissues; fluctuant and fluid filled initially but more firm with organization.

- Neoplasia—variable growth; consistent; painful.

Draining Tracts

- Mycobacterial disease
- Mycetoma—botryomycosis, actinomycotic mycetoma, eumycotic mycetoma
- Neoplasia
- Phaeohyphomycosis
- Sporotrichosis
- Systemic fungal infection—blastomycosis, coccidioidomycosis, cryptococcosis, histoplasmosis, trichosporosis

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—normal or neutrophilia with or without regenerative left shift. Neutropenia and degenerative left shift if sepsis present.
- Urinalysis and serum chemistry profile—depends on system affected.
- Prostatic—pyuria.
- Liver and/or pancreatic—high liver enzymes and/or total bilirubin.
- Pancreatic (dogs)—high amylase/lipase.
- Diabetes mellitus—persistent hyperglycemia and glucosuria.

OTHER LABORATORY TESTS

- FeLV and FIV—for cats with recurrent or slow-healing abscesses.
- CSF evaluation—increase in cellularity and protein expected with brain abscess.
- Adrenal function—evaluate for hyperadrenocorticism.

IMAGING

- Radiography—soft-tissue density mass in affected area; may reveal foreign body.
- Ultrasonography—determine if mass is fluid filled or solid; determine organ system affected; reveal flocculent-appearing fluid characteristic of pus; may reveal foreign object.
- Echocardiography—helpful for diagnosis of pericardial abscess.
- CT or MRI—helpful for diagnosis of brain abscess.

DIAGNOSTIC PROCEDURES

Aspiration

- Reveals a red, white, yellow, or green liquid.
- Protein content $> 2.5\text{--}3.0 \text{ g/dL}$.
- Nucleated cell count—3,000–100,000 (or more) cells/ μL ; primarily degenerative neutrophils with lesser numbers of macrophages and lymphocytes.
- Pyogenic bacteria—may be seen in cells and free within the fluid.

- If the causative agent is not readily identified with a Romanowsky-type stain, specimens should be stained with an acid-fast stain to detect mycobacteria or *Nocardia* and PAS stain to detect fungus.

Biopsy

- Sample should contain both normal and abnormal tissue in the same specimen.
- Impression smears—stained and examined.
- Tissue—submit for histopathologic examination and culture.

(CONTINUED)

- Contact the diagnostic laboratory for specific instructions.

Culture

- Affected tissue and/or exudate— aerobic and anaerobic bacteria and fungus.
- Blood and/or urine—isolate bacterium responsible for possible sepsis.
- Bacterial sensitivity.

PATHOLOGIC FINDINGS

- Pus-containing mass lesion accompanied by inflammation.
- Palpable—variably firm or fluctuant mass.
- Ruptured—may see pus draining directly from the mass or an adjoining tract.
- Exudate—large numbers of neutrophils in various stages of degeneration; other inflammatory cells; necrotic tissue.
- Surrounding tissue—congested; fibrin; large number of neutrophils; variable number of lymphocytes; plasma cells; macrophages.
- Causative agent variably detectable.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Depends on location of abscess and treatment required.
- Outpatient—bite-induced abscesses.
- Inpatient—sepsis; extensive surgical procedures; treatment requiring extended hospitalization.
- Establish and maintain adequate drainage.
- Surgical removal of nidus of infection or foreign object(s) if necessary.
- Institution of appropriate antimicrobial therapy.

NURSING CARE

- Depends on location of abscess.
- Apply hot packs to inflamed area as needed.
- Use protective bandaging and/or Elizabethan collars as needed.
- Accumulated exudate—drain abscess; maintain drainage by medical and/or surgical means.
- Sepsis or peritonitis—aggressive fluid therapy and support.

ACTIVITY

Restrict until the abscess has resolved and adequate healing of tissues has taken place.

DIET

- Sufficient nutritional intake to promote a positive nitrogen balance.
- Depends on location of abscess and treatment required.

CLIENT EDUCATION

- Discuss need to correct or prevent risk factors.
- Discuss need for adequate drainage and continuation of antimicrobial therapy for an adequate period of time.

SURGICAL CONSIDERATIONS

- Appropriate debridement and drainage—may need to leave the wound open to an external surface; may need to place surgical drains.
- Early drainage—to prevent further tissue damage and formation of abscess wall.
- Remove any foreign objects(s), necrotic tissue, or nidus of infection.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Antimicrobial drugs—effective against the infectious agent; gain access to site of infection.
- Broad-spectrum agent—bactericidal and with both aerobic and anaerobic activity; until results of culture and sensitivity are known. Dogs and cats: amoxicillin (11–22 mg/kg PO q8–12h); amoxicillin/clavulanic acid (12.5–25 mg/kg PO q12h); clindamycin (5 mg/kg PO q12h); and trimethoprim/sulfadiazine (15 mg/kg PO IM q12h). Cats with *Mycoplasma* and l-forms: doxycycline (5 mg/kg PO q12h).
- Aggressive antimicrobial therapy—sepsis or peritonitis.

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

Monitor for progressive decrease in drainage, resolution of inflammation, and improvement of clinical signs.

PREVENTION/AVOIDANCE

- Percutaneous abscesses—prevent fighting.
- Anal sac abscesses—prevent impaction; consider anal saculectomy for recurrent cases.
- Prostatic abscesses—castration possibly helpful.
- Mastitis—prevent lactation (spaying).
- Periorbital abscesses—do not allow chewing on foreign object(s).

POSSIBLE COMPLICATIONS

- Sepsis.
- Peritonitis/pleuritis if intra-abdominal or intrathoracic abscess ruptures.
- Compromise of organ function.
- Delayed evacuation may lead to chronically draining fistulous tracts.

EXPECTED COURSE AND PROGNOSIS

Depends on organ system involved and amount of tissue destruction.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- FeLV or FIV infection
- Immunosuppression

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

- Minimal for pyogenic bacteria.
- Mycobacteria and systemic fungal infections carry some potential.

PREGNANCY/FERTILITY/BREEDING

Teratogenic agents—avoid use in pregnant animals.

SEE ALSO

- Actinomycosis
- Anaerobic Infections
- Colibacillosis
- Mycoplasmosis
- Nocardiosis
- Sepsis and Bacteremia

ABBREVIATIONS

- CSF = cerebrospinal fluid
- CT = computed tomography
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- MRI = magnetic resonance imaging
- PAS = periodic acid-Schiff

Suggested Reading

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**Client Education Handout
available online**

ACETAMINOPHEN (APAP) TOXICOSIS



BASICS

DEFINITION

Results from accidental animal ingestion or owner administration of over-the-counter acetaminophen-containing analgesic and antipyretic medications.

PATHOPHYSIOLOGY

When the normal biotransformation mechanisms for detoxification (glucuronidation and sulfation) are saturated, cytochrome P450-mediated oxidation produces a toxic metabolite (*N*-acetyl-p-benzoquinone imine) that is electrophilic, conjugates with glutathione, and binds to sulphydryl groups leading to hepatic necrosis.

Dogs

- Liver is most susceptible to toxicity.
- Signs commonly observed at exposures > 100 mg/kg.
- Methemoglobinemia may develop at doses > 200 mg/kg.

Cats

- Cannot effectively glucuronidate; more limited capacity for acetaminophen elimination than dogs.
- Saturate glucuronidation and sulfation biotransformation routes.
- RBCs are most susceptible to oxidative injury following glutathione depletion.
- Develop toxic cytochrome P450 metabolite at much lower doses than dogs.
- Poisoned by as little as 50–60 mg/kg (often as little as one-half tablet); deacetylation of acetaminophen to p-aminophenol (PAP) causes oxidative damage to RBCs, rapidly producing methemoglobinemia by binding to sulphydryl groups on hemoglobin.
- Slower-developing hepatotoxicosis may not be fully expressed before development of fatal methemoglobinemia.

SYSTEMS AFFECTED

- Hemic/Lymph/Immune—RBCs are damaged by glutathione depletion, allowing oxidation of hemoglobin to methemoglobin.
- Hepatobiliary—liver necrosis (more common in dogs).
- Cardiovascular (primarily cats)—edema of the face, paws, and (to a lesser degree) forelimbs through an undefined mechanism.

GENETICS

Cats—genetic deficiency in the glucuronide conjugation pathway makes them vulnerable.

INCIDENCE/PREVALENCE

Common drug toxicity in cats; less frequent in dogs.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Cats more often than dogs

SIGNS

General Comments

Relatively common—owing to widespread human use.

Historical Findings

- Depression
- Hyperventilation
- Darkened mucous membranes
- Signs may develop 1–4 hours after dosing

Physical Examination Findings

- Progressive depression
- Salivation
- Vomiting
- Abdominal pain
- Tachypnea and cyanosis or muddy mucous membranes—reflect methemoglobinemia
- Edema—face, paws, and possibly forelimbs; after several hours
- Chocolate-colored urine—hematuria and methemoglobinuria; especially in cats
- Icterus
- Hypothermia
- Shock
- Death

CAUSES

Acetaminophen toxicosis

RISK FACTORS

- Nutritional deficiencies of glucose and/or sulfate
- Simultaneous administration of other glutathione-depressing drugs



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other causes of liver injury

- Hepatotoxic mushrooms
- Blue-green algae
- Aflatoxins
- Iron, copper, zinc
- Xylitol
- Cycad palms
- NSAIDs

Other causes of methemoglobinemia

- Onions/garlic
- Naphthalene
- Chlorates
- Nitrites
- Sulfites
- Phenol
- Benzocaine
- Propylene glycol (cats)

CBC/BIOCHEMISTRY/URINALYSIS

- Methemoglobinemia and progressively rising serum concentrations of liver enzymes (ALT, AST)—characteristic.
- As hepatic function becomes impaired—decreased BUN, cholesterol, and albumin, and increased serum bilirubin.
- Heinz bodies (cats)—prominent in RBCs within 72 hours.
- Anemia, hemoglobinemia, and hemoglobinuria or hematuria.

OTHER LABORATORY TESTS

Acetaminophen plasma, serum, or urine concentrations

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

- Methemoglobinemia.
- Pulmonary edema.
- Centrilobular necrosis and congestion of the liver.
- Renal tubular edema and degeneration with proteinaceous tubular casts.



TREATMENT

APPROPRIATE HEALTH CARE

- With methemoglobinemia—must evaluate promptly.
- With dark or bloody colored urine or icterus—inpatient.

NURSING CARE

- Gentle handling—imperative for clinically affected patients.
- Induced emesis and gastric lavage—useful within 4–6 hours of ingestion.
- Anemia, hematuria, or hemoglobinuria—may require whole blood transfusion.
- Fluid therapy—maintain hydration and electrolyte balance.
- Oxygen therapy may be needed.
- Drinking water—available at all times.
- Food—offered 24 hours after initiation of treatment.

(CONTINUED)

ACETAMINOPHEN (APAP) TOXICOSIS**ACTIVITY**

Restricted

DIET

N/A

CLIENT EDUCATION

- Warn client that treatment in clinically affected patients may be prolonged and expensive.
- Inform client that patients with liver injury may require prolonged and costly management.

SURGICAL CONSIDERATIONS

N/A

**MEDICATIONS****DRUG(S) OF CHOICE**

- Activated charcoal 2 g/kg PO; immediately after completion of emesis or gastric lavage.
- N*-acetylcysteine (Mucomyst) 140 mg/kg diluted in D5W as loading dose PO, IV; then 70 mg/kg diluted in D5W PO, IV, q6h for 5–7 additional treatments.
- S-adenosylmethionine (SAMe) as a glutathione donor; 40 mg/kg PO × 1 dose, then 20 mg/kg q24h PO × 7 days.
- Added benefit of using methylene blue, cimetidine, and/or ascorbic acid is controversial.

CONTRAINDICATIONS

Drugs that contribute to methemoglobinemia or hepatotoxicity.

PRECAUTIONS

Drugs requiring extensive liver metabolism or biotransformation—use with caution; expect their half-lives to be extended.

POSSIBLE INTERACTIONS

Drugs requiring activation or metabolism by the liver have reduced effectiveness.

**FOLLOW-UP****PATIENT MONITORING**

- Continual clinical monitoring of methemoglobinemia—vital for effective management; laboratory determination of methemoglobin percentage every 2–3 hours.
- Serum liver enzyme activities (ALT, ALP) every 12 hours; monitor liver damage.

PREVENTION/AVOIDANCE

- Never give acetaminophen to cats.
- Give careful attention to the acetaminophen dose in dogs.

POSSIBLE COMPLICATIONS

Liver necrosis and resulting fibrosis—may compromise long-term liver function in recovered patients.

EXPECTED COURSE AND PROGNOSIS

- Rapidly progressive methemoglobinemia—serious sign.
- Methemoglobin concentrations ≥ 50%—grave prognosis.
- Progressively rising serum liver enzymes 12–24 hours after ingestion—serious concern.
- Expect clinical signs to persist 12–48 hours; death owing to methemoglobinemia possible at any time.
- Dogs and cats receiving prompt treatment that reverses methemoglobinemia and prevents excessive liver necrosis—may recover fully.
- Dogs—death as a result of liver necrosis may occur within 72 hours.
- Cats—death as a result of methemoglobinemia occurs 18–36 hours after ingestion.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Keratoconjunctivitis sicca (KCS) may develop in small-breed dogs as a sequela.

AGE-RELATED FACTORS

Young and small dogs and cats—greater risk from owner-given single-dose acetaminophen medications.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Imposes additional stress and higher risk on exposed animals.

SYNONYMS

- Paracetamol
- Tylenol

SEE ALSO

Poisoning (Intoxication) Therapy

ABBREVIATIONS

- PAP = p-aminophenol
- ALT = alanine aminotransferase
- AST = aspartate transaminase
- RBC = red blood cell
- D5W = 5% dextrose injection

INTERNET RESOURCES

<http://www.aspca.org/pet-care/poison-control/>

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Client Education Handout
available online

ACIDOSIS, METABOLIC (TRADITIONAL APPROACH)



BASICS

DEFINITION

A process in the body that leads to a decrease in pH below the reference interval for that species. A decline in blood pH is specifically termed acidemia. Associated with a decrease in plasma bicarbonate concentration (HCO_3^-) (dogs, > 18 mEq/L; cats, > 16 mEq/L) and base excess (BE) (< -4 mmol/L) with a compensatory decrease in carbon dioxide tension (PCO_2).

PATOPHYSIOLOGY

- Metabolic acidosis may develop either from a loss of HCO_3^- (hyperchloremic acidosis) or a gain in acid (high anion gap acidosis). It is usually secondary to an accumulation of metabolically produced strong anions (strong ion gap or high anion gap acidosis), accumulation of weak acids (hyperphosphatemia), corrected hyperchloremia (hyperchloremic acidosis), or as a compensatory mechanism for respiratory alkalosis.
- High anion gap acidosis:** Increase in the concentration of other strong anions through addition (e.g., ethylene glycol toxicity), excessive production (e.g., lactate produced by prolonged anaerobic metabolism), or renal retention (e.g., renal failure) of strong anions other than chloride causes metabolic acidosis without increasing chloride concentration (so-called normochloremic or high AG metabolic acidosis).
- Hyperphosphatemic acidosis:** Increase in plasma weak acids (e.g., inorganic phosphate) is associated with metabolic acidosis and increased anion gap. At pH of 7.4, a 1 mg/dL increase in phosphate concentration is associated with a 0.58 mEq/L decrease in HCO_3^- and a 0.58 mEq/L increase in AG. Hyperphosphatemia commonly develops with decreased renal phosphorous excretion (e.g., renal failure, hypoparathyroidism, etc), cellular lysis (e.g., tumor lysis syndrome, trauma, rhabdomyolysis), bone neoplasms (increased bone resorption), and hypervitaminosis D.
- Hyperchloremic acidosis:** Hyperchloremic acidosis may be caused by chloride retention (e.g., renal failure, renal tubular acidosis) that typically occurs in response to HCO_3^- loss. Chloride and HCO_3^- are reciprocally related; a loss of HCO_3^- generally results in retention of chloride. Other mechanisms for hyperchloremic acidosis include: excessive loss of sodium relative to chloride (e.g., diarrhea, Addison's) and administration of substances containing more chloride than sodium as compared with normal extracellular fluid composition (e.g., administration of KCl, 0.9% NaCl). Acidemia is usually not severe in patients with hyperchloremic acidosis.

SYSTEMS AFFECTED

• **Cardiovascular**—a fall in pH results in an increase in sympathetic discharge but simultaneously causes a decrease in the responsiveness of the cardiac myocytes and vascular smooth muscle to the effects of catecholamines. In mildly acidemic conditions (pH > 7.2), the effects of increased sympathetic stimulation predominate and result in a mild increase in heart rate and cardiac output. More severe acidemia (pH < 7.1), especially if acute, may decrease cardiac contractility and predispose the heart to ventricular arrhythmias and ventricular fibrillation.

• **Respiratory**—increased $[\text{H}^+]$ stimulates peripheral and central chemoreceptors to increase alveolar ventilation; hyperventilation decreases PCO_2 , which counters the effects of low plasma HCO_3^- on pH. In dogs, a decrease of approximately 0.7 mmHg in PCO_2 is expected for each 1 mEq/L decrease in plasma HCO_3^- . Little is known about compensation in cats, but it appears to be almost nonexistent.

• **Renal/Urologic**—the kidneys increase net acid excretion, primarily by increasing excretion of NH_4^+ and chloride. This compensatory mechanism is not very effective in cats.

SIGNALMENT

Any breed, age, or sex of dog and cat

SIGNALMENT

Historical Findings

- Chronic disease processes that lead to metabolic acidosis (e.g., renal failure, diabetes mellitus, and hypoadrenocorticism), acute circulatory shock (hemorrhagic), exposure to toxins (e.g., ethylene glycol, salicylate, and paraldehyde), diarrhea, administration of carbonic anhydrase inhibitors (e.g., acetazolamide and dichlorphenamide).

Physical Examination Findings

- Generally relate to the underlying disease.
- Depression, stupor, seizures, and/or generalized muscle weakness in severely acidotic patients.
- Tachypnea in some patients results from compensatory increase in ventilation.
- Kussmaul's respiration, typically seen in human beings with metabolic acidosis, is not commonly observed in dogs and cats.
- Vomiting and/or diarrhea.

CAUSES

Associated with Hyperchloremia (Hyperchloremic Metabolic Acidosis)

- Renal:** Renal tubular acidosis; carbonic anhydrase inhibitors.
- GI:** Diarrhea.
- Other:** Chloride-rich fluids (e.g., 0.9% NaCl, KCl supplementation); total parenteral nutrition with cationic amino acids: lysine, arginine, and histidine; rapid correction of hypocapnia (chronic respiratory alkalosis); NH_4Cl or HCl.

Associated with Normochloremia (High Anion Gap Metabolic Acidosis)

- Renal:** uremic acidosis, acute renal failure.
- Ketoacidosis:** diabetic ketoacidosis, starvation liver disease.
- Lactic acidosis:** impaired perfusion, impaired carbohydrate metabolism.
- Toxins:** ethylene glycol, salicylate, paraldehyde, and methanol intoxication.
- Hyperphosphatemia (see Hyperphosphatemia):** raises the anion gap. At a pH of 7.4, each 1 mg/dL increase in phosphate concentration is associated with a 0.58 mEq/L increase in anion gap.

RISK FACTORS

- Chronic renal failure, diabetes mellitus, and hypoadrenocorticism
- Poor tissue perfusion or hypoxia—lactic acidosis
- Tumor lysis syndrome or osteosarcoma—hyperphosphatemia
- Trauma, snake envenomation, or malignant hyperthermia—rhabdomyolysis



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Low plasma HCO_3^- and hyperchloremia may also be compensatory in animals with chronic respiratory alkalosis, in which PCO_2 is low and pH is high or near normal, despite decreased HCO_3^- and increase in chloride concentration. Blood gas determination is required to differentiate.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

Potassium bromide is measured as chloride in most analyzers, so potassium bromide administration artificially decreases the anion gap.

Disorders That May Alter Laboratory Results

- Too much heparin (> 10% of the sample) decreases HCO_3^- .
- Blood samples stored at room temperature for > 15 minutes have low pH because of increased PCO_2 .
- Hypoalbuminemia lowers AG; negative charges of albumin are the main component of the anion gap.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Low total CO_2 —total CO_2 in serum samples handled aerobically closely approximates the serum HCO_3^- concentration; unfortunately, patients with chronic respiratory alkalosis also have low total CO_2 , and the distinction cannot be made without blood gas analysis.
- Metabolic acidoses are traditionally divided into hyperchloremic and high anion gap by means of the anion gap. Anion gap, the difference between the measured cations and the

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ACIDOSIS, METABOLIC (TRADITIONAL APPROACH)

A

measured anions, is calculated as $AG = [Na^+] - (HCO_3^- + Cl^-)$ or $AG = ([Na^+] + [K^+]) - (HCO_3^- + Cl^-)$, depending on the preference of the clinician or laboratory. Normal values with potassium included in the calculation are usually 12–24 mEq/L in dogs and 13–27 mEq/L in cats. The negative charges of albumin are the major contributors to the normal anion gap; this should be taken into account when evaluating anion gap in patients with hypoalbuminemia. At pH 7.4 in dogs, a decrease of 1 g/dL in albumin is associated with a decrease of 4.1 mEq/L in the anion gap. • Normal anion gap (i.e., hyperchloremic metabolic acidosis). • High anion gap (i.e., normochloremic metabolic acidosis). • Hyperglycemia—see Hyperglycemia. • Azotemia—see Azotemia. • Hyperphosphatemia—see Hyperphosphatemia. • High lactate concentration—see Lactic Acidosis. • Hyperkalemia—see Hyperkalemia (*formulas to adjust potassium concentration based on pH changes should not be used*).

OTHER LABORATORY TESTS

Blood gas analysis reveals low HCO_3^- , low PCO_2 , and low pH.

DIAGNOSTIC PROCEDURES

None

**TREATMENT**

- Acid-base disturbances are secondary phenomena; successful resolution depends on diagnosis and treatment of the underlying disease process.
- Restore blood volume and perfusion deficits before considering $NaHCO_3$.
- Treat patients with blood pH ≤ 7.1 aggressively while pursuing the definitive diagnosis.
- Discontinue drugs that may cause metabolic acidosis.
- Nursing care—Isotonic, *buffered* electrolyte solution is the fluid of choice for patients with mild metabolic acidosis and normal liver function.

**MEDICATIONS****DRUG(S) OF CHOICE**

- $NaHCO_3$ may help patients with hyperchloremic, hyperphosphatemic, or uremic acidosis, but not patients with lactic acidosis or diabetic ketoacidosis.
- $NaHCO_3$ may be considered for alkaline diuresis in salicylate toxicity.
 - Estimation of HCO_3^- dose: dogs, $0.3 \times$ body weight (kg) $\times (21 - \text{patient } HCO_3^-)$; cats, $0.3 \times$ body weight (kg) $\times (19 - \text{patient } HCO_3^-)$. Give half of this dose slowly IV and reevaluate blood gases before deciding on the need for additional administration. An empirical dose of 1–2 mEq/kg followed

by reevaluation of blood gas status is safe in most patients.

- Potential complications of $NaHCO_3$ administration: volume overload resulting from administered sodium, tetany from low ionized calcium concentration, increased affinity of hemoglobin for oxygen, paradoxical CNS acidosis, overshoot metabolic alkalosis, and hypokalemia.
- Hyperchloremic acidosis: $NaHCO_3$ may be effective and considered whenever pH < 7.1 .
- Uremic acidosis: efficacy of $NaHCO_3$ in acute therapy of uremic acidosis is related to the shift of phosphate inside the cells and consequent amelioration of hyperphosphatemic acidosis.
- Lactic acidosis: $NaHCO_3$ increases lactate production and is of little to no value in lactic acidosis. Therapy should be directed at augmenting oxygen delivery to the tissues and reestablishing cardiac output. Small titrated doses of $NaHCO_3$ can be used as a temporizing measure to maintain HCO_3^- above 5 mEq/L, if needed.
- Diabetic ketoacidosis: $NaHCO_3$ adversely affects outcome in humans with diabetic ketoacidosis even when pH < 7.0 .
- Administration of $NaHCO_3$ to ketoacidotic patients cannot be recommended at any pH. Therapy should be direct at insulin and fluid administration. Reestablishing plasma volume and renal perfusion will allow the kidneys to excrete ketoanions, replacing them with chloride.

CONTRAINdications

- Avoid $NaHCO_3$ in patients with respiratory acidosis because it generates CO_2 .
- Patients with respiratory acidosis cannot adequately excrete CO_2 , and increased PCO_2 will further decrease the pH.
- Avoid diuretics that act in the distal nephron (e.g., spironolactone).
- Avoid carbonic anhydrase inhibitors (e.g., acetazolamide, dichlorphenamide).
- Avoid $NaHCO_3$ in acute (< 10 minutes) cardiac arrest as it may impair tissue oxygen unloading.

PRECAUTIONS

Use $NaHCO_3$ cautiously in patients with congestive heart failure because the sodium load may cause decompensation of the heart failure.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None

**FOLLOW-UP****PATIENT MONITORING**

Recheck acid-base status; frequency dictated by the underlying disease and patient response to treatment.

POSSIBLE COMPLICATIONS

- Hyperkalemia in acute hyperchloremic acidosis
- Myocardial depression and ventricular arrhythmias

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Hyperkalemia
- Hyperchloremia

AGE-RELATED FACTORS

None

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYS

- Dilutional acidosis—metabolic acidosis resulting from increased free water in plasma.
- Hyperchloremic acidosis—normal anion gap acidosis.
- Hyperphosphatemic acidosis—metabolic acidosis resulting from high phosphate concentration.
- Non-respiratory acidosis.
- Normochloremic acidosis—high anion gap acidosis.
- Organic acidosis—metabolic acidosis resulting from accumulation of organic anions (e.g., ketoacidosis, uremic acidosis, and lactic acidosis).

SEE ALSO

- Azotemia
- Diabetes Mellitus with Ketoacidosis
- Hyperchloremia
- Hyperkalemia
- Hyperphosphatemia
- Lactic Acidosis

ABBREVIATIONS

- AG = anion gap
- BE = base excess
- CNS = central nervous system
- H^+ = hydrogen ion
- HCO_3^- = bicarbonate
- $NaHCO_3$ = sodium bicarbonate
- O_2 = oxygen
- PCO_2 = carbon dioxide tension

Suggested Reading

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ACNE—CATS



BASICS

OVERVIEW

- Inflammatory dermatitis affecting the chin and lips
- Symptoms may be recurrent or persistent
- Precise etiology unknown

SIGNALMENT

- Cats
- Prevalence for sex, age, or breed not reported

SIGNS

- Cats may have a single episode, a life-long recurrent problem, or a continual disease.
- Frequency and severity of each occurrence varies with the individual.
- Comedones, mild erythematous papules, serous crusts, and dark keratin debris develop on the chin and less commonly on the lips.
- Swelling of the chin.
- Severe cases—nodules, hemorrhagic crusts, pustules, cysts, fistulae, severe erythema, alopecia, and pain.
- Pain often associated with bacterial furunculosis.

CAUSES & RISK FACTORS

Precise etiology unknown; may be a disorder of keratinization, poor grooming, abnormal sebum production, immunosuppression, viral infection, or stress.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Bacterial folliculitis
- Demodicosis
- Malassezia* infection
- Dermatophytosis
- Neoplasia of sebaceous or apocrine glands
- Eosinophilic granuloma
- Contact hypersensitivity

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Skin scrapings—demodicosis.
- Fungal culture—dermatophytosis.
- Cytology—bacteria, *Malassezia*.
- Biopsy—rarely needed; necessary in selected cases to characterize changes such as cystic follicles, to differentiate acne from other diseases such as demodicosis, infections (bacterial, yeast, or dermatophytes), or to diagnose neoplasia.

PATHOLOGIC FINDINGS

- Mild disease—follicular distention with keratin (comedo), hyperkeratosis, and follicular plugging.
- Severe disease—mild to severe folliculitis and perifolliculitis with follicular pustule formation leading to furunculosis and pyogranulomatous dermatitis.
- Bacteria and *Malassezia* in these lesions are considered secondary invaders and not causative agents.
- Demodex* mites can be primary agents of this disease.



TREATMENT

- Initial treatment—gentle clipping and soakings to soften crusts.
- Continue one or a combination of the therapies listed below until all lesions have resolved.
- Discontinue treatment by tapering medication over a 2- to 3-week period.
- Recurrent episodes—once the recurrence rate is determined, an appropriate maintenance protocol can be designed for each individual.
- Continual episodes—life-long maintenance treatment necessary.



MEDICATIONS

DRUG(S)

Topical

- Shampoo—once or twice weekly with antiseborheic (sulfur-salicylic acid, benzoyl peroxide, or ethyl lactate).
- Cleansing agents—benzoyl peroxide, salicylic acid, chlorhexidine-phthosphingosine.
- Wet wipes—Douxo Chlorhexidine pads®, Malaseb® wipes, MalAcetic® wipes, GlycoZoo® wipes.
- Antibiotic ointment—mupirocin 2%.
- Other topicals—clindamycin or erythromycin solution or ointment.
- Combination topicals—benzoyl peroxide-antibiotic gels (e.g., Benzamycin).
- Topical retinoids—Tretinoin (Retin-A 0.01% gel).
- In severe inflammatory periods 10–14 days of oral prednisolone (1–2 mg/kg q24h) may help to reduce scar tissue formation.

Systemic

- Antibiotics—amoxicillin with clavulanate, cephalosporin, or fluoroquinolone.
- Severe cases may warrant treatment with isotretinoin (Accutane) or cyclosporine, modified (Atopica).
- Demodicosis—oral ivermectin 400 µg/kg daily until mites are cleared.

CONTRAINdications/POSSIBLE INTERACTIONS

- Benzoyl peroxide and salicylic acids—can be irritating.
- Some wipes contain alcohols that can be irritating.
- Systemic isotretinoin—use with caution, if animal will not allow application of topical medications; potential deleterious side effects in human beings (drug interactions and teratogenicity); container should be labeled for animal use only and kept separate from human medications to avoid accidental use; currently difficult to obtain for animal patients.



FOLLOW-UP

- Monitor for relapses.
- Maintenance cleansing programs can be used to reduce relapses. Affected cats are likely to have variable numbers of comedones life-long, often are just cosmetic and treatment is not necessary.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Systemic isotretinoin should not be used on breeding animals.

Suggested Reading

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BASICS

OVERVIEW

- Also called muzzle folliculitis and furunculosis.
- Chronic inflammatory disorder of the chin and lips of young animals.
- Characterized by folliculitis and furunculosis; rarely comedogenic as seen in “true acneiform” lesions of human beings.
- Recognized almost exclusively in short-coated breeds.
- Genetic predisposition and local trauma may play a more important role than hormonal effects.

SIGNALMENT

- Dogs.
- Predisposed short-coated breeds—boxer, Doberman pinscher, English bulldog, Great Dane, Weimaraner, mastiff, rottweiler, German shorthaired pointer, pit bull terrier.

SIGNS

- Ventral chin and lip margins may be minimally to markedly swollen with numerous erythematous papules and pustules.
- Initial lesions are sterile; bacteria may not be isolated and lesions may not respond to antibiotics.
- Advanced stages—lesions may be exudative, indicating secondary deep bacterial folliculitis-furunculosis.
- Lesions may be painful on palpation; most are non-painful and non-pruritic.
- Chronic resolved lesions may be scarred and lichenified.

CAUSES & RISK FACTORS

Some short-coated breeds appear to be genetically predisposed to follicular hyperkeratosis and secondary bacterial infection.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Dermatophytosis
- Demodicosis
- Foreign body
- Contact dermatitis

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Bacterial culture and sensitivity testing—in patients with suppurative folliculitis and furunculosis that are non-responsive to initial antibiotic selection.
- Biopsy—histologic confirmation for cases in which diagnosis is in question.
- Skin scrape—demodicosis.
- Dermatophyte culture—dermatophytosis.

PATHOLOGIC FINDINGS

- Clinical signs and histopathologic findings are diagnostic.
- Initial lesions—hairless follicular papules; characterized histopathologically by marked follicular keratosis, plugging, dilatation, and perifolliculitis.
- Bacteria—not present and cannot be isolated from lesions in early stages.
- As disease progresses, papules enlarge and rupture, promoting a suppurative folliculitis and furunculosis.



TREATMENT

- Depends on the severity and chronicity of the disease.
- Reduce behavioral trauma to the chin (e.g., rubbing on the carpet, chewing bones that increase salivation).
- Frequent cleaning with benzoyl peroxide shampoo or gel.
- Mupirocin 2% ointment to reduce the bacterial numbers on the surface of the skin.
- Instruct owners to avoid expressing the lesions, which may cause internal rupture of the papule and massive inflammation.



MEDICATIONS

DRUG(S)

Topical

- Benzoyl peroxide shampoo or gel (antibacterial).
- Mupirocin 2% ointment (antibacterial-staphylococcus).
- Tretinoin (Retin-A)—may reduce follicular keratosis.
- Corticosteroids—may be necessary to reduce inflammation; limit frequency of use to avoid local and systemic effects.

Systemic

- Antibiotics appropriate for deep bacterial infection—when indicated (e.g., cephalaxin, 22 mg/kg PO q8-12h for 6–8 weeks).
- May need to perform bacterial culture and sensitivity test.
- Isotretinoin (Accutane)—1–2 mg/kg/day.
- Oral corticosteroids: tapering dosages of prednisolone (initial 0.5 mg/kg/day) to reduce significant inflammation; not for continued use.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Benzoyl peroxide—may bleach carpets and fabrics; may be irritating.
- Mupirocin ointments—greasy; may be prudent to reserve for use in multidrug-resistant cases.
- Topical retinoids—may be drying and irritating.
- Topical steroids—may cause adrenal suppression and thinning of skin with repeated use.
- Isotretinoin—may cause keratoconjunctivitis sicca, hyperactivity, ear pruritus, erythema of mucocutaneous junctions, lethargy with vomiting, abdominal distension, anorexia with lethargy, collapse, and swollen tongue; CBC and chemistry screen abnormalities include high platelet count, hypertriglyceridemia, hypercholesterolemia, and high alanine transaminase.



FOLLOW-UP

PATIENT MONITORING

- Continue antibiotics until lesions have healed.
- Repeat bacterial culture/sensitivity if lesions worsen.
- Discontinue topical corticosteroids when possible.

EXPECTED COURSE AND PROGNOSIS

- Long-term topical treatment may be required.
- Chronic scarring may be prevented by early and aggressive therapy.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Synthetic retinoids—teratogens; do not use in pregnant animals, animals intended for reproduction, or intact female animals; should not be handled by women of childbearing age.

Suggested Reading

Miller WH, Griffin CE, Campbell KL. Muzzle folliculitis and furunculosis. In: Muller & Kirk's Small Animal Dermatology, 7th ed. St. Louis, MO: Elsevier, 2013, pp 201 and 640.

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ACRAL LICK DERMATITIS



BASICS

OVERVIEW

- Chronic lesions directly caused by self-trauma.
- A cycle of licking, pruritus, and secondary infection develops.

SYSTEMS AFFECTED

Skin/Exocrine

SIGNALMENT

- Dogs.
- Most common in large breeds—especially Doberman pinschers, Labrador retrievers, Great Danes, Irish and English setters, golden retrievers, Akitas, Dalmatians, boxers, Shar-Peis, and Weimaraners.
- Age at onset—varies (especially with cause).
- No sex predilection.

SIGNS

- Excessive licking of the affected area.
- Alopecic, eroded, thickened, and raised firm plaques with scabs and exudation, usually located on the dorsal aspect of the carpus, metacarpus, tarsus, or metatarsus.
- Lesions often occur singly or may be multiple.

CAUSES & RISK FACTORS

- Focal trauma to the area initiating a lick-itch cycle.
- Anything causing a local irritation or lesion may initiate response.
- Associated diseases—staphylococcal furunculosis, hypersensitivity, endocrinopathy, demodicosis, dermatophytosis, foreign body reaction, neoplasia, underlying joint disease or arthritis, trauma, neuropathy, psychogenic, or sensory nerve dysfunction.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Neoplasia
- Bacterial furunculosis
- Focal demodicosis
- Focal dermatophytosis

CBC/BIOCHEMISTRY/URINALYSIS

Normal except in cases of endocrinopathy.

OTHER LABORATORY TESTS

Endocrinopathy—free T₄/TSH; ACTH stimulation test or LDDST.

IMAGING

Radiology—neoplasia; local trauma; radiopaque foreign bodies; bony proliferation may be seen secondary to the chronic irritation; evidence of underlying arthritis if over a joint.

DIAGNOSTIC PROCEDURES

- Skin scrapings—demodicosis.

- Dermatophyte culture—fungal infection.
- Epidermal cytology—bacterial infection.
- Bacterial culture and sensitivity—tissue cultures may differ from surface culture.
- Food-elimination diet—determine food allergy.
- Intradermal allergy testing—atopy.
- Biopsy—to rule out neoplasia, other infections.
- Behavioral history.
- Neurologic and orthopedic evaluation.

PATHOLOGIC FINDINGS

Histopathology—epidermal hyperplasia, plasmacytic dermal inflammation, folliculitis, furunculosis, perihidradenitis, hidradenitis, and vertical streaking fibrosis.



TREATMENT

- Behavioral therapy: attempt to identify psychological causes and remediate.
- Physical restraints—Elizabethan collars and bandaging permit healing.
- Therapeutic laser—one controlled study did not demonstrate efficacy.
- Diet—no modification unless food hypersensitivity is suspected.
- Difficult to treat, especially if no underlying cause is found; warn owner that patience and time are necessary.
- Surgery (laser or standard)—may cause increased licking and attention to a larger affected area; if underlying causes are not addressed, recurrence is likely.



MEDICATIONS

DRUG(S)

Antibiotics

- Based on bacterial culture and sensitivity.
- Administer until infection is completely resolved; often at least 6 weeks.

Systemic

- Antihistamines—e.g., hydroxyzine (1–2 mg/kg PO q12h); chlorpheniramine (4–8 mg/dog PO q12h; maximum of 0.5 mg/kg q12h).
- SSRIs: e.g., fluoxetine (1 mg/kg PO q24h); paroxetine (0.5–1 mg/kg PO q24h).
- Dopamine antagonists: e.g., naltrexone (2.2 mg/kg PO q12–24h).
- TCAs: e.g., amitriptyline (1.1–2.2 mg/kg PO q12h; doxepin (3–5 mg/kg PO q12h; maximum 150 mg q12h); clomipramine (1–3.5 mg/kg PO q12–24h).
- Combine and/or withdraw administration of these medications carefully.

Topical

- Flunixin meglumine and flucinolone in dimethyl sulfoxide (combined).
- Topical capsaicin products.
- Intralesional corticosteroids rarely helpful.

- Topical medications should be applied with gloves.
- Animals should be kept from licking the area for 10–15 minutes.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Doxepin—caution using with monoamine oxidase inhibitors, clonidine, anticonvulsants, oral anticoagulants, steroid hormones, antihistamines, or aspirin.
- Antihistamines—may cause sedation.
- Psychotropic medications should be combined and/or withdrawn carefully.
- Cardiotoxicity and hepatotoxicity—rare cases in animals on TCAs. Routine monitoring recommended.



FOLLOW-UP

- Monitor level of licking and chewing closely.
- Treat underlying disease to prevent recurrence.
- If no underlying disease is detected, suspect psychogenic causes (compulsive or self-mutilation disorder); prognosis is guarded.



MISCELLANEOUS

AGE-RELATED FACTORS

Dogs < 5 years old—strongly consider allergy

ZOONOTIC POTENTIAL

- Transmitted to humans only if dermatophytosis is the underlying cause; exceedingly rare.
- Methicillin resistant *Staphylococcus aureus* may have zoonotic implications.

ABBREVIATIONS

- ACTH = adrenocorticotropin hormone
- LDDST = low-dose dexamethasone suppression test
- SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant
- TSH = thyroid stimulating hormone

Suggested Reading

Shumaker AK, Angus JC, et al.

Microbiological and histopathological features of canine acral lick dermatitis. Vet Dermatol 2008, 19(5):288–298.

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BASICS

OVERVIEW

- Syndrome resulting from growth hormone (somatotropin) hypersecretion by tumorous or hyperplastic somatotrophs in the anterior pituitary.
- Clinical signs are due to growth hormone's direct catabolic/diabetogenic effects and its indirect anabolic effects mediated through insulin-like growth factor I, which is secreted by the liver in response to growth hormone stimulation.
- Elevated IGF1 activity induces excessive soft tissue growth, visceral organomegaly, bone remodeling and thickening (especially in bones formed from membranous ossification) resulting in arthropathy, broad facial features, and enlarged "clubbed" paws.
- Myocardial hypertrophy occurs in many cats, but heart failure is uncommon.
- The catabolic actions of GH result from insulin antagonism leading eventually to pancreatic β cell exhaustion and DM. Between 25 and 33% of diabetic cats may have acromegaly.
- Like most diabetic cats the potential for remission remains if the excessive GH production can be normalized; likelihood of remission is inversely related to the duration of DM.

SIGNALMENT

- Cat
- Median age—11 years (range of 6–17 years)
- Approximately 80% are males

SIGNS

- Initial signs relate to unregulated DM with the vast majority of cases presenting with polyuria, polydipsia, and often profound polyphagia accompanied with concurrent weight gain (weight loss has also been reported).
- Many patients gain weight and have increased body size due to increased bone and soft tissue mass, not from increased adipose tissue. Weight gain in an unregulated diabetic cat strongly suggests acromegaly.
- Broadening of facial features, prognathia inferior, and increased paw size reflect long-standing or severe disease.
- Organomegaly—most commonly bilateral renomegaly and hepatomegaly.
- Murmur and/or gallop rhythm occasionally present; signs of heart failure uncommon.
- Lameness may develop.
- Neurologic signs referable to intracranial disease through an expanding pituitary mass lesion possible.
- Recent reports suggest the majority of acromegalic cats are indistinguishable phenotypically from non-acromegalic diabetic cats.

CAUSES & RISK FACTORS

- GH hypersecretion.
- Progestins do not cause GH secretion and acromegaly in cats as they do in dogs.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Uncomplicated DM or DM secondary to hyperadrenocorticism
- Pituitary-dependent hyperadrenocorticism and acromegaly can both produce insulin-resistant DM with an associated pituitary mass lesion. Differentiation may require use of a low-dose dexamethasone suppression test to rule out PDH.
- Acromegaly and PDH can occur concurrently.
- Other disorders causing weight loss with polyphagia, polyuria, and polydipsia such as hyperthyroidism are not usually associated with significant glucose intolerance.
- Insulin-resistant DM (> 2.0 U of insulin/kg/12h) is to be expected in all acromegalic cats and the dose tends to increase over time, with doses of 12–50 U/cat/12h not uncommon.
- Acromegaly should be suspected in any diabetic cat demonstrating signs of otherwise unexplained insulin resistance.

CBC/BIOCHEMISTRY/URINALYSIS

- Most abnormalities attributed to poorly controlled DM—hyperglycemia, glucosuria, and elevated fructosamine levels are consistent findings in most acromegalic cats.
- Hyperproteinemia.
- Traditionally associated with renal failure and hypertension, but more recent studies suggest this is not the case.

OTHER LABORATORY TESTS

- IGF1—diabetic cats receiving insulin can have higher IGF1 levels than normal; hence there is significant potential for overlap between acromegalic and non-acromegalic diabetic cats; however, dramatically elevated IGF1 levels (e.g., $> 1,000$ ng/ml) are strongly suggestive of the acromegaly.
- IGF1 is well preserved across the species, so valid assays are commonly available.
- GH—elevated basal serum levels are diagnostic. However, as GH is not well preserved across the species, a validated fGH assay has limited availability.

IMAGING

- Intracranial imaging to demonstrate a pituitary mass lesion; MRI is more sensitive than contrast-enhanced CT, although the difference is modest and from a cost-benefit perspective CT is generally preferred.
- Echocardiographic abnormalities may include left atrial enlargement, asymmetric

septal and left ventricular free-wall thickening, systolic anterior motion of the mitral valve, and diastolic dysfunction.

- Radiographic changes include increased oropharyngeal soft tissue, degenerative arthropathy with periarticular osteophytosis, spinal spondylosis deformans, and variable abdominal organomegaly.



TREATMENT

RADIOTHERAPY

- The only currently available means of reducing autonomous overproduction of GH from the anterior pituitary. Unfortunately, radiotherapy is more suited to reducing the size of the tumor than achieving clinically significant reductions in GH secretion.
- A total dose of between 3,500 and 5,000 cGy, administered in variably fractionated doses is often suggested. Recent reports suggest that the greatest success may be achieved with a total dose of 3,700 cGy administered as an incremental hypofractionated dosage protocol of 10 doses. Using this method, 13 of 14 acromegalic cats had markedly improved diabetic control.

SURGERY

- Hypophysectomy is considered the treatment of choice in human hypersomatotropism. It has also proven to be the only consistently effective and reliable method to cure HS in cats.
- An experienced neurosurgeon and appropriate pre-, peri- and postoperative care are essential for success. A transsphenoidal approach is currently preferred (incising the soft palate).
- In the long run, cats need to be supplemented with thyroid hormone and a glucocorticoid; synthetic ADH (DDAVP) supplementation can often be ceased 6–8 weeks postoperatively. When performed early in the disease process, diabetic remission is a realistic outcome and often occurs within 2 months after the procedure.



MEDICATIONS

Somatostatin and dopamine agonists have been used to try to inhibit GH secretion by the pituitary, mostly without success. Recently, a novel somatostatin analog, pasireotide (Novartis, Basel, Switzerland) has been shown to be effective at achieving this, although further research is required to evaluate the use of this drug, including dosing regimes, in the long run.

PALLIATIVE TREATMENT

- When definitive treatment is not possible, the focus should lie on gaining more control of the diabetes mellitus and treating possible comorbidities.
- Eventually most cats tend to need high dosages of insulin and/or combinations of short-acting and long-acting insulin types to ensure an adequate quality of life for both pet and owner.
- Nevertheless, a minority achieve an adequate quality of life.
- Regular veterinary assessment is recommended.
- Iatrogenic hypoglycemia is a major concern given the pulsatile nature of GH secretion (and therefore associated insulin resistance).

**FOLLOW-UP**

- Clinical signs that might be attributed to poor diabetic control (e.g., profound polyphagia) will not improve with improved diabetic control; thus levels of glycated proteins or blood glucose levels are better indicators of diabetic control than clinical signs.
- Serum IGF1 levels are not suitable for monitoring therapy as they do not change during or after radiotherapy.
- Reported survival times vary enormously—from a few months to many years, and dying from causes unlikely to be related to acromegaly.

**MISCELLANEOUS***Suggested Reading*

Berg RI, Nelson RW, Feldman EC, et al. Serum insulin-like growth factor-I concentration in cats with diabetes mellitus and acromegaly. *J Vet Intern Med* 2007, 21(5):892–898.

Niessen SJ, Petrie G, Gaudiano F, et al. Feline acromegaly: an underdiagnosed endocrinopathy? *J Vet Intern Med* 2007, 21(5):899–905.

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BASICS

OVERVIEW

- An infectious disease caused by Gram-positive, branching, pleomorphic, rod-shaped bacteria of the genus *Actinomyces*.
- *A. viscosus* and *A. hordeovulnaris*—most commonly identified isolates (though most isolates are not identified to the species level); survives in microaerophilic or anaerobic conditions.
- Rarely found as the single bacterial agent in a lesion; more commonly, it is a component of a polymicrobial infection.
- There may be synergism between *Actinomyces* and other organisms.
- Organ systems affected may include:
 - Skin
 - Respiratory
 - Cardiovascular
 - Musculoskeletal
 - Nervous

SIGNALMENT

- Dogs and cats (uncommon).
- Most common in young male dogs of sporting breeds.

SIGNS

- Infections—usually localized; may be disseminated; cervicofacial area commonly involved.
- Cutaneous swellings or abscesses with draining tracts—yellow granules (“sulfur granules”) may be seen in associated exudates.
- Pain, fever, and weight loss.
- Exudative pleural or peritoneal effusions; occasionally pericardial effusion noted.
- Cough, dyspnea, decreased ventral lung sounds (empyema).
- Retroperitonitis—lumbar pain; rear limb paresis or paralysis.
- Osteomyelitis of vertebrae or long bones—probably secondary to extension of cutaneous infection; lameness or a swollen extremity may develop.
- Motor and sensory deficits—reported with spinal cord compression by granulomas.
- Pyothorax and subcutaneous bite wounds are the most common presenting signs in cats.

CAUSES & RISK FACTORS

- *Actinomyces* spp. normal inhabitants of the oral cavity of dogs and cats.
- Loss of normal protective barriers (mucosa, skin), immunosuppression, or change in the bacterial microenvironment can predispose; thought to occur as an opportunistic infection.
- Specific risk factors—trauma (bite wound), migrating foreign body (grass awn or, in the western United States, a foxtail), and periodontal disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Nocardiosis—primary differential diagnosis; *Actinomyces* not reliably distinguished from *Nocardia* spp. by Gram staining, cytology, or clinical signs.
- Other causes of chronic

draining tracts and pleural or peritoneal effusions must be addressed.

CBC/BIOCHEMISTRY/URINALYSIS

- Nonspecific changes.
- Leukocytosis with a left shift and monocytosis—reported.
- Nonregenerative anemia—may develop.
- Hypoglycemia and hyperglobulinemia—reported.

IMAGING

- Radiographs of infected bone—periosteal new bone production, reactive osteosclerosis, and osteolysis.
- Thoracic radiographs—alveolar and interstitial lung patterns with possible lung consolidation; pleural effusion; pericardial effusion; subcutaneous masses on lateral thorax.
- Abdominal radiographs—peritoneal effusion; mass effect in abdomen.
- Vertebral column radiographs—periosteal new bone formation, especially T13–L3.

DIAGNOSTIC PROCEDURES

- Pus or osteolytic bone fragments submitted in anaerobic specimen containers for culture (see *Anaerobic Infections*) can provide a definitive diagnosis; inform the lab to check for actinomycosis; advisable to submit aerobic culture, as well.
- Fresh smears—Gram staining, cytology, and acid-fast staining; staining does not preclude the need for culture; *Actinomyces* does not stain acid-fast; *Nocardia* is variable.

PATHOLOGIC FINDINGS

Histopathologic examination—sulfur granules can be difficult to find so multiple tissue sections should be submitted; special stains may enhance visualization of organisms; granules are a useful diagnostic tool when present; pyogranulomatous or granulomatous cellulitis with colonies of filamentous bacteria is characteristic.



TREATMENT

- Exudative fluid (thorax, abdomen, subcutaneous tissue) should be drained and lavaged.
- A chest tube with continuous suction is needed for cats with pyothorax; dogs are best served with surgical exploration of the chest prior to tube placement in order to identify and remove any grass awns.
- Diseased lung lobes may need to be removed.
- Dogs with solitary masses involving the thoracic or abdominal wall may experience cure with radical surgical excision.



MEDICATIONS

DRUG(S)

- Important to distinguish between *Actinomyces* and *Nocardia* for appropriate antimicrobial selection.

- Antibiotics—a retrospective study suggests administration for a minimum of 3–4 months after resolution of all signs; may need to be directed against other associated microbes.
- Penicillins—considered the drug of choice; in most cases, oral therapy can be initiated and parenteral is not needed; amoxicillin should be administered at 20–22 mg/kg q8h PO.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Metronidazole—avoid use; actinomycosis unlikely to respond.
- Aminoglycosides—do not use; ineffective against anaerobic infections.
- *A. hordeovulnaris*—cell-wall deficient variant (l-phase); does not usually respond well to penicillin; consider clindamycin, erythromycin, and chloramphenicol.



FOLLOW-UP

PATIENT MONITORING

Monitor patients closely for recurrence in the months after therapy discontinued.

PREVENTION/AVOIDANCE

Avoidance of contact with grass awns and prevention of bite wounds.

POSSIBLE COMPLICATIONS

Concurrent immune-suppressive disease or therapy may complicate management.

EXPECTED COURSE AND PROGNOSIS

Redevelopment of infection at the initial site may be expected in about half of all cases.



MISCELLANEOUS

AGE-RELATED FACTORS

Young outdoor dogs.

ZOONOTIC POTENTIAL

There are no reported cases of actinomycosis being transmitted from animals to man; transmission by bite wound may be possible so appropriate attention should be given to bite wounds.

Suggested Reading

Edwards DF. Actinomycosis and nocardiosis. In: Greene CE, ed., Infectious Diseases of the Dog and Cat, 3rd ed. St. Louis, MO: Saunders Elsevier, 2006, pp. 451–461.

Thomovsky E., Kerl ME. Actinomycosis and nocardiosis. Compend Contin Educ Pract Vet 2008, 10:4–10.

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ACUTE ABDOMEN



BASICS

DEFINITION

An emergency condition characterized by historical and physical examination findings of a tense, painful abdomen. May represent a life-threatening condition.

PATHOPHYSIOLOGY

- A patient with an acute abdomen has pain associated with either distention of an organ, inflammation, traction on the mesentery or peritoneum, or ischemia.
- The abdominal viscera are sparsely innervated, and diffuse involvement is often necessary to elicit pain; nerve endings also exist in the submucosa-muscularis of the bowel wall.
- Any process that causes fluid or gaseous distension (i.e., intestinal obstruction, gastric dilatation-volvulus, ileus) may produce pain.
- Inflammation produces abdominal pain by releasing vasoactive substances that directly stimulate nerve endings.
- Many nerves in the peritoneum are sensitive to a diffuse inflammatory response.

SYSTEMS AFFECTED

- Behavioral—trembling, inappetence, vocalizing, lethargy, and abnormal postural changes such as the praying position to achieve comfort.
- Cardiovascular—severe inflammation, ischemia, and sepsis may lead to acute circulatory collapse (shock). May be associated with SIRS and septic shock.
- Gastrointestinal—vomiting, diarrhea, inappetence, generalized functional ileus; pancreatic inflammation, necrosis, and abscesses may lead to cranial abdominal pain, vomiting, and ileus.
- Hepatobiliary—jaundice associated with extrahepatic cholestasis from biliary obstruction (including pancreatitis) and bile peritonitis. Hyperbilirubinemia may occur secondary to sepsis.
- Renal/Urologic—azotemia can be due to prerenal causes (dehydration, hypovolemia, and shock), renal causes (acute pyelonephritis and acute renal failure), and post-renal causes (ureteral obstruction, urethral obstruction and uroperitoneum from bladder rupture).
- Respiratory—increased respiratory rate due to pain or metabolic/acid-base disturbances.

SIGNALMENT

- Dogs and cats.
- Dogs more commonly.
- Younger animals tend to have a higher incidence of trauma-related problems, intussusceptions, and acquired diet- and infection-related diseases; older animals have a greater frequency of malignancies.
- Male cats and dogs are at higher risk for urethral obstruction.

- Male Dalmatians in particular have a higher risk of urethral obstruction because of the high incidence of urate urinary calculi.
- German shepherds with pancreatic atrophy have a higher risk of mesenteric volvulus.
- Patients treated with corticosteroids and non-steroidal anti-inflammatory drugs are at higher risk for gastrointestinal ulceration and perforation.

SIGNS

General Comments

Clinical signs vary greatly depending on the type and severity of the disease leading to an acute abdomen.

Historical Findings

- Trembling, reluctance to move, inappetence, vomiting, diarrhea, vocalizing, and abnormal postures (tucked up or praying position)—signs that the owner may notice.
- Question owner carefully to ascertain what system is affected; for example, melena with a history of NSAID treatment may suggest GI mucosal disruption (ulceration).

Physical Examination Findings

- Abnormalities include abdominal pain, splinting of the abdominal musculature, gas- or fluid-filled abdominal organs, abdominal mass, ascites, pyrexia or hypothermia, tachycardia, and tachypnea.
- Once abdominal pain is confirmed, attempt to localize the pain to cranial, middle, or caudal abdomen.
- Perform a rectal examination to evaluate the colon, pelvic bones, urethra, and prostate, as well as for the presence of melena.
- Rule out extra-abdominal causes of pain by careful palpation of the kidneys and thoracolumbar vertebrae.
- Pain associated with intervertebral disc disease often causes referred abdominal guarding and is often mistaken for true abdominal pain. Renal pain can be associated with pyelonephritis.

CAUSES

Gastrointestinal

- Stomach—gastritis, ulcers, perforation, foreign bodies, gastric dilatation-volvulus.
- Intestine—obstruction (foreign bodies, intussusception, hernias), enteritis, ulcers, perforations.
- Rupture after obstruction, ulceration, or blunt or penetrating trauma, or due to tumor growth.
- Vascular compromise from infarction, mesenteric volvulus, or torsion.

Pancreas

- Pain associated with inflammation, abscess, ischemia.
- Pancreatic masses or inflammation obstructing the biliary duct/papilla may cause jaundice.

Hepatic and Biliary System

- Rapid distention of the liver and its capsule can cause pain.

- Biliary obstruction, rupture, or necrosis may lead to bile leakage and peritonitis. Gallbladder mucocele may be identified on ultrasound examination.

Hepatic abscess

Spleen

- Splenic torsion, splenic masses, splenic thrombus, splenic abscess.

Urinary Tract

- Distention is the main cause of pain in the urinary tract.
- Lower urinary tract obstruction can be due to tumors of the trigone area of the bladder or urethra, urinary calculi, or granulomatous urethritis.
- Traumatic rupture of the ureters or bladder are associated with blunt trauma and increased intra-abdominal pressure.
- Urethral tears can be associated with pelvic fractures from acute trauma.
- Free urine in the peritoneal cavity leads to a chemical peritonitis.
- Acute pyelonephritis, acute renal failure, nephroliths, and ureteroliths are uncommon causes of acute abdomen.

Genital Tract

- Prostatitis and prostatic abscess, pyometra; a ruptured pyometra or prostatic abscess can cause endotoxemia, sepsis, and cardiovascular collapse.
- Infrequent causes include ruptures of the gravid uterus after blunt abdominal trauma, uterine torsion, ovarian tumor or torsion, and intra-abdominal testicular torsion (cryptorchid).

Abdominal Wall/Diaphragm

- Umbilical, inguinal, scrotal, abdominal, or peritoneal hernias with strangulated viscera.
- Trauma or congenital defects leading to organ displacement or entrapment in the hernia will lead to abdominal pain if the vascular supply of the organs involved becomes impaired or ischemic.

RISK FACTORS

- Exposure to NSAIDs or corticosteroid treatment (increased risk when used concurrently)—gastric, duodenal, or colonic ulcers.
- Garbage or inappropriate food ingestion—pancreatitis.
- Foreign body ingestion—intestinal obstructions.
- Abdominal trauma—hollow viscus rupture.
- Hernias—intestinal obstruction/strangulation.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Renal-associated pain, retroperitoneal pain, spinal or paraspinal pain, and disorders causing diffuse muscle pain may mimic abdominal pain; careful history and physical

(CONTINUED)

examination are essential in pursuing the appropriate problem.

- Parvoviral enteritis can present similarly to intestinal obstructive disease; fecal parvoviral antigen assay and CBC (leukopenia) are helpful differentiating diagnostic tests.

CBC/BIOCHEMISTRY/URINALYSIS

- Inflammation or infection may be associated with leukocytosis or leukopenia.
- Anemia may be seen with blood loss associated with GI ulceration.
- Azotemia is associated with prerenal, renal, and post-renal causes.
- Electrolyte abnormalities can help to evaluate GI disease (i.e., hypochloremic metabolic alkalosis with gastric outflow obstruction) and renal disease (i.e., hyperkalemia with acute renal failure or post-renal obstruction).
- Hyperbilirubinemia and elevated hepatic enzymes help localize a problem to the liver or biliary system.
- Urine specific gravity (before fluid therapy) is needed to help differentiate prerenal, renal, and post-renal problems.
- Urine sediment may be helpful in acute renal failure, ethylene glycol intoxication, and pyelonephritis.

OTHER LABORATORY TESTS

- Venous blood gas analysis including lactate concentration may indicate acid-base abnormalities, and increased lactate may be associated with hypoperfusion.
- Canine and feline pancreatic lipase immunoreactivity can be useful in evaluating pancreatitis.

IMAGING

Abdominal Radiography

- May see abdominal masses or changes in shape or shifting of abdominal organs.
- Loss of abdominal detail with abdominal fluid accumulation is an indication for abdominocentesis.
- Free abdominal gas is consistent with a ruptured GI viscus or infection with gas-producing bacteria and is an indication for emergency surgery.
- Use caution when interpreting radiographs following abdominocentesis with an open needle. Free gas may be introduced with this technique.
- Use caution when evaluating postoperative radiographs; free gas is a normal postoperative finding.
- Ileus is a consistent finding with peritonitis.
- Characterize ileus as functional (due to metabolic or inflammatory causes) or mechanical (due to obstruction).
- Foreign bodies may be radiopaque.
- Upper GI barium contrast radiographs are useful in evaluating the GI tract, particularly for determination of GI obstruction.
- Loss of contrast or radiographic detail in the area of the pancreas can be observed with pancreatic inflammation.

Abdominal Ultrasound

- A sensitive diagnostic tool for the detection of abdominal masses, abdominal fluid, abscesses, cysts, lymphadenopathy, and biliary or urinary calculi.
- FAST ultrasound is a published technique meaning Focused Assessment with Sonography in Trauma.

Abdominal CT

- Very sensitive diagnostic tool that may be used especially when surgeon requires additional information.

DIAGNOSTIC PROCEDURES

Abdominocentesis/Abdominal Fluid Analysis

- Perform abdominocentesis on all patients presenting with acute abdomen. Four-quadrant approach may improve yield. Fluid can often be obtained for diagnostic evaluation even when only a small amount of free abdominal fluid exists, well before detectable radiographic sensitivity. Ultrasound is much more sensitive than radiography for the detection of fluid and can be used to direct abdominocentesis. Blind abdominocentesis can be performed safely without ultrasound guidance. Abdominal fluid analysis with elevated WBC count, degenerate neutrophils, and intracellular bacteria is consistent with septic peritonitis and is an indication for immediate surgery.
- Diagnostic peritoneal lavage can be performed by introducing sterile saline (10–20 mL/kg) and performing abdominocentesis with or without ultrasound guidance.
- Measurement of glucose concentration in abdominal effusion in comparison with peripheral blood may aid in the diagnosis of septic abdomen. A blood-to-abdominal fluid glucose difference of > 20 mg/dL is consistent with septic effusion.
- Pancreatitis patients may have an abdominal effusion characterized as a non-septic (sterile) peritonitis.
- Creatinine concentration higher in abdominal fluid than in serum indicates urinary tract leakage.
- Similarly, higher bilirubin concentration in abdominal fluid than in serum indicates bile peritonitis.

Sedation and Abdominal Palpation

- Because of abdominal splinting associated with pain, thorough abdominal palpation is often not possible without sedation; this is particularly useful for detecting intestinal foreign bodies that do not appear on survey radiographs.

Exploratory Laparotomy

- Surgery may be useful diagnostically (as well as therapeutically) when ultrasonography (or other advanced imaging) is not available or when no definitive cause of the acute abdomen has been established with appropriate diagnostics.

ACUTE ABDOMEN

A



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient management with supportive care until decision about whether the problem is to be treated medically or surgically. Early intervention with surgery is important when indicated.
- Aggressive therapy and prompt identification of the underlying cause is very important.
- Many causes of acute abdominal pain require emergency surgical intervention.
- Keep patient NPO if vomiting, until a definitive cause is determined and addressed.
- Intravenous fluid therapy is usually required because of the large fluid loss associated with an acute abdomen; the goal is to restore the normal circulating blood volume.
- If severe circulatory compromise (shock) exists, supplement initially with isotonic crystalloid fluids (90 mL/kg, dogs; 70 mL/kg, cats) over 1–2 hours; hypertonic fluids or colloids may also be beneficial if refractory to isotonic crystalloids or hypoproteinemic.
- Evaluate hydration and electrolytes (with appropriate treatment adjustments) frequently after commencement of treatment.

DIET

Early nutritional support important, especially in order to maintain GI mucosal barrier. Nutritional support can be enteral (oral, nasoesophageal, esophageal tube, gastrostomy tube, enterostomy tube) or parenteral.

SURGICAL CONSIDERATIONS

- Many different causes of an acute abdomen (with both medical and surgical treatments) exist; make a definitive diagnosis whenever possible prior to surgical intervention.
- This can prevent both potentially unnecessary and expensive surgical procedures and associated morbidity and mortality.
- It will also allow the surgeon to prepare for the task and to educate the owner on the prognosis and financial investment.



MEDICATIONS

DRUG(S)

Analgesics

- Pain medication may be indicated for control of abdominal discomfort.
- Opioids, such as hydromorphone or fentanyl, are often good choices.

Histamine H₂ Antagonists

- Reduce gastric acid production.
- Famotidine 0.5–1.0 mg/kg IV, SC or IM q12h.
- Ranitidine 2 mg/kg IV q12h

Proton Pump Inhibitor

Pantoprazole 1–1.5 mg/kg IV as a CRI over 24 hours.

Protectants

Sucralfate 0.25–1 g PO q8h.

Antiemetics

- Metoclopramide 0.2–0.4 mg/kg IV q6–8h (or 24-hour continuous rate infusion 1–2 mg/kg/24h).
- Maropitant: dogs, 1–2 mg/kg SC; cats, 1 mg/kg SC
- Ondansetron 0.5–1 mg/kg IV slowly q6–12h.
- Dolasetron 1 mg/kg IV q24h.

Antibiotics

- Antibiotics may be indicated if signs of infection (fever, elevated white blood cell count, positive culture) are seen or hemorrhagic diarrhea is present.
- Broad spectrum for Gram-positive, Gram-negative, and anaerobic bacteria.
- Gram stain and cultures prior to treatment if possible, but do not delay intervention pending results.

CONTRAINDICATIONS

Do not use metoclopramide if GI obstruction is suspected. Do not use barium if gastrointestinal perforation is suspected. Use iodinated contrast agent instead.

PRECAUTIONS

Gentamicin and most NSAIDs can be nephrotoxic and should be used with caution in hypovolemic patients and those with renal impairment. Opiates are preferred to NSAIDs for pain management as NSAIDs may cause GI complications.

**FOLLOW-UP****PATIENT MONITORING**

Patients usually require intensive medical care and frequent evaluation of vital signs and laboratory parameters.

**MISCELLANEOUS****SYNONYM**

Colic

SEE ALSO

- Gastric Dilation and Volvulus Syndrome
- Gastroduodenal Ulceration/Erosion (GUE)
- Gastrointestinal Obstruction
- Intussusception
- Pancreatitis

- Pyelonephritis
- Prostatitis and Prostatic Abscess
- Urinary Tract Obstruction

ABBREVIATIONS

- GI = gastrointestinal
- NSAID = nonsteroidal anti-inflammatory drug

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ACUTE RESPIRATORY DISTRESS SYNDROME



BASICS

DEFINITION

• Acute respiratory distress syndrome (ARDS) is a syndrome of acute onset of respiratory failure typified by diffuse bilateral pulmonary infiltrates on a dorsoventral thoracic radiograph with no clinical evidence of left atrial hypertension or volume overload. ARDS results from an overwhelming inflammatory reaction in the alveolocapillary membrane in response to a systemic or pulmonary inflammatory insult. The end result is increased vascular permeability leading to edema. • The 2012 Berlin Definition of ARDS defines three categories of severity based on $\text{PaO}_2/\text{FiO}_2$ ratio and level of PEEP employed during ventilation, with mild ARDS defined by a PF ratio of 200–300 mmHg with PEEP ≥ 5 mmHg, moderate ARDS as a PF ratio of 100–200 mmHg with PEEP ≥ 5 mmHg, and severe ARDS as a PF ratio < 100 mmHg with PEEP ≥ 5 mmHg.

PATOPHYSIOLOGY

• ARDS is due to a diffuse inflammatory insult that causes widespread damage to alveolar endothelial and epithelial cells resulting in thickening of the membrane and impaired gas exchange. This inflammatory insult can be triggered by primary pulmonary disease or it can be of non-pulmonary origin, and leads to exudative, proliferative, and fibrotic changes within the lung: • First, excessive accumulation and activation of neutrophils, monocytes, and platelets in the pulmonary microvasculature leads to increased alveolar endothelial permeability. This causes protein-rich edema fluid and inflammatory cells to leak into the interstitial and alveolar spaces. • Alveolar epithelial injury results from release of cytokines and other inflammatory mediators from leukocytes and platelets. • Epithelial injury involves both type I and type II alveolar epithelial cells, and results in alveolar flooding and surfactant dysfunction. This causes collapse and consolidation of alveoli with development of severe hypoxemia, and hyaline membrane formation in the alveolar spaces. • Microthrombi in the pulmonary vasculature, hypoxic pulmonary vasoconstriction, and release of endogenous vasoconstrictors lead to pulmonary arterial hypertension, which can lead to right-sided heart failure. • Proliferation of type 2 alveolar epithelial cells and pulmonary fibrosis occurs in the late stages of ARDS.

SYSTEMS AFFECTED

• Respiratory. • Cardiovascular—right-sided heart failure secondary to pulmonary hypertension; hemodynamic compromise may be associated with aggressive mechanical ventilator settings.

GENETICS

Certain humans are more prone to developing ARDS than others due to specific gene polymorphisms. This has not been investigated in the veterinary population.

INCIDENCE/PREVALENCE

Unknown

SIGNALMENT

Species

Dog and cat

Breed Predilections

A familial form of ARDS has been reported in a group of related Dalmatian dogs; it is clinically indistinguishable from ARDS.

Mean Age and Range

Unknown

SIGNS

Historical Findings

• Acute onset of respiratory distress in a patient with a significant underlying disease or exposure to known risk factors. • The patient is often hospitalized for its primary disease when it develops ARDS.

Physical Examination Findings

- Severe respiratory distress
- Crackles (if present) heard bilaterally on auscultation
- Fever—depends on underlying disease
- Cyanosis in more severe cases
- Signs relevant to the primary disease process.

CAUSES

Primary Pulmonary Causes

- Aspiration pneumonia
- Pneumonia
- Pulmonary contusion
- Near drowning
- Smoke inhalation
- An idiopathic form of ARDS associated with acute interstitial pneumonia or idiopathic pulmonary fibrosis has been reported in humans and dogs.

Non-pulmonary Causes

- SIRS
- Sepsis
- Neoplasia
- Pancreatitis
- Severe trauma and shock
- Severe bee sting envenomation

RISK FACTORS

- SIRS
- Sepsis
- Severity of illness
- Multiple transfusions



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Left-sided congestive heart failure
- Fluid overload
- Diffuse pneumonia
- Pulmonary hemorrhage

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis or leukopenia
- Other changes dependent on the underlying disease process

OTHER LABORATORY TESTS

• Arterial blood gases—low $\text{PaO}_2/\text{FiO}_2$ ratio (where PaO_2 is measured in mmHg and FiO_2 is 0.21–1.0). Normal $\text{PaO}_2/\text{FiO}_2$ ratio = 500; comparison of this ratio allows evaluation of severity of lung disease and allows direct

comparison of blood gases taken at different FiO_2 . PaCO_2 is often low; hypercapnia tends to be a late (preterminal) development.

- Total protein of airway edema fluid compared with serum total protein—ratio of edema fluid to serum total protein < 0.5 is supportive of low-protein hydrostatic pressure pulmonary edema (e.g., heart failure, fluid overload); edema fluid/serum total protein ratio > 0.7 suggests a high-protein, increased permeability pulmonary edema such as ARDS and pneumonia. • Coagulation panel may reveal hypocoagulable state supportive of DIC or cause of pulmonary hemorrhage.

IMAGING

Thoracic Radiographs

- Bilateral/diffuse pulmonary infiltrates.
- Severity of radiographic signs can lag behind clinical disease by 12–24 hours. • Can be difficult to distinguish from cardiogenic edema. Cardiac silhouette and pulmonary vascular size is usually normal in ARDS.

Echocardiography

- Attempt to rule out cardiogenic cause for pulmonary edema. • May be able to estimate degree of pulmonary hypertension.

DIAGNOSTIC PROCEDURES

Pulmonary artery catheter to measure pulmonary artery occlusion pressure can be used to rule out cardiogenic cause for edema; by definition, ARDS is associated with PAOP ≤ 18 mmHg.

PATHOLOGIC FINDINGS

Gross Pathology

Lungs are dark, heavy, and ooze fluid when cut.

Histopathology

- Acute phase—pulmonary vascular congestion with edema fluid and inflammatory cell accumulation in the interstitium and alveoli; epithelial cell damage, hyaline membrane formation, microthrombi, microatelectasis.
- Proliferative phase—hyperplasia of type 2 pneumocytes, interstitial mononuclear infiltration, organization of hyaline membranes, and fibroproliferation.



TREATMENT

APPROPRIATE HEALTH CARE

- There is no specific therapy. General aims are to maintain tissue oxygenation and to minimize iatrogenic lung injury while treating the underlying disease. • Oxygen therapy—no more than is required to maintain $\text{PaO}_2 > 60$ –80 mmHg to minimize oxygen toxicity. • Positive-pressure ventilation is essential in the management of ARDS patients. It is indicated in patients that are hypoxic despite oxygen therapy, patients requiring high levels of inspired oxygen for

ACUTE RESPIRATORY DISTRESS SYNDROME

(CONTINUED)

prolonged periods, or patients working so hard to breathe that they are at risk of exhaustion. • ARDS is thought to be exacerbated by ventilator-induced lung injury associated with alveolar overdistension compounded by cyclic opening and collapse of atelectatic alveoli. Therefore, lung-protective strategies of positive-pressure ventilation with moderate to high PEEP, low tidal volumes, and permissive hypercapnia are recommended to minimize ventilator-induced lung injury. Tidal volumes of 6 mL/kg have been found to increase survival significantly in human ARDS patients compared to tidal volumes of 12 mL/kg. • Recruitment maneuvers and high levels of PEEP can both cause significant hemodynamic compromise and patients should have constant direct arterial blood pressure monitoring.

- Intensive supportive care of the cardiovascular system and other organ systems is vital, as these patients are at high risk for development of multiple organ dysfunction.

NURSING CARE

- Monitor temperature closely, especially if using an oxygen cage, as animals with excessive work of breathing can easily become hyperthermic. • Ventilator patients require frequent position changes and physical therapy; regular oral care with a dilute chlorhexidine solution is important to reduce oral colonization with bacteria as a source of sepsis, and frequent endotracheal tube suctioning is needed to prevent occlusion. Inflate cuff carefully and change endotracheal cuff position regularly to prevent tracheal damage. • Blood pressure monitoring, as septic patients are prone to hypotension.
- Fluid therapy is important to support the cardiovascular system and to maintain normovolemia while avoiding fluid overload, as this will negatively affect lung function.

ACTIVITY

If not anesthetized for ventilation, strict cage confinement.

DIET

Nutritional support is important but challenging. Enteral feeding is desired over parenteral nutrition, but must consider high risk of regurgitation and aspiration in a recumbent patient.

CLIENT EDUCATION

Clients need to be aware of the guarded prognosis and high costs of therapy.

SURGICAL CONSIDERATIONS

The underlying disease may require surgery.



MEDICATIONS

DRUG(S) OF CHOICE

- No specific drug therapy.

- Antibiotics for the underlying disease where indicated.
- Vasoactive drugs to maintain blood pressure.
- Anesthetic drugs to allow positive-pressure ventilation.
- Analgesia as appropriate.
- Low-dose corticosteroid—use remains controversial with conflicting reports of efficacy for low-dose steroids in early or late ARDS.

ALTERNATIVE DRUG(S)

Furosemide may produce pulmonary venous dilation and improve lung function, as an intermittent bolus of 1 mg/kg IV q6–12h or as a CRI of 0.2 mg/kg/h IV. Beware dehydration and effects on organ function.



FOLLOW-UP

PATIENT MONITORING

Arterial blood gases, pulse oximetry, end-tidal carbon dioxide, thoracic radiographs, arterial blood pressure, ECG, temperature, urine output, CBC, coagulation profiles, serum chemistry, blood cultures, monitoring for other organ dysfunction.

PREVENTION/AVOIDANCE

- Aggressive therapy of primary disease processes to reduce the inflammatory insult to the lung. • Intensive cardiovascular monitoring and support of critically ill animals to ensure adequate tissue perfusion.
- Careful management of recumbent animals to reduce the chance of aspiration, especially if patient has neurologic disease or upper airway disorders that reduce the ability to protect the airway. • Judicious use of blood products in patients with inflammatory or severe systemic disease.

POSSIBLE COMPLICATIONS

- Multiorgan dysfunction syndrome—acute kidney injury, DIC, and gastrointestinal disease are the more common forms of organ dysfunction seen. • Barotrauma—can result in pneumothorax. Incidence is thought to be less with lower tidal volume ventilation strategies. • Ventilator-associated pneumonia—patients on PPV have increased risk of pneumonia that may be difficult to differentiate from worsening of the initial lung injury. Airway cultures should be considered in deteriorating patients.
- Oxygen toxicity may be unavoidable due to severity of hypoxemia in spite of PPV. Oxygen toxicity is indistinguishable from ARDS on histopathology making the incidence of this problem impossible to determine.

EXPECTED COURSE AND PROGNOSIS

- Mortality in human patients remains at 40–60%. • Mortality in veterinary patients likely approaches 100%.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Systemic inflammatory response syndrome, multiple organ dysfunction syndrome, sepsis.

SYNOMYMS

- Acute hypoxic respiratory failure • Acute interstitial pneumonia • Adult respiratory distress syndrome • High-protein pulmonary edema • Shock lung

SEE ALSO

- Dyspnea and Respiratory Distress • Panting and Tachypnea • Pulmonary Edema, Noncardiogenic • Sepsis and Bacteremia

ABBREVIATIONS

- ARDS = acute respiratory distress syndrome • CRI = constant rate infusion
- DIC = disseminated intravascular coagulation • PAOP = pulmonary artery occlusion pressure (formerly pulmonary capillary wedge pressure [PCWP]) • PEEP = positive end-expiratory pressure • PF ratio = $\text{PaO}_2/\text{FiO}_2$ ratio • PPV = positive-pressure ventilation • SIRS = systemic inflammatory response syndrome

INTERNET RESOURCES

<http://www.ardsnet.org>

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BASICS

OVERVIEW

- Malignant neoplasm derived from apocrine glands of the anal sac.
- Locally invasive.
- High metastatic rate, often to sublumbar lymph nodes.
- Frequently associated with hypercalcemia, secondary to parathyroid hormone-related peptide secretion.
- Prognosis guarded to fair.

SIGNALMENT

- Older dogs; extremely rare in cats.
- Females overrepresented in some studies.
- English cocker spaniels significantly overrepresented, springer and Cavalier King Charles spaniels also overrepresented.

SIGNS

Historical Findings

Signs may be due to physical obstructive nature of primary tumor (rectal mass, tenesmus) or enlarged local lymph node metastasis (tenesmus, constipation, stranguria), or systemic manifestations due to hypercalcemia (anorexia, polyuria/polydipsia, lethargy).

Physical Examination Findings

- Mass associated with anal sac; may be quite small despite massive metastatic disease.
- Sublumbar lymphadenopathy—on rectal or abdominal palpation.

CAUSES & RISK FACTORS

None definitively identified



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Anal sac abscess
- Perianal adenoma/adenocarcinoma
- Mast cell tumor
- Lymphoma
- Squamous cell carcinoma
- Perineal hernias

CBC/BIOCHEMISTRY/URINALYSIS

- Hypercalcemia—25–50% of cases.
- Secondary renal failure may develop.

OTHER LABORATORY TESTS

If hypercalcemia is present, and tumor cannot be identified, parathyroid hormone and PTHrP levels can be assessed—high PTHrP support neoplasia as the cause of hypercalcemia.

IMAGING

- Abdominal radiography—to evaluate sublumbar lymph nodes and lumbar and pelvic bones.
- Thoracic radiography—to evaluate for pulmonary metastasis.
- Abdominal ultrasonography—may identify mildly enlarged sublumbar lymph nodes not visible radiographically, also nodules in liver/spleen.
- MRI—recently shown to identify lymphadenopathy with greater sensitivity than ultrasound.

DIAGNOSTIC PROCEDURES

- Fine-needle aspiration of anal sac mass to rule out conditions other than adenocarcinoma; while differentiation of benign versus malignant neoplasm of perianal masses is difficult, apocrine gland adenocarcinoma of the anal sac will have a neuroendocrine appearance and can be differentiated from perianal gland tumors.
- Fine-needle aspiration of enlarged lymph nodes, liver, or splenic nodules to confirm metastasis.
- Incisional biopsy for histopathology required for definitive diagnosis, although excisional biopsy may be appropriate if location of mass and cytology are supportive of anal gland neoplasia.



TREATMENT

- Surgical resection—treatment of choice.
- Resection of primary tumor and enlarged lymph nodes may prolong survival.
- If mass is large and regionally invasive at diagnosis, surgery often palliative, not curative.
- Debulking all disease present may control hypercalcemia until tumor recurrence.
- Saline diuresis (200–300 mL/kg/day) preoperatively if hypercalcemia is severe.
- Radiation may help delay local recurrence and control growth of sublumbar metastases.



MEDICATIONS

DRUG(S)

- Limited reports of partial responses to platinum compounds in dogs—cisplatin (70 mg/m^2 IV with 6-hour saline diuresis— 18.3 mL/kg/h), carboplatin (300 mg/m^2 IV as a slow bolus) every 3 weeks.
- Mitoxantrone (5 mg/m^2 IV every 3 weeks for five treatments) in combination with radiation therapy used in one small case series.
- Possible role for melphalan after debulking surgery (7 mg/m^2 PO q24h for 5 days every 3 weeks).
- Toceranib phosphate reported to have some benefit (partial response or stable disease) in 28 dogs with measurable tumor.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Avoid platinum chemotherapeutic agents in dogs with renal insufficiency.
- Do not use cisplatin in cats.



FOLLOW-UP

PATIENT MONITORING

- Complete resection—physical examination, thoracic radiography, abdominal ultrasonography, and serum biochemistry at 1, 3, 6, 9, and 12 months postoperatively,

then every 6 months thereafter.

- Incomplete resection—monitor tumor size and blood calcium and renal values.

EXPECTED COURSE AND PROGNOSIS

- Guarded prognosis with both local progression and metastasis occurring.
- Cures may occur if tumor is found early and treated aggressively.
- Growth of the tumor may be slow and debulking lymph node metastatic disease may significantly prolong survival.
- Hypercalcemia is variably associated with a poor prognosis.
- Four papers (involving 200 dogs) showed median survival times of 6 to 20 months, depending on stage and treatment.
- A recent report on 16 dogs without metastasis showed a median survival time not met with a follow-up of 33 months.
- Dogs with lymph node metastasis lived significantly longer if the nodes were extirpated.
- Ultimately, dogs that cannot have their tumors excised completely succumb to hypercalcemia-related complications or mass effect from primary tumor or sublumbar nodal metastases.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Hypercalcemia as a paraneoplastic syndrome

ABBREVIATION

PTHrP = parathyroid hormone-related peptide

Suggested Reading

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Client Education Handout
available online

ADENOCARCINOMA, LUNG



BASICS

OVERVIEW

- Comprises 75% of primary pulmonary tumors in dogs and cats.
- Strongest predictors of outcome are tumor grade, node involvement, and clinical signs.
- May metastasize.
- May be associated with hypertrophic osteopathy.

SIGNALMENT

Dogs

- 1% of all tumors
- Mean age of affected animals 10 years
- No sex predilection, though more females in some reports
- Medium to large breeds overrepresented

Cats

- Rarer than in dogs
- Mean age of affected animals 11 years
- No breed predilection

SIGNS

Historical Findings

- Related to presence of a lung mass
- Nonproductive cough (> 50% of dogs)
- Dyspnea (may be related to pneumothorax)
- Tachypnea ◦ Hemoptysis • Paraneoplastic signs:
 - Lameness—bone metastasis or hypertrophic osteopathy (dogs or cats), weight-bearing lytic digit metastasis (cats)
 - Polyuria or polydipsia—hypercalcemia or hyperadrenocorticism from ectopic production of ACTH ◦ Fever

Physical Examination Findings

- May be asymptomatic or lack respiratory signs
- Tachypnea and dyspnea
- Fever
- Limb swelling
- Ascites, pleural effusion
- Caval syndrome

CAUSES & RISK FACTORS

Some evidence correlates risk to urban environment; controversial



DIAGNOSIS

- Fine-needle aspirate cytology
- Tissue biopsy or definitive resection

DIFFERENTIAL DIAGNOSIS

- Granulomatous lesion (fungal, foreign body, parasitic)
- Pulmonary abscess
- Other primary lung tumor:
 - Squamous cell carcinoma
 - Sarcomas (osteo-, chondro-, lipo-)
- Metastatic lung tumor
- Pneumonia
- Asthma
- Pulmonary thromboembolism
- Congenital cyst
- Lung torsion or hematoma

CBC/BIOCHEMISTRY/URINALYSIS

No specific abnormalities

OTHER LABORATORY TESTS

Coagulation tests

IMAGING

- Thoracic radiography—usually demonstrates a focal, solitary,

well-circumscribed mass; must be performed in cats presenting with multiple digit tumors to screen for primary lung tumor (lung-digit syndrome).

- Ultrasonography—may help with obtaining an aspirate or biopsy specimen from lung, or to evaluate abdomen.
- CT—most accurate assessment of surgical feasibility, lymphadenopathy (93% accuracy), metastatic disease.
- Dogs—most common in right caudal lung lobe and accessory lobe; cats—most common in left caudal lung lobe.

DIAGNOSTIC PROCEDURES

- Thoracocentesis with cytologic examination (for pleural effusion).
- Cytology—transthoracic fine-needle aspiration (83% agreement with histopathology).
- Percutaneous tissue biopsy—use Tru-Cut instrument.
- Open lung biopsy—specimen via thoracotomy, or minimally invasive thoracoscopy.

PATHOLOGIC FINDINGS

- Adenocarcinoma—classified according to location (bronchial, bronchiolar, bronchiolar-alveolar, or alveolar) and degree of differentiation.
- Thyroid transcription factor-1 positivity may distinguish primary from metastatic carcinoma.
- Cats tend to have less differentiated tumors, corresponding to more aggressive behavior.



TREATMENT

- Surgery—mainstay of treatment: partial or complete lobectomy with tracheobronchial lymph node biopsy or removal; thoracoscopic removal possible at limited centers and offers less postoperative morbidity.
- Radiotherapy—reports are anecdotal, but certain patients may benefit.
- Chemotherapy should be considered following surgery for tumors that are high grade, undifferentiated, and/or have nodal involvement. Intracavitary chemotherapy can be used to treat malignant pleural effusion.



MEDICATIONS

DRUG(S)

- Chemotherapy—vinorelbine concentrates in lungs and responses have been seen.
 - Doxorubicin, cisplatin, carboplatin, mitoxantrone, vinorelbine, and/or vindesine—rational choices for palliation
 - Platinum based or gemcitabine chemotherapy may be superior
 - Toceranib Phosphate (Palladia) has shown some anecdotal success
- Chemotherapy can be toxic; seek advice if unfamiliar with cytotoxic drugs.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Doxorubicin—monitor patients with underlying cardiac disease carefully; consider pretreatment with diphenhydramine and serial echocardiograms and ECGs.
- Cisplatin—do not give to cats (fatal); do not use in dogs with pre-existing renal disease; never use without appropriate and concurrent diuresis.



FOLLOW-UP

PATIENT MONITORING

- Serial thoracic radiographs—consider every 3 months; administer a minimum of two cycles of chemotherapy before evaluating response to treatment.
- Perform CBC (with any chemotherapy), biochemical analysis (cisplatin), and urinalysis (cisplatin) before each chemotherapy treatment.

POSSIBLE COMPLICATIONS

- Following diagnostic procedures or thoracotomy: pneumo- or hemothorax
- Resulting from chemotherapy: myelosuppression, fever, sepsis, nausea

EXPECTED COURSE AND PROGNOSIS

- Metastasis to the tracheobronchial lymph nodes—single best prognostic indicator; median survival without metastasis approaches 1 year and with metastasis, 60 days. More common (75%) in cats.
- Postoperative survival in dogs (~1 yr) is better than in cats (~4 mo), but around 2 years in either species if positive prognostic factors are present.
- Other patient, tumor, and treatment factors influencing prognosis—complete surgical excision; size of the primary tumor (< 5 cm better); metastasis (better if none); degree of cell differentiation (histologic score, better if well differentiated), lack of clinical signs prior to surgery.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Chemotherapy is not advised in pregnant animals.

ABBREVIATIONS

ACTH = adrenocorticotrophic hormone

Suggested Reading

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BASICS

DEFINITION

Malignant neoplasm involving the nasal cavity and paranasal sinuses.

PATHOPHYSIOLOGY

Progressive local and regional invasion of the nasal cavity, paranasal sinuses, and surrounding tissues by neoplastic epithelial and glandular epithelial cells.

SYSTEMS AFFECTED

- Respiratory—congestion, obstruction, dyspnea, epistaxis, mucopurulent nasal discharge
- Nervous—seizures, altered mentation
- Ophthalmic—exophthalmos, epiphora

INCIDENCE/PREVALENCE

- In dogs, less than 2% of all tumors are nasal tumors.
- In dogs, adenocarcinoma is more common than squamous cell carcinoma, chondrosarcoma, and other histologies, comprising 31.5% of all nasal tumors.
- In cats, nasal tumors comprise < 1% of all tumors. In cats, adenocarcinoma and lymphoma are most common.

GEOGRAPHIC DISTRIBUTION

Nasal adenocarcinomas are more commonly reported in urban areas.

SIGNALMENT

- Dog and cat.
- Median age in dogs is 10 years and 13 years in cats.
- In dogs, medium to large breeds affected more commonly with a possible overrepresentation of mesocephalic and dolichocephalic breeds.

SIGNS

Historical Findings

- Intermittent and progressive history of unilateral to bilateral epistaxis and/or mucopurulent discharge that initially responds to antibiotic therapy (median duration, 3 months).
- Sneezing and increased upper respiratory noises including reverse sneezing.
- Open-mouth breathing.
- Halitosis.
- Anorexia (more frequent in cats).
- Seizures (secondary to invasion of cranial vault).

Physical Examination Findings

- Nasal discharge (blood, mucopurulent)
- Decreased or absent airflow in the nasal passages (unilateral or bilateral)
- Facial deformity, exophthalmos, epiphora
- Pain upon nasal or paranasal sinus palpation or upon opening the mouth
- Regional lymphadenomegaly (rare)
- Abnormal mentation or other neurologic findings (rare)

CAUSES

Dolichocephalic morphology, p53 mutations, and COX-2 overexpression may all play a role.

RISK FACTORS

Urban environment and second-hand smoke may be risk factors.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other sinonasal tumors (e.g., squamous cell carcinoma, lymphoma, sarcomas, olfactory neuroblastoma)
- Intracranial neoplasia
- Viral infection—cats
- Fungal infections including aspergillosis (dogs) and cryptococcosis (cats)
- Bacterial sinusitis
- Parasites (e.g., nasal mites)
- Foreign body
- Trauma
- Tooth root abscess and oronasal fistula
- Coagulopathies
- Ehrlichiosis, leishmaniasis
- Systemic hypertension

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal
- Occasional blood loss anemia

OTHER LABORATORY TESTS

- Cytologic examination: occasionally helpful (e.g., aspirates of the subcutaneous mass if facial deformity)
- Coagulation profile

IMAGING

- Survey skull radiography—not sensitive; may show asymmetrical destruction of turbinates accompanied by a soft tissue mass effect; may see fluid density in the frontal sinuses secondary to outflow obstruction.
- Thoracic radiography—evaluate for lung metastasis (uncommon).
- CT or MRI best imaging method for local staging and observing integrity of cribriform plate or orbital invasion, and also used for therapeutic planning.

DIAGNOSTIC PROCEDURES

- Blood pressure.
- Oral exam under anesthesia.
- Rhinoscopy may permit visual observation of the mass and aid biopsy..
- Tissue biopsy necessary for definitive diagnosis. Biopsies may be performed blind, following advanced imaging, using pinch biopsy instrument including retroflex rhinoscopic biopsy of nasopharynx, cannula (closed suction), or hydropulsion techniques.
- Cytologic evaluation of regional lymph nodes to detect regional metastatic disease.

PATHOLOGIC FINDINGS

- Bilateral involvement and osteolysis common.

- Regional lymph node metastasis < 10% at time of diagnosis but up to 45% at necropsy.



TREATMENT

APPROPRIATE HEALTHCARE

- Radiation therapy is the standard of care.
- Radiation therapy can be administered with curative intent (definitive) or for palliation of clinical signs.
- Definitive radiation involves multiple fractions for a high total dose.
- Palliative radiation uses a low total dose to minimize toxicity while improving the quality of life through reduction of tumor size.
- Novel radiation techniques including IMRT and stereotactic radiation therapy may decrease risk of late toxicity while improving tumor control.
- Combining radiation therapy with novel drug therapy (toceranib phosphate (Palladia), others) appears safe and well tolerated.
- Radiation therapy followed by surgery to debulk residual mass may improve local control time but results in higher risk of late toxicity.
- Surgery alone considered ineffective with most tumors relapsing within 6 months.

NURSING CARE

- During radiation therapy, supportive care for radiation related mucositis may involve softening food, rinsing mouth with saline, dilute black tea, and administration of medications to control discomfort.
- These side effects are temporary but may cause discomfort for 10–14 days.

ACTIVITY

- Limit activity to minimize risk of epistaxis and dyspnea.
- Using a harness instead of a collar during walks may help minimize epistaxis.

DIET

- Soften food if needed during radiation therapy.
- Avoid extremes of temperatures and salty foods with radiation therapy-related mucositis.

CLIENT EDUCATION

Nasal adenocarcinoma may be painful even though the pet is not showing visible signs of pain.

- Consider the use of medications for discomfort and congestion.
- Radiation therapy is the most effective option and is well-tolerated using modern radiotherapy techniques.
- Radiation side effects may impact the patient's quality of life during treatment, but most pets enjoy a relatively normal quality of life following treatment.

ADENOCARCINOMA, NASAL

(CONTINUED)

- Intermittent congestion and sneezing may occur post therapy due to increased sensitivity from the tumors' destruction of the nasal turbinates.

SURGICAL/ANESTHETIC CONSIDERATIONS

Anesthetic recovery—ensure airway is maintained until animal is sternal to prevent apnea in patients with bilateral nasal obstruction.



MEDICATIONS

DRUG(S) OF CHOICE

- Chemotherapy is considered ineffective for durable tumor control, but may benefit some patients if radiation therapy is not a viable option. Various drugs have been described including cisplatin (dogs only), carboplatin, doxorubicin, and piroxicam. Toceranib phosphate (Palladia) exerts therapeutic activity against nasal carcinoma.
- Consult with an oncologist for more details.
- Adequate analgesic therapy should be employed as needed in patients suffering from invasive disease with bone destruction, signs of pain, and radiation therapy side effects.

CONTRAINDICATIONS

Cisplatin—never use in cats.

PRECAUTIONS

- Most chemotherapeutics have gastrointestinal, hematologic, and other potential side effects and should be administered and monitored by an oncologist.
- Piroxicam can cause gastric ulceration so careful monitoring of appetite, vomiting, and stool color (melena) is recommended.

POSSIBLE INTERACTIONS

Concurrent radiation therapy and chemotherapy will increase the risk of side effects but have not shown to significantly improve tumor control.

ALTERNATIVE DRUGS

- Palladia, a tyrosine kinase inhibitor, may have anticancer activity in some carcinomas including nasal adenocarcinomas. It is currently being investigated at the labeled dose alone and in combination with radiation therapy.
- Objective responses have been documented with use of Palladia alone.



FOLLOW-UP

PATIENT MONITORING

- CT or MRI are needed to assess response to therapy and are recommended 2–3 months post radiation treatment.
- Other staging tests including thoracic radiography or CT and lymph node evaluation are generally recommended in 3-month intervals during/following therapy.
- Routine staging with CT/MRI and monitoring of recurrent clinical signs can detect early recurrence.

POSSIBLE COMPLICATIONS

- Dyspnea
- Epistaxis
- Secondary infections
- Weight loss
- Anorexia
- Chemotherapy or radiation toxicity

EXPECTED COURSE AND PROGNOSIS

- Untreated—median survival around 2–6 months.
- Radiation therapy—median survival times around 12–18 months in dogs and 12–20 months in cats; 1-year survival rate 20–57% (dogs and cats); 2-year survival rate 20–48% (dogs and cats).
- Presence of cribriform lysis, brain involvement or metastatic disease (advanced stage) are poor prognostic indicators.
- Ophthalmic complications of radiation therapy—more likely in dogs than cats.
- Incidence and severity of ophthalmic toxicity are decreasing with advanced radiation therapy techniques now commonly used.
- Chronic rhinitis is possible following radiation therapy for sinonasal tumors and may require periodic symptomatic therapy.



MISCELLANEOUS

AGE-RELATED FACTORS

None

PREGNANCY/FERTILITY/BREEDING

Chemotherapeutic drugs and general anesthesia are a risk to the fetus and would not be recommended in pregnant animals.

SYNONYMS

- Nasal carcinoma
- Nasal tumor

SEE ALSO

- Squamous cell carcinoma, nasal
- Chondrosarcoma, nasal
- Lymphoma, nasal

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging

INTERNET RESOURCES

- <http://veterinarymedicine.dvm360.com/vetmed/Medicine/Canine-and-feline-nasal-tumors/ArticleStandard/Article/detail/735167>
- <http://smallanimal.vethospital.ufl.edu/clinical-services/oncology/types-of-cancer-and-treatment/nasal-tumors-dogs/>
- <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2643460/>

Suggested Reading

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- Langova V, Mutsaers AJ, Phillips B, Straw R. Treatment of eight dogs with nasal tumours with alternating doses of carboplatin and doxorubicin in conjunction with oral piroxicam. *Aust Vet J* 2004, 82:676–680.
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- Theon AP, Peaston AE, Madewell BR, et al. Irradiation of nonlymphoproliferative neoplasms of the nasal cavity and paranasal sinuses in 16 cats. *J Am Vet Med Assoc* 1994, 204(1):78–83.
- Author** Jayme Looper
Consulting Editor Timothy M. Fan
Acknowledgment The author and editors acknowledge the prior contribution of Louis-Philippe de Lorimier.



BASICS

OVERVIEW

- Malignant tumor of ductal or acinar origin arising from the exocrine pancreas.
- Usually metastatic by the time of diagnosis, affecting regional lymph nodes and visceral abdominal organs (liver) and associated peritoneal cavity.

SIGNALMENT

- Rare in dogs—0.5–1.8% of all tumors
- Rare in cats—2.8% of all tumors
- Older female dogs and Airedale terriers at higher risk than others
- Median age (dogs)—9.2 years
- Mean age (cats)—11.6 years

SIGNS

- Nonspecific—fever; vomiting; weakness; anorexia; icterus; malabsorption syndrome; weight loss.
- Abdominal pain—variable.
- Abdominal effusion—malignant.
- Metastasis to bone and soft tissue common.
- Pathologic fractures secondary to metastasis reported.
- Palpable abdominal mass (cats).
- Paraneoplastic syndromes of epidermal necrosis, hyperinsulinemia, and hyperglucagonemia may be present.
- Average duration of clinical signs (cats): 41 days, range 2–180 days.

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Primary pancreatitis; may be concurrent and complicate or delay early diagnosis
- Pancreatic pseudocyst
- Pancreatic nodular hyperplasia
- Hepatic neoplasia
- Other causes of vomiting and icterus
- Peritoneal carcinomatosis
- Other causes of abdominal effusion in cats

CBC/BIOCHEMISTRY/URINALYSIS

- Usually nonspecific changes (e.g., mild anemia and neutrophilia).
- Hyperamylasemia less reliable than hyperlipasemia.
- Lipase concentrations are often markedly elevated and may serve as a non-invasive biochemical marker of neoplasia in dogs.

OTHER LABORATORY TESTS

Rarely there may be significant metabolic alterations that affect glucagon, insulin, and amino acid concentrations.

IMAGING

- Abdominal radiographs may reveal a mass or loss of serosal detail associated with concurrent pancreatitis or peritoneal effusion.
- Ultrasonography may reveal one or more masses or concurrent pancreatitis (mixed echogenicity, large pancreas, hyperechoic peripancreatic fat). Pancreatic thickening, abdominal effusion, and single to multiple nodules of varying size may be identified. Sonographic findings may be impossible to distinguish from pancreatic nodular hyperplasia. Rarely the ultrasound of the pancreas may appear normal except for dilation of the pancreatic duct.

DIAGNOSTIC PROCEDURES

- Surgical biopsy—definitive.
- Fine-needle aspirate cytology—supportive. In many cases, where the tumor is not resectable, the fine-needle aspirates may provide strong enough evidence to start medical treatment.



TREATMENT

- None reported curative.
- Palliation of pain with aggressive analgesic combinations is necessary.
- Surgical intervention to alleviate intestinal and biliary obstruction, if necessary.
- Surgery is typically not a good option in many cases, due to the extent of the disease at the time of diagnosis.
- If surgery is an option, partial or total pancreatectomy may prolong survival.
- Treat concurrent pancreatitis.
- Antiemetics and supportive care (hydration and caloric requirements).



MEDICATIONS

DRUG(S)

- Gemcitabine is used in humans for the treatment of pancreatic carcinoma, and while used in dogs with cancer, it has not been established as the standard of care for dogs with pancreatic adenocarcinoma.
- Always consult a veterinary oncologist for updates in treating this rare neoplasm.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

POSSIBLE COMPLICATIONS

- Intestinal obstruction
- Biliary obstruction
- Pancreatic abscess
- Peritonitis
- Metastasis

EXPECTED COURSE AND PROGNOSIS

Progression to death is often rapid given that there is no successful curative treatment available. Despite the grave prognosis, individual patients treated with complete resection of their tumor and chemotherapy, in the absence of systemic metastasis, may have prolonged survival.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Gastrin-secreting pancreatic carcinoma (gastrinoma) has been reported in dogs and cats. Clinical signs are associated with hypergastrinemia, which results in inappropriate hydrochloric acid secretion by the stomach, leading to gastroduodenitis.

Suggested Reading

Linderman MJ, Brodsky EM, de Lorimier LP, Clifford CA, Post GS. Feline exocrine pancreatic carcinoma: a retrospective study of 34 cases. *Vet Comp Oncol* 2013, 11(3):208–218.

Cave T, Evans H, Hargreavest J, et al. Metabolic epidermal necrosis in a dog associated with pancreatic adenocarcinoma, hyperglucagonaemia, hyperinsulinaemia, and hypoaminoacidaemia. *J Small Anim Pract* 2007, 48:522–526.

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Quigley KA, Jackson ML, Haines DM. Hyperlipasemia in 6 dogs with pancreatic or hepatic neoplasia: Evidence for tumor lipase production. *Vet Clin Pathol* 2001, 30:114–120.

Author Nick Dervis

Consulting Editor Timothy M. Fan

Acknowledgment The author and editors acknowledge the prior contribution of Wallace B. Morrison.

ADENOCARCINOMA, PROSTATE



BASICS

OVERVIEW

- Prostatic adenocarcinoma is a malignant tumor that occurs in both neutered and intact male dogs.
- Although this neoplasm represents < 1% of all canine malignancies, it is the most common prostatic disorder in neutered male dogs.
- Metastases to regional lymph nodes, lungs, and the lumbosacral skeleton are common. Skeletal metastases can adopt an osteoblastic appearance.

SIGNALMENT

- Dog and rarely cat
- Medium- to large-breed intact or neutered male dogs
- Median age of 9–10 years

SIGNS

Historical Findings

- Tenesmus (with the production of ribbon-like stool)
- Weight loss
- Stranguria and dysuria
- Rear limb lameness or neurologic weakness
- Lethargy
- Exercise intolerance

Physical Examination Findings

- A firm, asymmetrical, and immobile prostate gland.
- Prostatomegaly is common, but is not always present.
- Pain may be elicited in response to abdominal or rectal palpation.
- Caudal abdominal mass, cachexia, pyrexia, and dyspnea may also be identified in advanced cases of disease.

CAUSES & RISK FACTORS

Neutered males are at increased risk for prostatic neoplasia



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other primary neoplasia (i.e., squamous cell carcinoma, transitional cell carcinoma).
- Metastatic or locally invasive neoplasia (i.e., transitional cell carcinoma).
- Acute or chronic prostatitis, benign prostatic hypertrophy, prostatic abscess, and prostatic cysts are possible differentials in intact male dogs but are highly unlikely in neutered dogs.

CBC/BIOCHEMISTRY/URINALYSIS

- Inflammatory leukogram possible.
- Alkaline phosphatase may be high if skeletal metastases exist.
- Post-renal azotemia may be present if urethral obstruction exists.
- It is prudent to evaluate urine samples via cystocentesis and free-catch techniques, as hematuria, pyuria, and malignant epithelial cells may be observed in free-catch samples but are unusual in samples obtained by cystocentesis.

OTHER LABORATORY TESTS

Serum and seminal plasma markers such as acid phosphatase, prostate specific antigen, and canine prostate specific esterase are not elevated in dogs with PAC.

IMAGING

- Thoracic radiography—metastases may appear as pulmonary nodules or increased interstitial markings.
- Abdominal radiography—sublumbar lymphadenomegaly, mineralization of the prostate, lytic lesions to the lumbar vertebrae or pelvis as a consequence of direct tumor extension from regionally infiltrated lumbar lymph nodes may be seen.
- Abdominal ultrasonography—focal to multifocal hyperechogenicity with asymmetry and irregular prostatic outline, ± prostatic mineralization.
- Contrast cystography may help differentiate prostatic from urinary bladder disease.

DIAGNOSTIC PROCEDURES

- Prostatic aspirate (percutaneous or transrectal).
- Prostatic wash.
- Prostatic biopsy performed percutaneously or surgically.
- Percutaneous biopsy has been associated with tumor seeding along the biopsy tract.



TREATMENT

- Prostatectomy if local disease (success of this procedure depends on the skill of the surgeon and extent of disease).
- Radiation therapy may palliate signs and prolong survival.
- Prostatic urethral stenting can alleviate urethral obstruction.
- Neutering—however, most tumors are not androgen responsive.



MEDICATIONS

DRUG(S)

- Chemotherapy—carboplatin, mitoxantrone, or doxorubicin; may offer short-term benefit.
- Pain relief with NSAIDs, morphine-derived drugs.
- Aminobisphosphonates for the relief of painful skeletal metastases.
- Stool softeners to relieve tenesmus.

CONTRAINdications/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

Ability to urinate and defecate, pain secondary to skeletal metastases, quality of life.

PREVENTION/AVOIDANCE

Keeping dogs sexually intact may decrease risk.

POSSIBLE COMPLICATIONS

- Urethral obstruction
- Metastasis to regional lymph nodes, skeleton, and lungs

EXPECTED COURSE AND PROGNOSIS

Guarded to poor, survival of 2–6 months depending upon presenting clinical symptoms. Treatment early in the course of disease with curative-intent radiation and systemic chemotherapy can extend survival times to 12 months.



MISCELLANEOUS

ASSOCIATED CONDITIONS

None

AGE-RELATED FACTORS

None

ABBREVIATIONS

- NSAID = nonsteroidal anti-inflammatory drug
- PAC = prostatic adenocarcinoma

Suggested Reading

Bryan JN, et al. A population study of neutering status as a risk factor for canine prostate cancer. Prostate 2007, 67:1174–1181.

Author Ruthanne Chun

Consulting Editor Timothy M. Fan



BASICS

OVERVIEW

- Accounts for < 1% of all reported neoplasms in dogs.
- Renal tumors tend to be highly metastatic via hematogenous dissemination, locally invasive, and often bilateral.
- Renal cystadenocarcinoma, a rare heritable syndrome with a less aggressive behavior and better long-term prognosis than renal adenocarcinoma, has been described in German shepherd dogs.

SIGNALMENT

- Adenocarcinoma—older (8–9 years) dogs, 1.6:1 male-to-female ratio, no breed predilection.
- Cystadenocarcinoma—German shepherd dogs, often female.

SIGNS

- Adenocarcinoma—insidious, non-specific signs such as weight loss, inappetance, lethargy, hematuria, and pale mucous membranes. Possibility for paraneoplastic polycythemia.
- Cystadenocarcinoma—may present for nodular dermatofibrosis, a syndrome of painless, firm, fibrous lesions of the skin and subcutaneous tissues.

CAUSES & RISK FACTORS

- Adenocarcinoma—unknown.
- Cystadenocarcinoma—heritable in German shepherd dogs.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other primary neoplasia (i.e., lymphoma, nephroblastoma)
- Metastatic neoplasia (i.e., hemangiosarcoma)
- Renal adenoma or cyst
- Pyelonephritis

CBC/BIOCHEMISTRY/URINALYSIS

- CBC may show paraneoplastic polycythemia or leukocytosis, or anemia.

- Biochemistry may be normal, or may reveal azotemia.
- Urinalysis may show hematuria, proteinuria, bacteriuria, or casts.

OTHER LABORATORY TESTS

Urine culture and sensitivity

IMAGING

- Thoracic radiographs—metastatic disease reported in up to 16% of patients.
- Abdominal radiographs—mass visualized in 81% of patients.
- Abdominal ultrasonography, CT, or contrast radiography—useful in identifying and staging the disease. Advanced imaging can guide decisions regarding surgical resectability.

DIAGNOSTIC PROCEDURES

- Renal biopsy (ultrasound-guided or surgical) for definitive diagnosis.
- Percutaneous fine-needle aspirate can be used for supportive diagnosis.



TREATMENT

- Aggressive surgical excision is the treatment of choice for unilateral disease.
- Successful chemotherapeutic management of either disease has not been described.
- Supportive management for patients in renal failure may be necessary.



MEDICATIONS

DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

- Renal failure—measure serum urea nitrogen and creatinine; urinalysis.
- Quality of life if bilateral or otherwise non-surgical disease.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Renal failure
- Metastatic disease
- Invasion of local vital structures (vena cava, aorta)

EXPECTED COURSE AND PROGNOSIS

- Adenocarcinoma—median reported survival of 49 dogs was 16 months (range 0–59 months).
- Cystadenocarcinoma—few large studies of this rare disease, reported median survival of 12+ months with no definitive therapy.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- The paraneoplastic syndromes of hypertrophic osteopathy, polycythemia, and a neutrophilic leukocytosis have been reported in isolated cases.
- Renal failure.
- Nodular dermatofibrosis and uterine leiomyomas are commonly associated with cystadenocarcinoma.

ABBREVIATION

- CT = computed tomography

Suggested Reading

Bryan JN, et al. Primary renal neoplasia of dogs. *J Vet Intern Med* 2006, 20:1155–1160.

Knapp DW. Tumors of the urinary system.

In: Withrow SJ, Vail DM, eds., *Small Animal Clinical Oncology*, 4th ed. Philadelphia: Saunders, 2007, pp. 649–658.

Author Ruthanne Chun

Consulting Editor Timothy M. Fan

ADENOCARCINOMA, SALIVARY GLAND



BASICS

OVERVIEW

- Tumor arising from major (e.g., parotid, mandibular, sublingual, or zygomatic) or minor salivary glands.
- Mandibular or parotid glands constitute 80% of cases.
- Mandibular gland most frequently affected in dogs.
- Parotid gland most frequently affected in cats.
- Locally invasive and regionally metastatic.
- Cats typically have more advanced disease than dogs at time of diagnosis.
- Metastasis—regional lymph node involvement in 39% of cats and 17% of dogs at diagnosis; distant metastasis reported in 16% of cats and 8% of dogs at diagnosis but may be slow to develop.
- Other salivary gland neoplasms—carcinoma; squamous cell carcinoma; mixed neoplasia.
- Epithelial malignancies—constitute roughly 85% of salivary gland tumors.
- Fibrosarcomas, lipomas, mast cell tumors, and lymphomas have involved the salivary glands by direct extension and invasion. A concurrent malignant fibrous histiocytoma (giant cell type) and malignant mixed tumor (likely of ductal origin) within the salivary gland has also been described.
- Adenomas comprise only 5% of salivary tumors.

SIGNALMENT

- Dog and cat.
- Mean age, 10–12 years.
- Siamese cats—may be at relatively higher risk.
- Male cats affected twice as often as female cats.
- No other breed or sex predilection has been determined.

SIGNS

- Unilateral, firm, painless swelling of the upper neck (mandibular and sublingual), ear base (parotid), upper lip or maxilla (zygomatic), or mucous membrane of lip (accessory or minor salivary tissue).
- Other signs may include halitosis, weight loss, anorexia, dysphagia, exophthalmus, Horner's syndrome, sneezing, and dysphonia.

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Squamous cell carcinoma
- Mucocele
- Abscess
- Soft tissue sarcoma, e.g., fibrosarcoma
- Lymphoma
- Sialadenosis

CBC/BIOCHEMISTRY/URINALYSIS

Results often normal

IMAGING

- Regional radiographs usually are normal; may see periosteal reaction on adjacent bones or displacement of surrounding structures.
- MRI or CT imaging allows superior discrimination of tumor for surgery and/or radiation treatment planning.
- Thoracic radiographs indicated to check for lung metastases.

DIAGNOSTIC PROCEDURES

- Cytologic examination of aspirate may differentiate salivary adenocarcinoma from mucocele and abscess.
- Needle core or wedge biopsy for histopathology—definitive diagnosis.



TREATMENT

- Aggressive surgical resection—when possible; most are invasive and difficult to excise completely.
- Radiotherapy—good local control and prolonged survival in three reported cases.
- Aggressive local resection (usually histologically incomplete) followed by adjuvant radiation can achieve local control and long-term survival, but further studies are needed to determine the most effective treatment, including the possible role for chemotherapy.



MEDICATIONS

DRUG(S)

Chemotherapy (mitoxantrone or carboplatin) efficacy is largely unreported; however, may

be indicated for treatment/palliation of metastatic disease.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

Evaluations—physical examination and thoracic radiographs every 3 months reasonable if aggressive surgery and/or radiation therapy employed.

POSSIBLE COMPLICATIONS

Temporary acute side effects (e.g., moist dermatitis and alopecia) expected with definitive radiation therapy in dogs, but uncommon in cats. Consultation with a radiation oncologist is recommended regarding specific, anatomic site-related side effects associated with planned dose and field size.

EXPECTED COURSE AND PROGNOSIS

- Improved survival time in dogs without evidence of nodal or distant metastasis at diagnosis; clinical stage not prognostic for cats.
- Median survival 550 days for dogs and 516 days for cats in retrospective study.
- Local control obtained through radiation and/or surgery remains critical.



MISCELLANEOUS

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging

Suggested Reading

Hammer A, Getzy D, Ogilvie G, et al.

Salivary gland neoplasia in the dog and cat: Survival times and prognostic factors. J Am Anim Hosp Assoc 2001; 37:478–482.

Author Anthony J. Mutsaers

Consulting Editor Timothy M. Fan

ADENOCARCINOMA, SKIN (SWEAT GLAND, SEBACEOUS)



BASICS

OVERVIEW

Malignant growth originating from sebaceous or apocrine sweat glands of the skin.

SIGNALMENT

- Apocrine sweat gland—rare in dogs, uncommon in cats.
- Sebaceous gland—rare in both dogs and cats.
- Middle-aged to older pets.
- Female dogs overrepresented for apocrine adenocarcinoma in one study.

SIGNS

- May appear as solid, firm, raised, superficial skin lesions.
- May be ulcerated and bleeding and accompanied by inflammation of the surrounding tissue.
- Apocrine sweat gland—often poorly circumscribed, ulcerated; very invasive into underlying tissue; may occur anywhere on the body, frequently affecting the trunk in dogs.
- Sebaceous gland—often ulcerated and inflamed, moderate risk of lymph node involvement.
- Dermal and lymphatic tracking can be observed early in disease course.

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other more frequent skin tumors
- Cutaneous histiocytic diseases
- Immune-mediated skin diseases
- Bacterial/fungal infections

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

N/A

IMAGING

Thoracic radiographs recommended at the time of diagnosis to assess for distant metastases.

DIAGNOSTIC PROCEDURES

- Biopsy for histopathology and definitive diagnosis
- Cytologic examination or biopsy of draining lymph nodes

PATHOLOGIC FINDINGS

- Apocrine gland adenocarcinomas are typically invasive into the underlying stroma and blood vessels, and often show poorly demarcated borders and a high mitotic index.
- Sebaceous gland adenocarcinomas often reveal lymphatic vessel invasion.



TREATMENT

- Aggressive *en bloc* surgical excision, including resection of draining lymph node, recommended for both types. Histopathologic analysis of lymph nodes assists with determining prognosis and establishing adjuvant treatment plan.
- Margins of entire tissue specimen must be evaluated histologically to assess completeness of resection.
- Radiation therapy may be recommended for treatment of draining lymph nodes after resection to prevent recurrence and development of regional metastasis; radiation therapy of primary tumor site recommended when wide and complete resection not possible.



MEDICATIONS

DRUG(S)

- Chemotherapy has been used anecdotally for the treatment of both tumor types, in both species.
- Contact a veterinary oncologist for any updated treatments that may be available.
- Nonsteroidal anti-inflammatory drugs and other analgesics are recommended, as indicated, for pain control.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

None



FOLLOW-UP

- Sebaceous gland adenocarcinoma—little is known about the metastatic potential of this malignancy, but may be rapidly metastatic to regional lymph nodes in some patients; long-term prognosis is anecdotally good with multimodal therapy combining aggressive surgery, chemotherapy, and radiation therapy.
- Apocrine gland adenocarcinoma—fair to good long-term prognosis; the histologic finding of vascular invasion is a negative prognostic factor predicting systemic metastases; aggressive surgical resection (local and regional tumor control) followed by adjuvant chemotherapy is recommended to improve survival. A study reported a post-excisional median survival time of 30 months in dogs.



MISCELLANEOUS

Suggested Reading

Carpenter JL, Andrews LK, Holzworth J. Tumors and tumor like lesions. In: Holzworth J, ed., Diseases of the Cat: Medicine and Surgery. Philadelphia: Saunders, 1987, pp. 406–596.

Pakhrin B, Kang MS, Bae IH, et al. Retrospective study of canine cutaneous tumors in Korea. *J Vet Sci* 2007, 8:229–236. Simko E, Wilcock BP, Yager JA. A retrospective study of 44 canine apocrine sweat gland adenocarcinomas. *Can Vet J* 2003, 44(1):38–42.

Hauck ML. Tumors of the skin and subcutaneous tissues. In: Withrow SJ, Vail DM, Page RL, eds., Small Animal Clinical Oncology, 5th ed. St. Louis, MO: Elsevier Saunders, 2013, pp. 305–320.

Haziroglu R, Haligur M, Keles H. Histopathological and immunohistochemical studies of apocrine sweat gland adenocarcinomas in cats. *Vet Comp Oncol* 2014, 12(1):85–90.

Author Louis-Philippe de Lorimier

Consulting Editor Timothy M. Fan

ADENOCARCINOMA, STOMACH, SMALL AND LARGE INTESTINE, RECTAL



BASICS

OVERVIEW

- Uncommon tumor arising from the epithelial lining of the gastrointestinal tract.
- Prognosis guarded to poor.

SIGNALMENT

- Dog more commonly affected than cat.
- Middle-aged to older (> 6 years) animals; age range 3–13 years.
- No breed predisposition.
- More common in males than females.

SIGNS

Historical Findings

- Stomach—vomiting, anorexia, weight loss, hematemesis, and melena.
- Small intestine—vomiting, weight loss, borborygmus, flatulence, and melena.
- Large intestine and rectum—mucus and blood-tinged feces and tenesmus.

Physical Examination Findings

- Stomach—nonspecific.
- Small intestine—may feel mid-abdominal mass; distended, painful loops of small bowel; melena on rectal exam.
- Large intestine and rectum—palpable mass per rectum, may form annular ring, or multiple nodular lesions protruding into the colon; bright red blood on feces.

CAUSES & RISK FACTORS

- Unknown.
- Nitrosamines—reported as causative agent in experimental literature.
- Possible genetic cause—gastric adenocarcinomas in related Belgian shepherds and Dutch Tervuren shepherds.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Foreign body
- Inflammatory bowel disease
- Lymphoma
- Parasites
- Leiomyoma
- Leiomyosarcoma
- Pancreatitis

CBC/BIOCHEMISTRY/URINALYSIS

- Stomach and small intestine—may see microcytic, hypochromic anemia (iron-deficiency anemia). Mild and persistent elevations in blood urea nitrogen in the face of normal creatinine can support intestinal blood loss.
- Large intestine and rectum—no characteristic changes.

OTHER LABORATORY TESTS

Fecal occult blood may be positive; diet may affect results—can recheck to confirm after feeding non-meat diet for 3 days.

IMAGING

- Ultrasound—may reveal a thickened stomach or bowel wall; may see mass in the gastrointestinal tract, enlarged lymph nodes.
- Positive contrast radiography—filling defect (stomach); intraluminal space-occupying or annular constriction (small bowel); gastric neoplasm most often found in distal two-thirds of stomach.
- Double contrast radiography—large intestine and rectum; polypoid or annular space-occupying masses.
- Advanced imaging with contrast CT or MRI can provide highest quality images of gastrointestinal tract.

DIAGNOSTIC PROCEDURES

- Ultrasound-guided fine-needle aspirate of bowel mass or enlarged lymph node may reveal carcinoma cells on cytology, which can be useful to rule out lymphoma.
- Endoscopic biopsy may be non-diagnostic because tumors are frequently deep to the mucosal surface; thus surgical biopsy frequently required.



TREATMENT

- Surgical resection—treatment of choice; seldom curative.
- Gastric—usually non-resectable.
- Small intestine—remove by resection and anastomosis; metastasis to regional lymph nodes and the liver common.
- Large intestine and rectal—may occasionally be resected by a pull-through surgical procedure; metastasis common; transcolonic debulking may provide palliation of obstruction.



MEDICATIONS

DRUG(S)

- Chemotherapy—only anecdotal reports, usually unsuccessful.
- Piroxicam 0.3 mg/kg PO q24 h can provide palliation for large intestinal and rectal tumors.
- Aggressive combination analgesics should be instituted.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Seek advice before initiating treatment with cytotoxic drugs.



FOLLOW-UP

Physical examination, thoracic radiographs, and abdominal ultrasound—at 1, 3, 6, 9, and 12 months post-surgery.

EXPECTED COURSE AND PROGNOSIS

Dogs

- Overall poor; pedunculated rectal tumors do best; most cases recur locally, develop metastasis, or both rapidly.
- Median survival gastric—2 months.
- Median survival small intestinal—10 months.
- Mean survival large intestinal—annular 1.6 months versus pedunculated 32 months.

Cats

- Guarded.
- Few reported cases, but may have prolonged survival (> 1 year).



MISCELLANEOUS

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging

Suggested Reading

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Author Laura D. Garrett

Consulting Editor Timothy M. Fan



BASICS

DEFINITION

A malignant tumor arising from the follicular or parafollicular cells (medullary/C-cells) of the thyroid gland.

PATHOPHYSIOLOGY

- About 60% of patients are euthyroid, 30% hypothyroid, and 10% hyperthyroid.
- Typically very invasive tumors with high rate of metastasis (lungs, retropharyngeal lymph nodes, liver), with up to 35–40% of dogs having metastasis at the time of diagnosis.
- Animals with bilateral tumors have a sixteen times greater risk of developing metastatic disease than animal with unilateral tumors.

SYSTEMS AFFECTED

- Cardiovascular**—hyperthyroid dogs are usually tachycardic and may have systemic hypertension; may see anemia and DIC in advanced disease.
- Endocrine/Metabolic**—affected dogs may be hypothyroid, euthyroid, or hyperthyroid; hypercalcemia may be seen as a paraneoplastic syndrome or secondary to concurrent parathyroid hyperplasia or parathyroid adenocarcinoma.
- Respiratory**—dogs may be dyspneic owing to a space-occupying mass adjacent to the trachea; metastasis to the lungs common. Large compressive masses can result in caval syndrome manifested as facial edema.

GENETICS

Unknown

INCIDENCE/PREVALENCE

Accounts for 1.2–3.8% of all canine tumors and represents 10–15% of all primary head and neck tumors.

GEOGRAPHIC DISTRIBUTION

May be more common in iodine-deficient areas.

SIGNALMENT

Species

Dog

Breed Predilections

Boxers, golden retrievers, Siberian huskies, and beagles at increased risk but seen in any breed.

Mean Age and Range

Older dogs (median 9–15 years; range 4–18 years)

Predominant Sex

No gender predilection.

SIGNS

General Comments

- Usually not diagnosed until a large mass is palpable.
- Approximately 65% are unilateral, 35% are bilateral.

Historical Findings

- Palpable mass/swelling in cervical neck, coughing, dyspnea, dysphagia, dysphonias, facial edema, neck pain.
- If functional thyroid tumor—may see polyuria, polydipsia, polyphagia, weight loss, restless behavior, diarrhea.
- If hypothyroid—may see poor hair coat, weight gain, lethargy.

Physical Examination Findings

- Freely movable or fixed cervical mass, unilateral or bilateral.
- Rarely may see Horner's syndrome, or cranial vena cava syndrome.
- If hyperthyroid—cardiac arrhythmias or murmurs.

CAUSES

Unknown

RISK FACTORS

- Untreated hypothyroidism has been shown to be a risk factor in a colony of beagles.
- Breed predilection.
- Iodine deficiency.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other primary neoplasms—lymphoma; soft tissue sarcoma; salivary gland adenocarcinoma; parathyroid carcinoma; carotid body tumor.
- Secondary tumors—metastatic oral squamous cell carcinoma; oral melanoma.
- Inflammatory—abscess or granuloma.
- Salivary mucocele.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal.
- May see non-regenerative normocytic normochromic anemia of chronic disease, leukocytosis.
- Rare—hypercalcemia; isosthenuria; DIC.

OTHER LABORATORY TESTS

Thyroid hormone (T_4 and/or free T_4 levels) and endogenous TSH levels.

IMAGING

- Thoracic radiography (3 view)—evaluation of lungs and other thoracic structures for metastasis.
- Cervical ultrasonography, computed tomography, and magnetic resonance imaging—evaluation of tissue of origin, vascularity, invasion, and cervical lymph nodes.
- Technetium-99 m scintigraphy to evaluate for ectopic thyroid tissue or metastatic lesions.
- Radioiodine studies—may provide information about the tumor's ability to produce thyroid hormone.

DIAGNOSTIC PROCEDURES

Biopsy

Tru-Cut not recommended owing to high risk of severe hemorrhage; open biopsy usually

required and allows for controlled hemostasis in the event of bleeding.

Cytology

- Examination of fine-needle aspirates from tumor and palpable regional lymph nodes.
- Specimen almost always heavily contaminated with blood owing to highly vascular nature of tumor.
- Homogeneous population of epithelial cells, sometimes with colloid and/or tyrosine-containing granules.
- Unable to differentiate malignant from benign thyroid cells; but almost all thyroid neoplasms in dogs are malignant.

PATHOLOGIC FINDINGS

Gross

- Characterized by high vascularity with areas of hemorrhage and necrosis.
- Usually poorly encapsulated; often invade adjacent tissues (e.g., trachea and esophagus, and surrounding vasculature); may adhere to the jugular vein, carotid artery, and vagosympathetic trunk.

Histopathology

- Three main types—follicular, papillary, and compact (solid); mixed follicular and solid tumors most common in dogs.
- C-cell (e.g., parafollicular, medullary) carcinomas less common.



TREATMENT

APPROPRIATE HEALTH CARE

- Definitive treatment is dependent on tumor stage (tumor size, mobility, and evidence of metastatic disease).
- Complete surgical excision recommended for freely movable thyroid tumors.
- Full course external beam radiation therapy recommended preoperatively for large tumors, as a sole therapy for non-resectable tumors, or postoperatively for incompletely surgically removed tumors.
- Palliative radiation and/or chemotherapy recommended for tumors that are metastatic at presentation.
- Also can use iodine-131 but doses are very large (60–100 mCi) and therefore there are limited facilities that offer this therapy.
- Toceranib phosphate (Palladia) can exert cytoreductive activity.

NURSING CARE

Varies with signs on examination.

ACTIVITY

Restrict activity if dyspneic.

DIET

N/A

CLIENT EDUCATION

- Warn owners of the importance of controlling heart rate and rhythm in hyperthyroid patients and of the possibility of episodes of collapse.

ADENOCARCINOMA, THYROID—DOGS

(CONTINUED)

- Warn owners of possible postoperative laryngeal paralysis and intraoperative hemorrhage.
- Warn owners of acute radiation therapy toxicities—moist desquamation, laryngitis, tracheitis, esophagitis.

SURGICAL CONSIDERATIONS

See "Appropriate Health Care"

Risks

- Marked hemorrhage—tumors highly vascular and invasive into surrounding structures including vasculature; may need blood transfusion and intensive postoperative care.
- Laryngeal paralysis—owing to trauma to recurrent laryngeal nerve.
- Damaged parathyroid glands—may occur during surgery.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Chemotherapeutic agents:
 - Chemotherapy is recommended as a sole therapy, or possibly in combination with surgery and/or radiation therapy.
 - Cisplatin (60 mg/m^2 every 3 weeks), carboplatin (300 mg/m^2 every 3 weeks), or doxorubicin (30 mg/m^2 every 3 weeks)—reported to effect partial remission in approximately 50% of cases.
 - Toceranib (2.5–3 mg/kg 3 times a week)—had biologic activity in 80% of cases (26% partial remission, 53% stable disease).
 - Cisplatin—nephrotoxic; must use with saline diuresis (18.3 mL/kg/hour IV over 6 hours; give cisplatin after 4 hours).
- Antiemetics for cisplatin therapy:
 - Maropitant 1 mg/kg SC before cisplatin, or
 - Dolasetron 0.6–1 mg/kg IV or PO q24 h, or
 - Butorphanol 0.4 mg/kg IM before and after cisplatin.
- Thyroid management:
 - Thyroxine—maintenance doses to decrease TSH production have been recommended; some tumors contain TSH receptors; value of hormone replacement therapy in affected dogs not determined.
 - Methimazole 5 mg PO q8 h for medium to large dogs; may be beneficial for hyperthyroid patients.
 - β -blockers—may be indicated for tachycardia or hypertension in hyperthyroid patients.

CONTRAINdications

- Doxorubicin is cumulatively toxic to cardiac myocytes causing decreased myocardial function. Do not give to animals with poor cardiac function or dilated cardiomyopathy.

- Cisplatin is nephrotoxic; do not give to animals with renal disease.

PRECAUTIONS

Chemotherapy can cause gastrointestinal, bone marrow, cardiac, and other toxicities—seek advice from a medical oncologist if unfamiliar with cytotoxic drugs.

POSSIBLE INTERACTIONS

Verapamil—may potentiate doxorubicin-induced cardiotoxicity.

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

- Serum calcium concentration—if bilateral thyroidectomy was performed; signs of hypocalcemia (agitation, panting, muscle tremors, tetany, and seizures) may be observed.

- Treat with 10% calcium gluconate (1–1.5 mL/kg IV over 10–20 minutes).
- Maintain serum calcium with dihydrotachysterol (vitamin D) orally.
- Thyroid hormone—supplementation with thyroxine may be necessary after bilateral thyroidectomy.
- TSH concentration—a goal of thyroxin supplementation is to downregulate the body's secretion of TSH.
- Site of primary tumor—physical examination and cervical ultrasound; thoracic radiographs every 3 months to detect pulmonary metastasis.

PREVENTION/AVOIDANCE

Unknown

POSSIBLE COMPLICATIONS

- Tumor—anemia; thrombocytopenia; hypercalcemia; DIC; respiratory distress.
- Chemotherapy—dilated cardiomyopathy; renal failure; pancreatitis; sepsis; gastrointestinal upset.
- Surgery—hemorrhage; hypothyroidism; hypoparathyroidism leading to hypocalcemia; laryngeal paralysis.
- Radiotherapy—acute side effects—moist desquamation, pharyngeal mucositis; esophagitis; tracheitis; late side effects—alopecia, and skin or coat color change (at radiation site).

EXPECTED COURSE AND PROGNOSIS

- Prognosis—related to stage of disease (tumor size, mobility and evidence of metastatic disease) with small, non-attached unilateral, non-metastatic tumors having best prognosis.
- MST after surgical removal of unilateral thyroid tumors is 1462 days vs. 365 days for patients undergoing bilateral thyroidectomy.

- For animals treated with full course external beam radiation therapy—progression-free survival at 1 year—80%, and 72% at 3 years in one study and in another study MST 24.5 months.

- Palliative radiation therapy in 13 dogs—MST 24 months.

- ^{131}I therapy in combination with surgery—MST 34 months, or ^{131}I alone MST 30 months.

- Animals treated with cisplatin alone (13 dogs)—overall response rate was 53%, median progression-free interval for responders was 202 days and overall MST was 98 days.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Non-thyroidal malignancies common
- Multiple endocrine neoplasia reported

AGE-RELATED FACTORS

None

PREGNANCY/FERTILITY/BREEDING

It is not recommended to breed animals with cancer. Chemotherapy is teratogenic—do not give to pregnant animals.

SYNOMYS

Thyroid carcinoma

ABBREVIATIONS

- DIC = disseminated intravascular coagulation
- MST = median survival time
- TSH = thyroid stimulating hormone

Suggested Reading

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AGGRESSION TO UNFAMILIAR PEOPLE AND UNFAMILIAR DOGS



BASICS

OVERVIEW

A variety of different motivations exist, including fear, territoriality, conflict and possessiveness. Aggression is directed toward a person or dog that does not live in the household. Regular visitors may also be targets. May be within the range of normal behavior, but may be compounded by fearfulness.

SYSTEMS AFFECTED

- Behavioral. • Sympathetic stimulation (e.g., tachypnea, tachycardia).

INCIDENCE/PREVALENCE

Stranger-directed aggression represents 32.5% of canine behavioral referral caseload.

SIGNALMENT

- Can occur at any age. Signs may begin to emerge as primary socialization wanes (approximately 12–16 weeks of age) or may arise or intensify at social maturity (approximately 18–36 months). Genetic concerns and poor prognosis if signs arise before 12 weeks.
- Territorial aggression more common in intact males—initial signs usually present by 1 year.
- Aggression toward unfamiliar people and dogs overrepresented in males.
- Breed predilection for inter-dog aggression in “fighting breeds” (e.g., pit bull terriers) and terriers.

SIGNS

- Aggression (barking, growling, lip-lifting, snarling, snapping, lunging, biting) toward unfamiliar people and dogs. May be accompanied by fearful or submissive body postures/facial expressions (head down, crouching, backing away, ears back, tail tucked, looking away, lip licking) or confident body postures (standing straight up, approach with tail up, ears forward).
- Territorial aggression arises in familiar locations or spaces (e.g., home, yard, car).
- May be confident, fearful or conflict.
- Fear aggression more likely when dog is cornered or cannot escape.
- May be more frequent or severe on- than off-leash.

CAUSES & RISK FACTORS

- May be a normal canine behavior.
- Strongly influenced by previous experience (e.g., early socialization, painful conditions, rough handling, inappropriate punishment, previous fear-evoking experience with unfamiliar people or dogs).
- Underlying medical conditions, especially pain.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Fear aggression • Territorial aggression
- Possessive aggression • Conflict aggression
- Generalized anxiety disorder

CBC/BIOCHEMISTRY/URINALYSIS

Usually unremarkable. Abnormalities suggest an underlying medical condition.

OTHER LABORATORY TESTS

Usually unremarkable

IMAGING

MRI if CNS disease suspected. Other imaging as needed to rule out underlying medical conditions.



TREATMENT

CLIENT EDUCATION

Treatment is aimed at controlling the problem, not at achieving a “cure.” Successful treatment, resulting in a decrease in aggressive incidents, depends on owner understanding of basic canine social behavior, risks involved, how to follow safety and management recommendations, correct identification of the aggression-eliciting stimuli, and effective implantation of reward-based behavior modification.

Safety Recommendations

- Owners’ main responsibility is safety by avoiding situations that may evoke a fearful or aggressive reaction. Avoidance is also necessary to insure the pet’s welfare and prevent further learning of aggressive behaviors.
- Owners should be advised that dog owners may be liable for bites and could face civil/criminal prosecutions should a person be injured.
- Successful treatment is more likely if a period of preventing exposure to aggression-provoking stimuli is instituted prior to behavior modification.
- Confining dog away from potential victims, avoid walks or parks where stimulus exposure might occur, or have dog under direct physical control of a responsible adult whenever an aggression-provoking situation could arise (e.g., public location, when visitors are at the house).
- Confining territorial dogs to where they cannot see/hear visitors approaching territory before they become aggressively aroused.
- Introduce a head halter (e.g., Gentle Leader) and basket muzzle for easier and safer control.
- Owners should be advised that punishment/dominance-based training can lead to

increased aggression, fear, agitation, and/or injuries and should be avoided. If safety cannot be insured, dogs should be removed from the household.

Behavior Therapy

- Structured interactions (also known as learn to earn or say please by sitting) where the dog is consistently taught to sit for anything it values (before feeding, petting, play, going for a walk) gives the dog control of its resources by sitting calmly, provides structure and predictability in all interactions, teaches impulse control and trains the dog that good things happen by sitting calmly.
- Commands: teach the dog to focus on the owner for guidance using eye contact and hand target (e.g., dog touch nose to owner’s hand).
- Teach the dog to sit and relax on verbal cue in neutral situations using food rewards; teach to go to mat, bed or crate to settle; teach to walk on loose leash. Train with head halter or muzzle if needed to insure safety. Private session with a force-free trainer should be considered to achieve basics before any exposure.

Behavior Modification: Systematic Desensitization and Counter-conditioning (DS/CC)

- When owner can effectively control and calm in the absence of stimuli, begin exposure by determining the limit (distance, location, person, dog) at which the dog will orient but not yet react. Have the dog focus on the owner or continue walking calmly (heel) and give favored (highest value) rewards to make positive associations with each stimulus exposure.
- Gradually (baby steps) increase stimulus intensity, staying below the threshold that would result in fear and/or aggression by decreasing distance, increasing distractions, or moving to more challenging environments.
- Progress is slow (typically months). Carefully monitor body language to avoid setbacks.
- If the dog is not calm, shows aggression or precursors to aggression (e.g., fixating on the stimulus) reduce the level of stimulation by moving farther away or taking the dog out of the situation. Future sessions should be at greater distances, or in locations or with stimuli where success can be achieved. For example, if the dog is calm when unfamiliar people pass on a walk, but when strangers pass the house the dog barks, revert to practicing DS/CC with the dog on walks and work up more slowly to practicing around the house.
- Owners must always be vigilant for the approach of stimuli that might incite fear or aggression.

SURGICAL CONSIDERATIONS

- Castration reduced aggression by at least 50% toward unfamiliar dogs in < 20% of

AGGRESSION TO UNFAMILIAR PEOPLE AND UNFAMILIAR DOGS (CONTINUED)

dogs studied and toward human territorial intruders in < 10% of dogs studied. Castration reduced inter-male aggression in 62% of dogs. • Military working German shepherds spayed at 5–10 months of age were more reactive 4–5 months post-surgery to approach by an unfamiliar person walking with an unfamiliar dog than intact dogs.



MEDICATIONS

SUPPLEMENTS

- Consider for mild fear or as an adjunct to drug therapy.
- Supplements are not a substitute for and should only be used to facilitate behavior modification.

L-theanine (Anxitane®)

- 2.5–5 mg/kg q12h.
- Active ingredient in green tea purported to increase serotonin, dopamine and GABA.
- Side effects: none reported.

Alpha-casozepine (Zylkene®)

- 15 mg/kg PO q24h (canine). Discontinue if no effect after 10 days.
- Purported to increase GABA.
- Side effects: none reported.
- Alpha-casozepine also in Royal Canin Calm Canine.

DRUG(S)

- There are no medications licensed for treatment of canine aggression. Owners must be aware that the use of medications is off-label. Note in the patient's record that owners were informed of potential risks and side effects. A signed informed consent form is advisable. NEVER use medications without concurrent behavior modification. Before prescribing medication, be sure that owners understand the risks and liability in owning an aggressive dog, will follow safety procedures, and do not expect medications to insure safety. In fact, medication may not be appropriate in all situations (e.g., households with small children, or individuals that have disabilities).
- There is a strong placebo effect when using drugs for behavior therapy in dogs. Studies have not shown a robust effect of drug treatment on aggression.

Selective Serotonin Reuptake Inhibitors

- Fluoxetine 0.5–2 mg/kg PO q24h.
- Paroxetine 0.5–1 mg/kg PO q24h.
- Sertraline 1–3 mg/kg PO q24h.
- Side effects: sedation, irritability, GIT effects, increased aggression; anorexia is common and usually transient.

Tricyclic Antidepressants

- Clomipramine 1–3 mg/kg q12h (label-restricted for aggression).
- Side effects: sedation, GIT effects,

anticholinergic effects, cardiac conduction disturbances if predisposed, and increased aggression.

Alpha-2 agonists

- Clonidine 0.01–0.05 mg/kg PO PRN 1.5–2 hours before eliciting trigger, up to q12h.
- Side effects: transient hyperglycemia, hypotension, collapse, and bradycardia (responsive to atropine), and increased aggression.

Serotonin 2 α antagonist/reuptake inhibitors

- Trazodone 2–5 mg/kg PRN prior to eliciting trigger up to q8h. Titrate to 8–10 mg/kg if no adverse effects.
- Side effects: sedation, anorexia, ataxia, GIT effects, cardiac conduction disturbances, and increased aggression.

PRECAUTIONS

- Use caution as any psychotropic medication may disinhibit, resulting in an increase rather than decrease in aggression. • Do not combine SSRIs, SARI, TCAs, MAO inhibitors (e.g., amitraz, selegiline), opioids (e.g., tramadol) or other medications that increase serotonin—can result in potentially fatal serotonin syndrome.



FOLLOW-UP

PATIENT MONITORING

- Clients need ongoing assistance and should receive at least one follow-up call within the first 1–4 weeks after consultation. Provisions for further follow-up should be made. Ongoing communication improves client compliance.

PREVENTION/AVOIDANCE

- Treatment recommendations are life-long—aggression may recur with treatment lapses and continued exposure to fear- and aggression-producing stimuli. Owners must always be vigilant and in control of the dog's behavior. • Appropriate early socialization and habituation may help prevent fear-based behaviors later in life. Puppies that are not socialized during the first three months of life are more likely to be fearful, defensive, and possibly aggressive later in life. Socialization may include attending well-structured, positive reinforcement puppy classes starting during the sensitive period for socialization from 7–12 weeks (perhaps up to 14–16 weeks). One study found that vaccinated puppies that attended puppy socialization classes were at no increased risk of parvovirus.

POSSIBLE COMPLICATIONS

Human injuries; euthanasia or relinquishment of patient

EXPECTED COURSE AND PROGNOSIS

There is no cure. Prognosis is more favorable if aggression is motivated by fear, at a low intensity, and occurs only in a few predictable situations. Prognosis is highly dependent on owner compliance.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Other fear- or anxiety-based conditions (e.g., noise phobias, separation anxiety) Aggression to other stimuli

ZOONOTIC POTENTIAL

Human injury from bite wounds

PREGNANCY/FERTILITY/BREEDING

Do not breed dogs with extremely fearful behavior or fear/aggression.

SEE ALSO

- Aggression toward Familiar People—Dogs
- Aggression, Food and Resource Guarding—Dogs
- Aggression—Between Dogs in the Household
- Fear and Aggression in Veterinary Visits

ABBREVIATIONS

- CNS = central nervous system • DS/CC = desensitization and counter-conditioning
- GABA = gamma-aminobutyric acid • GIT = gastrointestinal tract • MAO = monoamine oxidase • MRI = magnetic resonance imaging • SSRI = selective serotonin reuptake inhibitor • SARI = Serotonin 2 α antagonist/reuptake inhibitor
- TCA = tricyclic antidepressant

Suggested Reading

Herron ME, Shofer SS, Reisner IR. Survey of the use and outcome of confrontational and non-confrontational training methods in client-owned dogs showing undesired behaviors. Appl Anim Behav Sci 2009, 177:47–54.

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AGGRESSION TOWARD CHILDREN—DOGS

A



BASICS

OVERVIEW

Children are the most frequent victims of reported dog bites and tend to be injured more severely than adults.

SIGNALMENT

Any breed, age, gender, and neuter status.

Breed

- Breed reports vary with demographics. Breed identification may be unreliable.
- Breeds most commonly presenting to a behavior referral service that had bitten a child include English springer spaniel, German shepherd, Labrador retriever, golden retriever, and American cocker spaniel.
- Most fatal attacks (uncommon) are attributed to rottweilers, pit bulls, and their mixes. • Larger breeds and mixed breeds may be more likely to inflict severe injury.
- Smaller breeds can also be dangerous.

Sex

- More frequent in males than females.
- Neutering will not significantly reduce the risk.

Age

- Any age, but more frequent in socially mature dogs (2+ years old). • Risk may increase in geriatric dogs because of pain, sensory impairment, or irritability.

CAUSES & RISK FACTORS

Clinical Categories/Motivation for Aggression

- Fear-related • Pain-related • Play-related
- Conflict-related • Predatory • Territorial
- Resource (food/toy/bed) guarding

Dog-Associated Risk Factors

- Disease and associated irritability. • Pain-related aggression and resource guarding are the most common reasons for bites to familiar children < 6 years old. Generalized anxiety.
- Fearful behavior. • Dog lying down, particularly under or on furniture. • Parent/littermate aggression.

Environmental/Social Risk Factors

- Younger children most likely bitten by the family pet or other familiar dogs. • Presence of infants (risk of predatory attacks).
- Presence of young children. • Presence of food, edible toys. • Punishment-based training. • Inadequate supervision by parents/caregivers. • History of growling, snapping, biting. • Hugging, kissing, bending over anxious, fearful, or conflict-aggressive dog.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

See "Clinical Categories/Motivations for Aggression"

CBC/BIOCHEMISTRY/URINALYSIS

Baseline profile to rule out medical contributing factors.

OTHER LABORATORY TESTS

- Anecdotal evidence (only) correlates canine hypothyroidism with increased aggression; however, no data-based evidence.
- Unnecessary supplementation with thyroid hormone may predispose to agitation or aggression.

DIAGNOSTIC PROCEDURES

Thorough physical examination. A detailed history of the bite event and the behavior of both dog and child to determine motivation.



TREATMENT

SAFETY WITH FAMILIAR DOGS

- Never leave infants or young children unsupervised with dogs. Securely separate infants from dogs when alone, if both asleep.
- If one adult is present, separate dog from young children. • If more than one adult is present, assign responsibility for one adult to dog, and one to child. • Do not allow child to approach or interact with dog when dog is lying down. • Do not allow child to remove any object from dog. • Do not allow child to hug, kiss, bend over, or lie down beside dog.
- Separate dog when eating or chewing valued items.

SAFETY WITH UNFAMILIAR DOGS

- Do not tether unsupervised. • Do not allow young children to interact with unfamiliar dogs. • Securely lock gates in yards. • Avoid underground electric fences, which do not prevent entry of children into yard.

BEHAVIOR MODIFICATION THROUGH LEARNING/TRAINING

- Redirect dog's attention: teach "look" or "touch" cues. • Establish secure, separate "safe haven" for dog. • Restrict fearful or reactive dog on lead and offer food at safe distance from children, to turn a negative situation into a positive one. • Do not rely on training alone; safe practices require prevention.



MEDICATIONS

DRUGS

Anxiolytic drug may be indicated for dogs with generalized or situational anxiety or fearful behavior.

Selective Serotonin Reuptake Inhibitors

- Fluoxetine 0.5–2.0 mg/kg q24 h
- Sertraline 0.5–3 mg/kg q24 h

Tricyclic Antidepressants

Clomipramine 1–3 mg/kg q12 h

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Psychotropic medication can increase agitation and anxiety or disinhibit aggression. Use with safety recommendations to prevent bites. • Avoid the following combinations:
 - SSRI + TCA ◦ SSRI or TCA + tramadol
 - SSRI or TCA + MAOI including amitraz
 - SSRI + NSAID (caution, due to increased risk of GI or other hemorrhage).



FOLLOW-UP

PREVENTION/AVOIDANCE

- Do not rely on training alone to eliminate aggression. • Preventive measures are most important in management of canine aggression to children. • Even well-trained, socialized dogs may bite.

POSSIBLE COMPLICATIONS

- Family may not acknowledge risks.
- Disease may aggravate aggression. • Family may not be compliant. • Psychotropic drug may be unrealistically relied upon or ineffective. • Young children may be impulsive and difficult to control.

EXPECTED COURSE AND PROGNOSIS

- Aggressive behavior can often be reduced and controlled. However, lifetime compliance is needed. • Prognosis is poor if social/physical environment cannot be controlled.
- In some cases it may be necessary to rehome or euthanize dog, while in others the dog's behavior may improve as the child grows older.



MISCELLANEOUS

ABBREVIATIONS

- GI = gastrointestinal • MAOI = monoamine oxidase inhibitor • NSAID = nonsteroidal anti-inflammatory drug
- SSRI = selective serotonin reuptake inhibitor • TCA = tricyclic antidepressant

Suggested Reading

Herron ME, Shofer FS, Reisner IR. Survey of the use and outcome of confrontational and non-confrontational training methods in client-owned dogs showing undesired behaviors. Appl Anim Behav Sci 2009, 117:47–54.

Reisner IR, Shofer FS, Nance ML. Behavioral assessment of child-directed canine aggression. Inj Prev 2007, 13:348–351.

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AGGRESSION TOWARD FAMILIAR PEOPLE—DOGS



BASICS

DEFINITION

Aggression, directed toward household members or people with an established relationship with the dog, often in situations involving access to resources. May be status-related/dominance, conflict, impulsive, competitive or possessive aggression.

PATOPHYSIOLOGY

These dogs may show anxiety or be impulsive and unpredictable. When the aggression is guarding of resources, or in response to fear eliciting stimuli (e.g., threats, punishment, possibly handling) might be normal.

SYSTEMS AFFECTED

Behavioral

GENETICS

Pedigree analyses have shown increased occurrence in related dogs. May be genetic factors associated with impulse dyscontrol in English springer spaniel and English cocker spaniel. May be more common in show than field lines.

INCIDENCE/PREVALENCE

20–44% of behavioral referral caseloads.

GEOGRAPHIC DISTRIBUTION

Regional breed differences exist.

SIGNALMENT

Species

Dog

Breed Predilections

Spaniel (English springer and cocker), terrier, but may be exhibited by any breed.

Mean Age and Range

Usually manifested by social maturity (12–36 months of age). May be seen in younger dogs.

Predominant Sex

Males (castrated and intact).

SIGNS

General Comments

Detailed history-taking is needed to make a diagnosis, assess risks, and devise a safe and realistic treatment plan. Mild signs of aggression (e.g., staring, growling, baring teeth) often precede bites. Details of early aggressive episodes are vital to establish the diagnosis and prognosis. Often anxiety or fear based but may be motivated by desire to control, e.g., personal space, resources.

Historical Findings

- Aggression (barking, growling, lip-lifting, snarling, snapping, lunging, biting) directed toward family members. Aggression may occur around resources such as resting areas, food, or toys, handling (e.g., petting and reaching toward), or favored possessions (including resting with one family member

when another approaches). Aggression may be seen in other contexts, e.g., denied access to items or activities, when resting, when confronted or punished, or during uncomfortable or fear-evoking interactions (e.g., ear cleaning, grooming, bathing).

History-taking should attempt to establish triggers and frequency/severity of aggressive episodes.

- Aggression may not be directed uniformly toward each household member.

- Confident/dominant body postures (stiffening, staring, standing straight up, ears forward, tail up, and/or approaching/direct contact with the person) may be associated with aggressive behavior, or the motivation may be fear (tensing, head down, crouching, backing away, ears back, tail tucked, looking away, lip licking). Owners may report a combination of confident and submissive postures representing uncertainty (conflict).
- Owners may describe dog as “moody” and may be able to predict when aggression is likely to occur. Early on the dog may show fear (e.g., eye aversion, tail tucked, avoidance) that may diminish and the dog may give less warning as it becomes more confident that aggression will be effective (negative reinforcement).
- Anxiety may be noted in pet-owner interactions and other situations.

Physical Examination Findings

- Usually unremarkable.
- Medical conditions, especially pain, may contribute to the expression of aggression.

CAUSES

- May be part of normal canine social behavioral repertoire, but its expression is influenced by environment, learning, and genetics.
- Display of aggression may be influenced by underlying medical conditions (especially pain), early experiences (learning that aggression is effective to control situations), and inconsistent or lack of clear rules and routines in the household and in human-pet interactions.

RISK FACTORS

Inconsistent or inappropriate physical punishment and inconsistent owner interactions.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Fear-based aggression
- Conflict aggression
- Anxiety conditions
- Disease conditions associated with aggression (e.g., painful conditions, endocrinopathies)

CBC/BIOCHEMISTRY/URINALYSIS

Usually unremarkable. Abnormalities may indicate an underlying or contributing medical condition.

OTHER LABORATORY TESTS

As indicated to rule out underlying diseases. Rule out hypothyroidism.

IMAGING

MRI if CNS disease is suspected; other imaging may be needed to rule out other medical conditions.



TREATMENT

ACTIVITY

Insure behavioral needs are being met.

DIET

Low-protein/tryptophan-supplemented diets may help reduce aggression.

CLIENT EDUCATION

General Comments

- Treatment is aimed at controlling the problem, not achieving a “cure.”
- Successful treatment, resulting in a decrease in aggressive incidents, depends on owner understanding of basic canine social behavior and communication, risks involved in living with an aggressive dog, and how to implement safety and management recommendations.
- Owners must be aware that the only certain way to prevent future injuries is euthanasia.
- Owners must be educated about the risks of using physical punishment and training techniques that rely on “dominating” their dogs. Improper and inappropriate use of physical punishment/dominance techniques such as alpha rolls, corrections with choke chains or prong collars, or even yelling “no” can lead to human injury, increased aggression and anxiety, and disruption of the human-animal bond.

Safety Recommendations

- If owners elect not to euthanize, they must be aware that their main responsibility is preventing human injury by diligently avoiding all situations that might evoke an aggressive response including situations that incite fear even if not aggression.
- Treatment must begin with prevention of exposure to all aggression-provoking stimuli prior to any behavior modification.
- Use patient history to identify each situation or trigger for owners to avoid. This may include not allowing on furniture or beds where aggression might arise, not giving valuable treats or toys (e.g., rawhides) except when confined away from family members, and limiting physical contact with the dog including petting in any place or situation where the dog might resist or bite. Instead provide the dog with opportunities (control) to avoid undesirable interactions (e.g., safe haven, crate). Reward the dog for entering the safe haven and for leaving (coming out).
- Do not physically punish or reprimand the dog.
- Introducing a head halter (e.g., Gentle Leader) with a lightweight 8- to 10-foot leash attached or a basket muzzle whenever in contact with people or in any situation where problems might arise, makes controlling potentially dangerous situations

(CONTINUED)

AGGRESSION TOWARD FAMILIAR PEOPLE—DOGS

A

easier and safer. • Use the long leash to safely remove the dog from situations that may elicit aggression; do not reach for the dog directly.

Behavioral Therapy

- Behavior modification—use non-confrontational methods and reward-based training to achieve desirable outcomes and teach the dog behaviors without experiencing fear or becoming aggressive. • Structured interactions (also known as learn to earn or say please by sitting) where the dog is consistently taught to sit for anything it values (before feeding, petting, play, going for a walk) gives the dog control of its resources by sitting calmly, provides structure and predictability in all interactions, teaches impulse control and trains the dog that good things happen by sitting calmly. Owners must ignore the dog until it sits or train “sit”, whenever soliciting attention. • Use positive reinforcement (e.g., food, toys, play, petting) for response substitution (or counter commanding) to teach behaviors that are incompatible with those that have resulted in aggression.

Desensitization and Counter-Conditioning

- Decreasing reactivity to situations that have resulted in aggression by making positive associations with each interaction. Do not begin until owner can insure success with reward-based training and sit for all interactions. • Teach the dog strategies to relax (sit, down, go to your bed) on verbal cue in neutral situations using food rewards.
- Expose the dog to a sufficiently reduced stimulus where no fearful or aggressive reaction is elicited (e.g., owner passing by resting dog at sufficient distance). • Reward calm, non-fearful/aggressive behavior (e.g., verbal praise, tossing favored treats).
- Gradually increase the level of stimulation, staying below the threshold that would result in fear and/or aggression. • Progress is slow (typically months) and careful monitoring is essential to understand and respect the dog’s limits. • Train on cue those behaviors needed to manage specific problems, e.g., go to your bed (for dogs that are protective of resting areas) or “drop it” (for resource guarding).

SURGICAL CONSIDERATIONS

- Castration reduced aggression by at least 50% toward family members in approximately 30% of dogs studied.
- Females that start to show dominance aggression at less than 6 months of age may be less aggressive if spaying delayed until mature.

**MEDICATIONS****DRUG(S)**

- There are no medications licensed for treatment of canine aggression. Owners must

be aware that the use of medications is off-label. Note in the patient’s record that owners were informed of potential risks and side effects. A signed informed consent form is advisable. NEVER use medications without concurrent behavior modification. Before prescribing medication, be sure that owners understand the risks and liability in owning an aggressive dog, will follow safety procedures, and do not expect medications to insure safety. In fact, medication may not be appropriate in all situations (e.g., households with small children or individuals with disabilities).

- There is a strong placebo effect when using drugs for behavior therapy in dogs. Studies have not shown a robust effect of drug treatment on aggression.

Selective Serotonin Reuptake Inhibitors

- Fluoxetine 0.5–2 mg/kg PO q24 h.
- Paroxetine 0.5–2 mg/kg PO q24 h.
- Sertraline 1–3 mg/kg PO q24 h.
- Side effects: sedation, irritability, GIT effects, increased aggression; anorexia is common and usually transient.

Tricyclic Antidepressants

- Clomipramine 1–3 mg/kg q12 h in dogs (label restriction for aggression)
- Side effects: sedation, GIT effects, anticholinergic effects, cardiac conduction disturbances if predisposed, and increased aggression.

CONTRAINdications

Use caution as any psychotropic medication may reduce fear-based inhibition resulting in an increase rather than decrease in aggression.

PRECAUTIONS

Any psychotropic medication may increase rather than decrease aggression.

Corticosteroids are contraindicated in food-aggressive dogs; polyphagia can lead to increased frequency/intensity of aggression.

POSSIBLE INTERACTIONS

Do not combine SSRIs, TCAs, MAO inhibitors (e.g., amitraz, selegiline), opioids (e.g., tramadol), and other medications that increase serotonin—can result in potentially fatal serotonin syndrome.

**FOLLOW-UP****PATIENT MONITORING**

Clients need ongoing assistance and should receive first follow-up call within the first 1–4 weeks after consultation. Provisions for further follow-up (by phone or in person) should then be made.

PREVENTION/AVOIDANCE

Treatment, including safety recommendations, are life-long—aggression

may recur if preventive strategies not maintained.

POSSIBLE COMPLICATIONS

Human injuries; euthanasia or relinquishment of patient.

EXPECTED COURSE AND PROGNOSIS

There is no cure. Prognosis is more favorable if aggression is at a low intensity and occurs in relatively few predictable situations. Prognosis is highly dependent on owner compliance.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Other forms of aggression, including interdog aggression, resource guarding, and aggression to unfamiliar people or dogs. Aggressive dogs often have underlying anxiety.

ZOONOTIC POTENTIAL

Human injury.

PREGNANCY/FERTILITY/BREEDING

Do not breed aggressive dogs.

SYNONYMS

- Competitive aggression • Conflict aggression • Dominance-related aggression
- Rage syndrome • Status-related aggression

ABBREVIATIONS

- CNS = central nervous system • GIT = gastrointestinal tract • MAO = monoamine oxidase • MRI = magnetic resonance imaging
- SSRI = selective serotonin reuptake inhibitor • TCA = tricyclic antidepressant

SEE ALSO

- Aggression Toward Unfamiliar People and Unfamiliar Dogs—Dogs • Aggression, Food and Resource Guarding—Dogs
- Aggression—Between Dogs in the Household

Suggested Reading

Herron ME, Shofer SS, Reisner IR. Survey of the use and outcome of confrontational and non-confrontational training methods in client-owned dogs showing undesired behaviors. Appl Anim Behav Sci 2009, 177:47–54.

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Consulting Editor Gary M. Landsberg

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**Client Education Handout
available online**

AGGRESSION TOWARD HUMANS—CATS



BASICS

DEFINITION

Human-directed aggression in cats

PATHOPHYSIOLOGY

The more common causes for human-directed aggression in cats include play, fear/pain-related, redirected, maternal, and petting intolerance. Context is going to contribute greatly when making the correct diagnosis. For example, play aggression is likely to be seen in a young, solitary cat, while pain-related/fear aggression is a common behavior seen in the clinic setting.

SYSTEMS AFFECTED

- Behavioral
- Gastrointestinal—decreased appetite if fear and/or pain-related
- Hemic/Lymphatic/Immune—chronic stress effects on immune function
- Ophthalmic—dilated pupils in response to autonomic nervous system stimulation
- Skin/Exocrine—may show displacement behaviors such as overgrooming

GENETICS

There is no known genetic basis for human-directed aggression in cats.

INCIDENCE/PREVALENCE

Aggression is second only to inappropriate elimination for feline cases seen by veterinary behavior specialists.

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Cats of any age, gender/ neuter status, breed can be affected. Play-motivated aggression more likely in juvenile, solitary cat.

SIGNS

- Play-motivated: cat approaches its “victim,” crouches in wait, stalks and chases; tail is twitching and ears are forward. Typically will attack moving target.
- Fear/Pain-related: ears back, body and tail lowered, piloerection, pupils dilated; may hiss and growl. Avoidance of person(s) who elicit the aggression. Attacks possible if approached and/or cornered. Extreme cases: expression of anal glands, urination, and/or defecation.
- Hiding behavior.
- Redirected: cat is highly aroused by stimulus and seeks out less appropriate target.
- Aggression can be very severe given the cat's level of arousal.
- Maternal: usually predictable and self-limiting. Queen will act to protect her kittens.
- Petting intolerance: cat signals its “displeasure” by twitching its tail and skin when being petted in an undesired location and/or for too long. Ears are usually back;

mydriasis; may hiss and growl before turning to bite person.

CAUSES & RISK FACTORS

- Play-motivated: lacking in opportunities for normal play—no other cats, insufficient and/or inappropriate toys; history of owner using hands/feet to play with kitten and/or playing roughly with the kitten.
- Fear: poor socialization with humans and/or feral living, an aversive event associated with a person, or people in general.
- Pain-related: obvious medical/physical condition.
- Redirected: occurs during interference in, or interruption of, situations that have caused the cat to become aggressively aroused—such as a cat fight (between familiar household cats), the presence of a cat outside or noise.
- Maternal: recent birth of litter.
- Petting intolerance: exact etiology unknown. Cats tend to groom each other on head/neck so human grooming of cat in other locations may contribute to aggressive reaction.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

See causes above

CBC/BIOCHEMISTRY/URINALYSIS

Rule out contributing medical conditions based on presentation.

OTHER LABORATORY TESTS

- Senior cats: a complete thyroid panel.
- Urinalysis if inappropriate elimination and/or urine marking is presented as part of the aggression.

IMAGING

Based on clinical examination and/or suspected pain component

DIAGNOSTIC PROCEDURES

Thorough behavioral history including a description of the cat's postures during aggression and injuries inflicted, context, presence of outside cats, early historical information, litter box use, food consumption, and hiding behaviors.

PATHOLOGIC FINDINGS

N/A



TREATMENT

APPROPRIATE HEALTH CARE

Applicable only if health/medical issue diagnosed.

NURSING CARE

Applicable only if health/medical issue diagnosed.

ACTIVITY

- Play-motivated: cat should be provided with increased opportunity for appropriate play—either in the form of toys, human interaction, or additional housemate.
- Redirected: cat should be denied access to windows where outside cats can be seen.

DIET

- Hill's Science Diet c/d Multicare Feline Urinary Stress
- Royal Canin Feline Calm
- Either may be beneficial in helping to decrease anxiety.

CLIENT EDUCATION

- Play-motivated: normal play behavior and the importance for opportunities for appropriate play.
- Fear: avoidance of fear-inducing situations—ongoing exposure may worsen signs, cause severe stress, and compromise animal welfare.
- Redirected: importance in addressing primary stimuli—such as outside cats.
- Maternal: normal maternal and kitten-protective behavior—same as for fear-motivated aggression.
- Petting intolerance: normal feline grooming patterns; observation of cat's warnings so that behavior does not escalate.

Behavior Modification Exercises

Desensitization and Counter-Conditioning (DS & CC)

- Desensitization: exposing cat to the fear-inducing stimulus (scary person) at a low level so the cat does NOT react fearfully or aggressively. Over time, the intensity of the stimulus is increased (i.e., the distance between the cat and stimulus is decreased) without causing fearful responses.
- Counter-conditioning: rewarding the cat with a special treat, toy, grooming, petting, for relaxation.

Classical Conditioning (CC)

Classical conditioning: pairing the stimulus (person threatening to the cat) with a tasty treat, toy, petting. Example: scary person = tuna fish.



MEDICATIONS

The short-term use of medication may be necessary to decrease overall levels of anxiety and reactivity in more severe cases.

DRUG(S) OF CHOICE

Azapirones

Buspirone 0.5–1.0 mg/kg PO q12h. Most useful for fearful and withdrawn cats. Decreases anxiety and may increase “self-confidence.” Anecdotal reports of “increase in affection”; therefore might be useful in severe cases of petting intolerance. Response noted in 1–2 weeks.

(CONTINUED)

AGGRESSION TOWARD HUMANS—CATS

A

Selective Serotonin Reuptake Inhibitors (SSRIs)

- Fluoxetine, paroxetine, sertraline 0.5–1.5 mg/kg PO q24h.
- SSRIs must be given daily. May take 4–8 weeks to reach peak effects.

Tricyclic Antidepressants (TCAs)

- Amitriptyline 0.5–2.0 mg/kg PO q12–24h.
- Clomipramine 0.25–1.3 mg/kg PO q24h.
- TCAs must be given daily. May take 4–8 weeks to reach peak effects.

Benzodiazepines

- Alprazolam 0.125–0.25 mg/cat PO q8–24h.
- Diazepam 0.1–1.0 mg/kg PO q12–24h (rarely used due to potential hepatopathies).
- Can be given “as needed” for specific encounters with people inducing the fear response and during desensitization, counter-conditioning and classical conditioning sessions.
- Can be used in conjunction with azapirones, SSRIs, and TCAs.

**CONTRAINDICATIONS/
PRECAUTIONS/POSSIBLE
INTERACTIONS**

- None of the drugs listed are approved for use in cats.
- All of the medications are to be administered orally, as they have not been shown to be effective through transdermal dosing.
- Azapirones: side effects are uncommon but occasional excitement is noted. Should not be given in combination with an MAOI. Avoid use in the aggressor cat; may increase any “bully” behavior.
- Neither SSRIs nor TCAs should be given with each other, nor in combination with MAOIs.
- SSRIs: side effects include mild sedation and decreased appetite, constipation, and urinary retention. Competitive inhibition of cytochrome P450 liver enzymes; when administered concurrently with medication utilizing the P450 enzymes, elevated plasma levels of the medications may increase, causing toxic levels.
- TCAs: side effects include sedation, constipation, diarrhea, urinary retention, appetite changes, ataxia, decreased tear production, mydriasis, cardiac arrhythmias, tachycardia, and changes in blood pressure.
- Benzodiazepines: side effects include sedation, ataxia, muscle relaxation, increased appetite, paradoxical excitation, and increased friendliness. Idiopathic hepatic necrosis has been reported in cats.

- Specific recommendations for the use of diazepam: baseline physical exam, CBC, and blood chemistries to confirm good health. Repeat the blood chemistries at 3–5 days. Elevated ALT or AST, discontinue the medication.

ALTERNATIVE DRUGS**Pheromones**

- Used alone or concurrently with drugs
- Feliway—available in diffuser, spray and wipes—facial pheromone
- NurtureCALM 24/7 collar—maternal pheromone

Supplements

- Used alone or concurrently with drugs
- Anxitane—contains L-theanine, a calming compound found in green tea
- Zylkene—contains alpha-casozepine, a GABA agonist

**FOLLOW-UP****PATIENT MONITORING**

Weekly follow-up is recommended in the early stages of treatment, especially when on medication(s). Monthly follow-up once stable. For cats on medication, follow-up blood testing recommended every 6–12 months.

PREVENTION/AVOIDANCE

- Play-motivated: provide opportunities for appropriate play.
- Fear: avoidance of the fear-inciting stimuli if at all possible. Early socialization to people and events may help prevent some occurrences of fear-related responses to people.
- Pain: treat underlying condition(s).
- Redirected: address possible arousing stimuli—indoors and outdoors.
- Maternal: as for fear.
- Petting intolerance: limit amount of time petting the cat; desensitization and counter-conditioning to increase petting time.

POSSIBLE COMPLICATIONS

Potential human injury in all of the above cases, especially if the cat is approached or cornered and/or when highly aroused.

EXPECTED COURSE AND PROGNOSIS

Progress occurs slowly. Relearning is a process and each case is individual. If medications are indicated, begin at a low dose and work up as necessary. To discontinue medication, wait

until the new behavior is stable (8–12 weeks) and wean off slowly, usually over weeks. If aggressive behavior recurs, return to the last dose that controlled the anxiety/reactivity and continue treatment.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

Play-motivated: typically seen in young, solitary cat in household.

ZOONOTIC POTENTIAL

People injured during an aggressive attack should seek prompt medical attention. Infection by *Bartonella henselae* can result from a cat scratch or bite.

PREGNANCY/FERTILITY/BREEDING

Avoid medications in breeding/nursing cats.

SYNONYMS

N/A

SEE ALSO

- Aggression Overview—Cats
- Fears, Phobias, and Anxieties—Cats

ABBREVIATIONS

- CC = classical conditioning
- DS & CC = desensitization and counter-conditioning
- MAOI = monoamine oxidase inhibitor
- SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant

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AGGRESSION, FOOD AND RESOURCE GUARDING—DOGS



BASICS

OVERVIEW

- Aggressively guarding food (e.g., in food bowl, rawhides, bones, stolen/found items) or objects (e.g., toys, stolen objects).
- Usually within the range of normal behavior; genetics, learning or early experience may contribute to excessive expression of aggression.

SYSTEMS AFFECTED

Behavioral

SIGNALMENT

No breed or sex predilections.

SIGNS

Aggression (barking, growling, lip-lifting, snarling, snapping, lunging, biting) toward people or other animals in the presence of valued food items or objects.

CAUSES & RISK FACTORS

- May be part of normal canine behavior. Strongly influenced by previous experiences of successfully defending food, or objects through aggression and by resource availability/novelty.
- Underlying medical conditions and medications, especially those causing polyphagia, or calorie-restricted diets may increase level of food aggression.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Fear aggression
- Social status/dominance or conflict aggression

CBC/BIOCHEMISTRY/URINALYSIS

Usually unremarkable. Abnormalities suggest an underlying or contributing medical condition.

OTHER LABORATORY TESTS

Usually unremarkable.

IMAGING

MRI if CNS disease suspected. Other imaging as needed to rule out underlying medical conditions.

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

CLIENT EDUCATION

- Treatment is aimed at control, not achieving a "cure." Successful treatment resulting in a decrease in aggressive incidents, depends on owner understanding of basic canine social behavior, risks involved in living with an aggressive dog, and ability to follow safety and management recommendations.
- If safety cannot be insured, pet should be removed from the home.

Safety Recommendations

- The owner's main focus must be on preventing injury by diligently avoiding situations that may evoke an aggressive reaction.
- Owners may be more compliant with avoidance recommendations if they understand both the risk and the potential liability if the dog causes injury.
- Successful treatment is more likely if a period of preventing exposure to aggression-provoking stimuli is instituted prior to behavior modification.
- Always confine the dog away from potential victims or the dog must be under the direct physical control of a responsible adult whenever an aggression-provoking situation could arise.
- Give food and any other objects that the dog might guard in a confinement/safe haven location away from people and other animals; prevent access to items that may evoke aggression.
- Teach the dog to be comfortable wearing a head halter (e.g., Gentle Leader) and basket muzzle for safer control of potentially dangerous situations.
- Punishment/dominance-based training techniques are contraindicated as they cause further fear, agitation, defensive aggression, and further learning (fear of approach and negative reinforcement if successful).

Behavior Modification

- Command-response-reward program (say please by sitting): to increase owners' control of resources, make the dog more responsive to the owner, and create structure and predictability in the dog's life.

- Use positive reinforcement (e.g., food, toys, play) to teach behaviors that are incompatible to those that lead to aggression including a calm sit and watch before giving any food, chews or toys, and "drop it" to release toys for valuable rewards.
- Prevent access to items that might be stolen or guarded by supervising with leash if necessary, dog proofing or confinement training.
- "Booby trap" items by applying an aversive substance such as hot sauce.
- Systematic desensitization and counter-conditioning to specific aggression-provoking stimuli if safety and owner compliance can be insured.
- Find the threshold (distance, location) at which the dog shows no anxiety or aggression when in possession of food or chews and make positive associations by tossing small food treats each time the owner walks by—the goal is for the dog to associate the owner's presence with positive outcomes. If successful, training can very gradually proceed to closer proximities—level of improvement will be limited by safety and the dog's motivation to retain the resource.



MEDICATIONS

DRUG(S)

Medications are generally not indicated in the treatment of resource guarding.



FOLLOW-UP

PATIENT MONITORING

Clients usually need ongoing assistance with at least one follow-up call within the first 1–3 weeks after the consultation. Provisions for further follow-up should be determined at that time.

PREVENTION/AVOIDANCE

Management recommendations (avoiding triggers) are life-long..

POSSIBLE COMPLICATIONS

Human injuries; euthanasia or relinquishment of patient.

(CONTINUED)

AGGRESSION, FOOD AND RESOURCE GUARDING—DOGS

A

EXPECTED COURSE AND PROGNOSIS

There is no cure. Prognosis for improvement is more favorable if aggression is at a low intensity, occurs in only a few predictable situations, and can be effectively and practically prevented.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Fear and dominance/conflict aggression

ZOONOTIC POTENTIAL

Human injury and bite wounds

PREGNANCY/FERTILITY/BREEDING

Do not breed dogs with extreme aggression.

SEE ALSO

- Aggression Toward Unfamiliar People and Unfamiliar Dogs—Dogs
- Aggression Toward Familiar People—Dogs
- Aggression Between Dogs in the Household—Dogs

ABBREVIATIONS

- CNS = central nervous system
- MRI = magnetic resonance imaging

Suggested Reading

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Author Meredith E. Stepita

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AGGRESSION, INTERCAT AGGRESSION



BASICS

DEFINITION

Intercat aggression—offensive or defensive aggression between cats consisting of staring, displacing, vocalizing (growling, yowling, shrieking), spitting, hissing, swatting, lunging, chasing/stalking, and/or biting other cats.

PATHOPHYSIOLOGY

- May be normal behavior or abnormal.
- May be caused by underlying medical disease (e.g., CNS) or the indirect result of concurrent medical disease lowering the threshold for irritable responses (e.g., pain, hyperthyroid). • May be multiple motivations including predatory/play, disputes over territory, sexual, fear, anxiety, and redirected.

SYSTEMS AFFECTED

- Behavioral. • Skin/Exocrine—secondary to traumatic injury. • Immune—chronic stress may alter the immune response. • Secondary infection (cat bite abscesses) are not uncommon. • Nervous.

GENETICS

No specific genetic basis, although some evidence to suggest that friendliness is mostly genetic and related to paternal effects.

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Breed Predilections

None

Mean Age and Range

- Can occur at any age when due to changes in social environment (e.g., addition of a new cat, return of a cat from the veterinarian) or redirected. • Previously stable cat relationships can deteriorate as cats reach social maturity (2–4 years of age).

Predominant Sex

- Intact males more likely to initiate intercat aggression (related to territory, and/or proximity to females). • Females will defend their young from unfamiliar individuals.
- Male kittens are more likely to initiate intercat aggression related to the predatory components of play.

SIGNS

Historical Findings

- May arise spontaneously and vary in frequency and intensity. • Owners most likely to seek behavioral intervention if there are physical injuries, the welfare of the aggressor and /or victim is compromised, or fighting becomes sufficiently distressing. • Human intervention in an attempt to interrupt fighting may result in human-directed aggression/injury.

Aggressor (usually offensive)

- Covert signs: staring, displacing other cats, stiff body language/movements while approaching the other cat. • Overt signs: Growling, yowling, spitting, hissing, swatting, lunging, chasing/stalking, and/or biting other cats, dilated pupils, may be accompanied by body language of fear (e.g., the classic Halloween cat stance—piloerection, back arched, tail up) or more offensive body language (stiff muscles, tail head elevated but rest of tail down, back straight or slightly slanted toward the head, ears forward or to the side), excessive facial marking, and perhaps urine marking.

Victim (usually defensive)

- Covert: avoidance of aggressor, hiding, change in grooming and eating habits, hypervigilance, dilated pupils. • Overt: hissing, swatting, running, vocalizing (including growling), Halloween cat stance, may escalate to defensive attack if cornered.

Elimination Outside of the Litter Box

- Aggressor may block access to the litter box area, forcing victims to choose alternative elimination locations; secondary substrate and/or location preferences and aversions can develop. • Both victims and aggressors may urine mark. • Extremely fearful cats may urinate or defecate in midst of aggressive events.

Physical Examination Findings

- None except injury from fights or if underlying medical issues. • Stress may affect eating and self-grooming (increased or decreased).

CAUSES

- Lack of appropriate socialization to other cats prior to 7 weeks of age. • May be a component of normal social behavior. • Social and environmental instability such as the addition of a new cat, loss of a resident cat, odor stimuli (return of a cat from the veterinarian or giving one cat a bath), aging or illness of one or both cats, cats reaching social maturity. • Household change, e.g., moving, changing furniture or resting areas.
- Genetically unrelated cats and cats that have recently moved in together are more likely to show aggressive behaviors toward each other.
- Resident cats commonly need prolonged exposure to new cats before accepting them into group. • Resource limitation (not enough vertical and/or horizontal space, lack of appropriate hiding areas, and limited food, water, and litter boxes, etc.) in multi-cat households. • Exposure to arousing stimuli (cats in the yard, visitors, noises, scents, etc.) can cause redirected aggression after which aggression might persist. • Medical problems including CNS disorders, hyperthyroidism, or any disorder that causes pain and/or increased irritability.

RISK FACTORS

- Singleton and/or bottle-raised kittens.
- Lack of social exposure and experience with conspecifics during the socialization period (2–7 weeks) and beyond. • Male intact cats in multi-cat households. • Postpartum females with kittens in multi-cat households.
- Separating and returning housemate (e.g., following veterinary visit, groomer).
- Changes in social group such as the addition of a “new” cat to a home of resident cats. • Scratching and biting during the first introduction risks future intercat aggression.
- Access to the outdoors and/or intrusion of unfamiliar cats onto the territory. • Crowding or lack of adequate social space and access to resources (food, water, litter boxes, and resting stations).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Behavioral Differentials

- Fear-related aggression—cat may hiss, spit, arch the back, display piloerection and attempt to flee unless escape is thwarted; pupil dilation will accompany a fear response.
- Status-related aggression—may occur with change or instability of social hierarchy and the control of access to resources; it is undecided if cats have dominance hierarchies or if conflict is better explained by territorial defense. • Territorial aggression—in response to threat to the territory; boundaries are often delineated by marking with urine, feces, or scent glands. • Redirected aggression—exposure to agitating stimuli (cats in the yard, visitors, noises, scents, etc.) with aggression directed toward a target other than the agitating stimuli. • Failure of recognition—aggression between feline housemates after returning from separation (e.g., veterinary visit, grooming); most likely due to change in odor and visual cues of victim. • Maternal aggression—aggression during the periparturient period; females guard kittens and nesting sites from unfamiliar individuals.
- Intermale aggression—between males in response to territorial disputes, hierarchical status, or mates; aggression may be more pronounced at social maturity. • Sexual aggression—male typical behavior of chasing, pouncing, biting on the nape of the neck, and mounting with or without intromission.
- Predatory/play-related aggression—predatory components of play directed toward another cat; the recipient is often an older cat that is not interested in playing.

Medical Differentials

- Any illness causing malaise, pain, or increased irritability • Endocrine, e.g., hyperthyroidism • Neurologic: space-occupying lesions, e.g., meningioma, lymphoma, encephalitis, seizures, feline

(CONTINUED)

AGGRESSION, INTERCAT AGGRESSION

A

ischemic encephalopathy, trauma, sensory or cognitive decline • Infectious: rabies, toxoplasmosis, aberrant parasitic migrations (e.g., cuterebriasis), FIV, FeLV • Iatrogenic: medications that increase irritability or disinhibit aggression (e.g., mirtazapine, benzodiazepines, buspirone) • Toxins: lead, illicit substances

CBC/BIOCHEMISTRY/URINALYSIS

Baseline CBC, biochemistry, urine to rule out medical causes and as a baseline if drug therapy indicated.

OTHER LABORATORY TESTS

- FeLV/FIV • Cats > 6 years should have total T₄ measured

IMAGING

As indicated based on history and physical signs

DIAGNOSTIC PROCEDURES

- Obtain a detailed behavioral and medical history of the patients. • Identify if there is a clear aggressor and/or victim and if aggression is overt or covert. • If multiple cats determine which cats spend time together, mutually groom each other, and which cats physically avoid each other. • Identify the preferred core areas of each cat for feeding, play, and resting and locations of any house soiling or marking.
- Identify: the number, location, types of litter boxes and their management. • Media in the form of video, photographs, and/or drawn floor plans can provide spatial details and information regarding body language during social interactions. • Note any other changes in demeanor, routine, eating, and grooming.

PATHOLOGIC FINDINGS

None unless concurrent medical diseases

**TREATMENT****APPROPRIATE HEALTH CARE**

- Treat as outpatients with behavior and environmental modification (\pm medication)
- Current on routine vaccinations, including rabies

NURSING CARE

Supportive care if any injuries from fighting.

ACTIVITY

May need to be restricted if confinement required to prevent the perpetuation of aggression and negative emotional responses. Provide sufficient alternate outlets for each cat during confinement area and during release.

DIET

None (except possible therapeutic diet trial discussed below)

CLIENT EDUCATION

For chronic, severe cases or for aggression that does not respond to treatment, may require permanent separation either by rehoming one of the cats or by splitting up the residence.

For Cases that have a Low Frequency of Intense, Injurious Aggressive Outbursts

- Separate the cats when they cannot be supervised (create "safe zones"). • Either keep them separate in the same areas each day in an effort to form separate core territories for each cat, or "time share" the space between cats.
- Confine the newly introduced cat or the aggressor to the smaller, less familiar area.
- For multiple cats, separate by stability of relationship between cats. Any despotic/bully cats should be confined alone. • Consider "artificial allomarking" to form a communal scent between the cats that are fighting; a towel (facecloth) may be rubbed (cephalocaudally) to obtain the scent of one cat and then rubbed onto the other cat and vice versa. • Towels should be left in the environment to allow for habituation to each other's scent especially if the cats are kept separated. • Reward cats with food, play, and/or attention for being in the same room together without having aggressive events. Cats should stay at a distance that allows for calm participation. • Engage cats in daily sessions of pleasurable activities (e.g., play, training, eating delectable food treats) at distances that do not incite aggression. Gradually move the fun sessions closer to each other, making sure to stay at a distance that does not trigger overt/covert aggression.
- Teach the cats a "come and/or go to place" cue using positive reinforcement at times, in situations, and with sufficient rewards that the cats are most able to learn. • Interrupt or redirect the cats by cueing to come or go to its place, or by luring one or both cats to their safe zones with food and treats, wand toys, tossed toys, or laser pointers before aggression starts or as initial signs are seen (e.g., staring, tail twitching, pupil dilation). • Aversives and/or punishers can increase aggressive behavior and increase negative associations with other cats, so must be avoided or used cautiously. • The goal of management and safety is to prevent aggressive events. In an emergency, use of a laundry basket or blanket placed between or over the cats, can stop aggression, and direct the cat to its safe area until calm, but should not be considered as a treatment. • Bell the aggressor (using a quick release or safety collar) so both the owners and victim can quickly identify his/her location.
- Increase the number of resources and locations (e.g., food, water, scratching, perching, bedding, play and feeding toys) throughout the residence including each cat's core area. The efficacy of multimodal environmental enrichment should not be underestimated. • Increase litter boxes to the number of cats plus one divided among multiple locations so that one cat cannot keep another from accessing the boxes; locations with more than one exit/entry are ideal.
- Increase the number of hiding places and resting areas; especially concentrate on

increasing vertical space (e.g., resting areas on shelves, window sills). • No new cats should be added to the house.

For Cases where the Cats Cannot be in the Same Room without Immediately Becoming Agitated

- Separate cats completely when unsupervised. • Meet each cat's needs for play, litter boxes, food, water, perching, resting, and attention. • A large wire dog kennel or vertical orientated wire cat cage (with shelving) may be better tolerated than smaller cat kennels and can be used for controlled exposure.
- Cats may be taught to tolerate harnesses and leashes so that they can be used during training and controlled reintroduction. This is especially valuable for the aggressor. • Set up desensitization and counter-conditioning sessions daily; initially utilize physical and visual barriers. • Introduce the cats (in their kennels or on leash and harness) at a distance from each other that prevents overt/covert aggression. Feed the cats or engage in play for classical counterconditioning. • Over many sessions gradually reduce the distance between the cats, being careful to stay far enough apart during each session that no overt or covert behavioral signs of aggression and/or fear are seen. Start and end all sessions on a successful note. • Teach the cats a "come and/or go to place" cue using operant counterconditioning and positive reinforcement. Practice these cues several times daily so each cat learns to respond reliably. Behavioral cues are best taught when animals are not stressed. • When ready to allow the cats more freedom with each other, follow the instructions for less severe interact aggression (above).

SURGICAL CONSIDERATIONS

Neutering intact males is approximately 90% effective in reducing roaming, intercat aggression, and urine spraying.

Neutering/spaying is effective in reducing mounting/sexual behavior.

**MEDICATIONS****DRUG(S) OF CHOICE**

All medications are extra-label, insure that the client is informed, and review target desirable outcomes and potential adverse effects.

For the Aggressor and/or Victim**Selective Serotonin Reuptake Inhibitors (SSRI)**

- Fluoxetine or paroxetine 0.5–1 mg/kg PO q24 h.
- Drugs of choice for aggression, anxiety, and/or urine marking, may decrease impulsivity.
- Side effects may include gastrointestinal upset, decreased appetite, sedation, urinary

retention (paroxetine), and increased agitation/irritability.

Tricyclic Antidepressant (TCA)

- Clomipramine 0.3–0.5 mg/kg PO q24 h: serotonin selective tricyclic: for anxiety and aggression

• Side effects include gastrointestinal upset, sedation, urinary retention, constipation, and lowered seizure threshold. Do not use in patients with arrhythmias or cardiomyopathies.

Pheromones

Feliway and Feliway Multicat (CEVA) and Felifriend (CEVA, presently available in Europe) are feline facial pheromones that may be helpful in cases of intercat aggression when used with a multimodal plan.

For the Victim

Azapirone

Buspirone 0.5–1 mg/kg PO q8–24 h (feline dose): reserved for victims to increase social confidence.

- Side effects rare; may include decreased sociability and increased agitation/irritability. May increase intercat aggression as victim may be more confident and fight back."

Benzodiazepines

- Lorazepam 0.125–0.25 mg/cat PO up to q12–24 h or oxazepam 0.2–0.5 mg/kg PO q12–24 h for anxious or fearfully aggressive cats and as an appetite stimulant helping to facilitate classical counter conditioning. May be used as needed with peak effects seen within 1 hour.
- Side effects may include increased appetite, ataxia, inhibited learning, and disinhibition of aggression.
- Note: controlled substance; dependence can develop; Medication should be gradually weaned if used consistently for longer than 2 weeks.

CONTRAINDICATIONS

- Benzodiazepines should be used cautiously or avoided in cats with hepatopathies.
- Paroxetine and TCAs may produce anticholinergic side effects. Fluoxetine also occasionally reported to cause urine retention.
- SSRIs and TCAs should be used with caution in patients with histories of cardiac abnormalities, seizures, and liver disease.

PRECAUTIONS

- Any behavioral drug has the potential to produce paradoxical reactions, including fear, anxiety, hyperexcitability and/or aggression.
- Medications that alter serotonin levels have the potential to produce serotonin syndrome.

POSSIBLE INTERACTIONS

- Avoid concurrent use of SSRIs and TCAs or MAO inhibitors such as selegiline and use

cautiously or avoid with buspirone, tramadol, and tryptophan due to possible serotonin syndrome. • Caution with concurrent medications considered substrates of P450.

ALTERNATIVE DRUGS

- Amitriptyline (TCA) 0.5–1 mg/kg PO q12–24 h: for anxious cats especially if comorbid recurrent FIC/FLUTD; not selective for serotonin reuptake inhibition and likely less effective for the aggressor. • Dietary supplementation with alpha-casozepine (Zylkene: Veotquinol), ROYAL CANIN Veterinary Diet CALM (contains alpha-casozepine, L-tryptophan, and nicotinamide) or Hill's Prescription Diet Multicare Feline Urinary Stress (contains L-tryptophan and milk protein hydrolysate).



FOLLOW-UP

PATIENT MONITORING

- Clinicians should monitor patients 2 weeks after treatment initiation and monthly for the first few months by phone or email; a follow-up visit should be scheduled 4–8 weeks into treatment if drugs dispensed to assess response and adjust dose if necessary.
- Benzodiazepines may rarely cause cases of fatal hepatopathies; patients should be rechecked immediately if any adverse events, including anorexia. • Medication should be used for at least 4–6 weeks after resolution of signs, then gradually weaned by reducing the dosage no faster than 25% per day on a weekly basis. • Some patients require long-term medication; recheck laboratory work every 6 months to 1 year depending on health and age..

PREVENTION/AVOIDANCE

- Proper socialization 2–7 weeks and ongoing. Gradual introduction more closely resembles the natural process through which new cats enter an existing group at the periphery and may be accepted over time. Intercat aggression may be more common when unfamiliar cats are suddenly placed together. A negative initial encounter is often associated with future intercat aggression. Related and familiar cats are less likely to have intense intercat aggression. In stable multi-cat households, avoid adding additional cats.

POSSIBLE COMPLICATIONS

Abrupt withdrawal of behavioral medications may result in aggression and rebound anxiety.

EXPECTED COURSE AND PROGNOSIS

- The prognosis for most cases is fair; it is complicated by prolonged duration, high intensity, underlying medical conditions, and

incomplete owner compliance. In one study 62% (30/48) were considered cured and 37% (17/48) not cured (cat given away, euthanized or permanently separated). • Recent and mild (low-intensity, low-frequency) cases may have better long-term outcomes.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Urine marking/spraying • House soiling
- Excessive grooming • Fearful/anxiety-related behavior • Human-directed or interspecies aggression

AGE-RELATED FACTORS

Predatory/Play-related aggression more common in young active and playful cats housed indoors with more sedentary or aged individuals.

ZOONOTIC POTENTIAL

Humans intervening while cats are fighting may be injured and contract infections through cat bites and/or scratches.

PREGNANCY/FERTILITY/BREEDING

Most behavioral medications are contraindicated in breeding animals.

SYNONYM

Feline intraspecies aggression

ABBREVIATIONS

- FeLV = feline leukemia virus
- FIC/FLUTD = feline idiopathic cystitis/feline lower urinary tract disease
- FIV = feline immunodeficiency virus
- MAOI = monoamine oxidase inhibitor
- SSRI = selective serotonin reuptake inhibitor • T₄ = thyroxine • TCA = tricyclic antidepressant

SEE ALSO

- Aggression, Overview—Cats • Pediatric Behavior Problems—Cats

INTERNET RESOURCES

<http://indoorpet.osu.edu/cats/>

Suggested Reading

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BASICS

DEFINITION

- Aggression is a behavioral strategy used to manage aversive situations.
- May be normal and appropriate in certain contexts.
- May be abnormal with serious deleterious effects on the cat's physical and emotional well-being.
- Aggressivity: describes both mood and temperament traits relating to the propensity to show aggression when environmental circumstances dictate it might be used.

OVERVIEW OF TYPES

Play Aggression (Toward People)

- Typically refers to a cat who scratches and bites the owners during play.
- Not true aggression but overzealous play without proper impulse control due to lack of training or proper intraspecific social feedback.
- The cat's intent is not to harm the person.
- Behavior encouraged and rewarded by owners through rough play with a kitten; when larger and stronger, becomes perceived as aggression rather than overzealous play.

Predatory Aggression (Toward People or Other Animals)

- Cats have an innate drive to "hunt" or show predation behavior, which includes stalk, hide, and pounce.
- Predation is not a direct function of hunger.
- Typically stimulated by fast movements and can progress to the cat hiding and waiting for an animal or person to walk by.
- Play is a common way for young cats to perfect predation skills; play aggression and predatory aggression may overlap.

Redirected Aggression (Toward People or Other Animals)

- Cats who see, hear, or smell a trigger and direct aggressive behavior toward the closest bystander.
- In some cases, one person or animal in the home becomes the designated victim, and the cat may bypass a nearby individual and look for the preferred victim.
- Some cats may stay aroused for 24–72 hours after a triggered event.
- Common triggers inciting redirected aggression are seeing another cat or wildlife outside or loud noises.

Fear/Defensive Aggression (Toward People or Other Animals)

- The cat will show body postures indicative of fear/anxiety and may use aggression as a strategy to manage an aversive situation.
- Typical behaviors shown include a combination of any of the following: hissing, spitting, piloerection, arched back, turning away, running away, cowering, rolling on its back and pawing (defensive position, not submissive position) if cornered.

Territorial Aggression (Toward People or Other Animals)

- Some cats, particularly male cats, show territorial behaviors in domestic home settings due to size and the presence of more resources (e.g., people, food, resting areas, feeding areas, elimination sites, etc.) to defend in a smaller area.
- Territorial behaviors include marking with urine, feces, or bunting (the rubbing of the cheeks on surfaces to deposit pheromones) and scratching (also deposits pheromones and leaves visual marker) and may be associated with aggression.
- In severe cases, the aggressor may seek out the other individuals and attack.
- Body posture with territorial aggression is assertive and confident.

Pain Aggression (Toward People and Animals)

Cats who are in pain may show aggression (hiss, growl, scratch, bite) when they are physically handled or prior to or after movements such as jumping onto or off a piece of furniture.

Maternal Aggression

A female cat may show aggressive behaviors toward individuals approaching her kittens.

Impulse Control Aggression

Cats who show intense aggressive responses to mild stimuli without much or any warning may have an impulse control disorder arising from dysfunctional serotonin neural circuits.

Frustration-Induced Aggression (To People and Other Animals)

Some cats have very outgoing, social personalities and exhibit aggression if the captive life indoors does not meet their behavioral needs.

Contact-Induced/Petting Aggression (Toward People)

- Cats will show early signs of aversion when people stroke their cats, with their ears going back and tail swishing.
- If physical contact continues, they typically bite.
- Owners often miss the early warning signs.
- When cats groom one another, they typically limit the grooming to the head region.
- Some cats appear to be particularly sensitive to being stroked along the dorsum, the common method used by owners.

Intercat Aggression within a Home

- Fifty percent of cat owners report fighting (scratching and biting) after introducing a new cat to the home.
- The number of cats, gender, and age are not significant factors in predicting which cats will show aggression.
- Any of the above categories of aggression are all possibilities for fights between or among cats.
- Fear/anxiety is the most common cause of intraspecific aggression.

CONTRIBUTING FACTORS TO THE PATHOPHYSIOLOGY

Behavior problems are typically multifactorial in cause, and Figure 1 is a diagram illustrating some of the more common components that

need to be evaluated to accurately diagnose and treat aggression cases.

SYSTEMS AFFECTED

- Behavioral—vary with type of aggression, occur alone or in combination: tail swishing/twitching, ears turned sideways or flattened, stiffening of shoulders/legs, crouching, dilation of pupils, hissing, spitting, growling, piloerection, staring, chasing, stalking, pawing, lunging.
- Cardiovascular—signs associated with sympathetic activation and HPA activation.
- Endocrine and Metabolic—long-term aggression associated with fear/stress/anxiety, symptoms associated with long-term activation of the HPA system.
- Gastrointestinal—with chronic HPA stimulation may see a cat more prone to anorexia and GI ulcers. With acute fear aggression: evacuation of the bowel and possible diarrhea. IBD possible in chronic stress.
- Hemic/Lymphatic/Immune—decreased immune response with chronic HPA stimulation; stress leukogram.
- Musculoskeletal—an outcome of the aggression may result in damage to the muscles from damage by the nails and teeth.
- Both the victim and the aggressor may suffer injuries. With chronic activation of the HPA, may see muscle wasting.
- Nervous—increased reactivity for up to 72 hours following an aggressive outburst. May see an increase in aggression with decreased provocation as the synapses in the amygdala become sensitized. Some animals may have decreased serotonin, causing aggressive outbursts. Depending on the type of aggression, may see ritualized motor patterns, shaking, or trembling.
- Ophthalmic—dilated pupils with sympathetic stimulation.
- Renal/Urologic—may see associated spraying or small amounts of urine on horizontal surfaces. May exhibit signs consistent with FLUTD with aggression that is due to stress/anxiety/fear.
- Respiratory—tachypnea in acute cases or when stressed.
- Skin/Exocrine—damage due to fights. Damage due to excessive grooming associated with fear-based aggression/anxiety/distress.

SIGNALMENT

- There is preliminary evidence that behavioral traits in cats vary by breed and gender.
- Males were more likely to show aggression to cats than females.
- Abyssinian, Russian blue, Somali, Siamese, and chinchilla breeds showed more aggression.
- Maine Coon, ragdoll, and Scottish folds showed the least aggressiveness.

SIGNS

- May appear at social maturity (2–4 years of age) except for play-related and should occur in specific social contexts/interactions. If onset occurs in an older cat, medical causes should be ruled out first.
- General comments: most owners are able to detect overt signs of aggression (biting, hissing, growling) but may

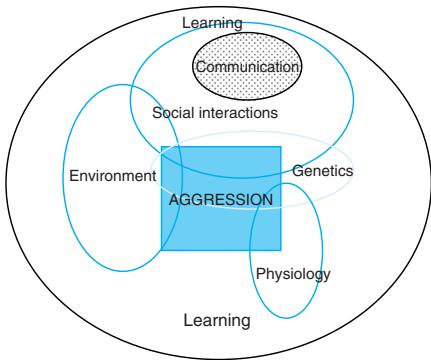


Figure 1.

miss more subtle signs of aggression that typically occur between cats (staring) and the resulting anxious behaviors that can result in aggression (meatloaf position, averting gaze, etc.). Videotapes of intercat interactions allow the clinician to assess the behavior.

CAUSES

- Underlying medical issues can cause aggression.
- Temperament/behavior is influenced by genetics, rearing, socialization, environment in which the cat lives, and types of interactions the cat has with people.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- CNS diseases (e.g., infections, toxins, tumors, partial seizures, focal seizures)
- Hyperthyroid
- Hepatic encephalopathy
- Any condition causing pain (e.g., arthritis, pancreatitis, dental disease, anal sacculitis)
- Lead poisoning
- Rabies
- Diabetic neuropathy (pain-induced aggression when paws touched)

CBC/CHEMISTRY/URINALYSIS

Physical examination, baseline blood and urine screening followed by additional diagnostics as indicated based on history, examination and laboratory results.

OTHER LABORATORY TESTS

- Discuss *Bartonella* testing in any cat that bites or scratches people.
- Thyroid levels.
- Urinalysis ± culture if housesoiling is part of the aggression issue.
- Feline serology (FCV, FeLV, FIV).



TREATMENT

- Never use physical correction/punishment; may escalate the aggression.
- Never try to physically handle or manipulate a cat in an aggressive state.
- Avoid known triggers.
- Identify triggers and desensitize and

counter-condition the cat to the triggers.

- Implement safety measures (nail caps, wearing long pants/long sleeves, keep flattened cardboard boxes around home to place between yourself and your cat, redirect the behavior in early arousal phase).
- Behavior modifications to redirect the cat and reduce arousal (specific plans are dependent upon the specifics of each case).
- Train your cat to commands such as "sit," "go to place," etc.
- Implement environmental enrichment.
- Teach owners to identify early signs of arousal so the cat can be redirected or so they can avoid the cat.
- After a very aggressive outburst, keep aggressor isolated in a room for at least 24 hours (as long as the cat remains aroused after an attack).
- Pheromones.
- Medications.



MEDICATIONS

DRUGS OF CHOICE

- SSRIs: fluoxetine or paroxetine 0.5 mg/kg PO q24h.
- TCAs: clomipramine 0.5 mg/kg PO q24h.
- Buspirone at 0.5–1.0 mg/kg q8–24h or benzodiazepines such as oxazepam at 0.2–0.5 mg/kg q12–24h might reduce fear and build confidence in the fearful cat that does not retaliate or fight back.

CONTRAINDICATIONS

- Cats with renal or hepatic disease
- Caution with TCAs and SSRIs in diabetics
- TCAs in patients with cardiac abnormalities

POSSIBLE INTERACTIONS

- TCAs and SSRIs should not be used together.
- Mirtazapine should not be used in combination with a TCA or SSRI.
- Any other medication the cat is on, the practitioner should look up which liver enzyme system is utilized in metabolism to maximize safety in combining medications.

ALTERNATIVE DRUGS

- Amitriptyline 0.5–1.0 mg/kg PO q12–24h
- SAMe: 100 mg PO q24h • Zylkene 75 mg (15 mg/kg or greater) PO q24h • Feliway Multicat diffuser l-theanine 25 mg PO q24h
- Zylkene 75 mg PO SID



FOLLOW-UP

PATIENT MONITORING

- Call owners once every 1–2 weeks for the first 2 months after a treatment plan has been recommended. Determine implementation of safety recommendations and the behavioral plan.
- If medications are involved, the medication dose should be reevaluated every 3–4 weeks.
- Frequency of follow-up will be dictated by the severity of the case and owner compliance.
- CBC, chemistry, T_4 prior to

medication. Recheck liver and kidney values 2–3 weeks after starting medication. Recheck bloodwork annually in young healthy patients, semiannually in older patients.

- Repeat physical exams in older patients semiannually, as painful conditions may start to contribute to/exacerbate the pain.

EXPECTED COURSE AND PROGNOSIS

- Ultimately depends on the specific kind of aggression and the compliance of clients with the suggested treatment plan.
- Most cases of aggression need a combination of behavioral modification, environmental modification, training, and, when necessary, medication to maximize chances of improvement.
- Some types of aggression can resolve or improve within a few weeks, whereas others may take several months or longer.
- Some forms of aggression have a poor prognosis.



MISCELLANEOUS

AGE-RELATED FACTORS

- Older cats—cognitive decline, CNS disease, arthritis, meningioma, other medical conditions.
- Age 2–4—social maturity, when cats may start to show certain kinds of aggression.

ABBREVIATIONS

- CNS = central nervous system
- FCV = feline calicivirus
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- FLUTD = feline lower urinary tract disease
- GI = gastrointestinal
- HPA = hypothalamic-pituitary-adrenal
- IBD = inflammatory bowel disease
- SAMe = S-adenosyl-L-methionine-tosylate disulfate
- SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant

SEE ALSO

- Aggression—Intercat Aggression
- Aggression Toward Humans—Cats

Suggested Reading

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Client Education Handout
available online



BASICS

DEFINITION

- Action by one dog directed against another organism with the result of, limiting, depriving, or harming that organism.
- Aggression refers to any behavior along an aggression continuum, from a stare, to immobility (freeze), growl, snarl, lunge, air snap, single bite, multiple bite, multiple attacks, and chase and attack.
- Numerous functional types have been posited. Here, aggression is classified on the basis of (1) affective aggression, (2) predatory aggression, and (3) play-related aggression. Affective (emotional) aggression is the focus of this chapter. Affective states, such as fear and arousal, and motivational factors, such as hunger and sexual drive, influence the probability of overt aggression, such as biting. Affective aggression may be human-directed or dog-directed. Within these contexts, there may be additional specificity, such as human-directed aggression toward unfamiliar persons, or human-directed aggression directed toward familiar persons. Often dogs display aggression in a single context.
- Human-directed aggression toward familiar persons in response to controlling gestures is historically called dominance aggression, although newer terminology, such as conflict aggression, may be used to avoid often-erroneous semantic assumptions inherent in the term “dominance.”
- Human-directed aggression toward unfamiliar persons specific to home location is called territorial aggression.
- Predatory aggression refers to behaviors associated with chasing and hunting prey. It is often considered nonaffective and may be socially facilitated by other dogs. Predatory behaviors may be triggered by movement or high-pitched sounds and may be misdirected to humans or objects.
- Play-related aggression involves aggressive gestures, such as growling and biting, in the context of play and is commonly displayed toward other dogs or humans. It is often initiated by signs of play, such as the play bow.
- In all cases, medical factors that might contribute to aggression (including pain) must be evaluated.

PATHOPHYSIOLOGY

- Affective aggression involves arousal of the sympathetic nervous system. Some pathologic conditions are associated with an increase in aggression because of CNS effects such as pain or irritability.
- Abnormalities in the CNS serotonin neurotransmitter system have been implicated in one type of impulsive human-directed aggression, colloquially called “rage,” directed toward familiar persons over controlling gestures.
- Aggression often has a learned component whereby dogs learn to use aggression to manage distance from fearful stimuli or control resources.

SYSTEMS AFFECTED

- Behavior.
- Other, if there is an underlying medical etiology.

GENETICS

- In some breeding programs, aggressive tendencies and bite styles have been selected for (or against).
- One study in the United States linked English springer spaniels that display human-directed dominance aggression to one breeding sire, implicating a heritable component.
- One study of human-directed dominance aggression among English cocker spaniels reported that males were more aggressive than females, and dogs with solid coat color were more aggressive than those with parti coat color.

INCIDENCE/PREVALENCE

- Canine aggression is the most common diagnostic category seen by board-certified veterinary behaviorists in North America.
- According to the Centers for Disease Control and Prevention (2009), about 4.7 million people are bitten by dogs each year in the US, although this number is considered an underestimation as the majority of dog bites are not reported.
- In the US, it is estimated that one in five of those who are bitten require medical attention for dog bite-related injuries.
- Among children and adults, males are more likely than females to be bitten.
- Based on emergency room data in the US, the rate of dog bite-related injuries is highest for children aged 5–9 years.

- In the majority of cases, people are bitten by dogs that are known to them.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog

Breed Predispositions

- Any breed or breed mix.
- Pit bull, German shepherd dog, and rottweiler are the most common breed types implicated in fatal dog bites in the US.
- In the US, English springer spaniels appear to be at risk for human-directed “dominance” aggression.

Mean Age and Range

Any age

Predominant Sex

- Any sex.
- Males—intact or castrated are most commonly implicated in cases of human-directed “dominance” type aggression. Intact males are overrepresented in dog-bite fatalities.
- Females—spayed are most commonly implicated in aggression to other female dogs in the home. In some studies, spayed females are less likely than males to display human directed aggression.

SIGNS

General Comments

- Any dog can display aggression. Many factors, including individual dog temperament and experience, influence the propensity to bite.
- Dogs may display warning signs—including immobility, growls, snarls, or air snaps that may provide time to avoid overt aggression. These signs should not be punished, as this might decrease the probability of warning signs without affecting the underlying risk, or may further intensify the aggressive (defensive) response. Instead, the animal should be safely removed from the situation and the underlying triggers for the affective state should be addressed.

Historical Findings

- Variable.
- Basis for risk analysis and details of treatment program. Important questions: Who is the target? Who was present to manage the dog? How severe were the resulting injuries? What are the circumstances (including location, time) in which aggression occurred? Are there any reliable triggers for the aggressive behavior? Abnormalities in mentation or awareness might indicate a medical cause

Physical Examination Findings

- Usually unremarkable.
- Use extreme care when handling aggressive dogs.
- A comfortable, well-fitting basket muzzle is recommended prior to examination of any dog with a history of human-directed aggression. Basket-style muzzles allow dogs to pant.
- Abnormalities on the neurologic examination may suggest an organic disease process (e.g., rabies, pain, blindness). Dogs can display aggression preictal, postictal or ictal period.

CAUSES

- Part of the normal range of behavior; strongly influenced by individual temperament, experience, early socialization (before 12 weeks), and other variables.
- Harsh handling and confrontational responses can escalate aggression and should be avoided.
- May be a manifestation of an organic condition, such as hepatic encephalopathy or pain.
- In all cases, evaluate medical causes of aggression.

RISK FACTORS

- Inadequate socialization during the canine critical period (3–12 weeks).
- Traumatic/fearful/negative experience(s).
- Predisposing environmental conditions—lack of training, inadequate restraint, harsh handling.
- Inability of owner to safely confine or manage the dog in order to prevent future incidents. Helpful devices include a barrier fence, a muzzle, a collar or head halter, a leash.
- Previous aggression/bite history (number of incidents, number of bites per incident, target, severity of injury); legal citation for biting.

- Unpredictability of aggressive behaviors, lack of warning signals.
- Presence of children, elderly people, or other humans or animals at high risk living in or visiting household.

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- A thorough medical evaluation should be conducted on all cases of aggression.
- Identify pathologic conditions associated with aggression before making a purely behavioral diagnosis.
- Rule out developmental abnormalities (hydrocephaly, lissencephaly, hepatic shunts), metabolic disorders (hypoglycemia, hepatic encephalopathy, diabetes), neuroendocrinopathies (hypothyroidism, hyperadrenocorticism), dermatopathy, neurologic conditions (intracranial neoplasm, seizures), toxins, inflammatory diseases (encephalitis, rabies), cognitive dysfunction, acute or chronic pain, and iatrogenic causes, such as glucocorticoid administration.

CBC/BIOCHEMISTRY/URINALYSIS

- May be indicated to evaluate dog as candidate for behavioral medications.
- Abnormalities may suggest underlying metabolic, endocrine causes, or other medical conditions.
- Usually no significant findings outside laboratory range unless an underlying medical etiology is detected.

OTHER LABORATORY TESTS

- Thyroid testing.
- Others as indicated by history and physical exam.

IMAGING

- May be indicated to identify sources of pain or disease.
- MRI or CT—particularly if cerebral disease/neoplasia suspected.

DIAGNOSTIC PROCEDURES

- Collection of thorough behavioral history and evaluation of medical concerns.
- Postmortem fluorescent antibody test is indicated for any aggressive dog for which rabies is a differential diagnosis, including any dog not quarantined for 10 days after a bite injury to a human or other animal.

PATHOLOGIC FINDINGS

None

**TREATMENT****APPROPRIATE HEALTH CARE**

- Manage any underlying medical conditions.
- Management success—combination of multiple modalities: safe environmental control, behavior modification to teach animals appropriate behavior, and pharmacotherapy.
- Consult a veterinarian with experience and training in aggression management.
- Euthanasia should be discussed or recommended when the risk of injury is high. Note recommendation in medical record.
- Rehoming aggressive dogs may put those involved at liability risk.

NURSING CARE

A boarding facility able to safely manage the dog might be used until a safe management plan can be implemented, or until an outcome decision can be made.

ACTIVITY

Since frustration and arousal may increase the incidence of aggression, an appropriate and safe exercise regime should be incorporated into the treatment program.

DIET

There is modest evidence that a low-protein diet may reduce territorial aggression in dogs, an effect that might be enhanced with tryptophan supplementation.

CLIENT EDUCATION

- Safe practices should dictate all decisions. These practices include safe confinement, physical barriers, head halters, leash control, muzzle use, and supervision by a competent adult.
- Situations that have led to aggression in the past should be listed and a specific plan developed to avoid these situations and associated locations in the future, and a long-term management plan developed.
- The dog should calmly be removed from aggression-provoking situations.
- Safe, non-confrontational techniques that manage resources and use positive reinforcement to teach the dog appropriate responses should be employed.

(CONTINUED)

AGGRESSION, OVERVIEW—DOGS

A

- Confrontational management techniques, such as roll-overs, increase the probability of a defensive aggressive response, may lead to human injury, and should be strictly avoided.
- Management (“dominance”) techniques including punishment are associated with defensive fear responses by the dog and an increased risk of human-directed aggression. These should be avoided and replaced with positive management techniques.
- The client should be advised to consider personal and legal liability risks of keeping the dog. Human injury, bite-related lawsuits, and homeowner’s insurance claims can result from canine aggression. Such risk assessment may help the client objectively evaluate the situation.
- Euthanasia should be considered if safe management cannot be employed, or when the risk of injury is high.

SURGICAL CONSIDERATIONS

Castration of males may reduce the incidence of inter-male aggression.

**MEDICATIONS****DRUG(S) OF CHOICE**

- None approved by the FDA for the treatment of aggression.
- No drug will eliminate the probability of aggression.
- Use drugs only when a safe management plan has been implemented.
- Inform the client of the extra-label nature of medication and risk involved; document in the medical record, obtain signed informed consent.
- Drugs that increase serotonin may be helpful to reduce anxiety, arousal, and impulsivity.

- Treatment duration: minimum 4 months, maximum: lifetime.
- See Table 1 for drugs used to facilitate management of aggression in combination with a safe management plan.

CONTRAINdications

- Fluoxetine is generally contraindicated in cases of seizures.
- Clomipramine is contraindicated in cases of cardiac conduction disturbances or seizures; in one open trial, clomipramine was no more effective than control in cases of human-directed aggression.

PRECAUTIONS

Avoid the use of benzodiazepines (e.g., diazepam) in aggressive dogs because of the risk of behavioral disinhibition. Aggression may increase when dogs lose their fear of the repercussions of biting.

POSSIBLE INTERACTIONS

Do not use SSRIs or TCAs with monoamine oxidase inhibitors, including amitraz and selegiline, or with each other because of the risk of serotonin syndrome.

ALTERNATIVE DRUG(S)

- L-Tryptophan (10 mg/kg PO q12 h).
- Trazodone (4–8 mg/kg PO q12 h or PRN) may be used with the agents listed in Table 1 to reduce anxiety and arousal.
- Clonidine (0.01–0.05 mg/kg PO q12 h or PRN), may be used with the agents listed in Table 1 to reduce anxiety and arousal.

**FOLLOW-UP****PATIENT MONITORING**

Weekly to biweekly contact recommended in the initial phases to guide clients with behavior modification plans and medication management.

PREVENTION/AVOIDANCE

- To prevent aggressive incidents, avoid all situations that have led to aggression in the past, using safe confinement, gates, halters, collars, leashes, muzzles.
- Reduce the risk of aggression in young dogs (3–12 weeks) with a positive socialization program; avoid intimidation techniques and negative, fear-inducing situations.

POSSIBLE COMPLICATIONS

- Injury to humans or animals.
- Liability to client, veterinarian.
- In cases of dog-directed aggression, although not the intended target, humans who interfere are often seriously injured either by accident or by redirected aggression; owners should not reach for fighting dogs; pull apart with leashes.
- Aggressive dogs are at risk for relinquishment or euthanasia.

EXPECTED COURSE AND PROGNOSIS

- Aggressive dogs weighing over 18.5 kg are at increased risk for behavioral euthanasia.
- Aggressive dogs may be successfully managed, but should not be considered “cured.”
- Prognosis is case-dependent due to risk factors and management features of each situation.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

Onset of aggression in mature dogs suggests a medical cause; carefully evaluate sensory acuity, sources of pain, endocrinopathy, cognitive function.

Table 1

Drugs and dosages used to manage canine aggression.

<i>Drug</i>	<i>Drug Class</i>	<i>Oral Dosage in Dogs</i>	<i>Frequency</i>	<i>Side Effects-usually transient</i>
Fluoxetine	SSRI	1.0–2.0 mg/kg	q24 h	Decreased appetite, sleepiness
Paroxetine	SSRI	1.0–2.0 mg/kg	q24 h	Constipation
Sertraline	SSRI	2.0–4.0 mg/kg	q24 h	Sleepiness
Clomipramine	TCA	1.0–3.0 mg/kg	q12 h	Sleepiness, vomiting

ZOONOTIC POTENTIAL

- Dog bites are significant public health risk.
- Rabies is a potential cause of aggression.

PREGNANCY/FERTILITY/BREEDING

Tricyclic antidepressants are contraindicated in breeding males and pregnant females.

SYNONYM

Biting

SEE ALSO

- Aggression—Between Dogs in the Household
- Aggression, Food and Resource Guarding—Dogs
- Aggression to Unfamiliar People and Unfamiliar Dogs
- Aggression Toward Children—Dogs
- Aggression Toward Familiar People—Dogs

ABBREVIATIONS

- CNS = central nervous system
- CT = computed tomography
- FDA = US Food and Drug Administration
- MRI = magnetic resonance imaging
- SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant

INTERNET RESOURCES

- American Veterinary Medical Association Dog Bite Prevention: <https://www.avma.org/public/Pages/Dog-Bite-Prevention.aspx>
- Centers for Disease Control and Prevention Dog Bites: <http://www.cdc.gov/HomeandRecreationalSafety/Dog-Bites/>
- ASPCA Aggression in Dogs: <http://www.aspca.org/pet-care/virtual-pet-behaviorist/dog-behavior/aggression-dogs>

Suggested Reading

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Client Education Handout
available online

AGGRESSION—BETWEEN DOGS IN THE HOUSEHOLD



BASICS

OVERVIEW

Aggression toward other dog(s) within a household or those dogs that are otherwise familiar and spend time together regularly. Dogs can form stable social relationships quickly, sometimes within minutes of being introduced. Aggression usually revolves around resources (e.g., food, toys, owner attention, resting places), but may be fear-related or can occur at times of excitement/arousal (e.g., visitors or other dogs on the property). Usually within the range of normal behavior, but may be abnormal or excessive due to learning, early environment, or genetics (dogs bred for fighting).

SYSTEMS AFFECTED

Behavioral

SIGNALMENT

Species

Dog

Breed Predilections

- More common in purebreds with 50% being the same breed.
- Breed predilection in “fighting breeds” (e.g., pit bull terrier) and terrier.

Mean Age and Range

Signs usually develop at social maturity (approximately 18–36 months of age).

Predominant Sex

May be more common/intense between females.

SIGNS

- Aggression (barking, growling, lip-lifting, snarling, snapping, lunging, biting) toward other dogs in the home. This may be accompanied by fearful or submissive body postures/facial expressions (crouching, backing away, ears back, tail tucked, looking away, lip licking) or confident/dominant body postures (standing straight up, approaching/direct contact with the other dog, tail up, ears forward).
- History prior to the onset of fights may include subtle signs of social/resource control/dominance (e.g., staring, lying across doorways to block the other dog’s access to a room) and submission (e.g., turning away from the staring dog or not entering the same room as the other dog).
- Dogs fighting in a household may get along well except in specific situations, especially over resources, access to passageways/doorways, times of arousal. Dogs that fight over owner attention often described as “jealous.”
- Aggression typically occurs when the owner is present.

CAUSES & RISK FACTORS

- May be a normal canine behavior; strongly influenced by previous experience (e.g., early socialization, previous aggressive encounters

with other dogs, inappropriate punishment).

- Breed predilections due to selective breeding for interdog aggression.
- Aggression is likely to be more severe toward dogs of the same sex, especially two females.
- Instigators are usually newer to the household and younger than recipients.
- In cases of aggression within a household, there may be history of owners interfering in normal canine communication, especially when one dog appears to be denying another dog access to something that the owners think they should “share.” This shift may actually support one dog in what would be considered inappropriate “canine” behavior and result in escalation of the interdog aggression. For example, an owner calling dog “A” into a room when the other dog “B” has blocked its access even though “A” was willing to remain outside of the room or the owner punishing dog “B” for blocking dog “A’s” access. Both of these situations undermine dog “B” in its hierachal position while it was subtly asserting control to which dog “A” was willing to defer.
- Underlying medical conditions, especially pain, may increase the level of aggression.
- If the aggressor initiates or continues its attack despite deference from the other dogs, or if the deferent dog is overly fearful or defensive, then these may indicate abnormal responses that might have a poor prognosis (unable to socially communicate) or require drug therapy to manage the abnormal behavior.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Play behavior/excited non-aggressive arousal
- Possessive aggression
- Fear aggression
- Others depending on circumstances

CBC/BIOCHEMISTRY/URINALYSIS

Usually unremarkable. Rule out underlying medical contributing conditions with blood, urine and thyroid screening.

OTHER LABORATORY TESTS

As needed to rule out underlying medical conditions.

IMAGING

MRI if CNS disease suspected; as needed to rule out underlying medical conditions.

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

CLIENT EDUCATION

General Comments

- Treatment is aimed at controlling the problem, not achieving a “cure.” Successful treatment, as measured by a decrease in aggressive incidents, depends upon owner

understanding of basic canine social behavior and communication, risks involved in living with an aggressive dog(s), and willingness and ability to follow safety and management recommendations.

Safety Recommendations

- The owner’s primary responsibility is to insure safety by identifying and avoiding all situations that may evoke an aggressive response. Dogs within a household may initially need to be kept in separate housing areas to prevent fighting.
- Owners should be advised that they may be liable if their dog bites and could face civil/criminal prosecutions should a person be injured.
- If needed, owners must be instructed in methods of safely breaking up dog fights.
- Treatment is more likely to be successful if aggression-provoking stimuli can be effectively prevented prior to behavior modification.
- The dogs must be confined away from each other or under the direct physical control of a responsible adult whenever an aggression-evoking situation could arise (e.g., around food/valued resources).
- Teaching the dogs to be comfortable wearing a head halter (e.g., Gentle Leader) with a lightweight 8- to 10-foot leash attached or a basket muzzle makes controlling potentially dangerous situations easier and safer. If needed, use the long leash both for prevention and to safely remove the dog from situations that may elicit aggression; do not reach for the dog directly.
- The more dominant dog typically asserts control of resources (e.g., staring, growling) with confident body postures directed toward the more subordinate dog who relinquishes the resource by moving or looking away.
- When there is competition over resources, allow priority access to the more controlling/dominant individual and encourage and reinforce deference in the other dog(s).
- Priority access may vary between resources (individual motivation), and contexts (location, who accesses first)—separate (time out) any dog displaying an inappropriate response.
- For some dogs problems may be resolved if additional resources and sufficient distribution are provided to reduce competition.
- Alternately, dogs may need to be separated when given resources that are a source of repeated conflict.

Behavior Therapy

- Depending on the situation, supporting and reinforcing the hierachal positions of the dogs will result in rapid (e.g., 1–2 weeks) resolution of the problem and a drastic decrease in aggressive incidents between dogs. Fighting is likely to recur if support of the hierarchy by humans is not continued.
- Separately, teach each dog those behaviors that will serve as a foundation for

AGGRESSION—BETWEEN DOGS IN THE HOUSEHOLD

(CONTINUED)

management and control when together including sit and relax, down-settle and teaching to go to mat, bed or crate to settle.

- NEVER allow dogs to “fight it out” as serious injuries may occur.
- During times together, use verbal cues or leave leash attached to train desirable and prevent or interrupt undesirable behavior.
- Structured interactions (also known as learn to earn or say please by sitting) where each dog is consistently taught to sit for anything it values (before feeding, petting, play, going for a walk) provides structure and predictability in all interactions, teaches impulse control and gives the dog control of its resources by sitting calmly.
- Systematic desensitization and counter-conditioning to fear-provoking stimuli.



MEDICATIONS

DRUG(S)

- There are no medications licensed for the treatment of canine aggression. Owners must be aware that the use of medication is off-label.
- A signed informed consent form is advisable listing potential risks and side effects.
- NEVER use medications without concurrent behavior modification.
- Before prescribing medication, be sure that owners understand the risks in owning an aggressive dog, will follow safety procedures, and that they understand that medication will not insure safety.
- Medication may not be appropriate in all situations (e.g., households with small children, individuals that are immunocompromised or have disabilities).
- Studies have not shown a robust effect of drug treatment on aggression. Placebo effect may be strong.
- Medications are most likely to be helpful in situations where there is a strong fear/anxiety component, or where one or both dogs are behaviorally abnormal (e.g., reactivity, impulsivity, intensity) as opposed to situations where closely ranked dogs use aggression to establish resource control.

Selective Serotonin Reuptake Inhibitors

- Fluoxetine 0.5–2 mg/kg PO q24h.
- Paroxetine 0.5–1 mg/kg PO q24h.
- Sertraline 1–3 mg/kg PO q24h.
- Side effects: sedation, irritability, GIT effects, increased aggression; anorexia is common and usually transient.

Tricyclic Antidepressants

- Clomipramine 1–3 mg/kg PO q12h (caution: label restriction for aggression).
- Side effects: sedation, GIT effects, anticholinergic effects, cardiac conduction disturbances if predisposed, and increased aggression.

Alpha-2 agonists

- Clonidine 0.01–0.05 mg/kg PO PRN 1.5–2 hours before eliciting trigger, up to q12h.
- Side effects: transient hyperglycemia, anticholinergic, hypotension, collapse, and bradycardia (responsive to atropine), and increased aggression.

Serotonin 2a antagonist/reuptake inhibitors

- Trazodone 2–5 mg/kg PO PRN prior to eliciting trigger, up to q6h—may titrate up to 8–10 mg/kg if no adverse effects.
- Side effects: sedation, anorexia, ataxia, GIT effects, cardiac conduction disturbances, increased aggression.

CONTRAINdicATIONS

Use caution as any psychotropic medication may reduce fear-based inhibition resulting in an increase rather than decrease in aggression.

PRECAUTIONS

Any psychotropic medication may increase irritability and aggression. Corticosteroids are contraindicated in food-aggressive dogs; polyphagia can lead to increased frequency/intensity of aggression.

POSSIBLE INTERACTIONS

Do not combine SSRIs, TCAs, MAO inhibitors (e.g., amitraz, selegiline), opioids (e.g., tramadol), and other medications that increase serotonin—can result in potentially fatal serotonin syndrome.



FOLLOW-UP

PATIENT MONITORING

Clients usually need ongoing assistance and should receive at least one follow-up call within the first 1–3 weeks after the consultation. Provisions for further follow-up should be made at that time.

PREVENTION/AVOIDANCE

Treatment recommendations are life-long.

POSSIBLE COMPLICATIONS

Injuries to dogs and humans; euthanasia or relinquishment of patient.

EXPECTED COURSE AND PROGNOSIS

There is no cure. Prognosis for improvement is more favorable if aggression is at a fairly low intensity and occurs in only a few predictable situations. Prognosis is highly dependent on owner compliance. Relationship issues may recur with changes in housing, health or age.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Other fear- or anxiety-based conditions; territorial aggression.

ZOONOTIC POTENTIAL

Human injury and bite wounds when separating fighting dogs.

PREGNANCY/FERTILITY/BREEDING

Do not breed dogs with extreme interdog aggression.

SEE ALSO

- Aggression to Unfamiliar People and Unfamiliar Dogs
- Aggression, Food and Resource Guarding—Dogs

ABBREVIATIONS

- CNS = central nervous system
- GIT = gastrointestinal tract
- MAO = monoamine oxidase
- MRI = magnetic resonance imaging
- SSRI = selective serotonin reuptake inhibitor
- SARI = Serotonin 2a antagonist/reuptake inhibitor
- TCA = tricyclic antidepressant

Suggested Reading

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ALKALOSIS, METABOLIC (TRADITIONAL APPROACH)



BASICS

DEFINITION

A process in the body that leads to an elevation in pH above the reference interval for that species. An elevation in blood pH is specifically termed Alkalemia. Associated with an increase in plasma bicarbonate concentration (HCO_3^-) (dogs, > 24 mEq/L; cats, > 22 mEq/L) and base excess (BE) (> 4 mmol/L) with a compensatory increase in carbon dioxide tension (PCO_2).

PATHOPHYSIOLOGY

- Metabolic alkalosis may develop from either a gain in bicarbonate or a loss in acid.
- Bicarbonate gain subsequent to:
Contraction alkalosis due to free water deficit; iatrogenic administration of alkalinizing therapy (e.g., Na HCO_3^-); metabolism of organic ions (lactate, citrate, acetate, and ketones); hypokalemia; and renal ammoniogenesis.
- Acid loss subsequent to:
gastric or renal acid loss (loop or thiazide diuretic); mineralocorticoid excess; presence of non-reabsorbable anions; decreased weak acids (hypoalbuminemia and hypophosphatemia).
- Renal HCO_3^- excretion is often very efficient in eliminating an excess HCO_3^- load, but is hindered by decreased effective circulating volume; hypokalemia, hypochloremia, and hyperaldosteronism. Metabolic alkalosis persists only if renal excretion of HCO_3^- is impaired. This primarily occurs from continued high rate of alkali administration, or some stimulus for the kidneys to retain sodium in the presence of a relative chloride deficit.
- Hypochloremic (corrected) metabolic alkalosis results from loss of fluid rich in chloride and H^+ primarily from the alimentary tract or kidneys. Loss of chloride and H^+ is associated with an increase in plasma HCO_3^- concentration. With chloride loss and volume depletion, the kidneys reabsorb sodium with HCO_3^- instead of chloride, perpetuating the metabolic alkalosis. Hypochloremic alkalosis is divided into chloride-responsive and chloride-resistant.
- Chloride-responsive results primarily from the loss of chloride rich fluid and is characterized by decreased extracellular fluid volume, hypochloremia, and low urinary chloride levels. This type of alkalosis responds to administration of chloride salt.
- Chloride-resistant is characterized by excessive mineralocorticoid leading to increased effective circulating volume and is not responsive to chloride salt.
- Hypokalemia may contribute to metabolic alkalosis by shifting H^+ intracellularly; stimulating apical H^+/K^+ ATPase in the collecting duct; stimulating renal ammoniogenesis; impairing chloride ion reabsorption in the distal

nephron; and reducing glomerular filtration rate (GFR) which decreases the filtered load of HCO_3^- and in the presence of volume depletion, impairs renal excretion of the excess HCO_3^- .

• Hypoalbuminemic alkalosis is due to a decrease in the level of plasma albumin. Plasma albumin is a weak acid.

• Compensatory metabolic alkalosis occurs in response to respiratory acidosis. This is associated with a low pH and elevated PCO_2 .

SYSTEMS AFFECTED

- Nervous—muscle twitching and seizures occur rarely in dogs. Metabolic alkalosis and associated hypokalemia may precipitate hepatic encephalopathy in patients with liver failure.
- Urinary—the kidneys rapidly and effectively excrete excessive alkali. In patients with chloride deficiency (and less importantly, volume depletion), the kidneys cannot excrete the excess alkali. Therefore, metabolic alkalosis is maintained. In these patients, chloride administration is required for renal compensation to occur. Volume expansion will hasten compensation. Patients with mineralocorticoid excess have excessive chloride loss. Therefore, chloride administration does not lead to hyperchloremia and correction of metabolic alkalosis (so-called chloride-resistant metabolic alkalosis).
- Respiratory—low $[\text{H}^+]$ (elevated pH) reduces alveolar ventilation. Hypoventilation increases PCO_2 and helps offset the effects of high plasma HCO_3^- on pH. In dogs, for each 1 mEq/L increase in plasma HCO_3^- there is an expected increase of approximately 0.7 mmHg in PCO_2 . Limited data is available for cats, but the degree of respiratory compensation appears to be similar.

SIGNALMENT

Any breed, age, or sex of dog and cat

SIGNS

Historical Findings

- Administration of loop diuretics (e.g., furosemide) or thiazides
- Vomiting

Physical Examination Findings

- Signs related to the underlying disease or accompanying potassium depletion (e.g., weakness, cardiac arrhythmias, ileus, etc.).
- Muscle twitching caused by low ionized calcium concentration.
- Dehydration in volume-depleted patients.
- Muscle twitching and seizures in patients with neurologic involvement (rare).

CAUSES

- Chloride-responsive—gastrointestinal losses (e.g., gastric vomiting, nasogastric tube suctioning); renal losses (diuretic therapy); and rapid correction of chronic hypercapnia (respiratory acidosis).
- Chloride-resistant—hyperadrenocorticism and primary hyperaldosteronism.
- Oral administration of alkalinizing agents—sodium bicarbonate or

other organic anions with sodium (e.g., lactate, acetate, gluconate); administration of cation-exchange resin with non-absorbable alkali (e.g., phosphorus binders).

- Hypoalbuminemia—liver disease, protein losing nephropathy or enteropathy, nephrotic syndrome.
- Free water deficit—diabetes insipidus; water deprivation; post-obstructive diuresis; polyuric renal failure.
- Hypokalemia—see Hypokalemia.

RISK FACTORS

- Administration of loop or thiazide diuretics.
- Vomiting.
- Stomach drainage.
- Diseases associated with hypoalbuminemia (e.g., nephrotic syndrome, liver failure).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

High plasma HCO_3^- and hypochloremia may also occur in animals compensating for chronic respiratory acidosis, in which PCO_2 is high and pH is low despite high HCO_3^- and low chloride concentration; blood gas determination required to differentiate.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results
None

Disorders That May Alter Laboratory Results

- Too much heparin (> 10% of the sample) decreases pH, PCO_2 and HCO_3^- .
- Blood samples stored at room temperature for more than 15 minutes have low pH because of increased PCO_2 .
- Exposure to room air decreases PCO_2 .
- Venous samples may have pH 0.5–1 unit lower and PCO_2 5–10 mmHg higher than an arterial sample.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- High total CO_2 (total CO_2 in samples handled aerobically closely approximates HCO_3^-).
- Low blood ionized calcium concentration.
- Serum electrolyte abnormalities vary with underlying cause.
- Hypochloremia—consider hypochloremic metabolic alkalosis, the most common reason for metabolic alkalosis in dogs and cats, which usually results from diuretic administration or vomiting of stomach contents.
- High sodium but normal chloride concentration—consider chloride-resistant metabolic alkalosis (e.g., hyperadrenocorticism or primary hyperaldosteronism) or administration of alkali.
- Hypoalbuminemia—consider hypoalbuminemic metabolic alkalosis (e.g., liver failure, protein-losing enteropathy, and protein-losing nephropathy). In vitro, a 1 g/dL decrease in albumin concentration is associated with an increase in pH of 0.093 in cats and 0.047 in dogs.
- Hypokalemia—

hypokalemia likely results from intracellular potassium shifting due to metabolic alkalosis or the underlying problem (e.g., vomiting of stomach contents or loop diuretic administration). • Urinary chloride levels—chloride-responsive metabolic alkalosis has urine chloride levels < 10 mEq/L while chloride-resistant metabolic alkalosis involves urine chloride levels of > 20 mEq/L.

OTHER LABORATORY TESTS

Blood gas analysis reveals high HCO_3^- , PCO_2 , pH and base excess (BE). Unlike HCO_3^- , BE is independent of changes in and is considered a more reliable measure of metabolic acid-base changes.

IMAGING

None

DIAGNOSTIC PROCEDURES

- Blood pressure—the combination of hypertension, hypernatremia, and hypokalemia with metabolic alkalosis may indicate the presence of hyperaldosteronism.
- Diagnostic testing for hyperadrenocorticism or primary hyperaldosteronism (e.g., plasma renin and aldosterone levels).



TREATMENT

• Acid-base disturbances are secondary phenomena. Diagnosis and treatment of the underlying disease process is integral to the successful resolution of acid-base disorders.

• Severe alkalemia is uncommon, but may be life-threatening. Patients with chronic respiratory disease and respiratory alkalosis are at risk of developing severe alkalemia if they start vomiting or receive diuretics.

• Discontinue drugs that may cause metabolic alkalosis. • *Chloride-responsive*—the fluids of choice contain chloride; give patients with volume depletion an intravenous infusion of balanced, buffered isotonic electrolyte replacement fluid supplemented with KCl; patients with hypokalemia may require large doses of KCl (see Hypokalemia).

• *Chloride-resistant* metabolic alkalosis can only be corrected by resolution of the underlying disease; metabolic alkalosis is usually mild in these patients. • If the metabolic alkalosis is associated with hypokalemia and total body potassium deficits, correcting the deficit with KCl is a particularly effective way to reverse the alkalosis.

NURSING CARE

Supportive care to maintain euhydration, euvolemia, adequate nutrition, etc.



MEDICATIONS

DRUG(S) OF CHOICE

Hypochloremic Alkalosis

- If chloride-responsive alkalosis occurs during an edematous state (e.g., congestive heart failure), oral compounds containing chloride without sodium are recommended to correct the alkalosis. If diuresis is needed due to volume overload, a carbonic anhydrase inhibitor (e.g., acetazolamide) or a potassium-sparing diuretic (e.g., spironolactone, amiloride) can be used to correct the alkalosis.
- H2-blocking agents such as famotidine reduce gastric acid secretion and may be considered as adjunctive therapy if gastric losses are ongoing.
- Antiemetics may help prevent further gastric acid loss.

Hypoalbuminemic Alkalosis

- Treatment for hypoalbuminemic alkalosis should be directed at the underlying cause and the decreased colloid oncotic pressure.
- Foster enteral nutrition to increase endogenous albumin production.
- Consider species-specific plasma or albumin (canine albumin) therapy.

CONTRAINDICATIONS

- Avoid chloride-free fluids—they may correct volume depletion but will not correct hypochloremic alkalosis.
- Avoid using salts of potassium without chloride (e.g., potassium phosphate)—potassium will be excreted in the urine and will correct neither the alkalosis nor the potassium deficit.

PRECAUTIONS

Do not use distal blocking agents (e.g., spironolactone) in volume-depleted patients.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

Acid-base status—frequency dictated by the underlying disease and patient response to treatment.

POSSIBLE COMPLICATIONS

- Hypokalemia • Neurologic signs



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Hypokalemia • Hypochloremia

AGE-RELATED FACTORS

None

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Non-respiratory alkalosis.
- Chloride-responsive metabolic alkalosis—metabolic alkalosis that responds to chloride administration.
- Chloride-resistant alkalosis—metabolic alkalosis secondary to increased mineralocorticoid activity that does not respond to chloride administration.
- Hypochloremic alkalosis—metabolic alkalosis caused by low chloride concentration.
- Hypoalbuminemic alkalosis—metabolic alkalosis caused by low albumin concentration.
- Concentration alkalosis—metabolic alkalosis resulting from decreased free water in plasma.
- Contraction alkalosis—metabolic alkalosis formerly attributed to volume contraction, but now known to be caused by chloride depletion. Volume depletion is a common but not essential feature.

SEE ALSO

- Hypochloremia • Hypokalemia

ABBREVIATIONS

- BE = base excess • H^+ = hydrogen ion
- HCO_3^- = bicarbonate • PCO_2 = carbon dioxide tension

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BASICS

DEFINITION

- Common problem • Pattern of hair loss—varied or symmetrical • Causes—multifactorial

PATHOPHYSIOLOGY

Specific and unique for each cause

SYSTEMS AFFECTED

- Endocrine/Metabolic • Hemic/Lymphatic/Immune • Skin/Exocrine

SIGNALMENT

- No specific age, breed, or sex predilection.
- Neoplastic and paraneoplastic associated alopecias—generally recognized in older cats.

SIGNS

Depends on specific diagnosis

CAUSES

- Neurologic/behavioral—compulsive disorder.
- Endocrine—sex hormone alopecia, hyperthyroidism, hyperadrenocorticism, diabetes mellitus.
- Immunologic—allergic dermatitis, alopecia areata, alopecia mucinosa, lymphocytic mural folliculitis, pseudopelade.
- Parasitic—demodicosis, cheyletiellosis.
- Infections—dermatophytosis.
- Physiologic/metabolic—sebaceous adenitis.
- Neoplastic—paraneoplastic dermatitis, squamous cell carcinoma in situ, epitheliotrophic lymphoma, thymoma with exfoliative dermatitis.
- Idiopathic/inherited—alopecia universalis, hypotrichosis, spontaneous pinnal alopecia, anagen and telogen defluxion.
- Medication effect—corticosteroids.
- Viral—FeLV- and FIV-associated disease (giant cell dermatosis).

RISK FACTORS

FeLV/FIV—reported risk for demodicosis (not all cases associated with viral infection).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Endocrine Alopecia/Sex Hormone

- Non-inflammatory alopecias are rarely hormonal in etiology; search for other causes before exploring endocrine etiology.
- Hormonal causes—primarily castrated males; alopecia along the caudal aspect of the hind limbs, which may extend along the perineum.
- Excessive corticosteroid administration; may also cause curling of pinnal tips.
- Megestrol acetate—may produce lesions similar to/associated with diabetes mellitus or hyperadrenocorticism.

Compulsive Disorder

- Uncommon as sole source of symptoms.
- Often misdiagnosed in cases of allergic

dermatitis. • Often misdiagnosed as endocrine alopecia. • The pattern of alopecia is frequently symmetrical without associated inflammation.

Allergic Dermatitis

- Varies from mild partial alopecia with little inflammation to severe excoriation and ulceration.
- Barbering of the hair coat often occurs clandestinely leading to a misdiagnosis of endocrine alopecia.
- Distribution—varied; often the head and neck or ventral abdominal regions are most affected.
- Food allergy, atopic dermatitis, contact allergy, and ectoparasite hypersensitivity.

Hyperthyroidism

- Partial to complete alopecia from self-barbering.
- Varied pattern.
- Middle-aged to old cats.
- Often misdiagnosed in cases of allergic dermatoses, compulsive disorder, or other endocrine alopecia.

Diabetes Mellitus

- Partial alopecia with an unkempt or greasy hair coat and excessive scaling.
- Poor wound healing.
- Increased susceptibility to infections.
- Rarely, cutaneous xanthomatosis secondary to hyperlipidemia (nodular to linear, yellow-pink alopecic plaques that tend to ulcerate).

Hyperadrenocorticism

- Rare; characterized by alopecia and extreme fragility of the skin.
- Truncal alopecia, with or without a rattle and curling of the pinnal tips.
- Extreme skin fragility noted in approximately 70% of cases.
- Occurs secondary to pituitary or adrenal tumors.
- Iatrogenic form less common in cats than in dogs; associated with frequent repositol corticosteroid injections.

Paraneoplastic Alopecia

- Most cases associated with pancreatic exocrine adenocarcinomas, bile duct carcinomas, or exfoliative dermatitis with thymoma.
- Middle-aged to old cats (9–16 years).
- Pancreatic carcinoma/bile duct carcinoma: acute onset, progress rapidly, bilaterally symmetrical, ventrally distributed (also located along the bridge of the nose and periocular), hair epilates easily, rare pruritus, erythema with dry fissuring footpads, glistening appearance to alopecic skin, skin is often thin and hypotonic, rapid weight loss.
- Thymoma with exfoliative dermatitis: non-pruritic scaling dermatitis that starts on the head and neck. Brown waxy deposits accumulate around the eyes and nasal region. Surgical removal of the thymoma will cause resolution of the dermatitis within a few months (typically 4–5 months).

Sebaceous Adenitis

- Slowly progressive partial alopecia associated with scaling along the dorsum of the body and the extremities.
- Sebaceous glands are, theoretically, selectively destroyed by toxic intermediate metabolites or

immunologic mechanisms.

- Possible dramatic pigment accumulation along the eyelid margins.
- Questionable association with systemic disease or stressful event (e.g., inflammatory bowel disease, lupus-like syndromes, upper respiratory tract infections).

Squamous Cell Carcinoma In Situ

- Multicentric premalignant dermatosis in old cats.
- Associated with papilloma virus; Bowenoid *in situ* carcinoma.
- Slightly elevated, often pigmented, plaque-like or papillated lesions with scaling and partially alopecic surfaces.
- Often misdiagnosed as seborrhea before distinct lesions develop.
- About 25% may convert to squamous cell carcinoma *in situ* lesions along the borders (histologically).

Epitheliotropic Lymphoma

- Early stages—varying degrees of alopecia associated with scaling and erythema.
- Later stages—plaques and nodules.
- Old cats.

Alopecia Areata/Pseudopelade/Lymphocytic Mural Folliculitis (Lymphocytic Invasion of the Hair Follicle)

- Often associated with an immunologic inciting cause; may occasionally be pre-neoplastic.
- Alopecia areata—rare; complete alopecia in a patchy distribution with no inflammation; head, neck, ears; histologic lymphocytic accumulation around the hair bulb.
- Lymphocytic mucinotic mural folliculitis—diffuse alopecia of the face, eyelids, muzzle; skin has a thick waxy feel; histologic lymphocytic invasion of the follicular outer root sheath and epidermis.
- Pseudopelade—well-circumscribed non-pruritic alopecia that often starts on the face; nails may slough; lymphocytic invasion of the isthmus region of the hair follicle.

Feline Cutaneous Lymphocytosis (Pseudolymphoma)

- Characterized by dermal lymphocytic infiltrate rather than follicular or epidermal.
- Older cats; often solitary lesions of partial alopecia with scaling ± erythema and pruritus.

Alopecia Universalis (Sphynx Cat)

- Hereditary.
- Complete absence of primary hairs; decreased secondary hairs.
- Thickened epidermis; normal dermis.
- Sebaceous and apocrine ducts open directly onto the skin surface; oily feel to skin.
- Wrinkled foreheads; gold eyes; no whiskers; downy fur on paws, tip of tail, and scrotum.
- Comedones with or without secondary folliculitis.

Feline Hypotrichosis

- Siamese and Devon Rex cats (autosomal recessive alopecia).
- Poorly developed primary telogen hair follicles.
- Born with a normal coat; becomes thin and sparse as young adult.

ALOPECIA—CATS

(CONTINUED)

Spontaneous Pinnal Alopecia

- Siamese cats predisposed. • May represent a form of alopecia areata or pattern baldness.

Anagen and Telogen Defluxion

- Acute loss of hair due to interference with the growth cycle. • Causes—stress, infection, endocrine disorder, metabolic disorder, fever, surgery, anesthesia, pregnancy, drug therapy.

Demodocosis

- Rare. • Partial to complete multifocal alopecia of the eyelids, periocular region, head, and neck; can generalize. • Variable pruritus with erythema, scale, and crust, and ceruminous otitis externa. • *Demodex cati* (elongated shape) often associated with metabolic disease (e.g., FIV, systemic lupus erythematosus, diabetes mellitus).
- Short/blunted *D. gatoi* mite is rarely a marker for metabolic disease; this form may be transferable from cat to cat and has been associated with pruritus most often affecting the lateral thorax and abdomen.

Cheyletiellosis

- Variable pruritus with scaling. • Not all animals in the household may be affected.

Dermatophytosis

Numerous clinical manifestations; always associated with alopecia.

CBC/BIOCHEMISTRY/URINALYSIS

Abnormalities may be noted with diabetes mellitus, hyperadrenocorticism, and hyperthyroidism.

OTHER LABORATORY TESTS

- FeLV and FIV—risk factors for demodicosis. • Thyroid hormones—document hyperthyroidism. • ANA titer—look for systemic lupus erythematosus.
- ACTH-response test, LDDST, and HDDST—diagnose hyperadrenocorticism.

IMAGING

- Abdominal ultrasound—assess adrenals in hyperadrenocorticism and look for neoplasia in animals with paraneoplastic syndrome.
- Chest radiographs/ultrasound to rule out thymoma. • CT scan—look for pituitary or other neoplasia tumors in animals with hyperadrenocorticism.

DIAGNOSTIC PROCEDURES

- Skin biopsy • Skin scrapes • Dermatophyte culture • Shirts/collar to prove self-trauma
- Food elimination trials • Intradermal allergy test

**TREATMENT**

- Therapy is specific for many of these disorders. • Behavioral modification or protecting hair coat with a shirt may prevent self-barbering. • Removal of an offending dietary item may alleviate the symptoms of food allergy. • If the pet is compliant,

shampoo and topical therapy may relieve secondary problems, such as hyperkeratosis in sebaceous adenitis, crusting in demodicosis, secondary bacterial infection, and malodor for greasy dermatoses.

**MEDICATIONS****DRUG(S)**

- Compulsive disorder—amitriptyline (10 mg/cat/day) as well as other behavior-modifying medications, such as gabapentin (5–10 mg/kg PO q12h).
- Endocrine alopecia (males)—testosterone supplementation.
- Allergic dermatitis—antihistamines, restricted-ingredient diet, corticosteroids, cyclosporine (7.3 mg/kg/day initially), allergen-specific immunotherapy, ectoparasite control.
- Hyperthyroidism—methimazole (tapazole) or radioactive iodine therapy.
- Diabetes mellitus—regulation of glucose levels (insulin).
- Hyperadrenocorticism—surgery; no known effective medical therapy.
- Paraneoplastic alopecia—no therapy or surgical excision of neoplasia; often fatal.
- Epitheliotropic lymphoma—retinoids (isotretinoin), corticosteroids, interferon, cyclosporine, lomustine.
- Sebaceous adenitis—retinoids, corticosteroids, cyclosporine.
- Squamous cell carcinoma in situ—surgical excision, retinoids (topical and oral), topical imiquimod cream.
- Alopecia areata—no therapy; possibly counterirritants.
- Demodicosis—lime sulfur dips at weekly intervals for four to six dips.
- Cheyletiellosis—topical parasiticides and environmental control.
- Dermatophytosis—griseofulvin (caution: idiosyncratic toxicity), itraconazole (hepatic toxicity, vasculitis), terbinafine.

PRECAUTIONS

Toxicity with griseofulvin and itraconazole (see Dermatophytosis).

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

Determined by specific diagnosis

PREVENTION/AVOIDANCE

Determined by specific diagnosis

POSSIBLE COMPLICATIONS

Determined by specific diagnosis

EXPECTED COURSE AND PROGNOSIS

Determined by specific diagnosis

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

- Dermatophytosis—can cause skin lesions in humans. • Cheyletiellosis—can cause irritation in humans.

PREGNANCY/FERTILITY/BREEDING

Retinoids and griseofulvin should not be administered to pregnant animals.

SEE ALSO

- Cheyletiellosis • Demodicosis
- Dermatophytosis • Diabetes Mellitus without Complication, Cats • Feline Paraneoplastic Alopecia • Hyperthyroidism
- Sebaceous Adenitis, Granulomatous

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone
- ANA = antinuclear antibody • CT = computed tomography • FeLV = feline leukemia virus • FIV = feline immunodeficiency virus • HDDST = high-dose dexamethasone-suppression test
- LDDST = low-dose dexamethasone-suppression test

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Client Education Handout
available online



BASICS

DEFINITION

- Common disorder.
- Characterized by a complete or partial loss of hair in areas where it is normally present.
- May be associated with multiple causes, be the primary problem, or be secondary to an underlying cause.

PATOPHYSIOLOGY

- Multiple causes.
- Represents removal of hair or disruption in the growth of the hair from hypersensitivity, infection, trauma, immunologic attack, mechanical “plugging,” endocrine abnormalities, neoplasia, drug reaction and/or blockage of the receptor sites for stimulation of the hair growth cycle.

SYSTEMS AFFECTED

- Endocrine/Metabolic
- Hemic/Lymphatic/Immune
- Skin/Exocrine

SIGNALMENT

Breed predilection listed below

SIGNS

- May be acute in onset or slowly progressive.
- Multifocal patches of circular alopecia—most frequently associated with folliculitis from bacterial infection and multifocal areas of demodicosis.
- Large, more diffuse areas of alopecia—may indicate a follicular dysplasia or metabolic component.
- The pattern and degree of hair loss are important for establishing a differential diagnosis.

CAUSES

Multifocal

- Localized demodicosis—partial to complete alopecia with erythema comedones, and mild scaling; lesions may become inflamed and crusted.
- Dermatophytosis—partial to complete alopecia with scaling; with or without erythema; not always ring-like.
- Staphylococcal folliculitis—circular patterns of alopecia with epidermal collarettes, erythema, crusting, and hyperpigmented macules.
- Injection reactions—inflammation with alopecia and/or cutaneous atrophy from scarring.
- Rabies vaccine vasculitis—well-demarcated patch of alopecia observed 2–3 months post-vaccination.
- Localized scleroderma—well-demarcated, shiny, smooth, alopecic, thickened plaque; extremely rare; still considered a controversial diagnosis.
- Alopecia areata—non-inflammatory areas of complete alopecia.

- Sebaceous adenitis of short-coated breeds (now termed “idiopathic periadnexal pyogranulomatous dermatitis”)—annular to polycyclic areas of alopecia and scaling.

Symmetrical

- Hyperadrenocorticism—truncal alopecia associated with atrophic skin, comedones, and pyoderma.
- Hypothyroidism—thinning of truncal haircoat; generalized alopecia is an uncommon presentation; alopecic “rat” tail.
- Non-inflammatory alopecia (alopecia X)—symmetrical truncal alopecia associated with hyperpigmentation; alopecia often starts along the collar area of the neck; Pomeranian, chow chow, Akita, Samoyed, Keeshonden, Alaskan malamute, and Siberian husky.
- Hyperestrogenism (females)—symmetrical alopecia of the flanks and perineal and inguinal regions with enlarged vulva and mammary glands; may also be associated with exogenous hormone exposure.
- Hypogonadism in intact females—perineal, flank, and truncal alopecia.
- Testosterone-responsive dermatosis in castrated males—slowly progressive truncal alopecia.
- Male feminization from Sertoli cell tumor—alopecia of the perineum and genital region with gynecomastia.
- Castration-responsive dermatosis—hair loss in the collar area, rump, perineum, and flanks.
- Estrogen-responsive dermatosis in spayed female dogs—alopecia of the perineum and genital regions.
- Seasonal/cyclic/canine flank alopecia—serpiginous flank alopecia with hyperpigmentation; boxer, English bulldog, Airedale terrier.

Patchy to Diffuse

- Demodicosis—often associated with erythema, folliculitis, and hyperpigmentation.
- Bacterial folliculitis—multifocal areas of circular alopecia to coalescing large patches of hair loss; epidermal collarettes.
- Dermatophytosis—often accompanied by scale, erythema, and hyperpigmentation.
- Sebaceous adenitis—alopecia with a thick adherent scale; predominantly on the dorsum of the body, including the head and extremities.
- Color mutant/dilution alopecia—brittle or coarse hair, thinning of the blue or fawn colored hair coat, and secondary folliculitis.
- Follicular dysplasia—slowly progressive alopecia.
- Anagen defluxion and telogen defluxion—acute onset of alopecia.
- Hypothyroidism—diffuse thinning of the hair coat.
- Hyperadrenocorticism—truncal alopecia with thin skin and formation of comedones.
- Epitheliotropic lymphoma—diffuse, generalized truncal alopecia with scaling and intense erythema, later nodule and plaque formation.

- Pemphigus foliaceus—hair loss associated with scale and crust formation.
- Keratinization disorders—alopecia associated with excessive scale and greasy surface texture.

Specific Locations

- Pinnal alopecia/pattern baldness—miniaturization of hairs and progressive alopecia; dachshund, greyhound, American water spaniel, Portuguese water spaniel, Boston terrier, Manchester terrier, whippet, Italian greyhound, Chihuahua.
- Traction alopecia—hair loss on the top and lateral aspect of the cranium secondary to having barrettes or rubber bands applied to the hair.
- Post-clipping alopecia—failure to regrow after clipping; may be associated with hair growth cycle disruption.
- Melanoderma (alopecia of Yorkshire terriers)—symmetrical alopecia of the pinnae, bridge of the nose, tail, and feet.
- Seasonal/cyclic/canine flank alopecia—serpiginous flank alopecia with hyperpigmentation; boxer, English bulldog, Airedale terrier.
- Black hair follicular dysplasia—alopecia of the black-haired areas only.
- Dermatomyositis—alopecia of the face, tip of ears, tail, and digits; associated with scale crusting and scarring.

Breed-Related Alopecia

- Alopecic breeds: Chinese crested, Mexican hairless, Inca hairless, Peruvian Inca Orchid, American hairless terrier (often associated with comedones, folliculitis, and furunculosis).
- Congenital hypotrichosis: cocker spaniel, Belgian shepherd, poodle, whippet, beagle, French bulldog, Yorkshire terrier, Labrador retriever, bichon frise, Lhasa apso, basset hound.
- Color dilution alopecia: blue or fawn Doberman pinscher, silver Labrador, cream chow chow, blond Irish setter, blue pit bull terrier, other breeds with dilute coat colors.
- Melanoderma with alopecia in Yorkshire terrier.
- Seasonal/cyclic/canine flank alopecia—serpiginous flank alopecia with hyperpigmentation; boxer, English bulldog, Airedale terrier.
- Pinnal alopecia/pattern baldness—miniaturization of hairs and progressive alopecia; dachshund, greyhound, American water spaniel, Portuguese water spaniel, Boston terrier, Manchester terrier, whippet, Italian greyhound, Chihuahua.
- Non-inflammatory alopecia (alopecia X)—symmetrical truncal alopecia associated with hyperpigmentation; alopecia often starts along the collar area of the neck; Pomeranian, chow chow, Akita, Samoyed, Keeshonden, Alaskan malamute, and Siberian husky.

ALOPECIA—DOGS

(CONTINUED)

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pattern and degree—important features for formulating a differential diagnosis.
- Inflammation, scale, crust, and epidermal collarettes—important for determining diagnosis.

CBC/BIOCHEMISTRY/URINALYSIS

Rule out metabolic causes such as hyperadrenocorticism

OTHER LABORATORY TESTS

- Thyroid testing—diagnose hypothyroidism.
- ACTH-response test, LDDST, and HDDST—evaluate for hyperadrenocorticism.
- Sex hormone profiles (questionable validity).

IMAGING

Ultrasonography—evaluate adrenal glands for evidence of hyperadrenocorticism.

DIAGNOSTIC PROCEDURES

- Response to therapy as a trial
- Fungal culture
- Skin scraping
- Cytology
- Skin biopsy—very useful to evaluate status of follicle/hair growth as well as epidermal changes associated with specific conditions.



TREATMENT

- Demodicosis—amitraz, ivermectin, milbemycin.
- Dermatophytosis—griseofulvin, ketoconazole, itraconazole, lime sulfur dips, terbinafine.
- Staphylococcal folliculitis—shampoo and antibiotic therapy.
- Sebaceous adenitis—keratolytic shampoo, essential fatty acid supplementation, retinoids, cyclosporine.
- Keratinization disorders—shampoos, retinoids, vitamin D, cyclosporine.
- Endocrine—ovariohysterectomy, castration, Lysodren, trilostane, adrenalectomy.



MEDICATIONS

DRUG(S) OF CHOICE

Varies with specific cause; see "Treatment."

CONTRAINDICATIONS

N/A

PRECAUTIONS

Toxicity with griseofulvin, retinoids, ivermectin, trilostane, lysodren, cyclosporine.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

Determined by cause

POSSIBLE COMPLICATIONS

N/A



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

Dermatophytosis can cause skin lesions in people.

PREGNANCY/FERTILITY/BREEDING

Avoid retinoids and griseofulvin in pregnant animals.

SEE ALSO

- Alopecia, Non-inflammatory—Dogs
- Demodicosis
- Dermatomyositis
- Dermatophytosis
- Hyperadrenocorticism (Cushing's Syndrome)—Dogs
- Hypothyroidism
- Pemphigus

- Sebaceous Adenitis, Granulomatous

- Sertoli Cell Tumor

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone
- HDDST = high-dose dexamethasone-suppression test
- LDDST = low-dose dexamethasone-suppression test

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available online



BASICS

DEFINITION

- Uncommon alopecic disorders that are associated with abnormal hair follicle cycling.
- Both endocrine and non-endocrine diseases can be associated with alopecia.
- Definitive diagnosis often requires ruling out the more common endocrine alopcias.
- Alopecia X has also been called growth hormone-responsive alopecia, castration-responsive alopecia, adrenal hyperplasia-like syndrome, among others.

PATOPHYSIOLOGY

- There are many factors that affect the hair cycle, both hormonal and non-hormonal.
- Increased sex hormones can affect the hair cycle. Estrogen is a known inhibitor of anagen, the growth phase of the hair follicle.
- The mechanism by which alopecia X influences the hair cycle is not known.
- Exposure to human exogenous hormone replacement therapy.

SYSTEMS AFFECTED

- Behavioral
- Endocrine/Metabolic
- Hemic/Lymphatic/Immune
- Skin/Exocrine

GENETICS

Breed predispositions exist for alopecia X; however, the mode of inheritance is unknown.

INCIDENCE/PREVALENCE

- Hyperestrogenism and hyperandrogenism are uncommon to rare causes of alopecia.
- Alopecia X is relatively common in predisposed breeds.

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dogs

Breed Predilections

- Hyperestrogenism and hyperandrogenism—no breed predilections.
- Alopecia X—miniature poodle and plush-coated breeds such as Pomeranian, chow chow, Akita, Samoyed, Keeshonden, Alaskan malamute, and Siberian husky.

Mean Age and Range

- Hyperestrogenism and hyperandrogenism—middle-aged to old intact dogs.
- Alopecia X—1–5 years of age; however, older dogs may develop the condition.

Predominant Sex

- Hyperandrogenism, primarily intact males.
- Hyperestrogenism, primarily intact females or males.
- Alopecia X, neutered or intact dogs of either sex.

SIGNS

Historical Findings

- Overall change in the hair coat—dry or bleached because the hairs are not being replaced; lack of normal shed.
- Males with hyperestrogenism may attract other male dogs.

Physical Examination Findings

- Alopecia—usually diffuse and bilaterally symmetrical truncal alopecia sparing the head and distal extremities. Uncommon with hyperandrogenism.
- Hair coat—may be dry or bleached.
- Secondary seborrhea, pruritus, pyoderma, comedones, ceruminous otitis externa, and hyperpigmentation—variable.
- Enlargement of nipples, mammary glands, vulva, prepuce—may be associated with hyperestrogenism.
- Macular melanosis and linear preputial dermatitis—may be associated with hyperestrogenism.
- Abnormal-sized or different-sized testicles—may be associated with hyperestrogenism or hyperandrogenism.
- Testicles may also appear normal in size.
- Tail gland hyperplasia and perianal gland hyperplasia—usually associated with hyperandrogenism.
- Systemic signs (PU/PD/polyphagia) are usually NOT present.

CAUSES

Hyperestrogenism—Females

- Estrogen excess associated with cystic ovaries, ovarian tumors (rare), or exogenous estrogen supplementation.
- Animals with normal serum estrogen concentrations may have increased numbers of estrogen receptors in the skin (undocumented).

Hyperestrogenism—Males

- Estrogen excess due to Sertoli cell tumor (most common), seminoma, or interstitial cell tumor (rare).
- Associated with male pseudohermaphroditism in miniature schnauzers.

Hyperandrogenism—Males

Androgen-producing testicular tumors (especially interstitial cell tumors).

Alopecia X

Hairs fail to cycle but an underlying endocrine cause has not been identified.

RISK FACTORS

- Intact male and female dogs are at increased risk for developing testicular tumors and ovarian cysts/tumors, respectively.
- Cryptorchid males are at increased risk for developing testicular tumors.
- Exogenous estrogen supplementation.
- Exposure to human exogenous hormone replacement therapy.
- There are no known risk factors for alopecia X other than breed predisposition.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Inflammatory causes of alopecia (pyoderma, demodicosis, and dermatophytosis)—should be ruled out; these diseases usually cause a patchy rather than diffuse pattern of alopecia.
- Sebaceous adenitis—an inflammatory cause of alopecia that may affect specific breeds (Samoyed, Akita).
- Hypothyroidism and hyperadrenocorticism—critical to rule out as these diseases may cause a very similar pattern of diffuse alopecia associated with lack of hair follicle cycling.
- Follicular dysplasias including color-dilution alopecia and black hair follicular dysplasia—alopecia should be color-restricted.
- Patterned alopecia of various breeds (dachshund, Boston terrier, greyhound, water spaniel, and others)—breed-specific alopcias of unknown cause.
- Seasonal/cyclic/canine flank alopecia—alopecia of the flank and dorsum, often serpiginous patterns with hyperpigmentation, more often in short-coated breeds (boxer, English bulldog, Airedale) and may recur seasonally.
- Post-clipping alopecia—hair fails to regrow following clipping; however, hair regrowth occurs within a year.
- Telogen defluxion—alopecia occurs 1–2 months following an illness or severe stressful episode and is usually more sudden in onset with relative ease of epilation.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually unremarkable.
- Anemia and/or bone marrow hypoplasia or aplasia can be associated with hyperestrogenism.

OTHER LABORATORY TESTS

- Serum sex hormone concentrations—often normal, treat according to suspected diagnosis based on clinical signs and ruling out other disorders.
- Serum estradiol concentrations—sometimes elevated in male dogs with testicular tumors or female dogs with cystic ovaries; however, normal fluctuation of estradiol occurs throughout the day, making interpretation of estradiol concentrations difficult.

IMAGING

Radiography, ultrasonography, and laparoscopy—identify cystic ovaries, ovarian tumors, testicular tumors (scrotal or abdominal), adrenal tumors, sublumbar lymphadenopathy, and possible thoracic metastases of malignant tumors.

DIAGNOSTIC PROCEDURES

- Preputial cytology—may demonstrate cornification of cells in males with hyperestrogenism (similar to a bitch in estrus).
- Skin biopsy.

ALOPECIA, NON-INFLAMMATORY—DOGS

(CONTINUED)

PATHOLOGIC FINDINGS

Histologic changes associated with endocrine dermatoses (telogen hairs, follicular keratoses, hyperkeratosis, excess trichilemmal keratinization [flame follicles], thin epidermis and thin dermis) may also be seen with non-inflammatory alopecias including hyperestrogenism and alopecia X. Histopathology will help rule out inflammatory causes of alopecia (pyoderma, demodicosis, dermatophytosis, sebaceous adenitis) and some of the other differentials listed above.

**TREATMENT****APPROPRIATE HEALTH CARE**

N/A

NURSING CARE

N/A

ACTIVITY

None

DIET

None

CLIENT EDUCATION

Alopecia X is a cosmetic condition resulting in coat loss only and there is no definitive cure for the hair loss. The risk of treatment should be emphasized. Hair regrowth will only occur in a portion of dogs regardless of treatment chosen and hair loss may recur months to years later in spite of continued treatment.

SURGICAL CONSIDERATIONS***Hyperestrogenism/Hyperandrogenism***

- Castration—scrotal testicular tumors.
- Exploratory laparotomy—diagnosis and surgical removal (ovariohysterectomy and castration) for ovarian cysts and tumors and abdominal testicular tumors.

Alopecia X

Neuter intact animals—a certain number will regrow hair following neutering. Hair regrowth can take up to 3 months to become evident.

**MEDICATIONS****DRUG(S) OF CHOICE*****General Treatments***

- Topical antiseborrheic shampoos—for comedones and seborrhea associated with alopecia.
- Antibiotics and topical antimicrobial shampoos—for secondary skin infections associated with alopecia.

Alopecia X

• Melatonin—3 mg q12h for small breeds and 6–12 mg q12h for large breeds; hair regrowth can take up to 3 months to become evident.

This treatment works in approximately 40% of cases. Because this treatment is the most benign, it is considered the treatment of choice following neutering. Once hair regrowth has occurred, discontinue treatment.

- Medroxyprogesterone acetate – 5–10 mg/kg SC q4 weeks for 4 treatments. Hair regrowth can take up to 6 months. This treatment works in approximately 40–50% of cases.

CONTRAINDICATIONS

None

PRECAUTIONS

- Melatonin at high doses can cause insulin resistance; therefore, use caution in treating dogs with diabetes mellitus.
- Medroxyprogesterone acetate can cause mammary nodules and cystic endometrial hyperplasia with long term use. Diabetes mellitus has been reported in a few dogs.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

- Mitotane—15–25 mg/kg—once daily as induction for 5–7 days, followed by twice weekly maintenance; hair regrowth occurs in a portion of dogs treated and can take up to 3 months to become evident. Use of this drug can result in an Addisonian crisis and other side effects as for treatment of Cushing's syndrome. Electrolytes and cortisol with ACTH stimulation testing should be monitored regularly.
- Trilostane—dosages as described for treatment of Cushing's syndrome; hair regrowth occurs in a portion of dogs treated and can take up to 3 months to become evident. Use of this drug can result in an Addisonian crisis and other side effects as for treatment of Cushing's syndrome. Electrolytes and cortisol with ACTH stimulation testing should be monitored regularly.
- Growth hormone administration and methyltestosterone may result in hair regrowth. Growth hormone can cause diabetes mellitus. Methyltestosterone can result in increased aggression, cholangiohepatitis, and seborrhea oleosa. Therefore, these drugs are not recommended.

**FOLLOW-UP****PATIENT MONITORING**

- Medroxyprogesterone acetate—complete physical examination and chemistry panel regularly.
- Mitotane—electrolytes and cortisol with ACTH stimulation testing regularly.
- Trilostane—electrolytes and cortisol with ACTH stimulation testing regularly.

PREVENTION/AVOIDANCE

None

POSSIBLE COMPLICATIONS

None

EXPECTED COURSE AND PROGNOSIS

- Female hyperestrogenism—improvement should occur within 3–6 months after ovariectomy.
- Estrogen- and androgen-secreting tumors—resolution of signs should occur within 3–6 months after castration.
- Alopecia X—hair regrowth will only occur in a portion of dogs regardless of treatment chosen and hair loss may recur in spite of continued treatment. Therefore, if hair regrowth occurs, discontinue treatment to preserve treatment for future recurrence of the alopecia. Risk of treatment should be weighed with the fact that this is a cosmetic disease.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Pyoderma, seborrhea, comedones may be associated with the alopecia.
- Behavioral changes associated with hyperestrogenism or hyperandrogenism.

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A—neutering is usually recommended for managing these conditions.

SYNOMYMS

Alopecia X—growth hormone-responsive alopecia, castration-responsive alopecia, adrenal hyperplasia-like syndrome, among others.

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone
- PU/PD = polyuria/polydipsia

INTERNET RESOURCES

<http://www.vet.utk.edu/hairloss/>

Suggested Reading

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available online



BASICS

OVERVIEW

- Facultative parasitic amoeba that infects people and non-human primates, including dogs and cats.
- Found primarily in tropical areas throughout the world, including North America.

SIGNALMENT

- Dog and cat.
- Mainly young and/or immunosuppressed animals are infected.

SIGNS

Dogs

- *Entamoeba histolytica* infections are usually asymptomatic.
- Severe infections—result in ulcerative colitis to cause dysentery (may be fatal).
- Hematogenous spread—results in failure states of the organs (invariably fatal).
- Granulomatous amoebic meningoencephalitis (caused by *Acanthamoeba* spp.)—causes signs similar to distemper (anorexia, fever, lethargy, oculonasal discharge, respiratory distress, and diffuse neurologic abnormalities).
- Syndrome of inappropriate secretion of antidiuretic hormone has been reported in a young dog with acanthamoebiosis causing granulomatous meningoencephalitis with invasion of the hypothalamus.

Cats

- Colitis—causing chronic intractable diarrhea (as per dogs).
- Systemic amebiasis or *Acanthamoeba*—not reported in cats.

CAUSES & RISK FACTORS

- *Entamoeba histolytica*—infection occurs by ingesting cysts from human feces.
- Encystment of trophozoites seldom occurs in dogs or cats so they are not a source of infection.
- One of the few organisms transmitted from man to pets but rarely from pets to man.
- Trophozoites (the pathogenic stage)—inhabit the colonic lumen as commensals or invade the colonic wall but can disseminate to other organs (rare) including lungs, liver, brain, and skin.
- Trophozoites damage intestinal epithelial cells by secreting enzymes that lyse cells and disrupt intercellular connections.
- Certain bacteria and a diet deficient in protein increase the virulence of the amoeba.
- The host's immune response to invasion exacerbates pathology.
- Colonic ulceration results when trophozoites in the submucosa undermine the mucosa.
- *Acanthamoeba castellani* and *A. culbertsoni*—free-living species found in freshwater, saltwater, soil, and sewage; can infect dogs.
- *Acanthamoeba* spp.—infection thought to be by inhalation of organisms from contaminated water or colonization of the skin or cornea; hematogenous spread or

direct spread from the nasal cavity through the cribiform plate to the central nervous system may occur, resulting in a granulomatous amoebic meningoencephalitis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Dogs

- Causes of bloody diarrhea or tenesmus, including constipation; food intolerance/allergy; parasitism (whip worms, leishmaniasis, balantidiasis); HGE; foreign body; irritable bowel syndrome; inflammatory bowel disease; diverticula; infectious (parvovirus, clostridial enteritis, bacterial overgrowth and other bacterial causes, fungal such as histoplasmosis or blastomycosis); neoplasia; ulcerative colitis; endocrinopathy (Addison's disease); toxic (lead, fungal, or plant); occasionally major organ disease causing colonic ulceration such as renal failure.
- Other causes of diffuse neurologic disease in young animals, including infectious (distemper, fungal such as *Cryptococcus*, *Blastomyces*, *Histoplasma*, bacteria, protozoa such as *Toxoplasma* and *Neospora*); toxic (lead, organophosphate); trauma; GME; extracranial (hypoglycemia; hepatic encephalopathy); inherited epilepsy; neoplasia.

Cats

- Other causes of diarrhea, including food intolerance/allergy; inflammatory bowel disease; parasitism (giardiasis, parasites such as hookworms, roundworms, trichomonas); infectious (panleukopenia, FIV, FeLV producing panleukopenia-like syndrome, bacterial including *Salmonella*, rarely *Campylobacter*); drug (acetaminophen); neoplasia; pancreatitis; and major organ dysfunction.

CBC/BIOCHEMISTRY/URINALYSIS

Normal; can reflect severe diarrhea.

OTHER LABORATORY TESTS

- Microscopic examination—colonic biopsies (H&E) obtained via endoscopy is the most reliable method.
- Trophozoites in feces—very difficult to detect; methylene blue staining improves chances.
- Trichrome and iron-hematoxyline—the ideal fecal stains but require a reference laboratory to perform.
- Fecal concentration techniques—no help.
- CSF—elevated WBC count (70% mononuclear cells), protein and xanthochromia in dogs with granulomatous amoebic meningoencephalitis due to *Acanthamoeba*.

IMAGING

MRI—shows brain granulomas.

DIAGNOSTIC PROCEDURES

Brain biopsy—required to definitively diagnose neurologic forms antemortem.



TREATMENT

- Colitis (caused by *E. histolytica*)—responds to metronidazole, although dogs continue to shed organisms.
- Systemic forms (particularly neurologic disease)—invariably fatal despite treatment.



MEDICATIONS

DRUG(S)

- Tinidazole (44 mg/kg PO q24h for 6 days) in dogs—found to be more effective than metronidazole in treating amebiasis in humans.
- Metronidazole (20 mg/kg PO q12h for 7 days).

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

High doses of metronidazole (usually > 30 mg/kg) for extended periods may cause neurologic signs in dogs.



FOLLOW-UP

Pets usually acquire infections from the same source as their owners; veterinarians must warn owners of possible risk.



MISCELLANEOUS

ABBREVIATIONS

- CSF = cerebrospinal fluid
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- GME = granulomatous meningoencephalopathy
- H&E = hematoxylin and eosin
- HGE = hemorrhagic gastroenteritis
- MRI = magnetic resonance imaging
- WBC = white blood cell

Suggested Reading

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Author Stephen C. Barr

Consulting Editor Stephen C. Barr

AMELOBLASTOMA



BASICS

OVERVIEW

- Common oral tumor of odontogenic (tooth structure) ectoderm origin.
- Biologically these tumors are benign histologically but possess locally invasive properties.
- Tumors may arise anywhere within the dental arcade.
- Several histologic subtypes exist with similar invasive behavior.

SIGNALMENT

- Middle-aged and old dogs
- Rare in cats

SIGNS

- Dogs may present with a smooth, firm, gingival mass that is usually non-ulcerated.
- It may be incidental finding during dental prophylaxis/procedures. If involving rostral dental arcade, incisor teeth can be displaced and enveloped by proliferative tissue.

CAUSES & RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Epulis
- Gingival hyperplasia
- Squamous cell carcinoma
- Amelanotic melanoma
- Plasma cell tumor
- Other tumors related to the odontogenic apparatus

CBC/BIOCHEMISTRY/URINALYSIS

Unaffected

OTHER LABORATORY TESTS

N/A

IMAGING

- Skull or dental radiographs may show bone lysis deep to the superficial mass. Not particularly useful for diagnostic or treatment planning.
- Regional and distant metastasis has not been described.
- Computed tomography is helpful for planning surgery or radiation therapy, especially in large or caudal tumors.

DIAGNOSTIC PROCEDURES

- Deep tissue biopsies are necessary and recommended for definitive diagnosis.
- Squamous cell carcinoma may be misdiagnosed as ameloblastoma.



TREATMENT

- Surgical excision such as hemi- or total mandibulectomy or maxillectomy with > 1–2 cm margins is recommended as a curative treatment option. Always submit resected tissue for histopathology, in order to confirm the original diagnosis, and evaluate soft tissue and bone margins.
- Radiation therapy may provide long-term control in large tumors, or when the owners decline surgery.
- Intralesional chemotherapy with bleomycin has been reported, but results are generally inferior to those of surgery or radiation.



MEDICATIONS

DRUG(S)

N/A

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

Careful oral examination at 1, 3, 6, 9, and 12 months after definitive treatment is recommended to monitor for local recurrence.



MISCELLANEOUS

Suggested Reading

Amory JT, Reetz JA, Sánchez MD et al.

Computed tomographic characteristics of odontogenic neoplasms in dogs. *Vet Radiol Ultrasound* 2014, 55(2):147–158.

Fiani N, Verstraete FJ, Kass PH, Cox DP.

Clinicopathologic characterization of odontogenic tumors and focal fibrous hyperplasia in dogs: 152 cases (1995–2005). *J Am Vet Med Assoc* 2011, 238(4):495–500.

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BASICS

OVERVIEW

- Amitraz—formamidine acaricide; applied topically to control ticks, mites, and lice.
- Amitraz-containing products (for dogs)—formulated as a 19.9% emulsifiable concentrate in 10.6-mL bottles for dilution and sponge-on; as a 9% impregnated 25-inch 27.5-g collar and an 18-inch 18.5-g collar; as a 14.34% component of a 0.023 fl. oz., 0.045 fl. oz., 0.113 fl. oz., 0.180 fl. oz., or 0.225 fl. oz. spot-on (discontinued); and as a 7.6% component of a 0.036 fl. oz., 0.072 fl. oz., 0.145 fl. oz., 0.217 fl. oz. spot-on
- Systems affected—nervous; cardiovascular; endocrine/metabolic (β cells of the pancreas); gastrointestinal.
- Clinical signs—most associated with α_2 -adrenoreceptor agonist.
- After high-dose oral administration (dogs)—peak plasma concentration reached at approximately 6 hours; elimination half-life as long as 24 hours; metabolites excreted in the urine.
- Ingestion of sustained-release- impregnated collars—constant release and continued systemic exposure until collar segments have passed in the stool.
- Toxicosis—generally occurs when pieces of impregnated collar are ingested, when concentrated or improperly diluted solutions are applied topically, or when solutions are ingested or applied to the wrong size animal.
- Idiosyncratic reactions may occur.

SIGNALMENT

- Thorough history—usually identifies topical or collar use; topically missing collar or pieces seen in dog's environment or in the stool.
- Dogs—common, owing to more common use.
- Cats—more sensitive than dogs although cats are less likely involved.
- Predilection for old and toy-breed animals.

SIGNS

Historical Findings

Develop acutely after exposure (topical or oral)

Physical Examination Findings

- Minor to severe depression/lethargy
- Weakness
- Ataxia
- Bradycardia
- Vomiting (pieces of collar)
- Hyperthermia/hypothermia
- Hyperglycemia; diabetic patients can show significant hyperglycemia following exposure
- Hypotension
- Polyuria
- Gastrointestinal stasis

- Mydriasis
- Death (prognosis is typically good with treatment)

CAUSES & RISK FACTORS

- Ingestion of impregnated collar or pieces of collar.
- Inappropriate direct dermal application.
- Ingestion of undiluted product.
- After application of properly diluted and applied solutions—less common.
- Elderly, sick, toy-breed, or debilitated animals—may be predisposed.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Recreational and prescription drugs—marijuana; opioids; barbiturates; benzodiazepines; phenothiazines; antihypertensive medications; skeletal muscle relaxants; antidepressants (tricyclic, SSRIs), and other depressant drugs or chemicals.
- Ivermectins, avermectins, milbemycins—generally very high dose or exceptionally sensitive breed.
- Macadamia nuts, tea tree oil, and albuterol inhaler toxicosis.
- Alcohols—ethanol; ethylene glycol (antifreeze); methanol (windshield washer fluid); isopropyl alcohol (rubbing alcohol).
- Tick bite paralysis, botulism, cranial trauma, diabetes, hyperadrenocorticism, hypothyroidism, severe anemia, cardiac failure, and anaphylactic shock—marked depression or weakness.
- Depends on clinical signs, history of exposure, or evidence of exposure and elimination of other causes.

CBC/BIOCHEMISTRY/URINALYSIS

- Hyperglycemia—common, related to insulin inhibition
- Elevated liver enzymes—uncommon

IMAGING

Abdominal radiography—may reveal a collar buckle in the gastrointestinal tract; collar itself is not radioopaque..

DIAGNOSTIC PROCEDURES

Identify amitraz on hair or in gastrointestinal contents—analytical methods described; useful only to prove exposure; no data available correlating concentration with clinical signs.

PATHOLOGIC FINDINGS

High-dose, prolonged exposure—increased liver weight; slight enlargement of hepatocytes; thinning of the zonae fasciculata and reticularis; slight hyperplasia of the zona glomerulosa of the adrenal glands.



TREATMENT

- Inpatient—severely affected patients.
- Mild sedation after correctly applied sponge-on solutions—often transient; may require no treatment.
- Mild signs after topical application—wearing gloves, scrub with a hand dishwashing detergent; rinse with copious amounts of warm water; institute non-specific supportive therapy (e.g., intravenous fluids, maintenance of blood pressure and normal body temperature, nutritional support); monitor 1–2 days until improvement is noted.
- Ingestion of collar possible—endoscopic retrieval of the collar—removal of large segments from the stomach may be beneficial; usually numerous small pieces are located throughout the gastrointestinal tract, making removal unrealistic.



MEDICATIONS

DRUG(S)

Collar Ingestion, Asymptomatic Patient

- Emetic—3% USP hydrogen peroxide (2.2 mL/kg PO; maximum 45 mL after feeding a moist meal); apomorphine and especially xylazine not recommended.
- Activated charcoal has not been shown to be effective.
- Bulk diet (whole wheat bread, lactulose, pumpkin, psyllium husk [Metamucil]).
- Warm tap water enema (5–10 mL/kg); will stimulate GI motility and help pass pieces of collar through the GI tract.

Marked Depression

- May require pharmacologic reversal of the α_2 -adrenergic effects.
- Atipamezole (Antisedan) 0.05 mg/kg 1/4th IV 3/4th IM; reverse clinical signs within minutes; repeat as needed; preferred over yohimbine because of its higher alpha-2 activities.
- Yohimbine (Yobine) 0.11–0.2 mg/kg IV, administered slowly; reverses depression and bradycardia within minutes; improves GI motility; objective is to keep the patient in a state of low-level depression with normal heart rate, blood pressure, body temperature, and blood glucose concentrations.
- Collar ingestion—monitor for recurrence of symptoms; may need additional yohimbine until collar segments appear in the stool.
- Yohimbine and atipamezole—may require repeated administration (as needed) possibly every 2–8 hours, because their half-life in dogs is short and amitraz elimination half-life is longer.

AMITRAZ TOXICOSIS

(CONTINUED)

- Atropine contraindicated because of potentiation of GI stasis.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Yohimbine and atipamezole—excessive administration may result in apprehension, CNS stimulation, and rarely seizures.

**FOLLOW-UP**

- Body temperature, blood pressure, serum glucose, and heart rate—important parameters.

- Close observation for recurrence of clinical signs—required for 24–72 hours.
- Yohimbine and atipamezole—requires readministration in severe cases, because reversal effects subside before collar segments have passed or before amitraz has been eliminated from the body.
- No long-term adverse effects expected.

**MISCELLANEOUS****AGE-RELATED FACTORS**

- Elderly, sick, or debilitated animals may take longer to fully recover.

ABBREVIATIONS

- CNS = central nervous system
- GI = gastrointestinal
- SSRI = selective serotonin reuptake inhibitor

Suggested Reading

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AMPHETAMINE AND ADD/ADHD MEDICATION TOXICOSIS



BASICS

DEFINITION

Acute gastrointestinal, neurologic, neuromuscular, and cardiac toxicosis as the result of excessive consumption of amphetamine or a derivative. May be due to ingestion of prescription medications or illegal drugs.

PATOPHYSIOLOGY

- Amphetamine and its derivatives belong to the CNS stimulant class phenylethylamines. Various substitutions of the basic phenylethylamine structure account for many pharmaceutical and illicit compounds found today.
- Amphetamine is a sympathomimetic that is structurally related to norepinephrine.
- Central action—stimulates cortical centers including cerebral cortex, medullary respiratory center, and reticular activating systems.
- Peripheral action—directly stimulates alpha and beta receptors and stimulates the release of norepinephrine from stores in adrenergic nerve terminals.
- Amphetamine may slow catecholamine metabolism by inhibition of monoamine oxidase.
- Several different product formulations including immediate and extended release and topical patch.
- Amphetamines are well absorbed orally; peak plasma levels are generally reached in 1–3 hours; this may be delayed with extended release formulations.
- Metabolism is minimal.
- The half-life, which varies from 7–34 hours, and rate of excretion of unchanged amphetamine in the urine are both dependent upon urine pH, with shorter half-lives associated with more acidic urine.
- Clinical signs may be seen at doses below 1 mg/kg.
- Oral lethal dose in dogs for most amphetamines ranges from 10 mg/kg to 23 mg/kg and for methamphetamine sulfate it is 9–11 mg/kg. Oral lethal dose for amphetamine sulfate is 20–27 mg/kg.
- Amphetamine and its derivatives are used in humans to treat ADD/ADHD, narcolepsy, and obesity.
- Illicit use of amphetamines in humans is also prevalent.

SYSTEMS AFFECTED

- Cardiovascular—stimulation most common: tachycardia and hypertension.
- Nervous—stimulation most common, depression uncommon.
- Neuromuscular—stimulation: muscle tremors and seizures.
- Respiratory—stimulation, tachypnea.
- Ophthalmic—mydriasis.

- Gastrointestinal—anorexia, vomiting, diarrhea.

INCIDENCE/PREVALENCE

N/A

SIGNALMENT

Species

Dogs and cats, although more prevalent in dogs.

Breed Predilections

N/A

Mean Age and Range

N/A

Predominant Sex

N/A

SIGNS

Historical Findings

- Abnormal behavior—usually hyperactivity, anxiety or pacing, anorexia, fast heart rate, panting; observed or evidence of exposure by owner/caretaker.
- Onset of signs typically begins within 30 minutes to 6 hours post-ingestion; depends on product formulation.

Physical Examination Findings

- Nervous—hyperactivity, agitation, restlessness, head bobbing, pacing, circling, vocalization, disorientation, hyperesthesia, ataxia, lethargy or depression (less common).
- Cardiovascular—tachycardia or bradycardia (less common, may be reflexive), hypertension.
- Neuromuscular—muscle fasciculation or tremors, seizures.
- Gastrointestinal—vomiting, diarrhea, anorexia, excessive salivation.
- Respiratory—tachypnea.
- Ophthalmic—mydriasis with possibly poor to unresponsive pupillary light response.
- Other—hyperthermia.

CAUSES

Accidental ingestion or administration, malicious poisoning.

RISK FACTORS

Households with children or adults currently taking prescription or illicit amphetamine or derivative.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Strychnine
- Organochlorine insecticides
- Methylxanthine
- 4-aminopyridine
- Metaldehyde
- Phenylpropanolamine
- Albuterol
- Nicotine
- Tremorgenic mycotoxins
- Hypernatremia

- Pseudoephedrine, phenylephrine
- 5 fluorouracil
- Ma huang, guarana, or ephedra

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—disseminated intravascular coagulopathy secondary to severe hyperthermia (rare).
- Chemistry—
- Azotemia: prerenal—secondary to dehydration; renal—secondary to rhabdomylosis and myoglobinuria (rare).
- Elevated liver enzymes—secondary to seizures and/or hyperthermia (rare).
- Hypoglycemia.
- Urinalysis—evidence of myoglobinuria, urine specific gravity (high—prerenal azotemia; isosthenuria—renal failure).

OTHER LABORATORY TESTS

- Electrolytes—imbalances secondary to GI effects.
- Acid-base status—acidosis may occur.
- Over-the-counter urine drug screens—watch for false positive or negative. Consult user handbook for further information.
- Amphetamines are present in blood, urine, and saliva; consult with local veterinary diagnostic lab or human hospital for availability and proper sample submission.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- EEG for presence of any tachyarrhythmia or less commonly bradyarrhythmia.
- Blood pressure—identification of hypertension.

PATHOLOGIC FINDINGS

On necropsy presence of amphetamines may be found in the gastric contents, urine, plasma, liver, kidney, or muscle.



TREATMENT

APPROPRIATE HEALTH CARE

Majority of cases require emergency inpatient intensive care management.

NURSING CARE

- Intravenous fluid therapy to correct dehydration and electrolyte imbalances as well as support renal function and promote excretion of amphetamines. Use blood pressure to help guide fluid rate.
- Cool intravenous fluids, fans, cool water baths for hyperthermia.

ACTIVITY

Minimize activity and stimuli.

DIET

Withhold food if moderately to severely affected. Bland diet for a few days post-exposure if significant gastrointestinal signs were noted.

AMPHETAMINE AND ADD/ADHD MEDICATION TOXICOSIS (CONTINUED)

CLIENT EDUCATION

In case of an exposure, owner should contact local veterinarian or veterinary poison center immediately.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

Decontamination

- Induce emesis—if a recent exposure and pet is not already symptomatic.
- Apomorphine—0.04 mg/kg IV, subconjunctival.
- Hydrogen peroxide 3%—2.2 mL/kg, maximum dose 45 mL.
- Gastric lavage if extremely large ingestion or patient is already symptomatic.
- Activated charcoal with a cathartic.

CNS Signs of Stimulation

- Acepromazine 0.05–1.0 mg/kg IV or IM
- Chlorpromazine 0.5 mg/kg IV, titrate up as needed.
- Cyproheptadine (serotonin antagonist): dogs, 1.1 mg/kg orally or rectally, may be repeated q8h as needed for signs consistent with serotonin syndrome; cats, 2–4 mg/cat, may repeat q12h as needed for signs consistent with serotonin syndrome
- Methocarbamol (for muscle tremors): 50–220 mg/kg IV, titrate to effect. Do not exceed 330 mg/kg/day.

Cardiovascular Signs

- Tachyarrhythmia—beta blockers such as propranolol 0.02–0.04 mg/kg IV or esmolol or metoprolol.
- Ventricular premature contractions—lidocaine: dogs at 2–4 mg/kg IV (to maximum of 8 mg/kg over a 10-minute period). Cats—start with 0.1–0.4 mg/kg and increase cautiously to 0.25–0.75 mg/kg IV slowly if no response. Cats are reportedly very sensitive to lidocaine, so monitor carefully if used.

Promote Elimination

Ascorbic acid or ammonium chloride—for urinary acidification to promote elimination; however, only use if can measure acid-base status.

CONTRAINDICATIONS

- While diazepam has been successfully used to treat amphetamine exposures, there is evidence that benzodiazepines may intensify neurologic signs.
- Urinary acidification if unable to monitor acid-base status or if myoglobinuria is present.
- Inducing emesis in a symptomatic patient.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

- Amphetamines inhibit the metabolism of adrenergic blockers (doxazosin, phenoxybenzamine, prazosin, terazosin), phenobarbital, and phenytoin.
- Amphetamines potentiate the metabolism of coumarin anticoagulants, monoamine oxidase inhibitors, opioid analgesics, and tricyclic antidepressants.

ALTERNATIVE DRUG(S)

Phenobarbital, pentobarbital, and propofol for CNS stimulatory signs.



FOLLOW-UP

PATIENT MONITORING

- Monitor in hospital until resolution of clinical signs.
- If severely affected, monitor liver and kidney values every 24 hours for 72 hours or until resolution.

PREVENTION/AVOIDANCE

All medications and illicit drugs should be kept out of pets' reach at all times.

POSSIBLE COMPLICATIONS

Acute renal failure secondary to myoglobinuria or DIC (rare).

EXPECTED COURSE AND PROGNOSIS

- Expected course of clinical signs is 12–72 hours, depending on dose, product formulation, effectiveness of decontamination and treatment, and rate of elimination.
- Prognosis—most patients do well with prompt and appropriate veterinary care. Seizures or severe hyperthermia may be a poor prognostic indicator.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

Pets exposed to human waste products from those taking amphetamines or derivatives could become symptomatic.

PREGNANCY/FERTILITY/BREEDING

Amphetamines are a known teratogen in humans. They have been found to cross the placenta in animals and may also be found in milk.

SYNONYMS

- Common brand names of prescription amphetamine drugs and their active ingredient: Adderall (amphetamine and dextroamphetamine); Ritalin, Metadate, and Concerta (methylphenidate); Daytrana (methylphenidate transdermal patch); Focalin (dexmethylphenidate); Vyvanse (lisdexamfetamine), Cylert (pemoline), Adipex-P (phentermine), Dexedrine (Dextroamphetamine).
- Illicit drug street names: ice, glass, crank, speed, uppers, ecstasy, meth, and many others.

SEE ALSO

- Antidepressant Toxicosis—SSRIs and SNRIs
- Antidepressant Toxicosis—Tricyclics
- Pseudoephedrine/Phenylephrine Toxicosis

ABBREVIATIONS

- ADD = attention deficit disorder
- ADHD = attention deficit hyperactivity disorder
- CNS = central nervous system
- DIC = disseminated intravascular coagulation
- ECG = electrocardiogram
- GI = gastrointestinal

INTERNET RESOURCES

- <http://www.aspapro.org/animal-poison-control-center-articles.php>
- <http://www.aspca.org/pet-care/animal-poison-control>
- <http://www.petpoisonhelpline.com/>

Suggested Reading

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BASICS

DEFINITION

A group of conditions of diverse cause in which extracellular deposition of insoluble fibrillar proteins (amyloid) in various organs and tissues compromises their normal function.

PATHOPHYSIOLOGY

- Patients usually affected by systemic reactive amyloidosis; tissue deposits contain AA, which is a fragment of an acute-phase reactant protein called SAA.
- Phases of amyloid deposition:
 - Predeposition phase: SAA concentration is high but without amyloid deposits; colchicine administration during this phase may prevent development of the disease.
 - Deposition phase (rapid portion): amyloid deposits increase rapidly; colchicine administration delays but does not prevent tissue deposition of amyloid; DMSO may promote resolution of amyloid deposits and a persistent decrease in SAA concentration.
 - Deposition phase (plateau portion): net deposition of amyloid changes little; neither DMSO nor colchicine is beneficial.
- Clinical signs in dogs and cats usually are associated with amyloid deposition in the kidneys.
- Dogs—amyloid deposits usually found in the glomeruli leading to proteinuria and nephrotic syndrome.
- Cats—amyloid deposits usually found in the medullary interstitium but may occur in glomeruli.
- Some Chinese shar-pei dogs with familial amyloidosis have medullary amyloidosis without glomerular involvement.
- Siamese and Oriental shorthair cats with familial amyloidosis have hepatic amyloidosis.
- A different type amyloid, pancreatic islet amyloid polypeptide, or amylin, deposits in the pancreas of old cats. Amylin is a hormone secreted along with insulin by the pancreatic beta cells. Chronic increased stimulus for secretion of amylin by beta cells (e.g., states of insulin resistance) lead to pancreatic islet cell amyloidosis.

SYSTEMS AFFECTED

Renal/Urologic—predisposition for renal AA deposition. Liver, spleen, adrenal glands, pancreas, tracheobronchial tree, and gastrointestinal tract also may be affected.

GENETIC

(See “Breed Predilections.”) No genetic involvement is clearly established; familial amyloidosis occurs in Chinese shar-pei, English foxhound, and beagle dogs, and in Abyssinian, Oriental shorthair, and Siamese cats.

INCIDENCE/PREVALENCE

Uncommon, occurs mostly in dogs; rare in cats, except Abyssinians.

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Dog—Chinese shar-pei, beagle, collie, pointer, English foxhound, and walker hound; German shepherd dog and mixed breeds are at lower risk.
- Cat—Abyssinian, Oriental shorthair, and Siamese.

Mean Age and Range

- Cats—mean age at diagnosis 7 years; range 1–17 years.
- Dogs—mean age at diagnosis is 9 years; range 1–15 years. Chinese shar-pei dogs—median age at diagnosis is 5 years; range 3.6–17 years.
- Prevalence increases with age.
- Abyssinian cats—range <1–17 years.
- Chinese shar-pei dogs—usually <6 years of age when signs of renal failure develop.
- Siamese cats with familial amyloidosis of the liver and thyroid gland usually develop signs of liver disease when 1–4 years old.

Predominant Sex

Dogs and Abyssinian cats—females at a slightly higher risk (<2:1). Female-to-male ratio is higher in Chinese shar-pei dogs (~2.5:1).

SIGNS

General Comments

- Depend on the organs affected, the amount of amyloid, and the reaction of the affected organs to amyloid deposits.
- Usually caused by kidney involvement; occasionally, hepatic involvement may cause signs in Chinese shar-pei dogs and Oriental shorthair and Siamese cats.

Historical Findings

- No clear history of a predisposing disorder in most (~75%) cases.
- Anorexia, lethargy, polyuria and polydipsia, weight loss, vomiting.
- Ascites and peripheral edema in animals with nephrotic syndrome.
- Chinese shar-pei dogs may have a history of previous episodic joint swelling and high fever that resolves spontaneously within a few days.
- Beagle dogs with juvenile polyarteritis may have a history of fever and neck pain that persist for 3–7 days.
- Oriental shorthair and Siamese cats may present with spontaneous hepatic hemorrhage leading to acute collapse and hemoabdomen.

Physical Examination Findings

- Related to renal failure—oral ulceration, emaciation, vomiting, and dehydration; kidneys usually small, firm, and irregular in affected cats; they may be small, normal-sized, or slightly enlarged in affected dogs.
- Signs of nephrotic syndrome (e.g., ascites, subcutaneous edema).
- Related to the primary inflammatory or neoplastic disease process.
- Thromboembolic phenomena—may occur in up to 40% of affected dogs; signs vary with the location of the thrombus; patients may develop pulmonary

thromboembolism (e.g., dyspnea) or iliac or femoral artery thromboembolism (e.g., caudal paresis).

- Chinese shar-pei dogs and Oriental shorthair and Siamese cats may have signs of hepatic disease (e.g., jaundice, cachexia, and spontaneous hepatic rupture with intraperitoneal bleeding).

CAUSES

- Neoplasia and chronic infectious and non-infectious inflammatory conditions can be found in 30–50% of dogs with reactive amyloidosis.
- Chronic inflammation—systemic mycoses (e.g., blastomycosis, coccidioidomycosis), chronic bacterial infections (e.g., osteomyelitis, bronchopneumonia, pleuritis, steatitis, pyometra, pyelonephritis, chronic suppurative dermatitis, chronic suppurative arthritis, chronic peritonitis, nocardiosis, chronic stomatitis), parasitic infections (e.g., dirofilariasis, leishmaniasis, hepatozoonosis), and immune-mediated diseases (e.g., systemic lupus erythematosus). Amyloid deposits can be found in up to 35% of FIV-positive cats.
- Neoplasia (e.g., lymphoma, plasmacytoma, multiple myeloma, mammary tumors, testicular tumors).
- Familial (e.g., Chinese shar-pei, English foxhound, and beagle dogs; Abyssinian, Siamese, and Oriental shorthair cats).
- Others—cyclic hematopoiesis in gray collies; juvenile polyarteritis in beagles.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Dogs—GN; proteinuria tends to be more severe in dogs with glomerular amyloidosis than those with GN but there is great overlap.
- Cats and Chinese shar-pei dogs with medullary amyloidosis—consider other causes of medullary renal disease (e.g., pyelonephritis, chronic interstitial disease).

CBC/BIOCHEMISTRY/URINALYSIS

- Nonregenerative anemia is found in some dogs and cats with amyloid-induced renal failure.
- Dogs—may see hypercholesterolemia (> 85%), azotemia (> 70%), hypoalbuminemia (70%), hyperphosphatemia (> 60%), hypocalcemia (50%), and metabolic acidosis.
- Hypercholesterolemia—common finding in cats with renal disorders (> 70% of cats with renal disease in one study) but does not reliably predict glomerular disease.
- Hypoproteinemia—more common than hyperproteinemia (24 vs. 8.5%) in dogs with amyloidosis; hyperglobulinemia common in cats.
- Proteinuria—with an inactive sediment common in dogs; mild or absent in animals with medullary amyloidosis without glomerular involvement (most mixed-breed cats, at least 25% of Abyssinian cats, and at least 33% of Chinese shar-pei dogs). In a retrospective study with 91 cases of renal

AMYLOIDOSIS

(CONTINUED)

amyloidosis in dogs, hypoalbuminemia was more common in non-Chinese shar-pei dogs (100%) versus shar-pei dogs (65%).

- Isosthenuria, and hyaline, granular, and waxy casts in some patients.

OTHER LABORATORY TESTS

Proteinuria—urinary protein:creatinine ratio to estimate severity.

IMAGING

Abdominal Radiographic Findings

- Kidneys usually small in affected cats.
- Kidneys small, normal-sized, or large in affected dogs.

Abdominal Ultrasonographic Findings

Kidneys usually hyperechoic and small in affected cats; may be small, normal-sized, or large in affected dogs.

DIAGNOSTIC PROCEDURES

Renal biopsy needed to differentiate amyloidosis from GN. In dogs other than Chinese shar-pei, amyloidosis is primarily a glomerular disease; diagnose by renal cortical biopsy. In most domestic cats, some Abyssinian cats, and some Chinese shar-pei dogs, medullary amyloidosis can occur without glomerular involvement; diagnose by renal medullary biopsy.

PATHOLOGIC FINDINGS

• Small kidneys in cats; small, normal, or large kidneys in dogs. • Amyloid deposits appear homogeneous and eosinophilic when stained by hematoxylin and eosin and viewed by conventional light microscopy. They demonstrate green birefringence after Congo red staining when viewed under polarized light. Evaluation of Congo red—stained sections before and after permanganate oxidation permits presumptive diagnosis of AA amyloidosis (vs. other types) because AA amyloidosis loses its Congo red affinity after permanganate oxidation. • The liver is very friable and usually contains extensive amyloid deposits in cats presented with acute hepatic hemorrhage.



TREATMENT

APPROPRIATE HEALTH CARE

- Hospitalize patients with chronic renal failure and dehydration for initial medical management. • Can manage stable patients and those with asymptomatic proteinuria as outpatients.

DIET

- Patients with chronic renal failure—restrict phosphorus and moderately restrict protein.
- Patients with hypertension—restrict sodium.

CLIENT EDUCATION

- Discuss progression of the disease. • Discuss familial predisposition in susceptible breeds.



MEDICATIONS

DRUG(S) OF CHOICE

- Identify underlying inflammatory and neoplastic processes and treat if possible.
- Manage renal failure according to the principles of conservative medical treatment (see Renal Failure, Acute, and Renal Failure, Chronic).
- Normalize blood pressure in patients with hypertension (see Hypertension, Systemic).
- Patients with thromboembolic syndrome and nephrotic syndrome caused by glomerular amyloidosis usually have a low plasma concentration of antithrombin; thus heparin is relatively ineffective. Aspirin (0.5 mg/kg PO q12h) has been suggested for dogs with glomerular disease; this low dosage is as effective in preventing platelet aggregation as is 10 mg/kg PO q24h.
- DMSO—may help patients by solubilizing amyloid fibrils, reducing serum concentration of SAA, and reducing interstitial inflammation and fibrosis in the affected kidneys; may cause lens opacification in dogs. Perivascular inflammation and local thrombosis may occur if undiluted DMSO is administered intravenously. Subcutaneous administration of undiluted DMSO may be painful. The authors have used 90% DMSO diluted 1:4 with sterile water subcutaneously at a dosage of 90 mg/kg 3 times per week in dogs. Whether or not DMSO treatment benefits renal amyloidosis in dogs remains controversial.

- Methylsulfonylmethane is an active metabolite of DMSO that can be given orally and lacks the smell of DMSO. It has been used empirically in dogs with amyloidosis, but there is no evidence that it benefits dogs with renal amyloidosis.
- Colchicine—impairs release of SAA from hepatocytes; prevents development of amyloidosis in humans with familial Mediterranean fever (a familial amyloidosis) and stabilizes renal function in patients with nephrotic syndrome but without overt renal failure; no evidence of benefit once the patient develops renal failure; may cause vomiting, diarrhea, and idiosyncratic neutropenia in dogs. Colchicine (0.01–0.04 mg/kg PO q24h) is used particularly in shar-pei dogs with episodic fever or polyarthritis before development of renal failure.

PRECAUTIONS

- Dosage of drugs excreted by the kidneys may need adjustment in patients with renal failure. • Use nonsteroidal anti-inflammatory drugs cautiously in patients with medullary amyloidosis; they can decrease renal blood flow in dehydrated patients.



FOLLOW-UP

PATIENT MONITORING

- Appetite and activity level daily by the owner; body weight weekly. • Serum albumin, creatinine, and BUN concentrations every 2–6 months in stable patients. • Can assess degree of proteinuria serially by urine protein:creatinine ratios.

PREVENTION/AVOIDANCE

Do not breed affected animals.

POSSIBLE COMPLICATIONS

- Renal failure • Nephrotic syndrome
- Systemic hypertension • Hepatic rupture causing intraperitoneal hemorrhage
- Thromboembolic disease

EXPECTED COURSE AND PROGNOSIS

Disease is progressive and usually advanced at the time of diagnosis. Prognosis improves if an underlying immune, inflammatory, or neoplastic disease is detected and successfully treated. Survival for dogs with glomerular amyloidosis varied from 3 to 20 months in 1 study; some dogs may occasionally live longer. Cats with renal failure because of amyloidosis usually survive < 1 year. Mildly affected cats may not develop renal failure and have an almost normal life expectancy.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Urinary tract infection • Polyarthritis in Chinese shar-pei • Polyarteritis in beagle

SEE ALSO

- Glomerulonephritis • Nephrotic Syndrome Proteinuria • Renal Failure, Acute • Renal Failure, Chronic

ABBREVIATIONS

- AA = amyloid A protein • DMSO = dimethylsulfoxide • GN = glomerular nephritis • SAA = serum amyloid A protein

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Client Education Handout
available online



BASICS

OVERVIEW

- Anaerobic bacteria (i.e., bacteria requiring low oxygen tension) comprise a large portion of the normal flora, especially on mucosal surfaces.
- May be Gram-positive or Gram-negative cocci or rods.
- Most common genera—*Bacteroides*, *Fusobacterium*, *Actinomyces*, *Propionibacterium*, *Pectostreptococcus* (enteric *Streptococcus*), *Porphyromonas*, and *Clostridium*.
- Most anaerobic infections are polymicrobial and contain at least two different anaerobe species admixed with facultative anaerobes or aerobic bacteria (especially *E. coli*).
- Individual organisms vary in potential to withstand oxygen exposure.
- Injurious toxins and enzymes may be elaborated by the organisms, leading to extension of the infection into adjacent, healthy tissue.
- All body systems are at potential risk for anaerobic infection.

SIGNALMENT

Dog and cat

SIGNS

General Comments

- Determined by the body system involved.
- Certain areas more commonly associated with anaerobic infection (mucous membrane proximity).
- It is possible to overlook anaerobes in an infectious process, leading to confusion in interpreting culture results and selection of antimicrobials.

Physical Examination Findings

- A foul odor associated with a wound or exudative discharge.
- Gas in the tissue or associated exudates.
- Discolored tissue, especially when black.
- Peritonitis, pyothorax, or pyometra.
- Severe dental disease.
- Wounds or deep abscesses that do not heal as anticipated.

CAUSES & RISK FACTORS

- Usually caused by normal flora of the body; a break in protective barriers allows bacterial invasion.
- Infection in the proximity of a mucous membrane should raise one's index of suspicion for anaerobe involvement.
- Predisposing factors—immunosuppression, bite wounds, dental disease, open fractures, abdominal surgery, and foreign bodies.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Wounds that fail to respond to appropriate medical therapy—if aerobic cultures are negative, suspect anaerobic organisms.
- Cats

with non-healing wounds—test for FeLV and FIV.

- Middle-aged and old animals—tumor invasion (e.g., in the gastrointestinal tract).

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilic leukocytosis and monocytosis common.
- Biochemical abnormalities depend on specific organ involvement.
- Systemic spread of infection suggested by leukocytosis, hypoglycemia, increased ALP, and hypoalbuminemia.

OTHER LABORATORY TESTS

- Culture of anaerobic bacteria is often unrewarding because of their fastidious nature and errors in sample handling and submission.
- Appropriate media and containers should be on-hand prior to sample collection; diagnostic laboratories can provide guidance.
- Samples should not be refrigerated prior to submission.
- Suitable samples for culture may include fluid (e.g., pleural, peritoneal, etc.) or tissue.

IMAGING

As required for the circumstances of the individual patient (e.g., suspected bone infection, peritonitis, etc.).

DIAGNOSTIC PROCEDURES

- Cytologic inspection reveals abundant degenerate neutrophils with morphologically diverse forms of intracellular and extracellular bacteria; presence of large filamentous bacteria is suggestive.
- If not performed in-house, Gram staining should be requested when the sample is submitted.



MEDICATIONS

- Thoracic drainage—important with pyothorax (see specific chapter).
- Hyperbaric oxygen—some potential use; limited in availability.

SURGERY

- Should not be delayed when anaerobes are suspected.
- Combined with systemic antimicrobial therapy—the best chance of a positive outcome.
- Usually indicated when anaerobic organisms complicate pyometra, osteomyelitis, and peritonitis.
- Cleanse the wound of toxins and devitalized tissue.
- Enhance drainage of pus.
- Improve local blood flow.
- Increase oxygen tension.

DRUG(S)

- Antimicrobial therapy alone—unlikely to be successful; poor drug penetration into exudates.
- Antibiotic selection—largely empiric, owing to the difficulty of isolating anaerobes and the delay in return of culture results.
- Because most anaerobic infections are polymicrobial, therapy targeted against both

anaerobes *and* any aerobic components offers the greatest chance of success.

- Amoxicillin with clavulanate—in many cases, considered the antibiotic of choice; convenient and accessible; clavulanate improves activity against *Bacteroides*.
- Imipenem—beta lactam with significant activity against serious, resistant infections.
- Cefoxitin—a cephalosporin with reliable activity against anaerobes.
- Clindamycin—may be especially useful for respiratory tract infections; concentrated within leukocytes.
- Chloramphenicol—good tissue penetration but bacteriostatic and associated with adverse effects, especially in cats; concern for human exposure also limits use.
- Metronidazole—useful against all clinically significant anaerobes (except *Actinomyces*).
- Aminoglycosides—uniformly ineffective.
- Trimethoprim-sulfa combinations—ineffective; poor penetration into exudates.
- Quinolones—routinely ineffective, although newer expanded-spectrum quinolones do have activity against anaerobes (e.g., pradofloxacin).



FOLLOW-UP

PATIENT MONITORING

Monitoring parameters will vary with the circumstances of each patient.

POSSIBLE COMPLICATIONS

Localized infection may progress to systemic infection if not appropriately identified and treated.

EXPECTED COURSE AND PROGNOSIS

Dependent upon identification and resolution of the underlying cause; long-term antibiotic therapy may be required.



MISCELLANEOUS

ASSOCIATED CONDITIONS

See “Causes & Risk Factors”

ABBREVIATIONS

- ALP = alkaline phosphatase
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus

Suggested Reading

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ANAL SAC DISORDERS



BASICS

OVERVIEW

- Anal sacs are reservoirs for secretions normally evacuated by compression during defecation.
- Normal gland secretions vary in consistency and color.
- Disorders include impaction, infection (sacculitis), abscess, and neoplasia.
- Treatment options include manual expression, flushing, antibiotics, and surgical excision.

SIGNALMENT

- Dogs and cats (rarely): no age or sex predisposition.
- Breeds predisposed:
 - Impaction—miniature and toy poodle, American cocker and English springer spaniel, Chihuahua.
 - Neoplasia (adenocarcinoma)—German shepherd dog, golden retriever, American cocker and English springer spaniel.

SIGNS

Impaction/Infection

- Anal pruritus—often manifested by “scooting”
- Perianal pruritus
- Hesitancy to defecate
- Tenesmus
- Tail chasing
- Foul-smelling, non-feces anal discharge
- Refusal to sit and/or lift tail
- Cats—excessive licking of the ventral abdomen and tail head
- Abscess—often unilateral; localized pain and discharge

CAUSES & RISK FACTORS

- Predisposing factors—soft feces or diarrhea leading to retention of secretions within anal sacs due to lack of expression; excessive glandular secretions; dermatologic disorders that alter the characteristics (cellularity and organism colonization) of anal sac secretions.
- Retained secretions may lead to infection and abscess formation.
- Other predisposing factors:
 - Obesity
 - Infection – hypersensitivity and/or endocrinopathy.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Adverse food reaction or food hypersensitivity
- Flea bite hypersensitivity

- Atopic dermatitis
- Tapeworm infestation
- Tail fold bacterial folliculitis
- Malassezia dermatitis
- Compulsive disorder (anal licking)
- Colitis or other intestinal disorder
- Keratinization disorder
- Anal sac neoplasia (including adenocarcinoma, squamous cell carcinoma)
- Perianal adenoma
- Perianal adenocarcinoma
- Perianal fistulae

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal
- Hypercalcemia—anal sac adenocarcinoma

OTHER LABORATORY TESTS

None unless indicated by an underlying cause

IMAGING

None unless indicated by an underlying cause

DIAGNOSTIC PROCEDURES

- Digital palpation of the anal sacs—normal anal sacs should not be palpable externally.
- Normal anal sac contents vary widely in gross appearance and microscopic characteristics; usually thin or watery, with minimal cellularity and primarily extracellular organisms, but may vary widely in numbers of inflammatory cells and bacteria.
- Impaction—generally more thick, pasty brown secretion; higher numbers of *Malassezia* and intracellular bacteria.
- Anal sacculitis and abscessation—purulent, often blood-tinged, foul-smelling discharge.
- Cytology of anal sac secretions—increased number of neutrophils, erythrocytes, *Malassezia*, and intracellular bacteria indicate infection; reports vary but Gram-positive cocci more common in normal secretions.
- Bacterial culture and sensitivity—normal secretions may contain *Proteus mirabilis*, *Streptococcus spp.*, *Escherichia coli*, *Bacillus spp.*, *Clostridium perfringens*, and *Pseudomonas aeruginosa*.



TREATMENT

- Gentle manual expression of contents for impaction and sacculitis.
- Sedation may be necessary to flush severely impacted or painful anal sacs.
- Infusion of antibiotic and/or corticosteroid medications directly into the anal sacs.
- Drainage of abscesses.
- Use of appropriate oral antibiotics and/or antiyeast medication.
- Anal sac excision with chronic disease.
- Surgical excision and staging of anal sac neoplasia; combine with chemotherapy.

- Identification of underlying causes of predisposing disease.
- Feeding high-fiber diets may help natural expression of anal sacs.



MEDICATIONS

DRUG(S)

- Infection—use of appropriate antibiotics: cephalaxin (22 mg/kg q12h), amoxicillin trihydrate-clavulanate potassium (10–15 mg/kg q12h), clindamycin (11 mg/kg q24h), trimethoprim-sulfamethoxazole (15 mg/kg q12h); metronidazole (10–15 mg/kg q12h); enrofloxacin (dogs, 10–20 mg/kg q24h; cats, 5 mg/kg/day), and orbifloxacin (5 mg/kg q24h).
- Chronic disease associated with perianal fistulae; cyclosporine, modified (name brand preferred: Atopica 5 mg/kg q24h) and/or topical tacrolimus.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- Reassess patients weekly initially; then as necessary to monitor healing.
- Manually express anal sac contents and/or flush contents until sacs empty without intervention.
- CBC, serum chemistry profile, and urinalysis with culture—recommended every 3–12 months for patients on chronic corticosteroid or cyclosporine therapy.



MISCELLANEOUS

SEE ALSO

- Adenocarcinoma, Anal Sac
- Perianal Fistula

Suggested Reading

- Muse R. Diseases of the anal sac. In: Bonagura JD, Twedt DC, eds., Kirk's Current Veterinary Therapy, 14th ed. St. Louis, MO: Saunders, 2009, pp. 465–468.
- Zoran DL. Rectoanal disease. In: Ettinger SJ, ed., Textbook of Veterinary Internal Medicine, 6th ed. Philadelphia: Saunders, 2005, pp. 1408–1420.

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BASICS

DEFINITION

- Acute manifestation of a Type I hypersensitivity reaction mediated through the rapid introduction of an antigen into a host having antigen-specific antibodies of the IgE subclass.
- The binding of antigen to mast cells sensitized with IgE results in the release of preformed and newly synthesized chemical mediators.
- Anaphylactic reactions may be localized (atopy) or systemic (anaphylactic shock).
- Anaphylaxis not mediated by IgE is designated an anaphylactoid reaction and will not be discussed.

PATOPHYSIOLOGY

- First exposure of the patient to a particular antigen (allergen) causes a humoral response and results in production of IgE, which binds to the surface of mast cells; the patient is then considered to be sensitized to that antigen.
- Second exposure to the antigen results in cross-linking of two or more IgE molecules on the cell surface, resulting in mast cell degranulation and activation; release of mast cell granules initiates an anaphylactic reaction.
- Major mast cell-derived mediators include histamine, eosinophilic chemotactic factor, arachidonic acid, metabolites (e.g., prostaglandins, leukotrienes, and thromboxanes), platelet-activating factor, and proteases, which cause an inflammatory response of increased vascular permeability, smooth muscle contraction, inflammatory cell influx, and tissue damage.
- Clinical manifestations depend on the route of antigen exposure, the dose of antigen, and the level of the IgE response.

SYSTEMS AFFECTED

- Gastrointestinal—salivation, vomiting, and diarrhea
- Hepatobiliary (dogs)—because of portal hypertension and vasoconstriction
- Respiratory (cats)—dyspnea and cyanosis
- Skin/Exocrine—pruritus, urticaria, and edema

GENETICS

Familial basis reported for Type I hypersensitivity reaction in dogs.

INCIDENCE/PREVALENCE

- Localized Type I hypersensitivity reactions not uncommon.
- Systemic Type I hypersensitivity reactions rare.

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Dogs—numerous breeds documented as having a predilection for developing atopy.
- Cats—no breeds documented as having predilection for atopy.

Mean Age and Range

- Dogs—age of clinical onset ranges from 3 months to several years of age; most affected animals 1–3 years old.
- Cats—age of clinical onset ranges from 6 months to 2 years.

Predominant Sex

- Dogs—atopy more common in females.
- Cats—no reported sex predilection.

SIGNS

General Comments

- Initial clinical signs vary depending on the route of exposure to the inciting antigen (allergen).
- Shock—end result of a severe anaphylactic reaction.
- Shock organ—dogs, liver; cats, respiratory and gastrointestinal systems.
- May be localized to the site of exposure but may progress to a systemic reaction.

Historical Findings

- Onset of signs immediate (usually within minutes).
- Dogs—pruritus, urticaria, vomiting, defecation, and urination.
- Cats—intense pruritus about the head, dyspnea, salivation, and vomiting.

Physical Examination Findings

- Localized cutaneous edema at the site of exposure.
- Hepatomegaly in some dogs.
- Hyperexcitability possible in early stages.
- Depression and collapse terminally.

CAUSES

Virtually any agent; those commonly reported include venoms, blood-based products, vaccines, foods, and drugs.

RISK FACTORS

Previous exposure (sensitization) increases the chance of the animal developing a reaction.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other types of shock.
- Trauma.
- Depends on the major organ system involved or if reaction is localized; diagnosis can be made largely on the basis of history and clinical signs.

CBC/BIOCHEMISTRY/URINALYSIS

Because of the acute onset of disease, no tests available that reliably predict individual susceptibility.

OTHER LABORATORY TESTS

- Intradermal skin testing to identify allergens.
- Radioallergosorbent test to quantify the concentration of serum IgE specific for a particular antigen.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Limited because a severely allergic animal can develop an anaphylactic reaction when exposed to even small quantities of antigen.

PATHOLOGIC FINDINGS

- Lesions vary, depending on severity of reaction, from localized cutaneous edema to severe pulmonary edema (in cats) and visceral pooling of blood (in dogs).
- Other non-specific findings vary and are characteristic of shock.
- Non-specific characteristics of localized reactions include edema, vasculitis, and thromboembolism.



TREATMENT

APPROPRIATE HEALTH CARE

In an acutely affected animal, the reaction is considered a medical emergency requiring hospitalization.

NURSING CARE

Elimination of inciting antigen, if possible.

Systemic Anaphylaxis

- Goal—emergency life support through the maintenance of an open airway, preventing circulatory collapse, and reestablishing physiologic parameters.
- Administer fluids intravenously at shock dosages to counteract hypotension.

Localized Anaphylaxis

Goal—limit the reaction and prevent progression to a systemic reaction.

ACTIVITY

N/A

DIET

If a food-based allergen is suspected (uncommon), avoid foods associated with hypersensitivity reaction.

CLIENT EDUCATION

- Discuss the unpredictable nature of the disease.
- Discuss the need to recognize that the animal has an allergic condition that may require immediate medical care.

SURGICAL CONSIDERATIONS

None



MEDICATIONS

DRUG(S) OF CHOICE

Systemic Anaphylaxis

- Epinephrine hydrochloride parenterally (1:1,000; 0.01 mL/kg) for shock.
- Corticosteroids for shock—prednisolone sodium succinate (2 mg/kg IV q8h) or dexamethasone sodium phosphate (0.25 mg/kg IV q12h).
- Atropine sulfate (0.04 mg/kg IM) to counteract bradycardia and hypotension.
- Aminophylline (10 mg/kg IM or slowly IV) in severely dyspneic patients.

Localized Anaphylaxis

- Diphenhydramine hydrochloride (1–2 mg/kg IV or IM).
- Prednisolone (2 mg/kg PO).
- Epinephrine hydrochloride (0.15 mL SC at site of initiation).
- If shock develops, initiate treatment for a systemic anaphylaxis.

CONTRAINDICATIONS

None

PRECAUTIONS

Localized reaction can develop into systemic reaction.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

Closely monitor hospitalized patients for 24–48 hours.

PREVENTION/AVOIDANCE

If inciting antigen (allergen) can be identified, eliminate or reduce exposure.

POSSIBLE COMPLICATIONS

None

EXPECTED COURSE AND PROGNOSIS

- If localized reaction is treated early, prognosis is good.
- If the animal is in shock on examination, prognosis is guarded to poor.



MISCELLANEOUS

ASSOCIATED CONDITIONS

None

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

Shock, Cardiogenic

INTERNET RESOURCES

Merck Veterinary Manual:
www.merckvetmanual.com.

Suggested Reading

Shmuel DL, Cortes Y. Anaphylaxis in dogs and cats. J Vet Emerg Crit Care (San Antonio) 2013, 23(4):377–394.

Author Paul W. Snyder

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Client Education Handout
available online

ANEMIA OF CHRONIC KIDNEY DISEASE

A



BASICS

DEFINITION

Progressive decreases in PCV, RBC count, and hemoglobin and hypoplasia of erythroid elements of the bone marrow are predictable features of progressive CKD. Anemia is normocytic, normochromic, nonregenerative, and proportional to the stage of CKD. The underlying cause of the anemia of CKD is multifactorial. Although factors such as gastrointestinal blood loss, reduced red blood cell survival, deficiencies in iron and/or folate, cytokines and inflammatory mediators may be involved, the primary contributing factor to anemia of CKD is an inadequate production of erythropoietin (EPO) by the kidneys. Erythropoietin is a glycoprotein hormone that regulates red blood cell generation at the level of the bone marrow. Erythropoietin is produced in the peritubular interstitial cells of the kidney in response to decrease in tissue oxygen.

SIGNALMENT

Middle-aged to old dogs and cats mostly affected; seen in young animals with heritable, congenital, or acquired CKD.

SIGNS

- Anemia contributes to development of anorexia, weight loss, fatigue, lethargy, depression, weakness, apathy, cold intolerance, and behavior and personality changes characterizing CKD.
- Pallor of the mucous membranes.
- Tachypnea.
- Tachycardia.
- Systolic murmur.
- Syncope and seizures (rare).

CAUSES & RISK FACTORS

- All inherited, congenital, and acquired forms of CKD (e.g., pyelonephritis, glomerulonephritis, amyloidosis, polycystic kidney disease, and lymphoma).
- Exacerbated by iron deficiency, inflammatory or neoplastic disease, gastrointestinal blood loss, hemolysis, and myeloproliferative disorders.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Anemia of chronic infectious, inflammatory or neoplastic disease; myeloproliferative disease; chronic blood loss; aplastic anemia; endocrine disease; drug reaction; and chronic immune-mediated, toxic, viral, rickettsial, or parasitic anemia; hemodilution.
- Regenerative anemia excludes diagnosis of anemia of CKD.
- Generally masked until advanced CKD.

CBC/BIOCHEMISTRY/URINALYSIS

- Normocytic, normochromic, hypoproliferative anemia (progressive; anemia may be masked by dehydration).
- Reticulocytes—low corrected indices and absolute counts ($\leq 10,000/\mu\text{L}$).
- Moderate to advanced CKD—elevated BUN, creatinine, and phosphorus; variably high calcium; variably low bicarbonate and potassium.
- High BUN:creatinine ratio may predict concurrent” gastrointestinal blood loss.
- Impaired urine-concentrating ability, possible proteinuria, and variably active sediment.

OTHER LABORATORY TESTS

- Serum iron—normal or variably low.
- Transferrin saturation—normal or variably low ($< 20\%$).
- FeLV and FIV and/or haemobartonella testing (cats) or rickettsial titers or PCR (dogs) to exclude agent-induced myelodyscrasia.
- Serum erythropoietin—normal (inappropriately) or low.

IMAGING

- Small, irregular kidneys with loss or disruption of renal architecture detected by radiography or ultrasonography.
- Enlarged, polycystic, hydronephrotic, infiltrative.

DIAGNOSTIC PROCEDURES

Cytologic examination of bone marrow—erythroid hypoplasia; myeloid:erythroid ratio normal or high; stainable iron normal or variably low.



TREATMENT

- Stabilize azotemia in patients in with uremic crisis.
- Ensure adequate and appropriate nutrition.
- Stabilize any metabolic derangement (e.g., acidosis) that could contribute to shortened RBC lifespan and/or anorexia.
- Minimize micronutrient deficiencies that could negatively impact rbc production.
- Identify and manage GI blood loss (gastric acid suppression with H₂ blockers or proton pump inhibitors) (GI protectants such as sucralfate).
- Ensure that patient is iron replete (serum iron panel).
- Correct systemic hypertension.



MEDICATIONS

DRUG(S) AND FLUIDS

Blood Transfusion

- Short-term, rapid correction if hypoxic distress (typically PCV $\leq 15\%$)—give compatible whole blood or packed RBCs.

- Target PCV is 25–30%.

- May be given intermittently for prolonged management, although compatibility issues are likely to occur long term.
- EPO support for progressive or symptomatic anemia (dogs, PCV $\leq 25\%$; cats, PCV $\leq 23\%$).

Erythropoietin Replacement

- Epoetin alfa (r-HuEPO)—original synthetic erythropoiesis stimulating protein, replica of human erythropoietin (Epogen and Procrit); provides consistent, rapid, and long-term correction of anemia in dogs and cats with CKD; potential for anti-r-HuEPO antibody production and pure red cell aplasia.
- Darbepoetin alfa (Aranesp), a new hyperglycylated analogue of r-HuEPO with prolonged half-life and sustained effects; very effective with significantly less tendency for antibody induction; should be used preferentially to epoetin alfa.
- Target PCV—dogs, 30–35%; cats, 30%.
- Initial dosage: darbepoetin alfa—0.5–2.0 $\mu\text{g}/\text{kg}$ SC/IV once weekly until PCV reaches low end of target, then decrease to q2–4 weeks as needed to maintain target. Recommend PCV prior to EVERY injection to avoid overtreatment.
- Epoetin alfa—50–100 U/kg SC thrice weekly until low end of target, then decrease to once to twice weekly.
- If converting from epoetin alfa to darbepoetin—divide weekly units by 400 to establish μg to give once weekly.
- Individualize to each patient; life-long treatment required.
- If PCV exceeds target, discontinue until upper target range is achieved, then increase dosage interval.
- Serum iron and transferrin saturation should be normalized before initiating and during treatment. Injectable iron (10 mg/kg IM) should be administered when indicated on iron panel. Injectable iron is preferable and better tolerated than oral preparations.
- Species-specific erythropoietins for dogs and cats are not currently commercially available.
- Alternative erythropoietin-stimulating treatments are under development.

Anabolic Steroids

Little or no efficacy or indication for use.



FOLLOW-UP

PATIENT MONITORING

- PCV—weekly to semi-monthly for 3 months, then monthly to bimonthly.
- Blood pressure—semi-monthly to monthly.
- Iron and transferrin saturation—at 1, 3, and 6 months, then semiannually.
- Discontinue erythropoietin if patient develops evidence of erythrocythemia, local or systemic sensitivity, anti-r-HuEPO antibody

ANEMIA OF CHRONIC KIDNEY DISEASE

(CONTINUED)

formation, pure red cell aplasia, or refractory hypertension.

POSSIBLE COMPLICATIONS*Erythropoietin-Related*

- Development of erythrocythemia, seizures, hypertension, iron depletion, injection pain, and mucocutaneous reactions.
- Development of a pure red cell aplasia during the course of epoetin alfa treatment suggests formation of anti-r-HuEPO antibodies, which neutralize r-HuEPO and native erythropoietin, causing severe anemia in 20–30% of animals; often reversible with cessation of treatment.
- Development of anti-r-HuEPO antibodies occurs in less than 5% of patients with darbepoetin alfa therapy.
- Signs associated with production of anti-r-HuEPO antibodies while the patient is receiving epoetin alfa include decreasing PCV, erythroid hypoplasia, absolute reticulocyte counts approaching zero, and myeloid:erythroid ratio ≥ 8 .
- Erythropoietin replacements should be used cautiously or withheld if hypertension or iron deficiency develop; treatment can be reinstated once hypertension and iron deficiency are corrected.

Transfusion-Related

- Incompatibility reaction
- Circulatory or iron overload
- Systemic hypertension
- Transmissible infection

EXPECTED COURSE AND PROGNOSIS

- Correction of anemia increases appetite, activity, grooming, affection and playfulness, weight gain, and cold tolerance, and decreases sleeping.
- Use of erythropoietin replacement agents in dogs and cats requires careful assessment of the risks and benefits for individual patients.
- Short-term prognosis depends on the severity of the renal failure.
- Long-term prognosis is guarded to poor because of the underlying chronic renal failure.

**MISCELLANEOUS****ABBREVIATIONS**

- CKD = chronic kidney disease
- FeLV = feline leukemia virus

- FIV = feline immunodeficiency virus
- PCR = polymerase chain reaction
- PCV = packed cell volume
- RBC = red blood cell
- r-HuEPO = recombinant human erythropoietin

Suggested Reading

Chalhoub S, Langston C, Eatross A. Anemia of Renal Disease: What it is, what to do, and what's new. *J Feline Med Surg* 2011, 13:629–640.

Cowgill LD, James KM, Lew JK, et al. Use of recombinant human erythropoietin for management of anemia in dogs and cats with renal failure. *J Am Vet Med Assoc* 1998, 212:521–528.

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BASICS

OVERVIEW

- A disorder of hematopoietic precursor cells characterized by replacement of normal bone marrow with adipose tissue. There is decreased production of granulocytes, erythrocytes, and platelets, resulting in pancytopenia in the peripheral blood. The disease is sometimes also referred to as aplastic pancytopenia.
- In the acute form, neutropenia and thrombocytopenia predominate because of the shorter life spans of these cells; in the chronic form, nonregenerative anemia also occurs. In both forms, the bone marrow exhibits variable degrees of panhypoplasia.
- There are many precipitating causes of deficient hematopoiesis, including infectious diseases, drug administration, starvation and toxin exposure; immune-mediated mechanisms are often suspected.
- Hemic/lymphatic/immune systems affected.

SIGNALMENT

Dogs and cats, no apparent breed or sex predilection. In one study, the mean age of nine affected dogs was 3 years.

SIGNS

- Acute form: fever, petechial hemorrhages, epistaxis, hematuria, melena; i.e., signs due to neutropenia and thrombocytopenia.
- Chronic form: pale mucous membranes, weakness, lethargy; i.e., signs due to anemia, in addition to signs observed in acute forms.

CAUSES & RISK FACTORS

Often not identified

Infectious Agents

- FeLV, FIV
- Canine and feline parvovirus
- Rickettsial organisms (e.g., *Ehrlichia* spp.)

Drugs and Chemicals

- Estrogen (exogenous administration, Sertoli and interstitial cell tumors)
- Methimazole (cats)
- Chemotherapeutic drugs, including azathioprine, cyclophosphamide, cytosine arabinoside, doxorubicin, vinblastine, and hydroxyurea
- Antibiotics, including trimethoprim-sulfadiazine, cephalosporins, and chloramphenicol
- Griseofulvin
- NSAIDs, including phenylbutazone and meclofenamic acid
- Fenbendazole, albendazole
- Captopril
- Quinidine

- Thiacetarsamide
- Ionizing radiation
- Mycotoxins (cats)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Causes of pancytopenia with normal to increased bone marrow cellularity (e.g., myelodysplastic disorders, leukemia, myelofibrosis).

CBC/BIOCHEMISTRY/URINALYSIS

- Leukopenia characterized by neutropenia with or without lymphopenia.
- Normocytic, normochromic, nonregenerative anemia.
- Thrombocytopenia.

OTHER LABORATORY TESTS

- Immunologic tests for infectious diseases (e.g., serologic titers, ELISA, IFA).
- PCR for infectious agents.
- Serologic test for antierythrocyte antibodies (Coombs' test).

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Bone marrow aspiration—frequently an inadequate or fatty sample is obtained because of decreased hematopoietic tissue and replacement by adipocytes.
- Bone marrow core biopsy—permits an evaluation of architecture and reveals hypoplasia of cell lines and replacement by adipose tissue.



TREATMENT

Supportive treatment, antibiotics, blood component therapy, as dictated by clinical condition.



MEDICATIONS

DRUG(S) OF CHOICE

- Cyclosporine A—10–25 mg/kg PO q12h (dogs), 4–5 mg/kg PO q12h (cats).
- Recombinant hematopoietic growth factors (e.g., rhG-CSF: 5 µg/kg/day SC).
- Androgen and corticosteroid administration have been largely unsuccessful.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A

OTHER DRUGS

- Antibiotics to treat secondary infections if fever and neutropenia present.
- Whole or component blood transfusion if indicated.



FOLLOW-UP

PATIENT MONITORING

- Daily physical examination.
- CBC every 3–5 days to weekly.
- Repeat bone marrow evaluation if necessary.

PREVENTION/AVOIDANCE

- Castration of cryptorchid males.
- Vaccination for infectious diseases.
- Frequent monitoring of CBC in cancer patients receiving chemotherapy or radiation.

POSSIBLE COMPLICATIONS

- Sepsis
- Hemorrhage

EXPECTED COURSE AND PROGNOSIS

- Guarded to poor.
- Recovery of hematopoiesis may take weeks to months, if it occurs at all.
- Spontaneous recovery occasionally occurs, especially in younger animals.



MISCELLANEOUS

SEE ALSO

Pancytopenia

ABBREVIATIONS

- ELISA = enzyme-linked immunosorbent assay
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- IFA = immunofluorescent antibody (test)
- NSAID = nonsteroidal anti-inflammatory drug
- PCR = polymerase chain reaction
- rhG-CSF = recombinant human granulocyte colony-stimulating factor

Suggested Reading

Brazzell JL, Weiss DJ. A retrospective study of aplastic pancytopenia in the dog: 9 cases (1996–2003). Vet Clin Path 2006, 35:413–417.

Weiss DJ. Aplastic anemia. In: Weiss DJ, Wardrop KJ, eds., Schalm's Veterinary Hematology, 6th ed. Ames, IA: Blackwell Publishing Ltd., 2010, pp. 256–260.

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ANEMIA, HEINZ BODY



BASICS

OVERVIEW

- Heinz bodies cause hemolytic anemia and indicate oxidative damage to RBCs.
- Heinz bodies form when oxidants overwhelm protective reductive pathways in RBCs; irreversible denaturation of the globin chains in hemoglobin causes precipitation and attachment of altered hemoglobin to the cell membrane.
- RBCs with Heinz bodies are targeted for removal by macrophages in the spleen, and occasionally undergo intravascular lysis.
- The pitting function of the spleen may remove Heinz bodies, resulting in spherocytes.
- Heinz bodies are usually caused by exposure to chemical or dietary oxidants.
- Cats are particularly susceptible to Heinz body formation because their hemoglobin contains more sulfhydryl groups than that of dogs.
- Healthy cats may have Heinz bodies with no anemia, possibly because cats have a nonsinusoidal spleen with limited pitting function.
- Heinz bodies are reported in hyperthyroidism (cats), lymphoma (cats, dogs), and diabetes mellitus (cats, dogs), possibly due to increased endogenous oxidants (e.g., β -hydroxybutyrate in ketoacidosis). Anemia may or may not be present.
- Heinz bodies may be accompanied by methemoglobinemia (hemoglobin containing Fe^{3+}) and/or eccentrocytes (oxidative damage to RBC membranes causing adhesion of opposing membranes and displacement of hemoglobin to one side of the cell).

SIGNALMENT

- Dogs and cats
- No sex, breed, or age disposition

SIGNS

Historical Findings

- Exposure to oxidant.
- Sudden onset of weakness, lethargy, or anorexia.
- Reddish-brown urine (hemoglobinuria) if severe intravascular hemolysis.
- Signs related to underlying disease in animals with systemic disease and Heinz bodies.

Physical Examination Findings

- Pale and occasionally icteric mucous membranes
- Dark or chocolate-colored blood with methemoglobinemia
- Tachypnea, tachycardia

CAUSES & RISK FACTORS

- Dietary: onions (raw, cooked, dehydrated, and powdered), garlic (dogs), propylene glycol (cats), Chinese chives (dog).
- Drugs: acetaminophen, phenacetin (cats), phenazopyridine (cats), methylene blue, vitamin K1 or K3 (dogs), DL-methionine (cats), benzocaine (topical), phenylhydrazine (dog), propofol (cats).
- Miscellaneous: zinc (nuts, bolts, pennies, dermatologic creams), naphthalene (moth ball ingestion in dogs), skunk musk exposure (dogs).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of regenerative, hemolytic anemia (e.g., immune mediated, hemoparasites).
- Heinz bodies may be found in healthy or ill cats without anemia.

Diagnosis of a Heinz body anemia requires documentation of a regenerative anemia, supporting evidence of a hemolytic process (e.g. hyperbilirubinemia), identification of Heinz bodies on a blood smear, and elimination of other causes of hemolysis or blood loss.

CBC/BIOCHEMISTRY/URINALYSIS

- Regenerative anemia (decreased HCT, polychromasia, nucleated RBCs) is expected if there has been sufficient time for a bone marrow response; the severity of anemia depends on dose of oxidant and duration of exposure.
- Hemoglobin concentration and MCHC may be falsely increased due to Heinz body interference with hemoglobin measurement.
- Heinz bodies are visible on a routinely stained blood smear as small, pale red, round inclusions that may protrude from RBC surface. They may be difficult to identify if there is marked poikilocytosis.
- Single, small ($< 0.5 \mu m$) Heinz bodies may be found in RBCs of cats without anemia.
- Large and/or multiple Heinz bodies in an anemic cat suggest a Heinz body hemolytic anemia.
- Dogs may have concurrent eccentrocytosis on a blood smear.
- Hyperbilirubinemia and bilirubinuria are possible.
- Hemoglobinuria and methemoglobinuria are uncommon but occur with severe intravascular hemolysis.
- Neutrophilia and monocytosis may occur.

OTHER LABORATORY TESTS

- New methylene blue stains Heinz bodies blue, making them easy to identify and quantify on a blood smear, even with marked poikilocytosis.
- Measure methemoglobin if blood is dark or chocolate colored.
- Serum zinc concentration if indicated.

IMAGING

Abdominal radiographs may reveal gastrointestinal metal objects in zinc toxicity.



TREATMENT

- Immediate identification and removal of oxidant may be sufficient, though it often take several days after exposure for the severity of anemia to reach nadir.
- Consider administration of emetics with recent ingestion of an oxidant.
- Supportive care depends on the severity of the hemolytic crisis and includes IV fluids, RBC transfusions, oxygen, and restricted activity.
- Endoscopy

or surgery to remove metallic items in gastrointestinal tract.



MEDICATIONS

DRUG(S) OF CHOICE

Acetaminophen toxicity in cats—N-acetylcysteine (140 mg/kg PO or IV, followed by seven additional treatments of 70 mg/kg q8h).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Administration of methylene blue to treat methemoglobinemia may exacerbate Heinz body formation.

ALTERNATIVE DRUG(S)

The use of dietary antioxidants (e.g., bioflavonoids) is controversial but may help prevent further formation of Heinz bodies.



FOLLOW-UP

PATIENT MONITORING

Serial CBCs and review of blood smears are recommended to assess RBC regeneration and disappearance of Heinz bodies.

PREVENTION/AVOIDANCE

Counsel clients about preventing exposure to oxidants.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

Prognosis is good with removal of oxidant and supportive care once the hemolytic crisis is over.



MISCELLANEOUS

SEE ALSO

- Acetaminophen (APAP) Toxicosis
- Anemia, Regenerative
- Methemoglobinemia • Zinc Toxicosis

ABBREVIATIONS

- HCT = hematocrit
- MCHC = mean corpuscular hemoglobin concentration
- RBC = red blood cell

Suggested Reading

- Andrews D. Disorders of red blood cells. In: Handbook of Small Animal Practice, 5th ed. St. Louis: Saunders, 2008, pp. 632–635.
- Desnoyers M. Anemias associated with oxidative injury. In: Schalm's Veterinary Hematology, 6th ed. Ames, IA: Blackwell, 2010, pp. 239–245.

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BASICS

DEFINITION

Accelerated destruction or removal of RBCs due to a Type II hypersensitivity reaction.

PATHOPHYSIOLOGY

- Antibodies form against endogenous unaltered RBC surface antigens (primary IMHA) or altered RBC membrane antigens (secondary IMHA).
- Infectious organisms, drugs, exposure of previously unexposed antigens, or adsorption of preformed antigen-antibody complexes to the RBC membrane can alter RBC membrane antigens.
- Immunoglobulin deposits on RBC membrane, causing either direct intravascular hemolysis or accelerated removal by the monocyte/macrophage system.
- Intravascular hemolysis occurs when adsorbed antibodies (usually IgG) activate complement.
- In vivo agglutination of RBCs occurs when IgM or high titers of IgG molecules cause bridging of RBCs.
- Extravascular removal of RBCs occurs primarily in spleen, liver, bone marrow.
- Nonregenerative IMHA is believed to be caused by immune-mediated destruction of RBC precursors in the bone marrow.
- Rarely cold-acting antibodies cause in vivo hemolysis and erythrocyte agglutination in peripheral vasculature.

SYSTEMS AFFECTED

- Cardiovascular—tachycardia; low-grade heart murmur.
- Hemic/Lymphatic/Immune—immune-mediated destruction of RBCs, elaboration of proinflammatory mediators, DIC.
- Hepatobiliary—hyperbilirubinemia and icterus plus bilirubinuria when hepatic function is overwhelmed; centrilobular necrosis.
- Respiratory—tachypnea. PTE may result from hypercoagulable state.
- Skin—rarely cold-type IMHA may cause necrosis of extremities and ear tips.

GENETICS

Cocker spaniels are at increased risk (absence of dog erythrocyte antigen 7).

GEOGRAPHIC DISTRIBUTION

Secondary IMHA may have higher prevalence where associated infectious diseases are endemic.

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Cocker spaniel at highest risk. Also, English springer spaniel, Old English sheepdog, Doberman pinscher, collie, bichon frise, miniature pinscher, and Finnish spitz.
- Domestic shorthair cats.

Mean Age and Range

- Dogs, mean age 5–6 years (range 1–13 years)
- Cats, mean age 2 years (range 0.5–9 years)

Predominant Sex

- Female dogs at higher risk
- Male cats overrepresented

SIGNS

Historical Findings

- Lethargy/weakness/collapse
- Anorexia
- Exercise intolerance/dyspnea, tachypnea
- Vomiting and/or diarrhea
- Dark red urine
- Pica (cats)

Physical Examination Findings

- Pale mucous membranes, tachycardia, tachypnea.
- Splenomegaly/hepatomegaly.
- Icterus and pigmenturia (hemoglobin or bilirubin).
- Fever/lymphadenomegaly.
- Systolic murmur.
- Petechiae, ecchymoses, or melena (if concurrent thrombocytopenia or DIC).
- Other findings possible (e.g., joint pain) when IMHA is component of SLE.
- Necrosis of extremities and ear tips in cold-type IMHA (rare).

CAUSES AND RISK FACTORS

Primary IMHA

Poorly characterized immune dysregulation

Secondary IMHA

- Infectious causes: hemotropic *Mycoplasma* spp., *Ehrlichia* spp., *Anaplasma phagocytophilum*, *Anaplasma platys*, *Babesia* spp., *Leishmania*, *Dirofilaria immitis*, FeLV, FIP, chronic bacterial infection.
- Neoplasia: lymphoma, lymphoid leukemia, hemangiosarcoma, hemophagic histiocytic sarcoma.
- Drugs: beta lactam antibiotics, propylthiouracil, methimazole, sulfonamides.
- SLE
- Neonatal isoerythrolysis
- Hemolysis due to DEA incompatible blood transfusion
- Exposure to infectious agents, vaccination, chemicals/drugs, surgery, hormonal change, or other stressful event is hypothesized as potential trigger for IMHA.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Dogs

- Pyruvate kinase deficiency
- Phosphofructokinase deficiency
- Toxicity (zinc, onions, garlic, broccoli, copper, naphthalene, skunk musk)
- Snake/spider evenomation (coral snakes, recluse spiders)
- Severe hypophosphatemia
- Anemia due to hemorrhage (immune-mediated thrombocytopenia, rodenticide toxicosis)
- Microangiopathic anemia due to splenic neoplasia, DIC, splenic torsion

Cats

- Toxicity (acetaminophen zinc, onions, garlic)
- Severe hypophosphatemia

- Congenital feline porphyria
- Increased osmotic fragility (Abyssinian, Somali)

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—anemia, high MCV (3–5 days post-hemolytic episode), spherocytes, polychromasia, increased RBC distribution width, leukocytosis with neutrophilia and left shift, monocytosis, lymphocytosis (cats).
- Anemia is nonregenerative in 30% of dogs and 50% of cats.
- Serum biochemistry—hyperbilirubinemia, hemoglobinemia, high ALT.
- Urinalysis—hemoglobinuria, bilirubinuria.

OTHER LABORATORY TESTS

- Spontaneous saline agglutination test—before and after washing RBCs.
- Positive direct antiglobulin test (Coombs' test)—positive in up to 75% of animals with IMHA.
- Flow cytometric detection of membrane-bound immunoglobulin and complement.
- Reticulocytosis—absolute count > 60,000/ μL (dogs) or > 50,000/ μL (cats) in regenerative IMHA.
- Thrombocytopenia 60% of dogs.
- Prolonged APTT and PT, increased fibrin degradation products and d-dimer, decreased antithrombin in animals with DIC.
- Positive ANA titer and LE cell test (animals with SLE).
- Positive serologic titers or PCR in secondary IMHA due to infectious causes.
- Evidence of hematologic parasites in blood smears (secondary IMHA due to infectious causes).

IMAGING

- Radiographic findings—hepatomegaly/splenomegaly; thorax usually normal; may see evidence of PTE (patchy alveolar pattern, interstitial pattern, pleural fluid), but dogs with pulmonary embolism may have normal thoracic radiographs.
- Ultrasonographic findings—hepatomegaly/splenomegaly; liver/spleen can be mottled and hyperechoic or hypoechoic.

DIAGNOSTIC PROCEDURES

- Bone marrow aspirate usually reveals erythroid hyperplasia.
- With nonregenerative IMHA, maturation arrest or erythroid hypoplasia may be evident.
- In chronic IMHA, myelofibrosis may be present.

PATHOLOGIC FINDINGS

- Hepatosplenomegaly, centrilobular hepatic necrosis
- Splenic and hepatic extramedullary hematopoiesis
- Reactive lymphadenomegaly
- PTE and DIC



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient during acute hemolytic crisis; outpatient when PCV stabilized, ongoing hemolysis controlled, and clinical signs of anemia resolved.
- Inpatient if complications such as DIC, PTE, thrombocytopenia, gastrointestinal bleeding, or a need for

ANEMIA, IMMUNE-MEDIATED

(CONTINUED)

multiple transfusions. • Chronic low-grade extravascular hemolysis can be treated on outpatient basis if the patient not exhibiting clinical signs secondary to anemia.

NURSING CARE

- Fluid therapy to maintain vascular volume and correct dehydration. • Packed RBCs typed or cross-matched for naive recipient. Blood should be cross-matched for recipients that have received prior transfusions. Whole blood acceptable if packed RBCs not available. • Transfusion volume = recipient weight (kg) \times 85 (dog) or 50 (cat) \times desired PCV-current PCV/donor PCV. • Transfusion rate 0.25 mL/kg/hr for first 30 minutes then 5–10 mL/kg/h. • Monitoring for complications such as PTE, bleeding (especially GI), DIC, infection. • Cage rest.

CLIENT EDUCATION

- IMHA and complications (e.g., DIC, PTE) can be fatal. • Life-long treatment may be needed; disease may recur. • Side effects of treatment may be severe.

SURGICAL CONSIDERATIONS

- Splenectomy can be considered if medical management fails to control disease.
- Consider blood product administration preoperatively.



MEDICATIONS

DRUG(S) OF CHOICE

- Corticosteroids—prednisone 1–2 mg/kg/day q12h for 2–4 weeks. Use prednisolone in cats due to higher bioavailability. • Once PCV above 30%, decrease dose to 1 mg/kg q12h. Then taper by a maximum rate of 25–50% per month over a 3- to 6-month period, depending upon PCV and severity of side effects. If after 3–6 months disease is in remission on a low q48h dose, try discontinuing the drug. • Add additional immunosuppressive drug such as azathioprine (dogs) cyclosporine (cats) if poor response to prednisone after 5–7 days or if poor prognostic indicators (e.g., intravascular hemolysis, serum bilirubin >8–10 mg/dL, persistent autoagglutination, Evans syndrome). • Azathioprine dose 2 mg/kg/day, can decrease to 0.5–1.0 mg/kg q48h if bone marrow suppression. Monitor for immunosuppression, hepatotoxicosis, pancreatitis.
- For prevention of thromboembolism (dogs) consider unfractionated heparin 300 U/kg SC q6–8h (dose adjusted based on APTT prolongation or measurement of anti-Xa activity) or ultra-low-dose aspirin 0.5–1.0 mg/kg/day or enoxaparin (low-molecular-weight heparin) 0.8 mg/kg SC q6h or 1.5 mg/kg q12h, or clopidogrel 2–3 mg/kg PO q24h (loading dose 10 mg/kg/day).
- Address underlying cause (e.g., infection and drugs) if secondary IMHA.

CONTRAINDICATIONS

- No heparin, enoxaparin, or aspirin in dogs with severe thrombocytopenia (< 80,000/ μ L).
- Do not use multiple cytotoxic drugs concurrently.

PRECAUTIONS

- No azathioprine in cats because of risk of bone marrow toxicity. • Prednisone/prednisolone can cause signs of Cushing's syndrome and may increase risk of PTE, pancreatitis, diabetes mellitus, secondary infection, gastric ulcers (consider gastric protectants). • Cytotoxic drugs can cause bone marrow suppression, secondary infection, pancreatitis (azathioprine), GI upset (cyclosporine, azathioprine, mycophenolate mofetil), gingival hyperplasia, papillomatosis (cyclosporine), infertility.

POSSIBLE INTERACTIONS

Azathioprine and prednisone have been associated with development of pancreatitis.

ALTERNATIVE DRUG(S)

- Dexamethasone (0.25–0.5 mg/kg/day IV)—can be used instead of prednisone/prednisolone in animals that do not tolerate oral drugs, until oral intake is possible.
- Chlorambucil—for cats, 0.1–0.2 mg/kg PO q24h initially, then q48h. • Cyclosporine—microemulsion, e.g., Atopica—dogs, 5–10 mg/kg/day PO divided twice daily; cats, 0.5–3 mg/kg q12h. • Mycophenolate mofetil 10–17 mg/kg q24h.



FOLLOW-UP

PATIENT MONITORING

- Monitor heart rate, respiratory rate, temperature frequently. • Monitor for adverse reactions to treatment (e.g., transfusion reactions/overhydration). • If PTE suspected, monitor thoracic radiographs and arterial blood gases frequently. • During first days of treatment, check PCV daily until stable, then every 1–2 weeks for 2 months; if still stable, recheck PCV monthly for 6 months, then 2–4 times per year; rechecks need to be more frequent if patient is on long-term medication especially cytotoxic drugs. • CBC and reticulocyte count should be rechecked at least monthly during treatment; if the neutrophil count falls < 3,000 cells/ μ L, discontinue cytotoxic drugs until count recovers; reinstitute at lower dosage.
- Coombs' tests and reticulocyte counts to assist in drug tapering.

PREVENTION/AVOIDANCE

Consider need for vaccination on case-by-case basis in dogs that developed IMHA after vaccination.

POSSIBLE COMPLICATIONS

- Pulmonary/multiorgan thromboembolism (up to 80% of all cases at necropsy). • DIC.

- Centrilobular hepatic necrosis and renal tubular necrosis secondary to hypoxia.
- Infection secondary to immunosuppressive therapy. • GI ulceration due to high-dose glucocorticoids. • Iatrogenic hyperadrenocorticism.

EXPECTED COURSE AND PROGNOSIS

- Mortality: 30–80% (dog), 25% (cat).
- Causes of death include thromboembolism, infection due to immunosuppression, DIC, persistent anemia. • Hyperbilirubinemia > 5 mg/dL, autoagglutination, intravascular hemolysis, severe thrombocytopenia, hypoalbuminemia are associated with poorer prognosis. • Response to treatment may take weeks to months; nonregenerative IMHA may have more gradual onset than typical IMHA and may be slower to respond to treatment. • IMHA may recur despite previous/current therapy.



MISCELLANEOUS

SYNOMYMS

- Autoimmune hemolytic anemia
- Immune-mediated anemia

SEE ALSO

- Anemia, Regenerative • Chapters on causes of secondary IMHA • Cold Agglutinin Disease • Disseminated Intravascular Coagulation

ABBREVIATIONS

- ALT = alanine aminotransferase • ANA = antinuclear antibody • APTT = activated partial thromboplastin time • DEA = dog erythrocyte antigen • DIC = disseminated intravascular coagulation • FeLV = feline leukemia virus • FIV = feline immunodeficiency virus IMHA = immune-mediated hemolytic anemia • LE = lupus erythematosus • MCV = mean cell volume • PCR = polymerase chain reaction • PCV = packed cell volume • PTE = pulmonary thromboembolism • PT = prothrombin time • RBC = red blood cell • SLE = systemic lupus erythematosus

Suggested Reading

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Client Education Handout
available online



BASICS

OVERVIEW

- Adults—caused by chronic external hemorrhage.
- RBC produced by iron-limited erythropoiesis.
- Importance—prompts clinician to look for chronic external blood loss.

SIGNALMENT

- Fairly common in adult dogs.
- Rare in adult cats.
- Transient neonatal iron-deficiency anemia may occur at 5–10 weeks of age in kittens.

SIGNS

- Signs of anemia (e.g., lethargy, weakness, and tachypnea) and underlying disease.
- Intermittent melena with gastrointestinal blood loss.
- Possible heavy bloodsucking parasite load.

CAUSES & RISK FACTORS

- Chronic external blood loss.
- Common causes—GI lymphoma, hookworms, GI neoplasia.
- Less common—skin (e.g., severe flea infestation) and urinary tract.
- Blood donor overuse.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Any cause of anemia, especially hemorrhage.
- Microcytic anemia in portosystemic shunt disease may or may not be due to iron deficiency.
- Anemia of inflammatory disease iron-limited erythropoiesis.

CBC/BIOCHEMISTRY/URINALYSIS

- PCV usually but not always decreased, generally 10–40% in dogs.
- Anemia either regenerative or non-regenerative.
- Microcytosis—indicated by low normal or low MCV, accompanied by increased heterogeneity, detected by erythrocyte histogram widening or increased RDW.
- RBC changes include microcytosis, hypochromia due to thin cell geometry, and keratocyte and schistocyte formation.
- Newer erythrocyte indices MCVR and CHr, are sensitive for detecting iron-limited erythropoiesis; available on one hematology system.
- Lab tests indicate iron-limited erythropoiesis, but may not differentiate true

from functional iron deficiency. Clinical findings of inflammatory disease versus blood loss are required to differentiate cause of iron limited erythropoiesis. It is also possible that inflammatory disease and true iron deficiency may occur concurrently.

- RBC morphologic changes—hypochromia (increased central pallor), oxidative lesions (e.g., keratocytes), fragmentation.
- Decreased MCHC not sensitive or specific.
- Thrombocytosis may occur.
- Hypoproteinemia—consistent with blood loss.

OTHER LABORATORY TESTS

- Hypoferrremia (serum iron < 70 µg/dL) and transferrin saturation < 15% support the diagnosis.
- Serum iron values may be normal during iron repletion, if blood loss is intermittent.
- Fecal exam for hookworms.
- Fecal examination for occult blood or melena.

IMAGING

Imaging studies—GI disease that may account for blood loss.

DIAGNOSTIC PROCEDURES

As indicated by underlying disease.



TREATMENT

- Identify / correct cause of blood loss.
- Administer iron until hematologic features of iron deficiency resolve.
- If severe (i.e., PCV < 15%), transfusion may be required; whole blood (10–20 mL/kg IV) or packed RBC.



MEDICATIONS

DRUG(S)

Iron Supplementation

Parenteral Iron Supplementation

- Initiate iron therapy with injectable iron.
- Iron dextran—a slowly released form of injectable iron; one injection (10–20 mg/kg IM) followed by oral supplementation.

Oral Iron Supplementation

- Animals with severe iron deficiency may have impaired intestinal iron absorption, making oral therapy of little value until partial iron repletion has occurred.
- Follow injected iron with oral iron supplement for 1–2 months, or until resolved.
- Kittens undergo spontaneous iron repletion beginning at 5–6 weeks of age.

Oral Iron Supplements

- Ferrous sulfate powder—place in food or drinking water (100–300 mg PO q24h).
- Ferrous gluconate—one (325 mg) tablet PO q24h.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Oral iron is associated with unexplained death in kittens and should be avoided.



FOLLOW-UP

- Monitor CBC every 1–4 weeks; if the anemia is severe, more frequently as needed.
- Effective treatment associated with an increase in MCV and reticulocyte volume.
- Erythrocyte histogram—effective treatment associated with microcytic subpopulation reduction over time; it may take a few months to normalize the histogram.



MISCELLANEOUS

ABBREVIATIONS

- CHr = reticulocyte hemoglobin content
- GI = gastrointestinal
- MCHC = mean cell hemoglobin concentration
- MCV = mean cell volume
- MCVR = mean reticulocyte volume
- PCV = packed cell volume
- RBC = red blood cell
- RDW = red cell distribution width

Suggested Reading

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ANEMIA, METABOLIC (ANEMIAS WITH SPICULATED RED CELLS)



BASICS

OVERVIEW

- Sometimes occurs concomitantly with diffuse diseases of the liver, kidney, and, rarely, spleen.
- In most animals with liver disease, spiculated cells have 2–10 elongated, blunt, finger-like projections from their surfaces and are classified as acanthocytes.
- Acanthocytic anemias can be associated with renal disease; anemias of renal disease more often have oval red cells with irregular or ruffled membranes (burr cells).
- Rarely, acanthocytic anemias can be seen in association with splenic disease alone.
- Pathogenesis not entirely clear; abnormal lipid metabolism with free cholesterol loading of RBC membranes is most frequently implicated as cause.
- Dogs with disseminated abdominal hemangiosarcoma with liver involvement often have acanthocytes.

SIGNALMENT

Dogs and cats (infrequently)

SIGNS

- None in most animals (usually mild to moderate condition).
- Detection of spiculated RBCs on peripheral blood film can be first marker for liver, kidney, or splenic disease.
- In large-breed dogs with vague signs or large spleen, suggests possibility of splenic or hepatic hemangiosarcoma.

CAUSES & RISK FACTORS

- Any disease of the liver, kidneys, or possibly spleen.
- The likelihood of RBC morphologic abnormalities parallels the severity of organ involvement.
- Hemangiosarcoma involving the liver is a frequent cause.
- Observed in cats with fatty liver syndrome.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Determination of renal or hepatic causes based on results of biochemistry profile and urinalysis.

CBC/BIOCHEMISTRY/URINALYSIS

- Mild to moderately low PCV, RBC count, and hemoglobin.

- Normal mean corpuscular volume and mean corpuscular hemoglobin concentration in most animals.
- Normocytic, normochromic, and nonregenerative.
- Polychromasia on blood films only with accompanying blood loss (as with hepatic hemangiosarcoma).
- WBC changes variable, based on underlying cause of hepatic or renal pathology.
- Inflammatory conditions likely to be accompanied by inflammatory leukogram.
- Variable findings in liver and kidney function tests (serum biochemistry and urinalysis).

Hepatic Diseases

- High ALT, ALP, and γ -glutamyl transferase.
- High bile acids, serum ammonia.
- Possibly low albumin and serum urea nitrogen.
- Bilirubinuria, bilirubin crystals in urine.

Renal Diseases

- High serum urea nitrogen, creatinine, and phosphorus.
- Highly variable urinalysis findings, including isosthenuria (urine specific gravity 1.008–1.025 in dogs; 1.008–1.035 in cats).
- Tubular and/or protein casts.
- Pyuria.
- Proteinuria.
- Hematuria.

OTHER LABORATORY TESTS

None

IMAGING

Abdominal radiographs and ultrasound—evaluate hepatic, renal, and splenic structure.

DIAGNOSTIC PROCEDURES

Liver or kidney biopsy if indicated.



TREATMENT

Focus treatment on diagnosis and treatment of underlying hepatic, renal, or splenic disease.



MEDICATIONS

DRUG(S)

Variable according to underlying cause.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Variable according to underlying cause.



FOLLOW-UP

Monitor CBC periodically while treating the underlying condition.



MISCELLANEOUS

SEE ALSO

- Anemia of Chronic Kidney Disease
- Hemangiosarcoma, Spleen and Liver

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- PCV = packed cell volume
- RBC = red blood cell
- WBC = white blood cell

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Author Alan H. Rebar

Consulting Editor Alan H. Rebar



BASICS

DEFINITION

Low RBC mass without evidence of increased polychromasia or reticulocytosis in the peripheral blood.

PATHOPHYSIOLOGY

- Low erythroid production or release.
- Onset of anemia and its related signs insidious unless RBC survival is concurrently shortened by hemorrhage or hemolysis.
- May be caused by selective alteration in erythropoiesis or generalized bone marrow injury affecting leukocytes and platelets as well. • Mechanisms for selectively altered erythropoiesis include deficient hormonal stimulation, nutritional deficiency, cytokine-mediated iron sequestration, and disturbed metabolism in or destruction of precursors; generalized bone marrow injury usually caused by toxin, infection, or infiltrative process.

SYSTEMS AFFECTED

- Cardiovascular—heart murmur from low blood viscosity
- Hemic/Lymph/Immune
- Hepatobiliary—centrilobular degeneration from hypoxic injury

SIGNALMENT

- Varies with primary cause.
- Giant schnauzer, Australian shepherd dog, border collie, beagle—congenital cobalamin malabsorption.

SIGNS

General Comments

- Usually secondary.
- Signs associated with primary disease often precede signs of anemia.

Historical Findings

- Lack of energy, exercise intolerance, inappetence, and cold intolerance.
- Other findings reflect primary condition: polyuria and polydipsia (e.g., CRF), paint exposure from remodeling old houses (e.g., lead poisoning), treating female dogs for micturating or urinary incontinence or feminization in male dogs (e.g., hyperestrogenism), failure to thrive observed at 8–12 weeks of age (hereditary cobalamin malabsorption).

Physical Examination Findings

- Pallor, heart murmur (severe anemia), and possibly tachycardia or polypnea.
- Signs reflecting primary condition: oral ulcerations (e.g., CRF), cachexia (e.g., cancer), organomegaly (e.g., lymphoma), gastrointestinal or CNS signs (e.g., lead poisoning), symmetrical alopecia (e.g., hypothyroidism and hyperestrogenism).

CAUSES

Nonregenerative Anemia without Other Cytopenias

- Anemia of inflammatory disease (AID)—most common cause of mild nonregenerative anemia; can be seen within 3–10 days of infection, inflammation, tissue injury, immune-mediated processes, and neoplasia; increased liver production of hepcidin and release of cytokines from T-lymphocytes and macrophages lead to iron sequestration in macrophages, decreased iron absorption; low serum iron and transferrin, increased ferritin, decreased EPO production and function, and shortened RBC lifespan.
- Chronic renal failure—kidneys fail to produce adequate EPO; uremic toxins shorten RBC lifespan and impair response to EPO.
- Chronic liver disease—shortened RBC survival caused by changes in RBC membrane lipids; functional iron deficiency due to decreased transferrin synthesis and impaired mobilization of hepatic iron.
- Endocrine disease—thyroid hormones and cortisol stimulate erythropoiesis and facilitate the effect of erythropoietin.
- Immune-mediated destruction of precursors—pure red cell aplasia.
- Infectious destruction of precursors (although usually > one cell line is involved), e.g., FeLV and ehrlichiosis, *Cytauxzoon felis*.

Nutritional or Mineral Deficiency/Toxicity

- Iron deficiency—usually due to chronic external blood loss; initially regenerative, but as severity increases, anemia becomes nonregenerative.
- Cobalamin (vitamin B₁₂) and/or folate deficiency—rare in dogs and cats; can be caused by dietary insufficiency, malabsorption, or chronic drug administration (e.g., sulfas, methotrexate, anticonvulsants) that inhibits folate; congenital defect in cobalamin absorption in giant schnauzers, border collies, Australian shepherd dogs, and beagles; can occasionally cause normocytic anemia and hypersegmented neutrophils; megaloblastic changes possible in the marrow.
- Disruption of precursor metabolism—chronic lead toxicity and possibly high concentrations of aluminum, arsenic, and cadmium inhibit heme synthesis; cadmium and lead cause renal toxicity and impaired EPO production.

Nonregenerative Anemia with Other Cytopenias

- Toxicities—drugs or chemicals (e.g., cancer chemotherapeutics, chloramphenicol, phenylbutazone, trimethoprim-sulfadiazine, zonisamide, phenobarbital, griseofulvin, methimazole, fenbendazole, albendazole, and benzene), hormones (e.g., estrogen toxicity secondary to abortifacient therapy and Sertoli cell tumor).
- Infections—FeLV, FIV, ehrlichiosis, babesiosis, and parvoviral infection (recovery usually precedes development of anemia).
- Infiltrative processes—myelodysplasia, myeloproliferative

and lymphoproliferative diseases, metastatic neoplasia, myelofibrosis, and osteosclerosis.

RISK FACTORS

- Renal failure • Inflammatory or chronic disease • Liver failure • Sertoli cell tumor
- Cancer • Chronic blood loss • Cats from multicat households (FeLV) • Lead or arsenic exposure—chronic



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Regenerative anemia initially nonregenerative; sudden onset of signs more consistent with regenerative than nonregenerative anemia; exacerbation of a chronic condition may produce the appearance of an acute onset.

LABORATORY FINDINGS

Disorders That May Alter Laboratory Results

- Lipemia can falsely elevate hemoglobin and MCHC values.
- Lead toxicity-increased NRBCs may falsely elevate the WBC count.

Valid If Run in Human Laboratory?

- Dogs—yes.
- Cats—yes, if hematology instrument uses species-specific parameters; instruments designed strictly for human specimens may under-count small feline RBCs.

CBC/BIOCHEMISTRY/URINALYSIS

CBC and Blood Smear

- PCV, RBC count, and hemoglobin low.
- Anemia usually normocytic, normochromic, with normal MCV and MCHC.
- Macrocytosis (high MCV)—without polychromasia suggests nuclear maturation defect (cells skip a division); seen in cats with FeLV; rarely caused by vitamin B₁₂ or folate deficiency.
- Microcytosis (low MCV)—suggests cytoplasmic maturation defect (cells undergo extra division); iron deficiency most common cause; in late stages, concurrent hypochromasia (low MCHC) common in dogs but not in cats; seen in approximately one-third of patients with hepatic insufficiency or vascular shunting.
- Specific RBC morphologies—schistocytes common with iron deficiency ± visibly hypochromic RBCs (dogs); acanthocytes with liver disease; target cells with iron deficiency, liver disease, and hypothyroidism.
- Inflammatory leukogram supports AID.
- Thrombocytosis common in iron deficiency.
- High number of NRBCs without polychromasia or disproportionate to the degree of anemia and polychromasia seen with lead toxicity, EMH, heat stroke, and injury to bone marrow stroma by endotoxemia or hypoxia.
- RBC or WBC precursors in peripheral blood without orderly progression to more mature forms suggest myelodysplasia or myeloproliferative disease.
- Concurrent

ANEMIA, NONREGENERATIVE

(CONTINUED)

cytopenia in other cell lines without evidence of marrow responsiveness (e.g., band neutrophils and macroplatelets) suggests generalized bone marrow injury.

Serum Biochemistry and Urinalysis

- CRF: high BUN and creatinine with inadequate urine concentration (dogs, < 1.030; cats, < 1.035).
- Liver disease: high ALT, total bilirubin, or elevated bile acids suggests liver disease.
- Hypothyroidism: high serum cholesterol (> 500 mg/dL).
- Hypoadrenocorticism: Na/K < 23, lymphocytosis, and eosinophilia.

OTHER LABORATORY TESTS

- Reticulocyte count—value of < 95,000/ μ L (dogs) or < 60,000/ μ L (cats) (automated counts) accompanied by a low PCV confirms nonregenerative anemia.
- Direct antiglobulin test (Coombs')—spherocytosis, autoagglutination, or positive Coombs' test provides support for immune-mediated destruction of erythroid precursors.
- Serum iron profile—may be indicated for patients with microcytic anemia; with iron deficiency both serum iron and ferritin are low, while total iron-binding capacity varies; with AID, serum iron is low but serum ferritin is high (MCV and MCHC usually normal).
- Bile acids measurement—may be indicated for evaluation of microcytic anemia; high values suggest hepatic insufficiency or vascular shunting.
- Serum lead—indicated when NRBCs are present, especially with concurrent gastrointestinal or CNS signs; value > 30 μ L/dL (0.3 ppm) strongly supports lead intoxication.
- Serologic testing—FeLV test in any cat with nonregenerative anemia; *Ehrlichia canis*, *Anaplasma phagocytophilia*, and *Babesia* PCR assays indicated in dogs with unexplained anemia, especially when concurrent with thrombocytopenia.
- Endocrine testing—when clinical signs and laboratory tests suggest hypothyroidism (T_4 , free T_4 , and TSH concentrations) or hypoadrenocorticism (ACTH stimulation test).
- Serum cobalamin \pm urine methylmalonic acid concentrations—puppies at risk for hereditary cobalamin malabsorption.

DIAGNOSTIC PROCEDURES**Cytologic Examination of Bone Marrow and Core Biopsy**

- Cytologic examination of aspirate indicated in all patients unless primary cause is apparent (e.g., AID and CRF).
- Bone marrow core biopsy—useful in evaluation of bone marrow architecture and overall cellularity; important for diagnosis of aplastic marrow or myelofibrosis.
- Erythroid hypoplasia or aplasia confirms the problem, although history and other tests may be needed to determine the underlying etiology.
- Myeloid hyperplasia and high iron stores support AID.

- Classically, iron deficiency has expanded erythron and high numbers of metarubricytes; absence of iron stores supportive in dogs, but not cats.
- Increased erythrophagocytosis suggests injury to cells (e.g., immune-mediated and toxic causes).
- Incomplete maturation sequence suggests injury to specific maturation stage (e.g., immune-mediated and toxic causes) or possibly incomplete recovery from a previous injury (recheck in 3–5 days).
- Disorderly maturation and atypical cellular morphology suggest myelodysplastic syndrome.
- Hypercellular marrow with increased blast cells (> 20% of nucleated cells) indicates hematopoietic neoplasia; immunophenotyping can identify affected cell line(s); circulating neoplastic cells may or may not be seen.
- Non-marrow cells indicate metastatic neoplasia.

Abdominal Ultrasound

Evaluation of microcytic anemia; look for intestinal neoplasia or other source of external blood loss.

**TREATMENT**

- Anemia usually resolves with resolution of underlying disease.
- Conditions associated with severe anemia or pancytopenia often carry guarded-to-poor prognosis and may involve long-term treatment without complete resolution.
- Metabolic compensation occurs with slowly developing nonregenerative anemia; thus mild to moderately severe anemia (PCV > 15%) generally requires no supportive intervention.
- For patients with severe anemia (PCV < 10–15%), the degree of hypoxia may require transfusion (e.g., 6–10 mL/kg for packed RBCs; 10–20 mL/kg for whole blood). Less blood may be needed in animals with chronic anemia.
- Determine blood type prior to transfusion to ensure compatibility. Cross match against donor blood if blood typing reagents are not available, or if patient requires a second transfusion more than 4 days after the first transfusion.
- If blood volume and tissue perfusion are compromised by concurrent blood loss or shock, administer lactated Ringer's solution or colloids.
- With chronic anemia, volume overload is a concern—blood products and fluids should be given slowly.

**MEDICATIONS****DRUG(S)**

- Erythropoietin in patients with anemia of CRF (see Anemia of Chronic Kidney Disease).

- Iron supplementation in patients with iron deficiency anemia (see Anemia, Iron-Deficiency).
- May supplement with folic acid at rate of 4–10 mg/kg/day.
- May supplement with cobalamin (vitamin B₁₂) at rate of 100–200 mg/day PO (dogs) or 50–100 mg/day PO (cats); parenteral cyanocobalamin administration (50 μ g/kg or 0.5–1 mg/dog SC weekly to monthly) needed in dogs with inherited cobalamin malabsorption.

PRECAUTIONS

Monitor for transfusion reactions (see Blood Transfusion Reactions).

**FOLLOW-UP****PATIENT MONITORING**

- With severe anemia: PCV and blood smear examination every 1–2 days.
- Stable animals with chronic or slowly improving disease course: reevaluate every 1–2 weeks.

**MISCELLANEOUS****PREGNANCY/FERTILITY/BREEDING**

Some pregnant animals have mildly low PCV, caused by expanded blood volume.

SYNOMYMS

Non-responsive anemia

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- AID = anemia of inflammatory disease
- ALT = alanine aminotransferase
- CNS = central nervous system
- CRF = chronic renal failure
- EMH = extramedullary hematopoiesis
- EPO = erythropoietin
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- IL-1 = interleukin-1
- MCHC = mean corpuscular hemoglobin concentration
- MCV = mean cell volume
- NRBC = nucleated red blood cells
- PCR = polymerase chain reaction
- TSH = thyroid stimulating hormone

INTERNET RESOURCES

Erythrocytes: Overview, Morphology, Quantity; A.H. Rebar, P.S. MacWilliams, B.F. Feldman, et al.: <http://www.ivis.org/advances/Rebar/Chap4/chapter.asp?LA=1>

Suggested Reading

Abram-Ogg, A. Nonregenerative anemia. In: Ettinger SJ, Feldman EC, eds., Textbook of Veterinary Internal Medicine: Diseases of the Dog and Cat, 7th ed. St Louis, MO: Elsevier Saunders, 2010, pp. 788–797.

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ANEMIA, NUCLEAR MATURATION DEFECTS (ANEMIA, MELOBLASTIC)



BASICS

OVERVIEW

- Nonregenerative anemia characterized by arrested development of the nuclei of RBC precursors (as a result of interference with DNA synthesis) while the cytoplasm develops normally (nuclear-cytoplasmic asynchrony).
- Affected RBC precursors fail to divide normally and thus are larger than corresponding normal precursors with the same degree of cytoplasmic maturity (hemoglobinization); because their nuclei are deficient in chromatin (DNA), they have a distinctive open and stippled appearance; these giant precursors with atypical, immature nuclei are known as megaloblasts.
- Although these asynchronous changes are most prominent in RBC precursors, WBC and platelet precursors are similarly affected.

SIGNALMENT

- Dogs and cats.
- Spontaneous, clinically unimportant occurrence in toy poodles (occasional).
- Breed predilection: giant schnauzers, also border collies, Australian shepherds, and beagles with inherited cobalamin malabsorption.
- Defect usually acquired.

SIGNS

- In dogs, generally mild, usually not clinically important.
- In cats with FeLV-associated nuclear maturation anemia, FeLV-related signs can be anticipated. Anemia may be mild to severe.

CAUSES & RISK FACTORS

- Infectious—FeLV; retroviral infection the most common cause of megaloblastic anemia in cats. FIV has been reported as a cause much less frequently.
- Nutritional—folic acid and vitamin B₁₂ deficiencies (Giant Schnauzers and other with inherited cobalamin malabsorption).
- Toxic—phenytoin, methotrexate (folate antagonist), alkylating agents (cyclophosphamide), plant alkaloids (vincristine), antimetabolites (azathioprine).
- Congenital—toy and miniature poodles.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- In dogs, all other mild to moderate nonregenerative anemias, including anemia of inflammatory disease, renal disease, and lead poisoning.
- Differentiation based on the distinctive CBC and bone marrow findings listed.
- In cats, FeLV infection is the primary differential.

CBC/BIOCHEMISTRY/URINALYSIS

- In dogs, mild to moderate anemia (PCV: 30–40%).
- In cats, anemia can be mild to severe.
- Anemia classically macrocytic (high mean corpuscular volume) and normochromic (normal mean corpuscular hemoglobin concentration). However, mean corpuscular volume and mean corpuscular haemoglobin concentration can be normal.
- Large, fully hemoglobinized RBC; occasional to numerous megaloblasts, particularly at the feather edge; minimal to no polychromasia.
- In cats with FeLV, anemia may occur in association with a myelodysplastic syndrome or in conjunction with leukemia of a different cell line.

OTHER LABORATORY TESTS

FeLV

IMAGING

N/A

OTHER DIAGNOSTIC PROCEDURES

Bone Marrow Biopsy

- In dogs, usually hyperplastic, often in all cell lines.
- In cats, marrow findings are highly variable and may be hyper- to hypocellular.
- Maturation arrest with nuclear and cytoplasmic asynchrony may be seen in all cell lines.
- Many megaloblastic RBC precursors may be observed.
- Macrophagic hyperplasia with active phagocytosis of nucleated RBCs and megaloblasts (common).



TREATMENT

- Treat by targeting the underlying cause if possible.
- Except for that occurring with FeLV in cats, megaloblastic anemia is a relatively mild condition.
- Treat most patients on an outpatient basis.



MEDICATIONS

DRUG(S)

- In animals with drug toxicity, discontinue the offending drug.
- In all animals, consider supplementation with folic acid (4–10 mg/kg/day) or vitamin B₁₂ (dogs, 100–200 mg/day PO; cats, 50–100 mg/day PO).
- Giant schnauzers with inherited cobalamin malabsorption require parenteral treatment with vitamin B₁₂ (0.5–1 mg IM weekly to every few months).

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Drugs known to cause megaloblastic anemia (e.g., methotrexate and phenytoin) should be avoided in patients whose condition results from other causes.



FOLLOW-UP

- Monitor response to treatment by CBC (weekly) and occasional bone marrow collection and evaluation.
- Closely monitor FeLV-positive cats for evidence of onset of other signs of hematopoietic dyscrasias in the peripheral blood and bone marrow.
- Prognosis—depends on underlying cause; in FeLV-positive cats, prognosis guarded; in animals with drug-associated anemia, prognosis good when use of offending drug is interrupted.



MISCELLANEOUS

SEE ALSO

- Anemia, Nonregenerative
- Feline Leukemia Virus Infection (FeLV)

ABBREVIATIONS

- FeLV = feline leukemia virus
- PCV = packed cell volume
- RBC = red blood cell
- WBC = white blood cell
- FIV = feline immunodeficiency virus

Suggested Reading

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ANEMIA, REGENERATIVE



BASICS

DEFINITION

Decreased circulating RBC mass (indicated by low PCV, hemoglobin, and total RBC count) accompanied by appropriate, compensatory increase in RBC production by the bone marrow (e.g., reticulocytosis in the peripheral blood and RBC hyperplasia in the bone marrow).

PATOPHYSIOLOGY

- Caused by blood loss or hemolysis.
- Hemolysis—caused by intrinsic RBC defects (e.g., congenital RBC membrane defects or enzyme deficiencies) or extrinsic factors (e.g., RBC parasites, oxidative injury, hemolysins, osmotic changes, immune-mediated RBC destruction, heat stroke, and severe hypophosphatemia. • Intravascular hemolysis may lead to DIC.

SYSTEMS AFFECTED

- Cardiovascular—murmurs with marked anemia; tachycardia. • Hemic/Lymph/Immune—erythroid hyperplasia in bone marrow; splenic EMH; splenomegaly due to EMH and histiocytic hyperplasia can be feature of extravascular hemolytic anemia.
- Hepatic—anoxia causes centrilobular degeneration of the liver; hemosiderosis ± hemochromatosis possible with chronic hemolytic anemia (e.g., PK-deficient dogs) especially following repeated transfusions.
- Renal—severe intravascular hemolysis rarely leads to renal tubular necrosis and acute renal failure. • Musculoskeletal—progressive osteoclerosis seen in PK-deficient dogs.

SIGNALMENT

- PK deficiency—basenji, beagle, cairn terrier, Chihuahua, dachshund, Labrador retriever, miniature poodle, pug, West Highland white terrier, and American Eskimo; and Somali, Abyssinian, and domestic shorthair cats.
- PFK deficiency—English springer spaniel, American cocker spaniel, whippet, wachtelhund, and mixed breed dogs with spaniel parentage. • Marked RBC osmotic fragility—English springer spaniel and Abyssinian, Somali, Siamese, and domestic shorthair cats. • Feline congenital porphyria—Siamese and domestic shorthair cats. • Some dog breeds have a genetic predisposition for heritable coagulopathies such as factor VIII deficiency and von Willebrand disease. • Middle-aged female dogs, especially American cocker spaniel, English springer spaniel, Irish setter, Old English sheepdog, poodle, and Shetland sheepdog, are predisposed to immune-mediated syndromes, such as SLE and immune-mediated hemolytic anemia.

SIGNS

- Pallor. • Weakness, exercise intolerance.
- Anorexia. • Possible heart murmur, tachycardia, bounding pulses. • Possible jaundice and hemoglobinuria. • Petechiae, epistaxis, melena suggest blood loss due to vasculitis or a platelet problem. • Hematomas or cavity bleeds suggest a coagulation factor deficiency. • Clinical signs depend on degree of anemia and rapidity of onset. • Rapid loss of 15–25% blood volume or acute hemolysis results in shock and possible death. • With chronic anemia, compensatory increases in heart rate, and eventually heart size, lessens RBC circulation time; hemoglobin can drop to as low as 50% of minimum normal value without overt signs of hypoxia.

CAUSES

Immune Mediated

- Antibodies ± complement on membrane shorten RBC lifespan. Antibodies may target RBC membrane components or may be directed against tumor antigens, infectious agents, vaccines, or drugs (e.g., sulfonamides, penicillins, cephalosporins, methimazole, amiodarone) that are either directly adherent to RBC surface or part of immune complexes adherent to RBCs. • Anemia is usually regenerative, but up to 30% of cases will be nonregenerative due to immune-mediated destruction of erythroid precursors in bone marrow. • Hemolysis may be either intravascular, through IgM-mediated activation of complement, or extravascular, through IgG-mediated phagocytosis.
- Hemolytic antibodies are generally reactive at body temperature; rarely cold-reacting antibodies cause *in vivo* hemolysis and/or RBC agglutination in cooler, peripheral vasculature. • Transfusion of a blood type B cat with type A blood can result in rapid, severe, intravascular hemolysis; neonatal isoerythrolysis seen in kittens born to a blood type B queen mated to a blood type A tom.
- Canine blood type DEA 1.1 can cause hemolysis in a DEA 1.1-negative dog, although a single incompatible transfusion can be tolerated. • The newly identified blood types *Mik* (cats) and *Dal* (dogs) can cause significant hemolytic transfusion reactions in animals lacking these common RBC antigens.

Oxidant Injury

- Oxidants can cause Heinz body formation (aggregates of oxidized hemoglobin), eccentrocytes (oxidation of RBC membranes), and methemoglobinemia. • Heinz bodies are removed through extravascular hemolysis, while oxidized membrane components cause intravascular hemolysis. • Oxidants include onions, garlic, acetaminophen (especially in cats), zinc (from pennies minted after 1982, zinc oxide ointment, and zinc bolts), acute copper toxicosis, benzocaine, vitamin K₃ (dogs), propofol, phenolic compounds (moth balls), skunk musk, and phenazopyridine

(cats). • In cats, some systemic diseases (e.g., diabetes mellitus, hyperthyroidism, lymphoma) enhance Heinz body formation but do not necessarily cause anemia.

Erythrocyte Parasites

- Cats: *Mycoplasma haemofelis*, *M. haemominutum*, *M. turicensis*, and *M. haematoparvum*, *Cytauxzoon felis*. • Dogs: *Mycoplasma haemocanis*, *Babesia canis*, and *B. gibsoni*.

Mechanical RBC Fragmentation

- Caused by vasculitis, thromboembolic disease or disease of any vascular organ (e.g., liver, kidney, spleen, heart). • Rare cause of anemia unless accompanied by hemorrhage.

Inherited RBC Abnormalities

- PK deficiency—impaired ATP formation, leading to premature RBC destruction; autosomal recessive trait. • PFK deficiency—marked alkaline fragility caused by impaired synthesis of 2,3-diphosphoglycerate; hemolytic episodes triggered by hyperventilation-induced alkalemia, especially after vigorous exercise; autosomal recessive trait. • Increased RBC osmotic fragility, (unknown RBC defect) leads to recurrent severe anemia and splenomegaly. • Feline congenital porphyria—enzyme deficiency in heme synthetic pathway leads to accumulation of heme precursors, hemolytic anemia and brown-red discoloration of teeth and bones. Siamese tend to have severe hemolytic anemia, while domestic shorthair cats have a less severe autosomal dominant trait that causes mild anemia.

Hypophosphatemia

Severe hypophosphatemia, secondary to treatment with insulin or phosphate binders, impairs ATP production, leading to increased erythrocyte fragility and hemolysis.

Blood Loss

- Trauma • Bleeding neoplasms (e.g., hemangiosarcoma, intestinal adenocarcinoma) • Coagulopathies (e.g., warfarin poisoning, hemophilia, thrombocytopenia) • Bloodsucking parasites (e.g., fleas, ticks, and *Ancylostoma*)
- Gastrointestinal ulcers



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiated from nonregenerative anemia by high reticulocyte count.

LABORATORY FINDINGS

Disorders That May Alter Laboratory Results

- Lipemia can cause mild *in vitro* hemolysis, without appreciable anemia, and may falsely elevate MCHC. • Autoagglutination may falsely decrease the RBC count.
- Intraerythrocytic inclusions (e.g. basophilic

(CONTINUED)

- stippling or intraerythrocyte parasites may falsely increase automated reticulocyte count.
- Exercise and excitement can increase RBC count, PCV, and reticulocyte count through splenic contraction.

Valid If Run in Human Laboratory?

- Dogs—yes.
- Cats—yes, if hematology instrument uses species-specific parameters; instruments designed for analysis of human specimens may under-count small feline RBCs.

CBC/BIOCHEMISTRY/URINALYSIS

- PCV, RBC count, and hemoglobin low.
- Total protein often low with blood loss anemia and may be the only sign with acute blood loss; normal PCV may be maintained through transient splenic contraction.
- Severity of acute blood loss may be underestimated until the plasma volume has been restored by fluid administration and/or internal fluid shifts.
- RBC indices vary depending on the cause of anemia and degree of regenerative response—MCV, normal to high; MCHC, normal to low in most patients; MCHC, artificially high with intravascular hemolysis and hemoglobinemia.
- With iron deficiency, dogs may have a low MCV, MCH, and MCHC; cats have a low MCV but normal MCH and MCHC.
- Specific RBC morphologies may suggest cause of hemolysis: marked spherocytosis suggests immune-mediated disease (not as easily detected in cats whose RBCs generally lack central pallor); Heinz bodies or eccentrocytes suggest oxidant injury; numerous schistocytes suggest microangiopathy.
- Agglutinated RBCs indicate anemia is immune mediated; distinguish autoagglutination from rouleaux by generous sample dilution with saline.
- Hemolysis may cause inflammatory leukogram (neutrophilia with a left shift and monocytosis). Acute blood loss may be associated with stress leukogram (mild neutrophilia and lymphopenia).
- Blood loss may be accompanied by either thrombocytopenia or rebound thrombocytosis; iron deficiency is often accompanied by thrombocytosis.
- Hyperbilirubinemia and bilirubinuria accompany marked hemolysis; hemoglobinemia and hemoglobinuria seen with intravascular hemolysis.

OTHER LABORATORY TESTS

- In anemia automated absolute reticulocyte count (RBC count × reticulocyte %) > 60,000/ μL (cats) or > 95,000/ μL (dogs) suggests regenerative anemia.
- It takes 3–5 days for bone marrow to mount a peak regenerative response, so reticulocytosis may initially be absent with blood loss or hemolysis.
- Direct antiglobulin test (Coombs' test) indicated when immune-mediated hemolytic anemia suspected; a positive test and evidence of spherocytosis

(canine) in the peripheral blood is confirmatory; false negatives and false positives are possible.

- PCR test for PK deficiency: young Basenji, beagle, dachshund, Toy Eskimo, West Highland white terrier, and cairn breeds with persistent anemia, massive reticulocytosis and a negative Coombs' test.
- PCR test for PFK deficiency: spaniels and whippets with recurrent hemolytic crises.

DIAGNOSTIC PROCEDURES

- Bone marrow aspirate—needed only when reticulocytosis is lacking; RBC hyperplasia confirms regenerative response.
- Bone marrow biopsy—useful in evaluation of bone marrow architecture and overall cellularity; important for confirmation of nonregenerative process.



TREATMENT

- Emergency if anemia is severe and develops rapidly.
- Massive hemorrhage leads to hypovolemic shock and anoxia; acute hemolysis leads to anoxia.
- Cage rest and careful observation indicated, depending on severity of signs.

Blood Loss Anemias

- Traumatic blood loss leading to shock-crystallloid fluids can rapidly correct hypovolemia and restore circulation.
- RBC replacement (packed RBCs or whole blood) indicated if PCV < 15–20% and signs of severe hypoxia (i.e., extremely pale mucous membranes, weakness, tachycardia, pounding pulses, tachypnea). Initial dosage depends on product selected; 6–10 mL/kg for packed RBCs; 10–20 mL/kg for whole blood. Less blood may be needed in animals with chronic anemia. Determine blood type prior to transfusion, to ensure compatibility. Cross match against donor blood if blood typing reagents not available, or if patient requires second transfusion more than 4 days after first transfusion.
- Animals with chronic blood loss are normovolemic with increased cardiac output, therefore transfusion volumes and rates should be conservative to avoid cardiac failure.

Hemolytic Anemias

Blood transfusion may be indicated; in patients with immune-mediated process, RBCs probably survive similarly to patient's own RBCs, so transfusion should not be withheld if marked signs of anemia present.



MEDICATIONS

DRUG(S)

- Iron may benefit animals with chronic blood-loss anemia (see Anemia, Iron-Deficiency).

ANEMIA, REGENERATIVE

A

- Hemolytic anemias—varies with cause of hemolysis.



FOLLOW-UP

PATIENT MONITORING

- Initially, monitor of RBC mass (e.g., PCV, RBC count, and hemoglobin) and morphologic features on a blood film (i.e., polychromasia) every 24 hours to evaluate effectiveness of treatment and bone marrow responsiveness.
- As regeneration becomes apparent (rising RBC values and polychromasia), recheck patients every 3–5 days; return to normal values occurs about 14 days after acute hemorrhage but may take longer with immune-mediated process.
- Following transfusion, monitor for complications (see Blood Transfusion Reactions).



MISCELLANEOUS

SEE ALSO

- Anemia, Heinz Body • Anemia, Immune-Mediated • Anemia, Iron-Deficiency • Babesiosis • Bartonellosis
- Cytauxzoonosis • Lupus Erythematosus, Systemic • Zinc Toxicosis

ABBREVIATIONS

- ATP = adenosine triphosphate • DIC = disseminated intravascular coagulation
- EMH = extramedullary hematopoiesis
- MCH = mean corpuscular hemoglobin
- MCHC = mean corpuscular hemoglobin concentration • MCV = mean cell volume
- PCV = packed cell volume • PFK = phosphofructokinase • PK = pyruvate kinase
- RBC = red blood cell • SLE = systemic lupus erythematosus

INTERNET RESOURCES

Erythrocytes: Overview, Morphology, Quantity; A.H. Rebar, P.S. MacWilliams, B.F. Feldman, et al.: <http://www.ivis.org/advances/Rebar/Chap4/chapter.asp?LA=1>.

Suggested Reading

Mitchell K, Krush S. Immune-mediated haemolytic anemia and other regenerative anemias. In: Ettinger SJ, Feldman EC, eds., *Textbook of Veterinary Internal Medicine: Diseases of the Dog and Cat*, 7th ed. St Louis, MO: Elsevier Saunders, 2010, pp. 761–772.

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ANISOCORIA

**BASICS****DEFINITION**

Asymmetric pupils

PATHOPHYSIOLOGY

- Disruption of sympathetic (causing miosis) or parasympathetic (causing mydriasis) innervation to the eye.
- Ocular disease – numerous causes.

SYSTEMS AFFECTED

- Nervous
- Ophthalmic

GENETICS

None

INCIDENCE/PREVALENCE

Common

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

- Dog and cat
- All ages affected
- No gender predisposition

SIGNS

Unequal pupil size

CAUSES*Neurologic*

See Table 1

Ocular

See Table 2

RISK FACTORS

N/A

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- Must determine which pupil is abnormal—see Figure 1 and Tables 1 and 2.
- Distinguish between neurologic and ocular causes.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

- See Table 1.
- Ultrasound—use to identify ocular, retrobulbar or jugular groove lesions.
- MRI—use to identify CNS lesions.
- CT—use to identify tympanic bulla lesions.

DIAGNOSTIC PROCEDURES

- See Table 1.
- CSF tap—evaluate CNS inflammation/infection.
- ERG—evaluate retinal function.
- Pharmacologic testing—see Figure 1; postganglionic lesions cause denervation supersensitivity resulting in more rapid constriction or dilation with application of pharmacologic agents. Differentiation of pre- or postganglionic lesions can be difficult if based solely on pharmacologic testing.

PATHOLOGIC FINDINGS

Dependent on the underlying diagnosis

**TREATMENT**

Dependent on underlying disease

Table 1

Neurologic lesions causing anisocoria.

<i>Sign</i>	<i>PLR</i>	<i>Lesion Localization</i>	<i>Differential List</i>	<i>Diagnostic Test</i>
<i>Mydriasis—Inability to constrict the pupil</i>	No direct, present indirect	Ipsilateral optic nerve/chiasm Ipsilateral oculomotor nerve/nucleus	Neuritis, neoplasia Encephalitis, neoplasia, trauma, retrobulbar mass	MRI/CSF tap/ERG MRI/CSF tap Ultrasound orbit
<i>Miosis—Inability to dilate the pupil</i>	Present	Brainstem C1-T2 myelopathy or C6-T2 brachial plexus Vagosympathetic trunk Tympanic bulla Trigeminal nerve	Encephalitis, neoplasia, trauma Trauma, myelitis, neoplasia, IVDH (rare) Jugular venipuncture, trauma Otitis media, neoplasia, trauma Neuritis, neoplasia	MRI/CSF tap MRI/myelogram/CT MRI/ultrasound MRI/CT MRI

Table 2

Ocular diseases causing anisocoria.

<i>Lesion</i>	<i>Associated Signs</i>	<i>Causes</i>
Anterior uveitis	Miosis, aqueous flare, corneal edema, conjunctival hyperemia	Infectious/inflammatory disease, trauma, neoplasia
Glaucoma	Mydriasis Sluggish/absent PLR, increased intraocular pressure, corneal edema	Primary glaucoma, secondary glaucoma
Neoplasm	Miosis/mydriasis, iris color change	Lymphoma, melanoma
Posterior synechia	Variable pupil shape, sluggish/absent PLR, anterior uveitis	Secondary to anterior uveitis
Iris atrophy	Variable pupil shape, iridal thinning, sluggish PLR	Old age change
Iris hypoplasia	Sluggish/absent PLR, irregular pupil margin, other ocular abnormalities	Congenital
Pharmacologic blockade	Mydriasis Absent direct/consensual PLR Normal vision	Atropine
Spastic pupil syndrome	Miosis, normal vision	FeLV

(CONTINUED)

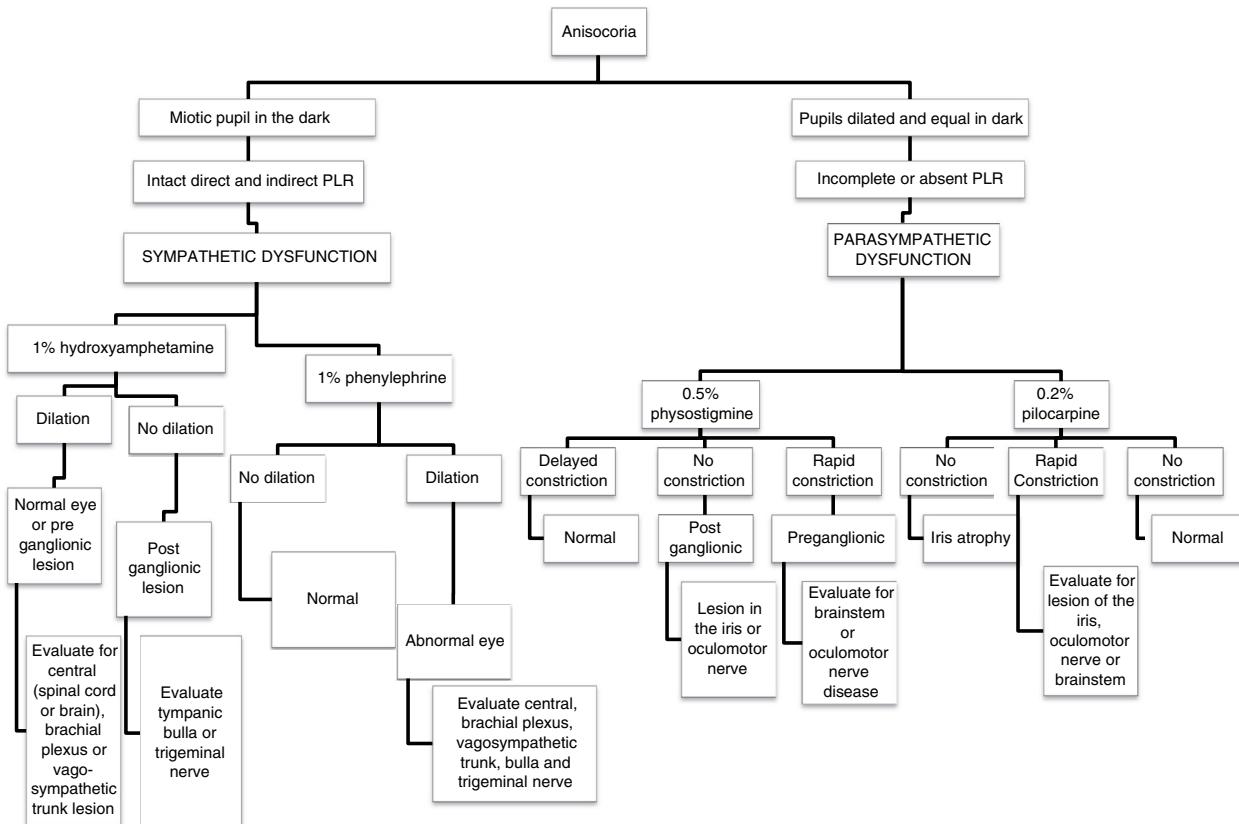
ANISOCORIA**A**

Figure 1.

**MEDICATIONS****DRUG(S) OF CHOICE**

Dependent on underlying disease

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

N/A

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

Dependent on the underlying disease

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

None

SEE ALSO

- Anterior Uveitis—Cats
- Anterior Uveitis—Dogs
- Glaucoma
- Horner's Syndrome
- Iris Atrophy
- Optic Neuritis and Papilledema

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- ERG = electroretinogram
- FeLV = feline leukemia virus

- MRI = magnetic resonance imaging
- PLR = pupillary light reflex

INTERNET RESOURCES

None

Suggested Reading

Cottrill NB, Differential diagnosis of anisocoria. In: Kirk's Current Veterinary Therapy, 14th ed. St Louis, MO: Saunders, 2009, pp. 1168–1174.

Lorenz MD, Kornegay JN. Blindness, anisocoria and abnormal eye movements. In: Handbook of Veterinary Neurology, 4th ed. St. Louis, MO: Saunders, 2004, pp. 283–295.

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**Client Education Handout
available online**

ANOREXIA



BASICS

DEFINITION

The lack or loss of appetite for food; appetite is psychological and its existence in animals is assumed. Hunger is physiologically aroused by the body's need for food. Anorexia may be partial (hyporexia) or complete. Anorexia results in decreased food intake, which then leads to weight loss. Pseudoanorexia is associated with the inability to prehend or swallow food rather than actual loss of appetite.

PATHOPHYSIOLOGY

- The control of appetite is a complex interaction between the central nervous system and the periphery. • The hypothalamus and brainstem contain peptidergic feeding-regulatory neurons that act as input stations for sensory and metabolic signals. These cell populations project to several brain regions and interconnect extensively. • Sensory signals that affect appetite include the odor, taste, texture, and temperature of food as well as gastric and duodenal distention. • Metabolic signals for hunger and satiety include a variety of peptides and hormones released during the fasting and fed states as well as plasma concentrations of glucose and fatty acids interacting with nutrient-specific receptors in the liver and gastrointestinal tract. • Leptin is primarily produced by adipocytes and acts on specific hypothalamic receptors to decrease metabolism and decrease appetite.
- Neuropeptide Y release from the gastrointestinal tract induces hunger and hyperphagia, and decreases energy expenditure after food restriction. • Ghrelin produced by the stomach is a prokinetic and decreases leptin and increases neuropeptide Y production. • Cholecystokinin and bombesin released from the gastrointestinal tract decrease appetite. • Serotonin is an important and perhaps final mediator centrally via a serotonergic tract that passes near the ventromedial hypothalamus. • Dopaminergic tracts in the hypothalamus help regulate food intake and are closely associated with the lateral hypothalamus (classical feeding center). • Environmental factors including the location and timing of meals as well as learned behaviors and circadian rhythms modulate appetite and may override other signals for satiety and hunger. • Appetite is stimulated by aldosterone and corticosterone and suppressed by glucagon and somatostatin.
- Inflammatory and neoplastic disease can cause hyporexia by releasing proinflammatory cytokines such as interleukin-1, tumor necrosis factor, and interferon. • The expected upregulation of dietary intake in response to elevated energy expenditure is frequently

absent in cancer patients. • Exogenous and endogenous toxins (e.g., renal and liver failure) cause hyporexia. • Any disorder that decreases cerebral arousal will potentially decrease food intake. • Gastroparesis associated with neoplasia, metabolic disorders, and primary gastrointestinal disease is associated with decreased appetite. • Fear, pain, and stress may decrease appetite.

SYSTEMS AFFECTED

All body systems

SIGNALMENT

Species

Dog and cat

Breed Predilections

N/A

Mean Age and Range

N/A

Predominant Sex

N/A

SIGNS

Historical Findings

- Refusal to eat is a common presenting complaint because pet owners strongly associate poor appetite with illness. • Patients with disorders causing dysfunction or pain of the face, neck, oropharynx, and esophagus may display an interest in food but cannot eat. These patients are referred to as being pseudoanorectic. • Animals lacking a sense of smell (anosmia) often show no sniffing behavior. • Weight loss may be noted.

Physical Examination Findings

- Clinical signs in animals with anorexia/hyporexia vary depending on the underlying cause but may include fever, pallor, icterus, pain, changes in organ size, ocular changes, abdominal distention, dyspnea, muffled heart and lung sounds, adventitious lung sounds, cardiac murmurs, and masses. Weight loss and muscle wasting may be evident depending upon the extent and duration of decreased food intake. • Pseudoanorectic patients commonly display weight loss, halitosis, excessive drooling, difficulty in prehending and masticating food, and odynophagia (painful swallowing).

CAUSES

Anorexia/Hyporexia

- Almost any systemic disease process can cause anorexia/hyporexia. • Psychological—unpalatable diet, food aversion, stress, alterations in routine and environment.
- Pain. • Toxicities and drug side-effects.
- Gastrointestinal disease. • Acid-base disorders. • Cardiac failure. • Endocrine and metabolic disease. • Neoplasia. • Infectious disease. • Immune mediated disease.
- Respiratory disease. • Musculoskeletal disease. • Neurologic disease. • Miscellaneous (e.g., motion sickness, high environmental temperature).

Pseudoanorexia

- Any disease causing painful or dysfunctional prehension, mastication, and swallowing.
- Stomatitis, glossitis, gingivitis, pharyngitis, and esophagitis (e.g., physical agents, caustics, bacterial or viral infections, foreign bodies, immune-mediated diseases, uremia).
- Retropharyngeal disorders (e.g., lymphadenopathy, abscess, hematoma, sialocele). • Dental disease or periodontal disease. • Retrobulbar abscess. • Oral, glossal, pharyngeal, or esophageal neoplasia.
- Neurologic disorders (e.g., rabies; neuropathies of cranial nerves V, VII, IX, X, XII; and central nervous system lesions).
- Musculoskeletal lesions (e.g., masticatory myositis, temporomandibular joint disease, fractures, craniomandibular osteopathy, myasthenia gravis, botulism, and cricopharyngeal achalasia). • Salivary gland neoplasia or inflammation.

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Perform a nutritional assessment. Gather information about the patient's diet (including all foods fed to the patient), food intake (current and normal) and obtain body and muscle condition scores. • Elicit a thorough history regarding the patient's environment, changes in routine, people, or other pets to help identify potential psychological etiologies. • Question owners about the patient's interest in food and ability to prehend, masticate, and swallow food. • A complete physical examination is required to determine the presence of systemic disease.
- Perform a thorough ophthalmic, dental, oropharyngeal, facial, and cervical examination (sedation or anesthesia may be required) in addition to observing the patient eating to rule out pseudoanorexia. • A database including a complete blood count, serum biochemistry panel, urinalysis, heartworm serology, retrovirus serology, abdominal, thoracic and cervical imaging studies, endoscopy, and histologic/cytologic examination of tissue/cell samples are often required to make a definitive diagnosis.
- Only if the history, physical examination, and database strongly suggest psychologic anorexia should further diagnostic work-up be forgone; in such cases, daily contact with the pet owner is essential until the anorexia has resolved.

CBC/BIOCHEMISTRY/URINALYSIS

- Abnormalities vary with different underlying diseases and causes of pseudoanorexia and anorexia. • Can be

(CONTINUED)

normal in patients with medical as well as psychologic causes of anorexia.

OTHER LABORATORY TESTS

Special diagnostic tests may be necessary to rule out specific diseases suggested by history, physical examination, and preliminary tests.

IMAGING

- Thoracic and abdominal imaging (radiographic and ultrasound) studies are often included in the minimum database to detect anatomic or functional abnormalities.
- Videofluoroscopy may be indicated to specifically evaluate pharyngeal and esophageal function.

DIAGNOSTIC PROCEDURES

- Vary with underlying condition suspected.
- Endoscopy may be useful for visualization of the pharyngeal and esophageal structures.



TREATMENT

- The mainstay of treatment is aimed at identifying and correcting the underlying disease. • Symptomatic therapy includes attention to fluid and electrolyte derangements, control of pain and/or nausea, reduction in environmental stressors, and modification of the diet to improve palatability. • Palatability can be improved by adding flavored toppings such as chicken and beef broth, seasoning with condiments such as garlic powder, increasing the moisture, fat or protein content of the food, and warming the food to body temperature. • When learned food aversion is suspected, food should be offered cautiously and removed immediately at the first signs of aversion. A patient showing signs of aversion to its normal diet may accept novel foods.
- Medications the patient is receiving should be reviewed for possible side-effects leading to reduced food intake. • Significantly malnourished dogs and cats are immediate candidates for assisted feeding (enteral or parenteral feeding). Well-nourished patients with debilitating disease should not go without food for longer than 3–5 days before assisted feeding is started. • The decision to institute enteral or parenteral feeding can be influenced by several factors. In animals with inadequate food intake that have $\geq 10\%$ body weight loss, hypoalbuminemia, poor body condition score, evidence of muscle wasting, and/or chronic disease processes, supplemental nutrition should be considered.
- Techniques for providing enteral nutrition include coax feeding and placement of a nasoesophageal, esophagostomy, gastrostomy, or jejunostomy tube. Force feeding should be avoided, particularly in cats in light of the association with conditioned food aversions.



MEDICATIONS

DRUG(S) OF CHOICE

- Diazepam is a short-acting appetite stimulant with sedative properties dosed at 0.1 mg/kg IV q24h or 1 mg PO q24h in cats.
- Oxazepam (2 mg/cat PO q12h) is a short-acting appetite stimulant and sedative.
- Cyproheptadine, an antihistamine with antiserotonergic properties, has been used as an appetite stimulant with mixed success at a dose range of 0.2–0.4 mg/kg PO 10–20 minutes prior to feeding.
- Mirtazapine is a serotonin antagonist that is dosed at 3.75–7.5 mg/dog PO q24h or 1.9 mg/cat PO q24–72h.
- Analgesics may promote appetite in painful conditions but their use must be balanced with the potential to cause gastrointestinal side-effects.
- Metoclopramide (0.2–0.4 mg/kg SC or PO q8–12h), ranitidine (2 mg/kg SC, IV, or PO q12h), or erythromycin (0.5–1 mg/kg PO q12h) are useful if anorexia is associated with gastroparesis or ileus.
- Antiemetics such as prochlorperazine (0.1–0.5 mg/kg PO q12h), maropitant (dogs: 1 mg/kg SC or 2 mg/kg PO q24h; cats: 1 mg/kg SC or PO q24h) or metoclopramide are useful to decrease nausea-associated anorexia.

CONTRAINdicATIONS

- Avoid antiemetics and prokinetics if gastrointestinal obstruction is present or suspected. • Drugs with sedative properties should be used with caution in severely debilitated animals.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Body weight, body and muscle condition score assessment, and hydration determination. • Monitor caloric intake to ensure return of appetite is sufficient to meet nutritional needs.

PREVENTION/AVOIDANCE

- Maximize patient comfort and wellbeing.
- Enhance the palatability of the diet.

POSSIBLE COMPLICATIONS

- Dehydration, malnutrition, and cachexia are most likely; these exacerbate the underlying disease. • A loss of more than 25–30% of body protein compromises the immune system and muscle strength, and death results from infection and/or pulmonary failure. • Feline hepatic lipidosis is a possible complication of anorexia in obese cats. • Breakdown of the intestinal mucosal barrier is a concern in debilitated patients.

EXPECTED COURSE AND PROGNOSIS

Varies with underlying cause



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

Nutritional support and glucose-containing fluids may be necessary to treat or prevent hypoglycemia in anorectic puppies and kittens.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

N/A

SEE ALSO

See "Causes"

ABBREVIATION

- CCK = cholecystokinin

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Client Education Handout
available online

ANTEBRACHIAL GROWTH DEFORMITIES



BASICS

DEFINITION

Abnormally shaped forelimbs and/or malalignments of the elbow or antebrachial carpal joints that result from maldevelopment of the radius or ulna in the growing animal.

PATHOPHYSIOLOGY

- Antebrachium—predisposed to deformities resulting from growth of one bone after premature growth cessation or decreased growth rate of the paired bone.
- Decreased rate of elongation in one bone behaves as a retarding strap; the growing paired bone must twist and curve around the short bone or overgrow at the elbow or carpus; causes joint malalignment.
- Normal growth—bones elongate through the process of endochondral ossification, which occurs in the physis; physis closure occurs when the germinal cell layer stops producing new cartilage and the existing cartilage hypertrophies, ossifies, and is remodeled into bone.
- Hereditary—may be a component of common elbow joint malalignment in many chondrodysplastic breeds (e.g., basset hound and Lhasa apso).
- Osteochondrosis or dietary oversupplementation—possibly associated with retardation of endochondral ossification (retained cartilaginous cores) in giant-breed dogs.
- Hypertrophic osteodystrophy—juvenile growth syndrome with phyeal and periosteal inflammation that may impede growth.
- Trauma—most common cause; if germinal cell layer of the physis is damaged, new cartilage production and bone elongation are stopped. Commonly occurs with fractures involving the distal ulnar or radial growth plates. A crushing-type fracture (Salter-Harris type V) may not be detected on radiographs of the injured antebrachium, and angular deformity only becomes evident over time due to lack of growth of the affected bone.

SYSTEMS AFFECTED

Musculoskeletal

GENETICS

- Skye terriers—reported as a recessive inheritable trait.
- Chondrodysplastic breeds (dogs)—disturbed endochondral ossification results in asynchronous growth of the paired bone system, resulting in altered growth and angular deformity. Affected dogs are predisposed to elbow malalignment.

INCIDENCE/PREVALENCE

- Traumatic—may occur in up to 10% of actively growing dogs that sustain injuries of the antebrachium; uncommon in cats.
- Elbow malalignment syndrome ± angular deformity (chondrodysplastic dog breeds)—fairly common and can be bilateral. Clinical abnormality in affected individuals is variable.
- Nutritionally induced—incidence

decreasing as nutritional standards are improved.

- Congenital agenesis of the radius (cats and rarely dogs)—occurs infrequently; results in severely bowed antebrachium and carpal subluxation.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Skye terrier—recessive inheritable form.
- Chondrodysplastic and toy breeds (especially basset hound, dachshund, Lhasa apso, Pekingese, Jack Russell terrier)—may be predisposed to elbow malalignment and incongruity.
- Giant breeds (e.g., Great Dane, wolfhound)—may be induced by rapid growth owing to excessive or unbalanced nutrition, osteochondrosis, or hypertrophic osteodystrophy.

Mean Age and Range

- Traumatic—any time during the active growth phase.
- Elbow malarticulations—during growth; may not be recognized until secondary arthritic changes become severe, occasionally at several years of age.

Predominant Sex

N/A

SIGNS

General Comments

- Longer-limbed dogs—angular deformities generally more common.
- Shorter-limbed dogs—tend to develop more severe joint malalignments.
- Age at the time of premature closure—affects relative degree of deformity and joint malarticulation; dogs with more growth potential remaining tend to develop more severe deformity.

Historical Findings

- Traumatic—progressive limb angulation or lameness 3–4 weeks after injury; owner may not be aware of causative event.
- Developmental elbow malalignments—insidious onset of lameness in one or both forelimbs; most apparent after exercise.

Physical Examination Findings

Premature Distal Ulnar Closure

- Results in three deformities of the distal radius—lateral deviation (valgus), cranial bowing (recurvatum), and external torsion resulting in supination of the manus.
- Relative shortening of limb length compared to the contralateral normally growing limb.
- Caudolateral subluxation of the radiocarpal joint and malarticulation of the elbow joint—may occur; causes lameness and painful joint restriction.

Premature Radial Phyeal Closure

- Affected limb—significantly shorter than the normal contralateral.
- Severity of lameness—depends on degree of joint malarticulation.
- Complete symmetrical

closure of distal physis—may note straight limb with a widened radiocarpal or radiohumeral joint space; may note caudal bow (recurvatum) to radius and ulna.

- Asymmetrical closure of medial aspect of distal radial physis—varus angular deformity; occasionally internal torsion and pronation.
- Closure of lateral aspect of distal radial physis—valgus angular deformity; external torsion.
- Closure of proximal radial physis with continued ulnar growth—malarticulation of the elbow joint; widened radiohumeral space, and proximal subluxation of the humeroulnar joint (increased humerus to anconeal process space).

CAUSES

- Trauma • Developmental basis
- Nutritional basis

RISK FACTORS

- Forelimb trauma • Excessive dietary supplementation



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Elbow dysplasia • Fragmented medial coronoid process • Ununited anconeal process • Panosteitis • Flexor tendon contracture • Hypertrophic osteodystrophy

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

- Damage to growth potential of the physis—commonly cannot be seen at the time of trauma; usually 2–4 weeks before radiographically apparent.
- Standard craniocaudal and mediolateral radiographic views—include entire elbow joint; from mid-humerus proximally extend to digits distally; take same series for comparison to normal contralateral limb.
- Degree of angular deformities and relative shortening—determined by comparing relative lengths of radius and ulna within the deformed pair to the normal contralateral pair.
- Degree of torsional deformity—determined by comparing position of the elbow and carpus on same view, i.e., lateral projection of elbow and 45° oblique of carpus on same view indicates torsional deformity.
- Cross-sectional imaging and creation of models using stereolithography is useful for full appreciation of the deformity.
- Elbow and carpal joints—evaluate for malalignment and degenerative change.. Presence of degenerative change is associated with less optimal outcome following surgical treatment.
- Elbow joint—evaluate for associated ununited anconeal process and fragmented medial coronoid process.

(CONTINUED)

ANTEBRACHIAL GROWTH DEFORMITIES

A

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

Cartilage of abnormal growth plate often replaced with bone. Angular deformity can occur due to retained cartilage core (osteochondrosis) of the ulna.



TREATMENT

APPROPRIATE HEALTH CARE

- Genetic predisposition—do not breed.
- Traumatic physeal damage—not seen at time of injury; revealed 2–4 weeks later.
- In young (<6 months) animals, surgical treatment is generally recommended as soon as possible following diagnosis. Treatment may require multiple surgical procedures.

NURSING CARE

N/A

ACTIVITY

Exercise restriction—reduces joint malalignment damage; slows arthritic progression.

DIET

- Decrease nutritional supplementation in giant-breed dogs—slows rapid growth; may reduce incidence.
- Avoid excess weight—helps control arthritic pain resulting from joint malalignment and overuse.

CLIENT EDUCATION

- Discuss heritability in chondrodysplastic breeds.
- Explain that damage to physeal growth potential is not apparent at time of forelimb trauma and that the diagnosis is often made 2–4 weeks following an injury.
- Discuss the importance of joint malalignment and resultant osteoarthritis as primary causes of lameness.
- Emphasize that early surgical treatment leads to a better prognosis.
- Depending on the patient's age, treatment may involve multiple procedures.

SURGICAL CONSIDERATIONS

- Premature distal ulnar physeal closure in a patient <5–6 months of age (significant amount of radial growth potential remaining)—treated with partial ulnar osteotomy, valgus deformities ≤ 25°: may improve and may not require additional surgery; young patients and those with more severe deformities: often require a second definitive correction after maturity.
- Radial or ulnar physeal closure in a mature patient (limited or no growth potential) requires definitive deformity correction, joint realignment, or both.
- Deformity correction—may be accomplished with a variety of osteotomy techniques; may be stabilized with several different internal or external fixation devices; must correct both torsional and angular deformities; performed at the point of greatest curvature.
- Joint malalignment (particularly elbow)—must

correct to minimize arthritis development (primary cause of lameness); obtain optimal joint alignment via dynamic proximal ulnar osteotomy (use triceps brachii muscle traction and joint pressure) or shortening longer bone (radial or ulnar osteotomy as indicated).

- Significant limb length discrepancies—distraction osteogenesis; osteotomy of the shortened bone is progressively distracted at the rate of 1 mm/day with an external fixator system to create new bone length.



MEDICATIONS

DRUG(S) OF CHOICE

Anti-inflammatory drugs—symptomatic treatment of osteoarthritis

CONTRAINDICATIONS

Corticosteroids—do not use owing to potential systemic side effects and cartilage damage seen with long-term use.

PRECAUTIONS

Warn client of possible gastrointestinal upset associated with chronic anti-inflammatory therapy.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Neutraceuticals (e.g., chondroitin sulfate and glucosamine)—may help minimize cartilage damage and osteoarthritis development, but not proven.



FOLLOW-UP

PATIENT MONITORING

- Postoperative—depends on surgical treatment.
- Periodic checkups—evaluate arthritic status and anti-inflammatory therapy.

PREVENTION/AVOIDANCE

- Selective breeding of susceptible breeds.
- Avoid dietary oversupplementation in rapidly growing giant-breed dogs.

POSSIBLE COMPLICATIONS

Routinely seen with various osteotomy fixation techniques (e.g., infection, non-union of osteotomy, fixator pin tract inflammation, undercorrection).

EXPECTED COURSE AND PROGNOSIS

- Generally, best results seen with early diagnosis and surgical treatment—minimizes osteoarthritis.
- Premature ulnar closure—tends to be easier to manage than premature closure of the radial growth plates. Prognosis is dependent on severity of the deformity, joint congruity, and presence of degenerative joint disease. The prognosis worsens with increasing severity.
- Limb lengthening by distraction osteogenesis—requires extensive postoperative management by the veterinarian and owner; high rate of complications.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Osteochondrosis • Hypertrophic osteodystrophy • Un-united anconeal process

AGE-RELATED FACTORS

The younger the patient at the time of traumatically induced physeal closure, the more severe the deformity and malarticulation.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYMS

Radius curvus

ABBREVIATIONS

- HOD = hypertrophic osteodystrophy
- OCD = osteochondrodysplasia • UAP = ununited anconeal process

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Client Education Handout available online

ANTERIOR UVEITIS—CATS



BASICS

DEFINITION

- Inflammation of the anterior uveal tissues, including iris (iritis), ciliary body (cyclitis), or both (iridocyclitis). • May be associated with concurrent posterior uveal and retinal inflammation (choroiditis; chorioretinitis).
- May be unilateral or bilateral.

PATHOPHYSIOLOGY

- Increased permeability of the blood-aqueous barrier related to infectious, immune-mediated, neoplastic, traumatic, or other causes; allows entrance of plasma proteins and blood cellular components into aqueous humor. • Disruption of blood-aqueous barrier is initiated and maintained by numerous chemical mediators, including histamine, prostaglandins, leukotrienes, serotonin, kinins, and complement.

SYSTEMS AFFECTED

- Ophthalmic. • Other systems may also be affected by underlying disease process.

INCIDENCE/PREVALENCE

- Relatively common condition. • True incidence/prevalence unknown.

GEOGRAPHIC DISTRIBUTION

Geographic location may affect incidence of certain infectious causes of uveitis.

SIGNALMENT

Species

Cat

Mean Age and Range

- Mean age 7–9 years. • Any age may be affected.

Predominant Sex

Males/neutered males more commonly affected than females.

SIGNS

Historical Findings

- Cloudy eye—due to corneal edema, aqueous flare, hypopyon, etc. • Painful eye—manifest by blepharospasm, photophobia, or rubbing eye; usually less pronounced than in dogs. • Red eye—due to conjunctival hyperemia and ciliary flush; less pronounced than in dogs in most cases. • Vision loss—variable.

Physical Examination Findings

Importance of a thorough physical examination in cats presenting with uveitis cannot be overstated.

Ophthalmic Findings

- Ocular discomfort—manifest by blepharospasm and photophobia • Ocular discharge—usually serous; sometimes mucoid to mucopurulent. • Conjunctival hyperemia—bulbar and palpebral conjunctiva both usually affected. • Corneal edema—diffuse; mild to severe. • Keratic precipitates—multifocal aggregates of

inflammatory cells adherent to corneal endothelium; most notable ventrally.

- Aqueous flare and cells—cloudiness of aqueous humor due to increased protein content and suspended cellular debris; best visualized with a bright, narrow beam of light shined through anterior chamber.
- Ciliary flush—Injection of deep perilimbal anterior ciliary vessels. • Deep corneal vascularization—circumcorneal distribution (brush border). • Miosis and/or resistance to pharmacologic dilation. • Iridal swelling—may be generalized or nodular. • Reduced IOP is consistent with anterior uveitis but is not a uniform finding. • Posterior synechia—adhesions between posterior iris and anterior lens surface. • Fibrin in anterior chamber.
- Hypopyon or hyphema—accumulations of white blood cells or red blood cells, respectively, in the anterior chamber; usually settles horizontally in ventral aspect of chamber but may be diffuse. • Chronic changes may include rubeosis iridis, iridal hyperpigmentation, secondary cataract, lens luxation, pupillary seclusion, iris bombe, secondary glaucoma, and phthisis bulbi.

CAUSES

- Infectious—mycotic (*Blastomyces* spp., *Cryptococcus neoformans*; *Coccidiodes immitis*; *Histoplasma capsulatum*); protozoal (*Toxoplasma gondii*; *Leishmania infantum*); bacterial (*Bartonella* spp., *Mycobacterium* spp. or any bacterial septicemia); viral (FIV, FeLV, feline coronavirus; FHV-1); parasitic (ophthalmomyiasis; ocular larval migrans).
- Idiopathic—lymphocytic-plasmacytic uveitis. • Immune-mediated—reaction to lens proteins (due to cataract or lens trauma).
- Neoplastic—primary ocular tumors (esp. diffuse iris melanoma, ocular sarcoma); metastasis to uveal tract (esp. lymphoma).
- Metabolic—hyperlipidemia; hyperviscosity; systemic hypertension. • Miscellaneous—trauma (blunt or penetrating); ulcerative keratitis; corneal stromal abscess; toxemia of any cause.

RISK FACTORS

None specific; immune suppression and geographic location may increase incidence of certain infectious causes of uveitis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Conjunctivitis—redness limited to conjunctival hyperemia (i.e., no ciliary flush); ocular discharge usually thicker and more copious than in uveitis; discomfort may be alleviated by topical anesthetic. • Glaucoma—elevated IOP is most consistent distinguishing feature of this disease; others may include dilated pupil, Haab's striae, and buphthalmos.
- Ulcerative keratitis—corneal fluorescein staining will detect ulcers; corneal edema

associated with ulcers is either localized to, or most severe at, site of ulcer; ocular discharge often thicker and more copious than with uveitis; discomfort may be alleviated by topical anesthetic. • Horner's syndrome—miosis, enophthalmos, and nictitans protraction are similar in both conditions, but Horner's is non-painful with no ocular discharge; ptosis with Horner's is distinguished from blepharospasm, as the latter is an active process; minor conjunctival hyperemia may be noted with Horner's, but cornea and anterior chamber are clear; clinical signs of Horner's syndrome resolve following topical application of ophthalmic 1–10% phenylephrine.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—often normal; changes may be present related to underlying disease.
- Biochemistry—often normal; most common abnormality in cats with uveitis is elevated serum proteins (usually due to polyclonal gammopathy). • Urinalysis—often normal; changes may be present related to underlying disease.

OTHER LABORATORY TESTS

- FeLV serum titers. • FIV serum titers.
- Coronavirus titers—not specific for FIP but may influence the index of suspicion for this disease. • *Toxoplasma gondii* IgM and IgG titers performed on serum and/or aqueous humor. • *Bartonella* spp. serology, PCR (serum or aqueous humor) and/or blood culture.

IMAGING

- Thoracic radiography—may show evidence of causative disease process (e.g., infiltrates related to infectious disease; evidence of metastatic neoplastic disease). • Ocular ultrasound—indicated if opacity of ocular media precludes direct examination; may reveal intraocular neoplasm or retinal detachment.

DIAGNOSTIC PROCEDURES

- Tonometry—low IOP consistent with uveitis; elevated IOP indicates glaucoma (primary disease or secondary to uveitis).
- Ocular centesis—if retinal detachment is present, cytology of subretinal aspirate may reveal causative agents; anterior chamber centesis may be performed for *Toxoplasma gondii* or *Bartonella* IgM and IgG titers on aqueous humor.

PATHOLOGIC FINDINGS

- Gross—see physical examination findings.
- Histopathologic—corneal edema; peripheral corneal deep stromal vascularization; keratic precipitates; preiridal fibrovascular membrane; peripheral anterior synechia; posterior synechia; entropion or ectropion uveae; leukocyte accumulation in iris, ciliary body, sclera, choroid (lymphocytic-plasmacytic, suppurative, or granulomatous infiltrates, depending on etiology); secondary cataract; with posterior segment involvement

(CONTINUED)

in inflammatory process, cyclitic membrane; vitreal traction bands and retinal detachment may be present. • Lymphoplasmacytic infiltrate of iris and ciliary body (either diffuse or nodular) is most common histopathologic finding.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient medical management generally sufficient.

ACTIVITY

No changes indicated in most cases.

DIET

No changes indicated.

CLIENT EDUCATION

- Inform of potential systemic diseases causing ophthalmic signs and emphasize importance of appropriate diagnostic testing.
- In addition to symptomatic uveitis treatment, treatment of underlying disease (when possible) is paramount to a positive outcome.
- Inform of potential complications and emphasize compliance with treatment and follow-up recommendations that will reduce the likelihood of complications.

SURGICAL CONSIDERATIONS

- None in most cases.
- Specific instances requiring surgical intervention include removal of ruptured lenses and surgical management of secondary glaucoma.
- Chronic uveitis leading to secondary glaucoma commonly necessitates enucleation of affected globes.
- Enucleation is recommended in cats with uveitis related to diffuse iris melanoma or other primary intraocular tumors.



MEDICATIONS

DRUG(S)

Corticosteroids

Topical

- Prednisolone acetate 1%—apply 2–8 times daily, depending on severity of disease; taper medication as condition resolves.
- Dexamethasone 0.1%—apply 2–8 times daily, depending on severity of disease; taper medication as condition resolves.
- Other topical corticosteroids (e.g., betamethasone, hydrocortisone) are considerably less effective in the treatment of intraocular inflammation.
- Taper treatment frequency as condition improves; stopping topical corticosteroids abruptly may result in rebound of ocular inflammation.

Subconjunctival

- Triamcinolone acetonide 4 mg by subconjunctival injection.
- Methylprednisolone 4 mg by subconjunctival injection.
- Often not

required. • Indicated only in severe cases as one-time injection, followed by topical and/or systemic anti-inflammatories.

Systemic

- Prednisone 1–3 mg/kg/day initially; taper dose after 7–10 days.
- Use only if systemic infectious causes of uveitis have been ruled out.

Nonsteroidal Anti-inflammatory Drugs

Topical

- Flurbiprofen—apply 2–4 times daily, depending on severity of disease.
- Diclofenac—apply 2–4 times daily, depending on severity of disease.

Systemic

- Meloxicam 0.2 mg/kg IV, SC, PO once, then 0.05 mg/kg IV, SC, PO q24h for 2 days, then 0.025 mg/kg q24–48h. Due to potential renal effects, limit duration of use to 4 days.
- Robenacoxib 1 mg/kg PO once daily; limit duration of use to 3 days.
- Ketoprofen 1 mg/kg PO q24h; limit duration of use to 5 days.

Topical Mydriatic/Cycloplegic

- Atropine sulfate 1%—apply 1–4 times daily, depending on severity of disease. Use lowest frequency adequate to maintain dilated pupil and ocular comfort; taper medication as condition resolves. Ointment is preferred over solution in cats as it causes less salivation.

CONTRAINDICATIONS

- Avoid the use of miotic medications (e.g., pilocarpine), including topical prostaglandins (e.g., latanoprost), in the presence of uveitis.
- Topical and subconjunctival corticosteroids are absolutely contraindicated in the presence of ulcerative keratitis.
- Corticosteroids (especially systemic) should be avoided in cats with systemic hypertension. Avoid systemic NSAIDs in cats with renal disease.

PRECAUTIONS

Owing to concern for secondary glaucoma, topical atropine should be used judiciously and IOP should be monitored periodically.

POSSIBLE INTERACTIONS

Systemic corticosteroids and nonsteroidal anti-inflammatory drugs should not be used concurrently.



FOLLOW-UP

PATIENT MONITORING

Recheck in 3–7 days, depending on severity of disease. IOP should be monitored at recheck to detect secondary glaucoma. Frequency of subsequent rechecks dictated by severity of disease and response to treatment.

POSSIBLE COMPLICATIONS

Systemic Complications

Occur as a result of the systemic etiology of the uveitis.

Ophthalmic Complications

- Secondary glaucoma—common complication of chronic uveitis in cats.

ANTERIOR UVEITIS—CATS

A

- Secondary cataract.
- Lens luxation.
- Retinal detachment.
- Phthisis bulbi.

EXPECTED COURSE AND PROGNOSIS

- Guarded prognosis for affected eyes.
- Depends on underlying disease and response to treatment.
- Cats with treatable underlying disease (e.g., toxoplasmosis) are more likely to have a favorable ophthalmic outcome than those with idiopathic lymphocytic-plasmacytic uveitis or untreatable underlying condition (e.g., FIP, FIV).



MISCELLANEOUS

AGE-RELATED FACTORS

- Younger cats more likely to be diagnosed with infectious etiology.
- Older cats at higher risk of idiopathic lymphocytic-plasmacytic uveitis and intraocular neoplastic causes.

ZOONOTIC POTENTIAL

- None in most cases.
- Some forms of systemic infection causing uveitis may pose a slight risk to immunocompromised owners.

PREGNANCY/FERTILITY/BREEDING

Avoid systemic corticosteroids. Because of systemic absorption, topical corticosteroids may also pose a risk, especially with frequent application.

SYNONYM

Iridocyclitis

SEE ALSO

- Horners Syndrome
- Red Eye

ABBREVIATIONS

- FeLV = feline leukemia virus
- FHV-1 = feline herpesvirus type 1
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- IOP = intraocular pressure

Suggested Reading

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Consulting Editor Paul E. Miller



Client Education Handout
available online

ANTERIOR UVEITIS—DOGS



BASICS

DEFINITION

- Inflammation of the anterior uveal tissues, including iris (iritis), ciliary body (cyclitis), or both (iridocyclitis).
- May be associated with concurrent posterior uveal and retinal inflammation (choroiditis; chorioretinitis).
- May be unilateral or bilateral.

PATHOPHYSIOLOGY

- Increased permeability of the blood-aqueous barrier related to infectious, immune-mediated, traumatic, or other causes allows entrance of plasma proteins and blood cellular components into aqueous humor.
- Disruption of blood-aqueous barrier is initiated and maintained by numerous chemical mediators, including histamine, prostaglandins, leukotrienes, serotonin, kinins, and complement.

SYSTEMS AFFECTED

- Ophthalmic.
- Other systems may also be affected by underlying disease process.

INCIDENCE/PREVALENCE

- Relatively common condition.
- True incidence/prevalence unknown.

GEOGRAPHIC DISTRIBUTION

Geographic location may affect incidence of certain infectious causes of uveitis.

SIGNALMENT

Species

Dog

Breed Predilections

- None for most causes.
- Uveitis associated with iridociliary cysts in golden retriever (a.k.a. golden retriever uveitis, pigmentary uveitis).
- Increased incidence of uveodermatologic syndrome in Siberian husky, Akita, Samoyed, and Shetland sheepdog.

Mean Age and Range

- Any age may be affected.
- Mean age in uveodermatologic syndrome—2.8 years.
- Mean age in golden retriever uveitis—8.6 years.

SIGNS

Historical Findings

- Red eye—due to conjunctival hyperemia and ciliary flush.
- Cloudy eye—due to corneal edema, aqueous flare, hypopyon, etc.
- Painful eye—manifest by blepharospasm, photophobia, or rubbing eye.
- Vision loss—variable.

Physical Examination Findings

The importance of a thorough physical examination in dogs presenting with uveitis cannot be overstated.

Ophthalmic Findings

- Ocular discomfort—manifest by blepharospasm, photophobia, and rubbing

- eye.
- Ocular discharge—usually serous; sometimes mucoid to mucopurulent.
- Conjunctival hyperemia—bulbar and palpebral conjunctiva both usually affected.
- Corneal edema—diffuse; mild to severe.
- Keratic precipitates—multifocal aggregates of inflammatory cells adherent to corneal endothelium; most notable ventrally.
- Aqueous flare and cells—cloudiness of aqueous humor due to increased protein content and suspended cellular debris; best visualized with a bright, narrow beam of light shined through anterior chamber.
- Ciliary flush—Injection of deep perilimbal anterior ciliary vessels.
- Deep corneal vascularization—circumcorneal distribution (brush border).
- Miosis and/or resistance to pharmacologic dilation.
- Iridal swelling.
- Reduced IOP is consistent with uveitis but is not a uniform finding.
- Posterior synechia—adhesions between posterior iris and anterior lens surface.
- Fibrin in anterior chamber.
- Hypopyon or hyphema—accumulations of white blood cells or red blood cells, respectively, in the anterior chamber; usually settles horizontally in ventral aspect of chamber but may be diffuse.
- Chronic changes may include rubeosis iridis, iridal hyperpigmentation, secondary cataract, lens luxation, pupillary seclusion, iris bombe, secondary glaucoma, and phthisis bulbi.

CAUSES

- Infectious—mycotic (*Blastomyces dermatitidis*, *Cryptococcus neoformans*, *Coccidiodes immitis*, *Histoplasma capsulatum*); protozoal (*Toxoplasma gondii*, *Neospora caninum*, *Leishmania donovani*); rickettsial (*Ehrlichia canis*, *Rickettsia rickettsii*); bacterial (*Leptospira* spp., *Bartonella* spp., *Brucella canis*, *Borrelia burgdorferi*, any bacterial septicemia); algal (*Prototheca* spp.); viral (adenovirus, distemper, rabies, herpes); parasitic (ocular filariasis, ocular larval migrans).
- Immune-mediated—reaction to lens proteins (due to cataract or lens trauma); uveodermatologic syndrome; post-vaccinal reaction to canine adenovirus vaccine; vasculitis.
- Neoplastic—primary ocular tumors (especially uveal melanoma, iridociliary adenoma/adenocarcinoma); metastasis to uveal tract (lymphosarcoma most common).
- Metabolic—hyperlipidemia; hyperviscosity; systemic hypertension.
- Miscellaneous—idiopathic; trauma; pigmentary uveitis of golden retrievers; ulcerative keratitis; corneal stromal abscess; scleritis; lens instability/luxation; dental/periodontal disease; toxemia.

RISK FACTORS

None specific; immune suppression and geographic location may increase incidence of certain infectious causes of uveitis; breed predispositions should be considered.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Conjunctivitis—redness limited to conjunctival hyperemia (i.e., no ciliary flush); ocular discharge usually thicker and more copious than in uveitis; discomfort may be alleviated with application of topical anesthetic.
- Glaucoma—elevated IOP is most consistent feature of this disease; others may include dilated pupil, Haab's striae, and buphthalmos.
- Lens luxation—corneal edema may be localized to site of lens contact with endothelium or may be diffuse as a result of associated uveitis and/or glaucoma; lens luxation is highly breed associated.

- Ulcerative keratitis—corneal fluorescein staining will detect ulcers; corneal edema associated with ulcers is either localized to, or most severe at, site of ulcer; ocular discharge often thicker and more copious than with uveitis; discomfort may be partially alleviated by topical anesthetic.
- Corneal endothelial dystrophy or degeneration—diffuse corneal edema is present, but IOP is normal; conjunctival hyperemia and signs of ocular discomfort are generally absent.
- Horner's syndrome—miosis, enophthalmos, and nictitans protraction are similar in both conditions, but Horner's is non-painful with no ocular discharge; ptosis with Horner's is distinguished from blepharospasm as the latter is an active process; minor conjunctival hyperemia may be noted with Horner's, but cornea and anterior chamber are clear; clinical signs of Horner's syndrome resolve following topical application of 1–10% phenylephrine.

CBC/BIOCHEMISTRY/URINALYSIS

Often normal; changes related to underlying disease may be present.

OTHER LABORATORY TESTS

- Serology for infectious diseases listed under "Causes" may be appropriate, depending on index of suspicion for infectious etiology.
- Clinical signs raising the suspicion of systemic disease including lethargy, pyrexia, weight loss, coughing, lymphadenopathy, etc., warrant serology for infectious diseases.

IMAGING

- Thoracic radiography may show evidence of causative disease process (e.g., systemic mycoses; metastatic neoplasia).
- Abdominal ultrasound may be warranted if suspicion for metastatic neoplastic disease is high.
- Ocular ultrasound is indicated if opacity of ocular media precludes direct examination; may reveal intraocular neoplasm or retinal detachment.

DIAGNOSTIC PROCEDURES

- Tonometry—low IOP consistent with uveitis; elevated IOP indicates glaucoma (primary disease or secondary to uveitis).
- Lymph node aspirates—if enlarged nodes

(CONTINUED)

are palpable, aspiration for cytology is indicated. • Ocular centesis—if retinal detachment is present, cytology of subretinal aspirate may reveal causative agents; anterior chamber centesis is generally unrewarding.

PATHOLOGIC FINDINGS

- Gross—see “Physical Examination Findings.”
- Histopathologic—corneal edema; peripheral corneal deep stromal vascularization; keratic precipitates; preiridal fibrovascular membrane; peripheral anterior synechia; posterior synechia; entropion or ectropion uvae; leukocyte accumulation in iris, ciliary body, sclera, choroid (lymphocytic, plasmacytic, suppurative, or granulomatous infiltrates, depending on etiology); secondary cataract; with posterior segment involvement in inflammatory process, cyclitic membrane; vitreal traction bands and retinal detachment may be present.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient medical management is generally sufficient.

NURSING CARE

None

ACTIVITY

- No changes indicated in most cases.
- Reduced exposure to bright light may alleviate discomfort.

DIET

No changes indicated.

CLIENT EDUCATION

- Inform of potential systemic diseases causing ophthalmic signs and emphasize importance of appropriate diagnostic testing.
- In addition to symptomatic uveitis treatment, treatment of underlying disease (when possible) is paramount to a positive outcome.
- Inform of potential complications and emphasize compliance with treatment and follow-up recommendations that will reduce the likelihood of complications.

SURGICAL CONSIDERATIONS

None in most cases. Specific instances requiring surgical intervention include removal of ruptured lenses, removal of cataracts causing uveitis (if prognosis for successful surgery is otherwise favorable), and surgical management of secondary glaucoma.



MEDICATIONS

DRUG(S) OF CHOICE

Corticosteroids

Topical

- Prednisolone acetate 1% apply 2–8 times daily, depending on severity of disease; taper medication as condition resolves.

- Dexamethasone 0.1%—apply 2–8 times daily, depending on severity of disease; taper medication as condition resolves.

- Other topical corticosteroids (e.g., betamethasone, hydrocortisone) are considerably less effective in the treatment of intraocular inflammation.

- Taper treatment frequency over several weeks as condition improves; stopping topical corticosteroids abruptly may result in rebound of ocular inflammation.

Subconjunctival

- Triamcinolone acetonide 4–6 mg by subconjunctival injection.
- Methylprednisolone 3–10 mg by subconjunctival injection.
- Often not required.
- Indicated only in severe cases as one-time injection followed by topical and/or systemic anti-inflammatories.

Systemic

- Prednisone 0.5–2.2 mg/kg/day initially; taper dose after 7–10 days.
- Use only if systemic infectious causes of uveitis have been ruled out.

Nonsteroidal Anti-inflammatory Drugs

Topical

- Less effective than topical corticosteroids.
- Flurbiprofen—apply 2–4 times daily, depending on severity of disease.
- Diclofenac—apply 2–4 times daily, depending on severity of disease.

Systemic

- Do not use concurrently with systemic corticosteroids; avoid in the presence of hyphema.
- Carprofen 2.2 mg/kg PO q12h or 4.4 mg/kg PO q24h.
- Tepoxalin 10 mg/kg PO q24h.
- Meloxicam 0.2 mg/kg PO q24h.
- Firocoxib 5 mg/kg PO q24h.

Topical Mydriatic/Cycloplegic

- Atropine sulfate 1%—apply 1–4 times daily, depending on severity of disease. Use lowest frequency adequate to maintain dilated pupil and ocular comfort; taper medication as condition resolves.

CONTRAINDICATIONS

- Avoid the use of miotic medications (e.g., pilocarpine, demecarium bromide), including topical prostaglandins (e.g., latanoprost), in the presence of uveitis.
- Topical and subconjunctival corticosteroids are contraindicated in ulcerative keratitis.
- Avoid systemic corticosteroids in dogs with systemic hypertension or systemic infections.

PRECAUTIONS

Out of concern for secondary glaucoma, topical atropine should be used judiciously and IOP should be monitored periodically.

POSSIBLE INTERACTIONS

Systemic corticosteroids and NSAIDS should not be used concurrently.

ALTERNATIVE DRUG(S)

N/A

ANTERIOR UVEITIS—DOGS

A



FOLLOW-UP

PATIENT MONITORING

Recheck in 3–7 days, depending on severity of disease. IOP should be monitored at recheck to detect secondary glaucoma. Frequency of subsequent rechecks dictated by severity of disease and response to treatment.

POSSIBLE COMPLICATIONS

- Many systemic complications, including death, may occur due to systemic etiology of uveitis.
- Ophthalmic complications include secondary cataract, secondary glaucoma, lens luxation, retinal detachment, phthisis bulbi.

EXPECTED COURSE AND PROGNOSIS

Extremely variable; depends on underlying disease and response to treatment.



MISCELLANEOUS

ZOONOTIC POTENTIAL

None in most cases. Some forms of systemic infection causing uveitis may pose a slight risk to immune-compromised owners.

PREGNANCY/FERTILITY/BREEDING

Avoid systemic corticosteroids. Because of possibility of systemic absorption, topical corticosteroids may also pose risk, especially with frequent application in small dogs.

SYNOMYS

Iridocyclitis

SEE ALSO

Red Eye

ABBREVIATIONS

- IOP = intraocular pressure
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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Consulting Editor Paul E. Miller



Client Education Handout
available online

ANTIDEPRESSANT TOXICOSIS—SSRIS AND SNRIS



BASICS

DEFINITION

- Toxicity secondary to the overdose of a selective serotonin reuptake inhibitor (SSRI), serotonin and norepinephrine reuptake inhibitor (SNRI) or co-ingestion of two types of serotonergic drugs.
- SSRIs include citalopram (Celexa), escitalopram (Lexapro), fluoxetine (Prozac), fluvoxamine (Luvox), paroxetine (Paxil), sertraline (Zoloft), vilazodone (Viibryd), vortioxetine (Brintellix). SNRIs include desvenlafaxine (Pristiq), duloxetine (Cymbalta), levomilnacipran (Fetzima), milnacipran (Ixel, Savella), tofenacin (Elamol, Tofacine), and venlafaxine (Effexor).

PATHOPHYSIOLOGY

- SSRIs and SNRIs are antidepressants that inhibit reuptake of serotonin, a neurotransmitter involved in aggression, anxiety, appetite, depression, migraine, pain, and sleep. The SNRIs also inhibit the reuptake of norepinephrine.
- Excessive stimulation of serotonin receptors can occur by enhanced serotonin synthesis, increased presynaptic serotonin release, inhibition of serotonin uptake into the presynaptic neuron, inhibition of serotonin metabolism, or serotonin agonism. Serotonin syndrome is characterized in humans as a combination of symptoms that include at least three of the following: myoclonus, mental aberration, agitation, hyperreflexia, tremors, diarrhea, ataxia, or hyperthermia.
- Toxic dosage varies widely among commonly available SSRIs and SNRIs and are not well defined in veterinary medicine.

SYSTEMS AFFECTED

- Cardiovascular—decreased vascular tone (hypotension), increased heart rate and stroke volume (tachycardia).
- Gastrointestinal—increased smooth muscle contractility (vomiting, diarrhea).
- Nervous—stimulation (agitation, restlessness, seizures) and altered mental status (vocalization, disorientation).
- Neuromuscular—autonomic dysfunction (hyperactivity) and neuromuscular hyperactivity (hyperreflexia, myoclonus, tremors).
- Ophthalmic—increased autonomic function (mydriasis).
- Respiratory—increased bronchial smooth muscle contraction (dyspnea).

INCIDENCE/PREVALENCE

Second most common human prescription medication toxicosis (after cardiac medications).

SIGNALMENT

Species

Dogs and cats

Mean Age and Range

Any age can be affected.

SIGNS

Historical Findings

- Agitation or lethargy
- Dilated pupils
- Vomiting
- Tremors
- Hypersalivation
- Diarrhea
- Seizures
- Nystagmus

Physical Examination Findings

- Agitation
- Ataxia
- Mydriasis
- Tremors
- Vomiting
- Disorientation
- Hyperthermia
- Vocalization
- Depression
- Tachycardia
- Hypotension
- Diarrhea
- Blindness
- Seizures
- Hypersalivation
- Death

CAUSES

- SSRI/SNRI overdose—accidental exposure, inappropriate administration, or therapeutic use.
- Ingestion of an SSRI/SNRI along with another class of medications that increases serotonin (TCAs, MAOIs, novel antidepressants, tramadol, fentanyl, meperidine, amphetamines, cocaine, dextromethorphan, 5-HTP, buspirone, bupropion, triptans, LSD).

RISK FACTORS

- Animals on a serotonergic drug.
- Underlying liver or kidney disease. Cats are attracted to venlafaxine and will eat multiple capsules.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Toxicologic: TCAs, MAOIs, metaldehyde, lead, ethylene glycol, hops, anticholinergics, antihistamines.
- Non-toxicologic: meningitis e.g., (rabies, canine distemper), neoplasia, heat stroke, malignant hyperthermia.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC/biochemistry: no changes are expected.
- Urinalysis: myoglobinuria secondary to rhabdomyolysis may be seen.

OTHER LABORATORY TESTS

- Blood gas: metabolic acidosis may be seen.

- Testing for SSRIs/SNRIs can be performed, but the tests are not clinically useful.
- Note: venlafaxine will give a false positive for PCP on many urine drug screens.

DIAGNOSTIC PROCEDURES

There are no diagnostic tests to confirm serotonin syndrome.



TREATMENT

APPROPRIATE HEALTH CARE

- Emesis (if asymptomatic and recent ingestion) or gastric lavage (if large number of pills ingested).
- Activated charcoal with cathartic (if severe signs are expected, may need to repeat due to long half-life).

NURSING CARE

IV fluids to help maintain blood pressure and body temperature, and to protect kidneys from myoglobinuria.

CLIENT EDUCATION

If animal appears blind, sight should return.



MEDICATIONS

DRUG(S) OF CHOICE

- Agitation:
 - Phenothiazines (acepromazine 0.025–0.05 mg/kg IV, titrate up as needed).
 - Cyproheptadine (dog, 1.1 mg/kg; cat, 2–4 mg PO q4–6h or can be given rectally if vomiting).
 - Benzodiazepines (diazepam 0.5–2 mg/kg IV) (see "Precautions").
- Tremors: methocarbamol (50–150 mg/kg IV, titrate up but do not exceed 330 mg/kg/day).

CONTRAINdicATIONS

- High risk of serotonin syndrome: other SSRIs, SNRIs, MAOIs, TCAs, amphetamines, 5-HTP, clarithromycin, dextromethorphan, lithium, St. John's wort.
- Low risk of serotonin syndrome: tramadol, fentanyl, amantadine, bupropion, carbamazepine, codeine.

PRECAUTIONS

- Benzodiazepines (e.g., diazepam) are reported by some sources to exacerbate serotonin syndrome and their use for SSRI/SNRI toxicosis is not universally recommended.

POSSIBLE INTERACTIONS

- Decreased metabolism of SSRIs/SNRIs: cimetidine, diuretics, quinidine, lithium.
- Increased levels of medications (decreased metabolism): theophylline, coumadin, digoxin.

(CONTINUED)

ANTIDEPRESSANT TOXICOSIS—SSRIS AND SNRIS

A

**FOLLOW-UP****PATIENT MONITORING**

Blood pressure, heart rate, urine color: monitor hourly, then less frequently as the animal remains stable.

PREVENTION/AVOIDANCE

- Keep medications out of the reach of animals.
- Follow label directions when giving serotonergic drugs to animals.

POSSIBLE COMPLICATIONS

Renal failure secondary to myoglobinuria from rhabdomyolysis. DIC secondary to hyperthermia.

EXPECTED COURSE AND PROGNOSIS

- Prognosis is good in most cases, with recovery in 12–24 hours.
- Patients that present in status epilepticus or with severe hyperthermia have a guarded prognosis.

**MISCELLANEOUS****AGE-RELATED FACTORS**

Young and elderly animals are more at risk for developing serious toxicosis.

PREGNANCY/FERTILITY/BREEDING

SSRIs and SNRIs can cause increased litter mortality and possible birth defects.

ABBREVIATIONS

- 5-HTP = 5-hydroxytryptophan
- MAOI = monoamine oxidase inhibitor
- PCP = phencyclidine (angel dust)
- SNRI = serotonin and norepinephrine reuptake inhibitor
- SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant

Suggested Reading

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ANTIDEPRESSANT TOXICOSIS—TRICYCLIC



BASICS

DEFINITION

- Toxicity secondary to the acute or chronic ingestion of a tricyclic antidepressant (TCA).
- TCA medications include amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, maprotiline (tetracyclic antidepressant), nortriptyline, protriptyline, trimipramine, and many others.

PATOPHYSIOLOGY

- TCAs block the reuptake of norepinephrine, dopamine, and serotonin at the neuronal membrane. They also have anticholinergic activity and are thought to have membrane stabilizing effects on the myocardium (particularly inhibiting fast sodium channels in the ventricular myocardium). They can also have slight alpha-adrenergic blocking activity and antihistaminic effects.
- TCAs are rapidly and well absorbed across the digestive tract. They can decrease GI motility and delay gastric emptying, resulting in delayed drug absorption.
- Lipophilic, protein bound, and well distributed across all tissues.
- They are metabolized by the liver and undergo enterohepatic recirculation. The inactive metabolites are eliminated in the urine.

SYSTEMS AFFECTED

- Nervous—increased dopamine, serotonin, and norepinephrine levels in the CNS contribute to CNS signs.
- Cardiovascular—anticholinergic effects and inhibition of norepinephrine reuptake contribute to tachycardia; alpha adrenergic blockade, cardiac membrane stabilization, and decreased cardiac contractility contribute to hypotension and arrhythmias.
- Gastrointestinal—anticholinergic effects may cause ileus and delayed gastric emptying.
- Ophthalmic—anticholinergic effects can cause pupillary dilation.
- Renal/Urologic—anticholinergic effects may cause urinary retention.

GENETICS

Species and individual differences in absorption, metabolism, and elimination can be significant.

INCIDENCE/PREVALENCE

Incidence is unknown.

SIGNALMENT

Species

Dogs and cats

Breed Predilections

None

Mean Age and Range

None

Predominant Sex

None

SIGNS

General Comments

- Signs can occur at therapeutic doses.
- Signs of toxicosis can occur within 30–60 minutes or be delayed by several hours.

Historical Findings

- Evidence of accidental consumption of the owner's or another pet's medication
- CNS depression (lethargy, ataxia)
- Vocalization
- Vomiting or hypersalivation
- Panting
- Agitation or restlessness
- Tachypnea or dyspnea
- Tremors
- Seizures

Physical Examination Findings

- CNS depression or stimulation
- Tachycardia
- Mydriasis
- Hypothermia
- Hypertension
- Pallor
- Cyanosis
- Hyperthermia
- Arrhythmias
- Hypotension
- Urinary retention
- Constipation

CAUSE

Accidental exposure, inappropriate administration, or therapeutic use.

RISK FACTORS

- Concurrent use of other antipsychotic medication
- Pre-existing cardiac disease



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Toxicity caused by other antipsychotic medication, stimulant substances (e.g., amphetamines, cocaine, methylxanthines, or pseudoephedrine) or substances capable of causing cardiac arrhythmias (e.g., quinidine, propranolol, albuterol, digoxin).
- Non-toxicologic differentials include hyperkalemia, cardiac ischemia, cardiomyopathy, and other diseases of cardiac conduction.

CBC/BIOCHEMISTRY/URINALYSIS

Expected to be normal

OTHER LABORATORY TESTS

- Blood gases—metabolic acidosis may be noted.
- OTC urine drug screen for TCAs—can be used to determine if exposure has occurred; not useful in determining degree of toxicity.

- Serum TCA levels—can be used to determine if exposure has occurred.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- ECG to monitor for arrhythmias
- Blood pressure monitoring

PATHOLOGIC FINDINGS

No specific lesions expected



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—not recommended for symptomatic patients, patients with cardiac disease, or patients ingesting greater than a therapeutic dose of TCAs.
- Inpatient—asymptomatic:
 - Decontamination with emesis (less than 15 minutes of exposure time), gastric lavage in large exposures, and activated charcoal.
 - Monitor at a clinic for a minimum of 6 hours after exposure.
- Inpatient—symptomatic: stabilize the CV and CNS systems and provide supportive care.

NURSING CARE

- Fluid therapy—restore hydration due to vomiting, regulate blood pressure when hypotension is noted.
- Thermoregulation as needed.
- Enema with warm water if not defecating within 6–12 hours.

DIET

NPO if vomiting

CLIENT EDUCATION

- With a prescribed TCA, instruct client to monitor for adverse or idiosyncratic effects, and to stop the medication and contact the clinic if they occur.
- Prevent exposure to non-prescribed medication.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

Decontamination

- Emesis within 15 minutes of ingestion *only if asymptomatic*; induce emesis with either hydrogen peroxide (dog, 1–2 mL/kg PO) or apomorphine (dog/cat, 0.03–0.05 mg/kg IV, IM, or 0.1 mg/kg SC, or 0.25 mg instilled in conjunctiva of eye).
- Gastric lavage under anesthesia may be considered with large exposures.

(CONTINUED)

ANTIDEPRESSANT TOXICOSIS—TRICYCLIC**A**

- After emesis (or if > 15 minutes of exposure), administer activated charcoal (1–2 g/kg PO) with a cathartic such as sorbitol (70% sorbitol at 3 mL/kg) or sodium sulfate (0.25 tsp/5 kg) if no diarrhea.
- Repeat one-half dose of activated charcoal in 4–6 hours if patient is still symptomatic.

Other

- Cyproheptadine: dogs, 1.1 mg/kg q8h PO or rectally; cats, 2–4 mg/cat q12–24h PO or rectally; used for treatment of serotonin syndrome.
- 20% intravenous lipid emulsion—prevents lipophilic TCAs from reaching the site of action by acting as a sequestant in an expanded plasma lipid phase; 1.5 mL/kg IV bolus followed by 0.25 mL/kg/min IV CRI for 1 hour. Can repeat bolus every 3–5 minutes as needed up to 3 mL/kg, not to exceed a total dose of 8 mL/kg.
- Sodium bicarbonate—used to maintain blood pH at 7.55; if not monitoring acid-base status, start with 2–3 mEq/kg IV over 15–30 minutes in a symptomatic patient.
- Diazepam 0.5–1 mg/kg IV, repeat if necessary; for agitation or seizures.
- Acepromazine 0.02 mg/kg IV, repeat if necessary; for agitation or mild hypertension.
- Phenobarbital—as needed for seizure control.

CONTRAINDICATIONS

- Atropine should not be used because TCAs have anticholinergic effects that are exacerbated by atropine.
- Magnesium sulfate should not be used as a cathartic. Ileus or reduced GI motility will enhance absorption of magnesium and may result in magnesium toxicity.
- Beta-blockers (e.g., propranolol, atenolol) should not be used for tachycardia because of their potential to exacerbate hypotension.
- Do not induce emesis in a patient already showing clinical signs.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

- TCAs increase risk of hyperthermia, seizures, and death with use of MAOIs.
- Sympathomimetic and anticholinergic medications increase the risk for arrhythmias or cardiac effects from TCAs.
- Levothyroxine increases the risk for arrhythmias when used with TCAs.

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

- Acid-base status—monitor for acidosis and if implementing sodium bicarbonate therapy.
- Blood pressure—monitor until asymptomatic.
- ECG—monitor until asymptomatic.

PREVENTION/AVOIDANCE

Keep medications out of reach of pets.

POSSIBLE COMPLICATIONS

Pulmonary edema can occur secondary to aggressive fluid therapy.

EXPECTED COURSE AND PROGNOSIS

- Due to the variable half-lives of the different TCAs, signs can last 24 hours or longer.
- The prognosis is generally good in patients exhibiting mild to moderate signs.
- The prognosis is guarded in patients exhibiting severe signs such as seizures, arrhythmias, or hypotension that are poorly responsive to therapy.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Serotonin syndrome may occur as a result of TCA ingestion.

AGE-RELATED FACTORS

None

PREGNANCY/FERTILITY/BREEDING

TCAs cross the placenta and be found in breast milk; the significance of this is not known at this time.

SEE ALSO

- Antidepressant Toxicosis—SSRIs and SNRIs
- Poisoning (Intoxication) Therapy

ABBREVIATIONS

- CNS = central nervous system
- CV = cardiovascular
- ECG = electrocardiogram
- GI = gastrointestinal
- MAOI = monoamine oxidase inhibitor
- OTC = over-the-counter
- TCA = tricyclic antidepressant

INTERNET RESOURCES

- <http://www.aspapro.org/poison>
- <http://www.petpoisonhelpline.com/>

Suggested Reading

Gwaltney-Brant S. Antidepressants: Tricyclic antidepressants. In: Plumlee KH, ed., Clinical Veterinary Toxicology. St. Louis, MO: Mosby, 2004, pp. 286–288.

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Volmer PA. Recreational drugs: Tricyclic antidepressants. In: Peterson ME, Talcott PA, eds., Small Animal Toxicology, 2nd ed. St. Louis, MO: Saunders Elsevier, 2006, pp. 303–306.

Wismer TA. Antidepressant drug overdoses in dogs. *Vet Med* 2000, 95:520–525.**Author** Cristine L. Hayes**Consulting Editor** Lynn R. Hovda

AORTIC STENOSIS



BASICS

DEFINITION

A narrowing of the left ventricular outflow tract (LVOT) that restricts blood flow leaving the ventricle. It is most commonly congenital, often heritable. The lesion is most commonly subvalvular in dogs, but may be valvular or supravalvular (more often in cats). Subvalvular aortic stenosis (SAS) in dogs is caused by fibrous tissue manifested as nodules, a ridge, ring or tunnel-like lesion. SAS may be associated with other defects including mitral valve dysplasia.

PATHOPHYSIOLOGY

Restriction to outflow generates pressure overload of the LV. Degree of obstruction is related to severity of secondary changes. Left ventricular pressure overload causes thickened LV walls, resulting in diminished blood supply relative to muscle demand and myocardial ischemia. This may result in arrhythmogenesis and if severe or infarcted, mechanical dysfunction. The restriction to blood flow causes high velocity, turbulent flow across the valve, which may cause endothelial damage, lead to aortic insufficiency (AI) and predisposing to endocarditis. SAS may lead to chamber enlargement, distortion of the mitral valve annulus and mitral regurgitation with a possible sequela of left-sided congestive heart failure. Sudden death is common with severe SAS and may be secondary to arrhythmias or infarction.

SYSTEMS AFFECTED

- Cardiovascular—LV pressure overload leading to arrhythmias, syncope, sudden death, heart failure, endocarditis
- Respiratory—possible pulmonary edema with CHF
- Multisystemic—possible due to low cardiac output or endocarditis

GENETICS

SAS is inherited in the Newfoundland, golden retriever, rottweiler and Dogue de Bordeaux. A mutation in the phosphatidylinositol-binding clathrin assembly protein gene (PICALM) is reported in Newfoundlands; a screening test is available. Dominant inheritance patterns are proposed with incomplete penetrance responsible for the disease appearing to skip generations. More than one gene or modifying genes may be involved.

INCIDENCE/PREVALENCE

SAS is one of the most common congenital heart defects of dogs. It is reported as second most common, but difficulty in diagnosing mild disease may underestimate true caseload. Aortic stenosis has been reported as a small contributor of feline congenital heart disease, about 6%. Approximately 2 out of 1,000 dogs and 0.2 per 1,000 cats evaluated at veterinary teaching hospitals are diagnosed with SAS.

(dogs), supravalvular aortic stenosis (cats), and dynamic LVOT obstruction (cats).

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and Cat

Breed Predilections

The Newfoundland, golden retriever, rottweiler, Bouvier des Flanders, Dogue de Bordeaux, German shepherd, and boxer have the highest incidence of SAS and a familial component or heritability is reported. Increased risk is also described for English bulldog, American Staffordshire terrier, bull Terrier, English bulldog, Great Dane, and Samoyed. No breed predilection is reported for cats.

Mean Age and Range

Clinical signs may be seen at any age. Although often inherited, SAS becomes identifiable during the first few weeks to months of life as the subvalvular lesion progresses. Full phenotype is appreciated by 1 year of age.

Predominant Sex

N/A

SIGNS

Historical Findings

Many dogs with SAS show no clinical signs and have no relevant historical findings. Historical findings are related to disease severity and may include syncope, exercise intolerance, sudden death, and signs due to CHF such as respiratory distress and/or coughing when severe.

Physical Examination Findings

- Systolic left basilar ejection murmur; may radiate to the apex, right side of the thorax, include the carotid arteries and if very loud the cranium. A precordial thrill may be palpable. Murmur intensity is loosely correlated to severity of stenosis. As the disease worsens during early life, some may have absence of or a quiet murmur that develops to a more characteristic finding by 1 year.
- Diastolic murmur may be present with significant AI. The combination of this diastolic murmur with the systolic ejection murmur is a to-and-fro murmur.
- Arrhythmias may be auscultated.
- Pulse deficits may be appreciated, often associated with ventricular arrhythmias.
- Weak pulses may be appreciated that are late or slow to rise with severe SAS (pulsus parvus et tardus).
- Tachypnea, respiratory distress and crackles may occur with CHF.

General Comments

- Boxers have a relatively small aorta compared to other breeds, which can be difficult to distinguish from mild SAS.
- Bull terriers are overrepresented for combined mitral valve dysplasia and SAS.

- Newfoundland dogs are overrepresented for combined patent ductus arteriosus and SAS.

- Volume overload of PDA can cause a relative aortic stenosis and be difficult to distinguish from PDA with mild SAS.

CAUSES

- Congenital heart disease.
- Secondary to valvular change as with aortic valve endocarditis or calcification.
- Dynamic or fixed LVOT obstruction in some cats with hypertrophic (obstructive) cardiomyopathy.
- A component of complex congenital heart disease as with some cases of mitral valve dysplasia.

RISK FACTORS

- Familial history of SAS.
- SAS predisposes to aortic valve endocarditis.
- Aortic valve endocarditis predisposes to valvar aortic stenosis.
- HCM predisposes cats to fixed or dynamic LVOT obstruction.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

The systolic murmur must be differentiated from other causes of similar murmurs. Innocent or physiologic murmurs are commonly auscultated in athletic dogs, or with anemia, fever, stress or excitement. Pulmonic stenosis, tetralogy of Fallot, and atrial septal defects cause a similar murmur. Weak pulses may also occur with conditions that reduce cardiac output such as heart failure, cardiomyopathy, and severe pulmonic stenosis. Other obstruction to flow may cause reduced pulse quality, such as aortic thromboembolism or rarely aortic coarctation/tubular hypoplasia.

CBC/BIOCHEMISTRY/URINALYSIS

Typically within normal limits

OTHER LABORATORY TESTS

Genetic testing for the mutation associated with Newfoundland SAS is a breeding tool to reduce frequency in this breed.

IMAGING

Thoracic Radiography

- Mild disease may be radiographically silent.
- LV hypertrophy may be subtle as pressure overload causes concentric hypertrophy.
- Left heart enlargement.
- Prominent aortic root and/or widened mediastinum.
- Lung fields typically normal unless CHF with pulmonary venous distention and interstitial to alveolar infiltrates.

Echocardiography

- Findings are variably present and associated with disease severity.
- Ridge, ring, nodule, or tunnel-like narrowing below the aortic valve with SAS.
- Thickened LV free wall or interventricular septum.
- Aortic valve thickening and increased echogenicity with valvar stenosis.
- Mitral regurgitation and

(CONTINUED)

thickening of valve leaflet possible.

- Post-stenotic dilatation of the aorta.
- Hyperechoic myocardium associated with ischemia.
- AI with secondary LV chamber enlargement and volume overload if significant.
- Left atrial enlargement may be seen with significant valve regurgitation.
- Elevated LVOT flow velocity ($> 2.4 \text{ m/s}$), with acceleration proximal to the stenosis and turbulent flow distal to the obstruction and valve.
- Transvalvular pressure gradient estimated by the LVOT flow velocity ($4 \times \text{flow velocity squared}$). Estimated gradients of 25–49 mmHg are considered mild; 50–79 mmHg moderate, and $\geq 80 \text{ mmHg}$ severe.
- With myocardial failure the estimated pressure gradient may be falsely low.
- Effective valve orifice, if calculated, is reduced.

DIAGNOSTIC PROCEDURES

- ECG may show changes consistent with LV hypertrophy (tall R waves, widened QRS complexes, left axis deviation); signs of myocardial ischemia (ST segment deviation or slurring). Ventricular arrhythmias may occur and contribute to syncope or sudden death.
- Holter monitoring may be used to quantify arrhythmia severity and therapeutic response.

PATHOLOGIC FINDINGS

Findings vary with severity but typically include LV concentric or mixed (if significant AI) hypertrophy. A subvalvular lesion of dense fibrous tissue is seen with variable. Myocardial ischemia, necrosis and replacement fibrosis may be evident. Post-stenotic dilatation of the aorta and associated valvular endothelial damage and sometimes left atrial enlargement is reported.



TREATMENT

APPROPRIATE HEALTH CARE

Therapy is limited prior to the onset of complications and aimed at preventing clinical signs and avoiding sudden death.

NURSING CARE

Aimed at relieving symptoms and complications such as arrhythmias, syncope and CHF.

ACTIVITY

Restriction is warranted with severe disease; exertion may increase incidence of arrhythmias, syncope and sudden death.

DIET

Modest salt restriction with CHF.

CLIENT EDUCATION

SAS is considered an inherited disease; affected animals should not be bred. Owners should be counseled on the risk of endocarditis and appropriate antibiotics for any wounds, infections or surgical procedures.

Alert owners to the risks of sudden death, CHF and increased anesthetic risk.

SURGICAL CONSIDERATIONS

No surgical or interventional technique has been shown to extend life beyond medical therapy. Balloon valvuloplasty or combined cutting and traditional balloon valvuloplasty may acutely reduce the pressure gradient and temporarily alleviate some clinical signs. However, the effects are not shown to be beneficial beyond those achieved with beta-blockers. Currently, data does not support surgery or intervention.



MEDICATIONS

DRUG(S) OF CHOICE

Beta adrenergic blockers are advocated with moderate to severe SAS, particularly with ventricular arrhythmias, syncope or ECG evidence of ischemia. They may reduce myocardial oxygen demand, eliminate or protect against ventricular arrhythmias, and reduce heart rate. Atenolol is most common (dogs, 0.5–1.5 mg/kg PO q12h; cats 6.25 mg/cat PO q12–24h).

- Therapy for ventricular arrhythmias, CHF, atrial fibrillation or endocarditis may be required.

CONTRAINdicATIONS

Beta blockers are contraindicated in animals with bronchoconstriction such as asthmatic cats. Starting beta-blockers with CHF is contraindicated and continued use in patients that develop CHF is controversial.

PRECAUTIONS

- Beta-blockers are negatively impact cardiac output and starting low doses with gradual up titration is warranted.
- Positive inotropes may worsen a fixed obstruction and are used with caution when treating CHF.
- Anesthetic drugs that cause hypotension, arrhythmias or cardiac depression should be avoided with severe SAS.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUGS

- Carvedilol (dogs, 0.5–1.5 mg/kg PO q12h)
- Metoprolol tartrate (dogs, 0.5–1.5 mg/kg PO q12h)



FOLLOW-UP

PATIENT MONITORING

Monitor by ECG, Holter monitor, thoracic radiography, and echocardiography. Treatment of complications such as CHF and arrhythmias may necessitate additional monitoring for renal/electrolyte, blood pressure, and rhythm disturbances.

PREVENTION /AVOIDANCE

N/A

AORTIC STENOSIS

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POSSIBLE COMPLICATIONS

Ventricular arrhythmias, syncope, myocardial infarction, sudden death, AI, mitral regurgitation, endocarditis.

EXPECTED COURSE AND PROGNOSIS

Mildly affected dogs may have a normal lifespan and quality without therapy. Severely affected dogs have limited lifespans and typically succumb to sudden death or CHF. In one study the average lifespan for dogs with severe SAS on atenolol was about 4.5 years.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Increased risk of infective endocarditis

AGE-RELATED FACTORS

SAS is not immediately apparent at birth but appears over few weeks to months of life.

PREGNANCY/FERTILITY/BREEDING

Contraindicated

SYNONYMS

Subaortic stenosis, discrete subaortic stenosis.

SEE ALSO

- Congestive Heart Failure, Left-Sided
- Endocarditis, Infective
- Cardiomyopathy, Hypertrophic—Cats
- Cardiomyopathy, Hypertrophic—Dogs

ABBREVIATIONS

- AI = aortic insufficiency
- CHF = congestive heart failure
- HCM = hypertrophic cardiomyopathy
- ECG = electrocardiogram
- LV = left ventricle
- LVOT = left ventricular outflow tract
- PDA = patent ductus arteriosus
- SAS = subvalvular aortic stenosis

INTERNET RESOURCES

N/A

Suggested Reading

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Stern JA, White SN, Lehmkohl LB, et al. A single codon insertion in PICALM is associated with development of familial subvalvular aortic stenosis in Newfoundland dogs. Hum Genet 2014, 133(9):1139–1148.

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Client Education Handout
available online

AORTIC THROMBOEMBOLISM



BASICS

DEFINITION

Aortic thromboembolism results from a thrombus or blood clot that is dislodged within the aorta, causing severe ischemia to the tissues served by that segment of aorta.

PATHOPHYSIOLOGY

- ATE is commonly associated with myocardial disease in cats, most commonly hypertrophic cardiomyopathy. It is theorized that abnormal blood flow (stasis) and a hypercoagulable state contribute to the formation of a thrombus within the left atrium. The blood clot is then embolized distally to the aorta. The most common site of embolization is the caudal aortic trifurcation (hind legs). Other less common sites include the front leg, kidneys, gastrointestinal tract, or cerebrum.
- ATE in dogs typically is associated with neoplasia, sepsis, infectious endocarditis, Cushing's disease, protein-losing nephropathy, or other hypercoagulable states. However, in one recent retrospective study, no concurrent condition was identified in 58% of dogs.

SYSTEMS AFFECTED

- Cardiovascular—the majority of affected cats have advanced heart disease and left heart failure.
- Nervous/Musculoskeletal—severe ischemia to the muscles and nerves served by the segment of occluded aorta causes variable pain and paresis. Gait abnormalities or paralysis results in the leg or legs involved.

GENETICS

Hypertrophic cardiomyopathy, a common associated disease, is likely heritable. Additionally, a family of domestic shorthair cats with remodeled hypertrophic cardiomyopathy who all died of ATE has been reported.

INCIDENCE/PREVALENCE

- Prevalence is not known in the general population of cats. In two large studies of cats with hypertrophic cardiomyopathy, 12–16% presented with signs of ATE. In two retrospective studies of cats with ATE, 11–25% of cats had previous evidence of heart disease.
- Rare in dogs.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Cat, rarely dog

Breed Predilections

Mixed-breed cats are most commonly affected. Abyssinian, Birman, and ragdoll purebred cats were overrepresented in one

study. In dogs, no breed predilection has been identified in the USA. A European study suggested that Cavalier King Charles Spaniels may be overrepresented.

Mean Age and Range

Age distribution is 1–20 years. The median age is approximately 8–9 years in cats. In dogs, the median age is 8–10 years.

Predominant Sex

Males > females (2:1) in cats. In dogs, no sex predilection in dogs in the USA. A European study suggested a male predilection.

SIGNS

The presence of the 5 "P's" is helpful to remember the classic clinical signs associated with ATE: Pain, Paralysis or Paresis, Pulselessness, Pallor, and Poikilothermic (cold).

Historical Findings

- Acute onset paralysis and pain are the most common complaints in cats. Vocalization and anxiety are also common.
- Lameness or a gait abnormality, typically of several week duration, is more common in dogs.
- Tachypnea or respiratory distress is common in cats.
- About 15% of cats may vomit prior to ATE.

Physical Examination Findings

- Usually paraparesis or paralysis of the rear legs with signs of lower motor neuron injury. Less commonly, monoparesis of a front leg. In dogs, the majority are paretic and ambulatory.
- Absent or diminished femoral pulses.
- Pain upon palpation of the legs.
- Gastrocnemius muscle often becomes firm several hours after embolization.
- Cyanotic or pale nail beds and foot pads.
- Tachypnea/dyspnea and hypothermia are common in cats.
- Since commonly associated with heart disease in cats, a cardiac murmur, arrhythmias, or gallop sound may be present.

CAUSES

- Cardiomyopathy (all types)
- Hyperthyroidism
- Neoplasia
- Sepsis (dogs)
- Hyperadrenocorticism (dogs)
- Protein-losing nephropathy (dogs)

RISK FACTORS

- In the cat, cardiomyopathy is a risk factor. Cardiomyopathic cats with a markedly enlarged left atrium, spontaneous echocardiographic contrast (smoke), or an intracardiac thrombus observed on an echocardiogram are at a higher risk for development of ATE.
- In the dog, hypercoagulable conditions, such as neoplasia, sepsis, endocarditis, protein losing nephropathies, or hyperadrenocorticism are risk factors.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Hind limb paresis secondary to other causes such as spinal neoplasia, trauma, myelitis, fibrocartilaginous infarction, or intervertebral disc protrusion. These conditions resulting in spinal cord injury present with signs of upper motor neuron disease, whereas ATE patients present with signs of lower motor neuron disease.

CBC/BIOCHEMISTRY/URINALYSIS

- High creatine kinase as a result of muscle injury.
- High aspartate aminotransferase and alanine aminotransferase as a result of muscle and liver injury.
- Hyperglycemia secondary to stress.
- Mild increases in blood urea nitrogen and creatinine due to low cardiac output and possible renal emboli.
- Electrolyte derangements, due to low output and muscle damage, such as hypocalcemia, hyponatremia, hyperphosphatemia and hyperkalemia are not uncommon.
- CBC and urinalysis changes are non-specific.

OTHER LABORATORY TESTS

Routinely available coagulation profiles typically do not reveal significant abnormalities because the hypercoagulability results from hyperaggregable platelets. In the dog, thromboelastography may suggest a hypercoagulable state with a clot strength (increased maximum amplitude) or shortened clotting time (decreased R).

IMAGING

Radiographic Findings

- Cardiomegaly is common in cats.
- Pulmonary edema and/or pleural effusion in approximately 50% of cats.
- Rarely, a mass is seen in the lungs, suggestive of neoplasia.

Echocardiographic Findings

- In cats, changes consistent with cardiomyopathy. Hypertrophic cardiomyopathy is most common, followed by restrictive or unclassified cardiomyopathy and then dilated cardiomyopathy.
- Most cases (> 50%) have severe left atrial enlargement (i.e., left atrial to aortic ratio of ≥ 2).
- A left atrial thrombus or spontaneous echocardiographic contrast (smoke) may be seen.

Abdominal Ultrasonographic Findings

- May be able to identify the thrombus in the caudal aorta.
- Typically not necessary to reach a diagnosis in the cat but often needed to reach a diagnosis in the dog.

(CONTINUED)

AORTIC THROMBOEMBOLISM

A

Advanced Diagnostic Imaging

- Nonselective or CT angiography should identify a negative filling defect in the caudal aorta representing the thrombus.
- Typically not necessary to reach a diagnosis.

DIAGNOSTIC PROCEDURES**Electrocardiography**

- Sinus rhythm and sinus tachycardia most common. Less common rhythms include atrial fibrillation, ventricular arrhythmias, supraventricular arrhythmias, and sinus bradycardia.
- Left ventricular enlargement pattern and left ventricular conduction disturbances (left anterior fascicular block) are common.

PATHOLOGIC FINDINGS

- Thrombus typically is identified at the caudal aortic trifurcation.
- Occasionally, a left atrial thrombus is seen.
- Emboli of the kidneys, gastrointestinal tract, cerebrum, and other organs also may be seen.

**TREATMENT****APPROPRIATE HEALTH CARE**

Initially, cats with ATE should be treated as inpatients because many have concurrent congestive heart failure and require injectable drugs, in addition to being in considerable pain and distress.

NURSING CARE

- Fluid therapy is cautiously used as most cats have advanced myocardial disease. If in congestive heart failure, IV fluid therapy may not be necessary.
- Supplemental oxygen therapy or thoracocentesis may be beneficial if in congestive heart failure.
- Initially, minimally handle the affected legs. However, as reperfusion occurs, physical therapy (passive extension and flexion of the legs) may speed full recovery.
- Do not perform venipuncture on the affected legs.
- These animals may have difficulty posturing to urinate and may need to have their bladders expressed to prevent overdistention or urine scald.

ACTIVITY

Restrict activity and stress

DIET

Initially, most cats are anorexic. Tempt these cats with any type of diet to keep them eating and avoid hepatic lipidosis.

CLIENT EDUCATION

- Short- and long-term prognosis is poor in both dogs and cats.
- Most cats will re-embolize. Most cats that survive an initial episode will be on some type of anticoagulant therapy that may require

frequent re-evaluations and an indoor lifestyle.

- Most cats that survive an initial episode will recover complete function to the legs; however, if ischemia was severe and prolonged, sloughing of parts of the distal extremities or persistent neurologic deficits may result. In one study, approximately 15% of cats had permanent neuromuscular abnormalities after surviving the initial embolic event.
- Based on 3 small retrospective studies in dogs, the prognosis is generally poor but may be better in dogs presenting with chronic (vs. acute) lameness and dogs treated appropriately with warfarin.

SURGICAL CONSIDERATIONS

- Surgical embolectomy typically is not recommended because these patients are high risk for surgery because of severe heart disease.
- Rheolytic thrombectomy has been used with limited success in a small number of cats with ATE.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Thrombolytic therapy (e.g., tissue plasminogen activator [TPA]) is used extensively in humans and infrequently in cats and dogs. These drugs are expensive and carry a significant risk for bleeding complications; to date, they have not demonstrated improved treatment efficacy and thus are rarely used in general practice. TPA is theorized to be more beneficial if given early, ideally, within the first 6 hours of the event.
- Clopidogrel is an antiplatelet aggregation drug. One may choose to give a loading dose of clopidogrel for treatment of an acute embolic event. The loading dose in the cat is 75 mg/cat PO once and then maintenance dose starting 24h later is 18.75 mg/cat (one-fourth of 75 mg tablet) PO q24h. The loading dose in the dog is approximately 10 mg/kg once and then a maintenance dose of 1 mg/kg q24h. When compared to aspirin, clopidogrel was superior in preventing re-embolization, resulting improved survival times in cats that had survived an ATE.
- Unfractionated heparin is the preferred anticoagulant drug in general practice for initial management of feline ATE. Heparin has no effect on the established clot; however, it prevents further activation of the coagulation cascade. In either a cat or dog, give an initial dose of 100–200 units/kg IV and then 200–300 units/kg SC q8h. Alternatively, heparin can be administered as a CRI, if there is concern about adequate bioavailability via the SC route, at a dose of 25–35 units/kg/h. Titrate the dose to prolong the activated partial thromboplastin time approximately two-fold.
- Aspirin is theoretically beneficial during and after an episode of thromboembolism because of its antiplatelet effects. The dose in cats is an 81 mg tablet PO q48–72h. Vomiting and diarrhea are not uncommon. Some specialists advocate a mini dose of 5 mg/cat q72h. Antithrombotic dose recommendations for dogs range from 0.5 to 2 mg/kg q24h. Always give aspirin with food.
- Buprenorphine in the cat is useful and widely available drug used for analgesia and sedation at a dose of 5–20 µg/kg IV, SC, or in cheek pouch q6–8h. For stronger analgesia, use fentanyl or hydromorphone.
- Acepromazine may be cautiously used for its sedative and vasodilatory properties at a dose of 0.01–0.02 mg SC q8–12h.
- Warfarin, a vitamin K antagonist, is the anticoagulant most widely used in humans and has been proposed for prevention of re-embolization in cats surviving an initial episode. The initial dose is 0.25–0.5 mg/cat PO q24h or 0.05–0.2 mg/kg PO q 24h in the dog. Overlap with heparin therapy for 3 days. The dose is then adjusted to prolong the prothrombin time approximately two times its baseline value or to attain an international normalized ratio of 2 to 3. Long-term management with warfarin can be challenging because of frequent monitoring and dose adjustments in addition to bleeding complications. In one study, dogs treated appropriately with warfarin had a better clinical outcome.
- Low molecular weight heparin has recently been proposed for the long-term prevention of feline ATE. LMWH has a more predictable relationship between dose and response than warfarin and does not need monitoring or dose adjustments. It also has a lower risk of bleeding complication. The main disadvantage of LMWH is high drug cost and the injectable route of administration. The two LMWHs that have been used in feline ATE are: dalteparin (100–150 units/kg SC q8–24h) and enoxaparin (1 mg/kg SC q12–24h). Best dose unknown. LMWH usually started q24h due to cost. Some studies suggest q6h dosing necessary for stable blood levels, but may increase bleeding risk.

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CONTRAINdications

N/A

PRECAUTIONS

- Anticoagulant therapy with heparin, warfarin, or the thrombolytic drugs may cause bleeding complications.
- Avoid a nonselective beta-blocker such as propranolol as it may enhance peripheral vasoconstriction.

AORTIC THROMBOEMBOLISM

(CONTINUED)

POSSIBLE INTERACTIONS

Warfarin may interact with other drugs, which may enhance its anticoagulant effects.

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

- ECG monitoring while the cat is in hospital is helpful to detect reperfusion injury and hyperkalemia related ECG changes.
- Monitoring electrolytes and renal parameters periodically may be helpful to optimize management of the cardiac disease.
- Examine the legs frequently to assess clinical response. Initially, APTT should be performed once daily to titrate the heparin dose.
- If warfarin is used, PT or INR is measured approximately 3 days after initiation of therapy and then weekly until the desired anticoagulant effect is reached. Thereafter, measure three to four times yearly or when drug regimen is altered.

PREVENTION/AVOIDANCE

Because of the high rate of re-embolization, prevention with either clopidogrel, aspirin, warfarin, or LMWH is strongly recommended.

POSSIBLE COMPLICATIONS

- Bleeding with the anticoagulant therapy.
- Permanent neurologic deficits or muscular abnormalities in the hind limbs may arise with prolonged ischemia.
- Recurrent congestive heart failure or sudden death.
- Reperfusion injury and death usually associated with hyperkalemic arrhythmias.

EXPECTED COURSE AND PROGNOSIS

- Expected course is days to weeks for full recovery of function to the legs.
- Prognosis, both short term and long term, is poor in cats.

In two large studies, ~ 60% of cats were euthanized or died during the initial thromboembolic episode. Long-term prognosis varies between 2 months to several years; however, the average is a few months with treatment. Predictors of poorer prognosis include hypothermia (< 99°F) and congestive heart failure. One study demonstrated a median survival time of 77 days in cats with congestive heart failure and 223 days in cats without congestive heart failure. Predictors of better prognosis include normothermia, single leg affected, and presence of motor function on initial exam.

- In dogs, the disease is rare and prognosis in general is also poor. One study suggested a better prognosis if the dog had chronic clinical signs and if treated with warfarin.
- Recurrence of ATE is common.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

See "Causes" and "Risk Factors"

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Saddle thromboembolism
- Systemic thromboembolism

SEE ALSO

- Cardiomyopathy, Dilated—Cats
- Cardiomyopathy, Hypertrophic—Cats
- Cardiomyopathy, Restrictive—Cats

ABBREVIATIONS

- APTT = activated partial thromboplastin time
- ATE = aortic thromboembolism
- CRI = constant rate infusion
- ECG = electrocardiogram
- INR = international normalized ratio
- LMWH = low molecular weight heparin
- PT = prothrombin time

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Client Education Handout available online



BASICS

OVERVIEW

- Tumors of endocrine cells that are capable of amine precursor uptake and decarboxylation and secretion of peptide hormones; the tumors are named after the hormone they secrete.
- APUD cells are generally found in the gastrointestinal tract and CNS.
- Gastrin- and pancreatic polypeptide-secreting tumors are discussed here; insulinoma and glucagonoma are discussed separately.
- Hypergastrinemia from gastrin-secreting tumors causes gastritis and duodenal hyperacidity, which can cause gastric ulceration, esophageal dysfunction from chronic reflux, and intestinal villous atrophy.
- High concentration of pancreatic polypeptide also causes gastric hyperacidity and its consequences.

SIGNALMENT

- Gastrinoma—rare in dogs and cats; age range 3–12 years, mean 7.5 years (dogs).
- Pancreatic polypeptide—extremely rare in dogs.

SIGNS

- Vomiting
- Weight loss
- Anorexia
- Diarrhea
- Lethargy, depression
- Polydipsia
- Melena
- Abdominal pain
- Hematemesis
- Hematochezia
- Fever

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other conditions associated with hypergastrinemia, gastric hyperacidity, and gastrointestinal ulceration
- Uremia
- Hepatic failure
- Drug-induced ulceration (e.g., NSAIDs or steroids)
- Inflammatory gastritis
- Stress-induced ulceration
- Mast cell disease

CBC/BIOCHEMISTRY/URINALYSIS

- Normal or reflect the chronic effects of general disease
- Iron-deficiency anemia secondary to gastrointestinal bleeding

- Increased BUN secondary to gastrointestinal bleeding
- Hypoproteinemia
- Electrolyte abnormalities with chronic vomiting

OTHER LABORATORY TESTS

- Serum gastrin concentration normal or high-normal in patients with gastrinoma. Treatment with H₂ antagonists or proton pump inhibitors increases serum concentrations of gastrin and could lead to false-positive diagnosis of gastrinoma, but withdrawal of these drugs results in return of gastrin concentrations to baseline in dogs without gastrinoma.
- Provocative test of gastrin secretion—increased gastrin concentration after intravenous calcium gluconate or secretin administration suggests gastrinoma; see Appendix II for protocol and interpretation.

IMAGING

Abdominal ultrasound sometimes demonstrates a pancreatic mass but is usually normal.

DIAGNOSTIC PROCEDURES

- Endoscopy with gastric and duodenal biopsy.
- Aspirate any detectable masses because of suspicion of mast cell disease.
- If no detectable masses exist, examine a buffy coat smear for mast cells.

PATHOLOGIC FINDINGS

- Endoscopic biopsy reveals gastrointestinal ulceration.
- Histopathologic examination of pancreatic tumors reveals findings consistent with islet cell tumor but not specific for hormone type.
- Immunocytochemical staining can aid in the specific diagnosis.
- Histopathologic examination also can reveal metastasis to liver and regional lymph nodes.



TREATMENT

- Tell owner that most APUDomas are malignant and have metastasized by the time of diagnosis and that long-term control is often difficult.
- Aggressive medical management can sometimes palliate signs for months to years.
- Surgical exploration and excisional biopsy of a pancreatic mass are important both diagnostically and therapeutically.
- Medical management is useful for gastric hyperacidity.



MEDICATIONS

DRUG(S)

- Histamine H₂-receptor antagonists—cimetidine, ranitidine, and famotidine; decrease acid secretion by gastric parietal cells.

- Omeprazole—a proton pump inhibitor; the most potent inhibitor of gastric acid secretion available; highly effective and expensive.
- Sucralfate—adheres to ulcerated gastric mucosa and protects it from acid; promotes healing by binding pepsin and bile acids and stimulating local prostaglandins.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Because sucralfate may be less effective in an alkaline environment, and may reduce the absorption of other drugs, it should be given 1–2 hours prior to antacid drugs.



FOLLOW-UP

PATIENT MONITORING

- Physical examination and clinical signs are the most useful measures of treatment effectiveness and disease progression.
- Gastroscopy can monitor progression of gastritis but is not necessary.
- Abdominal radiography or ultrasound may detect development of abdominal masses.

EXPECTED COURSE AND PROGNOSIS

- Difficult to predict.
- Patients with gastrinoma have been controlled on medical management for months to years.
- No cure available.



MISCELLANEOUS

SEE ALSO

Gastrroduodenal Ulceration/Erosion

ABBREVIATIONS

- APUD = amine precursor uptake and decarboxylation
- CNS = central nervous system
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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ARTERIOVENOUS FISTULA AND ARTERIOVENOUS MALFORMATION



BASICS

OVERVIEW

Abnormal, low-resistance connections between an artery and vein which bypass a capillary bed; arteriovenous malformations (AVM) are typically congenital and involve a vascular nidus, or complex of communicating vessels, while arteriovenous fistulae (AVF) are often acquired direct connections. Large AVMs and AVFs allow a significant fraction of the total cardiac output to bypass the capillary bed. The resulting increase in cardiac output may lead to circulatory volume overload and congestive heart failure (CHF). The anatomic location of AVMs is variable, most often reported in the liver of dogs. The location of AVFs is also variable, occurring frequently in the limbs or at the site of previous surgery/trauma.

SIGNALMENT

- Dog and cat (rare in both).
- No specific age, breed, or sex predilections known, though AVMs are typically seen in younger animals.

SIGNS

Historical Findings

- Animals with AVF often have a history of trauma to the affected area.
- Owner may notice a warm, non-painful swelling at the site.
- Other findings depend on the lesion location (e.g., ascites with hepatic AVM).
- The shunt may cause local organ dysfunction.

Physical Examination Findings

- Vary and depend on location of the AVM/AVF.
- Signs of CHF (e.g., coughing, dyspnea, tachypnea, exercise intolerance) may develop in animals with long-standing disease and high blood flow.
- Bounding pulses may be present because of high ejection volume and rapid runoff through the AVM/AVF.
- Continuous murmur (bruit) at the site caused by turbulent blood flow through the lesion.
- Cautious compression of the artery proximal to the lesion abolishes the bruit. When blood flow is high, this compression may also elicit an immediate reflex decrease in heart rate (Branham's sign).
- Edema, ischemia, and congestion of organs and tissues caused by high venous pressure in the proximity of the lesion.
- If the lesion is on a limb, pitting edema, lameness, ulceration, scabbing, and gangrene may result.
- Lesions near vital organs may cause signs associated with organ failure such as ascites (liver), seizures (brain), paresis (spinal cord), and dyspnea (lung).

CAUSES & RISK FACTORS

- AVMs are rare; frequently a congenital lesion.
- Acquired AVFs typically result from local damage to vasculature secondary to trauma, surgery, venipuncture, perivascular injection, or tumor.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- The lesion may look like a mass if peripherally located (limb, ear).
- Other differentials include an aneurysm or false aneurysm.
- Atypical clinical findings, depending on location, may suggest other disease processes; AVF or AVM may be a late diagnostic consideration.

CBC/BIOCHEMISTRY/URINALYSIS

May reflect damage to systems in the vicinity of the lesion, i.e., biochemical abnormalities suggesting hepatic, renal, or other organ dysfunction are possible.

OTHER LABORATORY TESTS

N/A

IMAGING

Thoracic Radiographic Findings

Cardiac enlargement and pulmonary overcirculation in some animals with hemodynamically significant lesions.

Ultrasonographic Findings

- AVM and AVF appear as cavernous, vascular structures.
- Doppler ultrasound may demonstrate high-velocity, turbulent flow within the lesion.

Cross-sectional Imaging

Computed tomography or magnetic resonance angiography can aid in the diagnosis, particularly when imaged with contrast injection to highlight the vascular anatomy.

Angiography

Selective angiography defines the lesion and may be necessary for definitive diagnosis. This is performed at the time of intervention, if transcatheter therapy is pursued. Placement of the catheter close to the lesion and rapid injection is necessary; high-volume blood flow dilutes the contrast medium quickly.

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Surgery can be difficult and labor-intensive and may require blood transfusion, though is the traditional treatment for clinically-significant lesions.
- Transcatheter therapies with coils, devices, or glue represent

newer treatment options. Coils or devices are often sufficient for treatment of AVF; AVMs typically require glue embolization, as closure of the nidus is required for complete cure. Potential advantages include less invasive treatment and intravascular access to remote lesions.

- AVMs and AVFs may recur. In some animals, surgical removal of the affected limb or organ (e.g., amputation, liver lobectomy) may be necessary.



MEDICATIONS

DRUG(S)

- Concurrent medical treatment depends on the site of the lesion and secondary clinical features.
- Medical treatment for CHF or other organ dysfunction may be required before surgery.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Avoid excessive fluid administration; animals with these lesions are often volume overloaded.



FOLLOW-UP

Postoperative reevaluation is needed to determine whether the AVM or AVF has recurred and if organ dysfunction has normalized.



MISCELLANEOUS

SEE ALSO

Congestive Heart Failure, Left-Sided

ABBREVIATIONS

- AVF = arteriovenous fistula
- AVM = arteriovenous malformation
- CHF = congestive heart failure

Suggested Reading

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ARTERIOVENOUS MALFORMATION OF THE LIVER



BASIC

OVERVIEW

- Intrahepatic arteriovenous (AV) malformations (also referred to as AV fistulae) are communications between proper hepatic arteries and intrahepatic portal veins; this anatomic union results in hepatofugal (away from the liver) splanchnic circulation.
- Blood flows directly from a hepatic artery into portal vasculature retrograde into the vena cava through multiple acquired portosystemic shunts (APSS).
- Associated with ascites.
- Uncommon, usually congenital, but may be acquired (surgical injury, trauma, neoplasia).

SIGNALMENT

- Dogs, less common in cats
- Age-related presentation (congenital): < 2 years
- No sex or breed predilection

SIGNS

General Comments

Vague or acute illness; present for signs caused by portal hypertension and APSS: ascites and hepatic encephalopathy (HE).

Historical Findings

- Dogs may have a normal transition to growth foods, unlike PSVA that demonstrate HE.
- May have an acute onset of ascites or HE.
- Vague signs include: lethargy, anorexia, vomiting, diarrhea, weight loss, polydipsia, dementia, abdominal distention, and uroliths causing obstructive uropathy.

Physical Examination Findings

- Lethargic, poor body condition, ascites; enlarged liver lobe containing the AV malformation; rarely palpated on initial examination.
- Rarely, bruit auscultated over AV malformation.

CAUSES & RISK FACTORS

- Usually congenital vascular malformations (single or multiple vessels) reflecting failed differentiation of common embryologic anlage.
- Rare: secondary to abdominal trauma, inflammation, neoplasia, surgical interventions, or diagnostic procedures (e.g., liver biopsy).
- Portal hypertension—reflects arterialization of valveless portal system—establishing APSS.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- CNS signs—*infectious disorders* (e.g., distemper); *toxicity* (e.g., lead); hydrocephalus; idiopathic epilepsy; metabolic disorders (e.g., hypoglycemia, hypokalemia or hyperkalemia); HE (e.g., acquired liver disease or PSVA).
- Abdominal effusion:—pure transudate (ascites; protein-losing nephropathy, protein-losing enteropathy, liver disease); modified transudate (congenital cardiac malformations, right-sided heart failure, pericardial tamponade, supradiaphragmatic vena caval obstruction, neoplasia, portal vein thrombosis); hemorrhage.
- Portal hypertension—chronic hepatic disease, ductal plate malformations/congenital hepatic fibrosis, non-cirrhotic or idiopathic portal hypertension, cirrhosis, portal thrombi.

CBC/BIOCHEMISTRY/URINALYSIS

- Erythrocyte microcytosis (APSS), target cells
- Hypoalbuminemia with normal or low serum globulins; ALP and ALT activity normal or moderately increased; variable low BUN and hypcholesterolemia, and anicteric
- Hyposthenuria or isosthenuria
- Ammonium biurate crystalluria

OTHER LABORATORY TESTS

- Coagulation tests—variable, may be normal; low protein C activity reflects APSS.
- Total serum bile acids—preprandial values variable, postprandial values increased; classic shunting pattern.
- Plasma ammonia—usually increased, inferred by ammonium biurate crystalluria.
- Peritoneal fluid—pure transudate (total protein < 2.5 g/dL) or modified transudate.

IMAGING

Radiography

- Abdominal effusion
- Microhepatia or normal sized liver due to enlarged lobe with AV malformation
- Renomegaly
- Normal thorax

Abdominal Ultrasonography

- Abdominal effusion
- Liver lobe with AV malformation—large compared to most other liver lobes that are atrophied due to portal hypoperfusion.
- Tortuous anechoic tubules represent AV structure with unidirectional pulsating or turbulent flow on color-flow Doppler.
- Hepatic artery and/or portal vein branches may appear tortuous.

- Hepatofugal portal flow (away from the liver)—through APSS.
- Renomegaly.
- Urolithiasis: urinary bladder or renal pelvis.
- Rule out portal thrombosis (luminal filling defect, abrupt blood flow termination).

Radiographic Contrast Angiography

- Not indicated in most cases.
- Venous portography—only confirms APSS.
- Hepatic arteriography—required to confirm AV communication (celiac trunk or anterior mesenteric artery contrast injection).

Multi-Sector CT

Non-invasive contrast imaging of hepatic vasculature; arterial and venous phases; 3-dimensional reconstruction illustrates AV malformation, large liver lobe, atrophied liver.

Echocardiography

Rule out right-sided heart disease, pericardial disease, and vena caval occlusion.

DIAGNOSTIC PROCEDURES

- Multi-sector CT and exploratory laparotomy.
- Liver biopsy—collect samples from *affected* and *unaffected* liver lobes; “normal” liver often demonstrates severe vascular arterialization (more severe than associated with PSVA).



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient—Treat HE and ascites prior to surgical approach or percutaneous selective acrylamide embolization.

NURSING CARE

- Diet—restrict nitrogen intake to ameliorate HE and hyperammonemia; restrict sodium to attenuate ascites formation.
- HE—resolve endoparasitism, electrolyte and hydration disturbances, treat infections, initiate treatments to alter enteric uptake and formation of HE toxins (see Hepatic Encephalopathy).
- Ascites—mobilize by restricting activity and sodium intake and instituting dual diuretic therapy (furosemide and spironolactone); reserve therapeutic abdominozentesis for tense ascites impairing ventilation, nutrition, sleep, or recumbent posture; (see Portal Hypertension, Portosystemic Shunting, Acquired, and below).

SURGICAL CONSIDERATIONS

- Resection of liver lobe containing AV malformation is complicated by coexistence of additional hepatic vascular malformations; clinical cure possible but unlikely.

- Percutaneous selective acrylamide vascular embolization; complicated by risk of thromboembolism of additional vasculature; temporary improvement; but treatment may be curative.
- Multiple microscopic vascular malformations continue portal hypertension and APSS.
- Do not ligate APSS nor band the vena cava.



MEDICATIONS

DRUG(S)

Hepatic Encephalopathy

See Hepatic Encephalopathy

Ascites

- Restrict sodium intake.
- Furosemide (0.5–2 mg/kg PO IM or IV q12–24h)—combine with spironolactone.
- Spironolactone (0.5–2 mg/kg PO q12h)—double initial dose as loading dose once.
- Chronic diuretic therapy—individualized to response, 4- to 7-day assessment intervals used to titrate dose to response, avoiding hydration, electrolyte, and HE complications.
- Diuretic-resistant ascites—may require therapeutic abdominocentesis; to initiate diuresis.
- Vasopressin V₂ receptor antagonists newly available may control ascites accumulation. (See Portosystemic Shunting, Acquired.)

Bleeding Tendencies

See Coagulopathy of Liver Disease

Gastrointestinal Hemorrhage

- *Histamine type-2 receptor antagonists* (famotidine 0.5–2 mg/kg PO, IV, or SC q12–24h); or *HCl pump inhibitors* (omeprazole 1.0 mg/kg/24h PO or pantoprazole 1 mg/kg/24h IV [omeprazole may induce p450 cytochrome-associated drug interactions and may have a 24–48h delay onset of action]; some clinicians recommend chronic treatment to minimize gastrointestinal bleeding and ulceration that may be chronic problems).
- *Gastroprotectant*—sucralfate: 0.25–1.0 g/10 kg PO q8–12h; titrate to effect, beware of drug interactions as sucralfate may bind other medications, reducing bioavailability.
- *Eliminate endoparasitism*.

CONTRAINDICATIONS

Avoid drugs dependent on hepatic biotransformation or first pass hepatic extraction (reduced by APSS) or that react with GABA-benzodiazepine receptors because of propensity for HE.



FOLLOW-UP

PATIENT MONITORING

Biochemistry—initially monthly until stabilized after surgery or AV malformation embolization, thereafter quarterly; monitor for hypoalbuminemia, infection, optimization of HE management and control of ammonium biurate crystalluria.

EXPECTED COURSE AND PROGNOSIS

- Prognosis fair if patient survives surgical resection of AV malformation or embolization.
- Most patients require indefinite nutritional and medical management (HE, ascites) because of coexisting microscopic vascular malformations across the liver; APSS persists requiring continued management of HE.



MISCELLANEOUS

SEE ALSO

- Ascites
- Hepatic Encephalopathy
- Hypertension, Portal
- Portosystemic Shunting, Acquired
- Portosystemic Vascular Anomaly, Congenital

ABBREVIATIONS

- APSS = acquired portosystemic shunt
- GABA = γ -aminobutyric acid
- HE = hepatic encephalopathy
- PSVA = portosystemic vascular anomalies

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BASICS

DEFINITION

Osteoarthritis or degenerative joint disease is the progressive and permanent deterioration of the articular cartilage of diarthrodial (synovial) joints due to primary (idiopathic) and secondary causes.

PATOPHYSIOLOGY

- DJD is initiated by mechanical stress—traumatic injury, instability, abnormal conformation, abnormal activity, etc.
- Metalloproteinases, serine proteases, and cysteine protease enzymes are released from damaged chondrocytes, causing collagen degradation and loss of collagen cross-linking in cartilage.
- Collagen synthesis is altered, resulting in decreased collagen/proteoglycan interaction and reduced hydrophylic matrix properties.
- Cartilage matrix is further compromised by increased breakdown of proteoglycans and manufacture of poorer-quality proteoglycans.
- Nitric oxide is released, which mediates cartilage breakdown and supports chronic inflammation.
- Chondrocyte apoptosis is facilitated by cyclooxygenase-2 enzymes.
- Synovial membrane inflammation results in decreased viscosity of the synovial fluid, reducing lubrication.
- Poorer-quality synovial fluid reduces oxygen and nutrient supply to the chondrocytes.
- Subchondral bone becomes sclerotic, worsening loading qualities of the bone and overlying cartilage.
- Pain of DJD results from stimulation of pain receptors in the tendons, ligament, subchondral bone, and joint capsule.
- The result of these processes is progressive cartilage degradation ranging from fibrillation to deep fissuring of cartilage.
- Full-thickness cartilage loss can eventually occur.
- Periarticular fibrosis occurs to reduce joint motion (and pain), leading to poorer vascularity of the synovial membrane.
- Osteophytes and enthesiophytes develop around and within the joint to increase the load-bearing surface area.
- These changes reduce functionality and may eventually lead to ankylosis.

SYSTEMS AFFECTED

Musculoskeletal—diarthrodial joints

GENETICS

- Primary DJD is rare.
- Dogs—causes of secondary DJD are varied, including hip and elbow dysplasias, osteochondrosis dissecans, patellar luxations, congenital shoulder luxation, Legg-Perthes, and cranial cruciate ligament rupture.
- Cats—causes of secondary DJD are patellar luxation, hip dysplasia, and arthropathy.

INCIDENCE/PREVALENCE

- Dog—very common; 20% of dogs older than 1 year have some degree of DJD.

- Cat—90% of cats over 12 years of age had evidence of DJD on radiographs.
- Clinical problems are more prevalent in larger, overweight, and very active animals.
- Primary DJD is rare.

SIGNALMENT

Species

Dog and cat

Mean Age and Range

- Secondary DJD due to congenital disorders (OCD, hip dysplasia) seen in immature animals; some present with DJD signs when older (hip and elbow dysplasia).
- Secondary to trauma—any age.

SIGNS

Historical Findings

- Dogs—decreased activity level, unwilling to perform certain tasks; intermittent lameness or stiff gait that slowly progresses; possible history of joint trauma, OCD, or developmental disorders; may be exacerbated by exercise, long periods of recumbency, and cold weather.
- Cats—overt lameness may not be seen. May have difficulty grooming, jumping onto furniture, or accessing the litter box; increased irritability.

Physical Examination Findings

- Stiff-legged or altered gait (e.g., bunny hopping in hip dysplasia) or non-use of leg.
- Decreased range of motion.
- Crepitus.
- Joint swelling (effusion and/or thickening of the joint capsule).
- Joint pain.
- Joint instability.

CAUSES

- Primary—no known cause.
- Secondary—results from an initiating cause: abnormal wear on normal cartilage (e.g., joint instability, joint incongruity, trauma to cartilage or supporting soft tissues) or normal wear on abnormal cartilage (e.g., osteochondral defects).

RISK FACTORS

- Working, athletic, and obese dogs place more stress on their joints.
- Dogs with disorders that affect collagen or cartilage (Cushing's disease, diabetes mellitus, hypothyroidism, hyperlaxity, prolonged, steroids).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Neoplastic (synovial sarcoma; rarely, chondrosarcoma; osteosarcoma).
- Septic arthritis (caused by bacteria; spirochetes; L forms in cats; *Mycoplasma*; *Rickettsia*; *Ehrlichia*; viruses, such as feline calicivirus; fungi, and protozoa).
- Immune-mediated arthritis (erosive vs. non-erosive).
- Other musculoskeletal conditions that cause

lameness.

- Neurologic conditions causing lameness or decreased activity/weakness.

OTHER LABORATORY TESTS

- Coombs' test, ANA, and rheumatoid factor may help to rule out immune-mediated arthritis.
- Serum titers for *Borrelia*, *Ehrlichia*, and *Rickettsia* to evaluate for infectious arthritis.

IMAGING

- Radiographic changes—include joint capsular distention, osteophytosis, enthesiophytosis, soft-tissue thickening, and narrowed joint spaces; in severely affected patients: subchondral sclerosis, and intra-articular calcified bodies (joint mice).
- Radiographic severity often does not correlate with clinical severity.
- Stress radiography may identify underlying instability and accentuate joint incongruity (e.g., distraction index, passive hip laxity of the coxofemoral joint is predictive of hip DJD).
- Bone nuclear scintigraphy can assist in localizing subtle DJD.

DIAGNOSTIC PROCEDURES

- Arthrocentesis and synovial fluid analysis—cell counts are normal or slightly increased (< 2,000–5,000 cells/mL) predominantly mononuclear (macrophages) and occasional synovial lining cells.
- Bacterial culture of synovial fluid—negative.
- Biopsy of synovial tissue to rule out neoplasia or immune-mediated arthritides (lymphocytic plasmacytic synovitis, SLE).

PATHOLOGIC FINDINGS

- Fibrillation or erosion of articular cartilage.
- Eburnation and sclerosis of subchondral bone.
- Thickening and fibrosis of the joint capsule.
- Synovial fluid can be grossly normal to thin and watery, usually increased volume.
- Synovial villous hypertrophy and hyperplasia.
- Osteophytes and enthesiophytes at joint capsule attachments and adjacent to the joint.
- Neovascularization or pannus in severe cases over joint surfaces.



TREATMENT

APPROPRIATE HEALTH CARE

- Medical—usually tried initially.
- Surgical options—to improve joint geometry or remove bone-on-bone contact areas.

NURSING CARE

- Physical therapy—very beneficial.
- Maintaining or increasing joint motion—passive range of motion exercises, massage, swimming.
- Pain management—cold and heat therapy.
- Muscle tone/strengthening—swimming (aerobic exercise with minimal weight bearing); controlled leash walks up hills or on soft surfaces, such as sand or dry or underwater treadmill.

ARTHRITIS (OSTEOARTHRITIS)

(CONTINUED)

ACTIVITY

Limited to a level that minimizes aggravation of clinical signs.

DIET

- Weight reduction for obese patients—decreases stress placed on arthritic joints.
- Omega n-6 and n-3 fatty acids decrease the production of certain prostaglandins and modulate inflammation.

CLIENT EDUCATION

- Medical therapy is palliative and the condition is likely to progress. • Discuss treatment options, activity level, and diet.

SURGICAL CONSIDERATIONS

• Arthrotomy—used to remove aggravating causes (e.g., fragmented coronoid process, un-united anconeal process, osteochondral flaps). • Arthroscopy—used to diagnose and remove aggravating causes; flushing the joint may be beneficial. • Reconstructive procedures—used to eliminate joint instability and correct anatomic problems (patella luxation, angular deformity). • Joint removal—femoral head and neck ostectomy, temperomandibular joint arthroplasty. • Joint replacement—total hip replacement is widely used, total elbow replacement still experimental. • Joint fusion (arthrodesis)—in selected chronic cases and for joint instability, complete or partial; carpus, hock: generally excellent outcome; shoulder, elbow, stifle; less predictable outcome.



MEDICATIONS

DRUG(S) OF CHOICE

NSAIDs

- Inhibit prostaglandin synthesis through cyclooxygenase enzymes.
- Deracoxib (3–4 mg/kg PO q24h, chewable).
- Carprofen (2.2 mg/kg PO q12h or q24h).
- Meloxicam (load 0.2 mg/kg PO, then 0.1 mg/kg PO q24h: liquid).
- Tepoxalin (load 20 mg/kg, then 10 mg/kg PO q24h).
- Cats—meloxicam (0.1 mg/kg PO q24h: liquid) or robenacoxib (1 mg/kg PO q24h for 3 days).

Chondroprotective/Regenerative Supplements

- Supply PSGAG molecules to repair and regenerate cartilage.
- Host of products, many with little production oversight so effects vary widely.
- Glucosamine and chondroitin sulfate—injectable Adequan, oral Cosequin, oral MSM, mixtures (e.g., Glycoflex II, SynFlex).

- Adequan—clinical study in dogs with hip dysplasiam; 4.4 mg/kg IM every 3–5 days for 8 injections had a positive, temporary effect.
- Cosequin—trials showed positive effects.

CONTRAINDICATIONS

- NSAIDs must not be given with steroids.
- Acetaminophen must not be given to cats.

PRECAUTIONS

- NSAIDs—may cause gastric ulceration.
- COX-2 selective drugs may interfere with liver function. • When switching NSAIDs—wait 3 days for washout before starting new drug.

POSSIBLE INTERACTIONS

Steroids and NSAIDS

ALTERNATIVE DRUG(S)

- Free-radical scavengers. • Glucocorticoids— inhibit inflammatory mediators and cytokines; however, chronic use delays healing and initiates damage to articular cartilage; potential systemic side effects documented; goal is low-dose (dogs, 0.5–2 mg/kg; cats, 2–4 mg/kg) q48h. • Prednisone—initial dose 1–2 mg/kg PO q24h for dogs and 4 mg/kg PO q24h for cats. • Triamcinolone hexacetonide—intra-articular injection of 5 mg in dogs showed a protective and therapeutic effect in one model.



FOLLOW-UP

PATIENT MONITORING

Clinical deterioration—indicates need to change drug selection or dosage; may indicate need for surgical intervention.

PREVENTION/AVOIDANCE

Early identification of predisposing causes and prompt treatment to help reduce progression of secondary conditions, e.g., surgical removal of osteochondral lesions.

EXPECTED COURSE AND PROGNOSIS

- Slow progression of disease likely. • Some form of medical or surgical treatment usually allows a good quality of life.



MISCELLANEOUS

SYNOMYMS

- Degenerative arthritis • Degenerative joint disease • Osteoarthritis • Osteoarthrosis

ABBREVIATIONS

- ANA = antinuclear antibody • COX-2 = cyclooxygenase-2 • DJD = degenerative joint disease • NSAID = nonsteroidal

anti-inflammatory drug • OCD = osteochondrodysplasia • PSGAGs = polysulfated glycosaminoglycans • SLE = systemic lupus erythematosus

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- Author** Walter C. Renberg
Consulting Editor Walter C. Renberg
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Client Education Handout
available online



BASICS

DEFINITION

Pathogenic microorganisms within the closed space of one or more synovial joints

PATOPHYSIOLOGY

- Usually caused by contamination associated with traumatic injury (e.g., a direct penetrating injury such as bite, gunshot wound, foreign object), a sequela to surgery, arthrocentesis or joint injection, hematogenous spread of microorganisms from a distant septic focus, or less commonly the extension of primary osteomyelitis
- Primary sources of hematogenous infection—urogenital, integumentary (including ears and anal sacs), respiratory, cardiac, and gastrointestinal systems

SYSTEMS AFFECTED

Musculoskeletal—usually affects one joint

GENETICS

N/A

INCIDENCE/PREVALENCE

Relatively uncommon cause of monoarticular arthritis in dogs and cats

GEOGRAPHIC DISTRIBUTION

May be an increased incidence in Lyme disease-endemic areas

SIGNALMENT

Species

- Most common in dogs
- Rare in cats

Breed Predilections

Any. Medium to large breeds—most commonly German shepherds, Dobermanns, and Labrador retrievers.

Mean Age and Range

Any age; usually between 4 and 7 years. Hematogenous: more common in immature animals.

Predominant Sex

Male

SIGNS

General Comments

Always consider the diagnosis in patients with acute, monoarticular lameness associated with soft tissue swelling, heat, and pain.

Historical Findings

- Lameness—acute onset most common, but can present as chronic lameness
- Lethargy
- Anorexia
- May report previous trauma—dog bite, penetrating injury, prior surgery or other invasive procedure of the joint

Physical Examination Findings

- Monoarticular lameness, rarely polyarticular
- Joint pain and swelling—commonly carpus, stifle, hock, shoulder, or cubital joint
- Localized joint heat

- Decreased range of motion
- Local lymphadenopathy
- Fever

CAUSES

- Aerobic bacterial organisms—most common: staphylococci, streptococci, coliforms and *Pasteurella*
- Anaerobic organisms—most common: *Propionibacterium*, *Peptostreptococcus*, *Fusobacterium* and *Bacteroides*
- Spirochete—*Borrelia burgdorferi*
- Mycoplasma*
- Fungal agents—*Blastomyces*, *Cryptococcus*, and *Coccidioides*
- Rickettsial—*Anaplasma*, *Ehrlichia*, *Rickettsia*
- Leishmania*
- Feline calicivirus

RISK FACTORS

- Predisposing factors for hematogenous infection—diabetes mellitus; hypoadrenocorticism (Addison's disease); immunosuppression
- Penetrating trauma to the joint including surgery
- Existing osteoarthritis or other joint damage
- Intra-articular injection, particularly if steroid injected



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Osteoarthritis
- Trauma
- Immune-mediated arthropathy
- Postvaccinal transient polyarthritidis
- Greyhound polyarthritis
- Feline progressive polyarthritis
- Crystal-induced joint disease
- Synovial sarcoma

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram—inflammatory left shift in some cases
- Other results normal

OTHER LABORATORY TESTS

Serologic testing for specific pathogens

IMAGING

Radiography

- Early disease—may reveal thickened and dense periarticular tissues; may see evidence of synovial effusion. Often difficult to diagnose early disease radiographically.
- Late disease—reveals bone destruction, osteolysis, irregular joint space, discrete erosions, and periarticular osteophytosis.

DIAGNOSTIC PROCEDURES

Synovial Fluid Analysis

- Increased volume
- Turbid fluid
- Decreased viscosity
- Decreased mucin clot reaction
- Make slides immediately; if additional fluid is obtained, place in EDTA tube

- Elevated WBC count—> 80% neutrophils with $> 40,000/\text{mm}^3$ (normal joint fluid < 10% neutrophils and $< 3,000/\text{mm}^3$)
- Neutrophils may show degenerative changes (chromatolysis, vacuolation, nuclear swelling, loss of segmentation)
- Neutrophils with phagocytosed bacteria—definitive diagnosis or bacteria in the synovial fluid

Synovial Fluid Culture

- Positive culture is definitive but not necessary for diagnosis.
- Must be collected aseptically; requires heavy sedation or general anesthesia.
- Place fluid sample in aerobic and anaerobic culturettes and in blood culture medium.
- Use 1:9 dilution of synovial fluid to blood culture media.
- Culturette samples—cultured immediately upon arrival to the laboratory.
- Blood culture medium—re-culturing after 24 hours of incubation increases accuracy by 50% and is the preferred method.
- Mycoplasma*, bacterial L-forms and protozoa require specific culture procedures—contact laboratory prior to sample collection.

Other

- Synovial biopsy—to rule out immune-mediated joint disease; no more effective than incubated blood culture medium for growing bacterial organisms.
- Blood and urine cultures if hematogenous source is suspected.

PATHOLOGIC FINDINGS

- Synovium—thickened; discolored; often very proliferative
- Histology—evidence of hyperplastic synoviocytes
- Increased numbers of neutrophils, macrophages, and fibrinous debris
- Cartilage—loss of proteoglycan, destruction of articular surface, pannus formation



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—initial stabilization; initiate systemic antibiotic therapy as soon as fluid is obtained for bacterial culture; consider joint drainage/lavage as soon as possible to minimize intra-articular injury.
- Identify and treat source if hematogenous spread is suspected.
- Outpatient—long-term management.

NURSING CARE

Alternating heat and cold packing—beneficial in promoting increased blood flow and decreased swelling.

ACTIVITY

Restricted until resolution of symptoms

DIET

N/A

CLIENT EDUCATION

- Discuss probable cause.
- Warn client about the need for long-term antibiotics and the likelihood of residual degenerative joint disease.

SURGICAL CONSIDERATIONS

- Acute disease with minimal radiographic changes—joint drainage and lavage via needle arthrocentesis, arthroscopic lavage or arthrotomy. An irrigation catheter (ingress/egress) can be placed in larger joints.
- Chronic disease—may require open arthrotomy with debridement of the synovium and copious lavage; if appropriate, an irrigation catheter (ingress/egress) may be placed to lavage the joint postoperatively.
- Lavage—use warmed physiologic saline or lactated Ringer's solution (2–4 mL/kg q8h) until effluent is clear. Do not add povidone/iodine or chlorhexidine to lavage fluid.
- Effluent fluid—cytologically monitored daily for existence and character of bacteria and neutrophils.
- Removal of catheters—when effluent fluid has no bacteria and the neutrophils are cytologically healthy.
- Arthroscopy allows for visual assessment of articular cartilage, lavage and biopsy, and is a less invasive method of thorough joint lavage than arthrotomy.
- Recent reports suggest there may be no difference between combined medical and surgical management and medical management alone.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Pending culture susceptibility data—bactericidal antibiotics, such as first-generation cephalosporin or amoxicillin-clavulanic acid, preferred.
- Choice of antimicrobial drugs—primarily depends on in vitro determination of susceptibility of microorganisms; toxicity, frequency, route of administration and expense also considered; most penetrate the synovium well; need to be given for a minimum of 4–8 weeks.
- NSAIDs—may help decrease pain and inflammation.

CONTRAINDICATIONS

Avoid fluorinated quinolones in pediatric patients; they induce cartilage lesions experimentally.

PRECAUTIONS

Failure to respond to conventional antibiotic therapy—may indicate anaerobic disease or other unusual cause (fungal, spirochete).

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

- If drainage and irrigation catheters have been placed—may be removed after 4–6 days or after reassessment of synovial fluid cytology.
- Duration of antibiotic therapy—2 weeks following resolution of clinical signs. Total treatment may be 4–8 weeks or longer depending on clinical signs and pathogenic organism.
- Persistent synovial inflammation without viable bacterial organisms (dogs)—may be caused by antigenic bacterial fragments or antigen antibody deposition.
- Systemic corticosteroid therapy (after joint sepsis has been resolved) and aggressive physical therapy—may be needed to maximize normal joint dynamics.

PREVENTION/AVOIDANCE

If clinical signs recur, early (within 24–48 hours) treatment provides the greatest benefit.

POSSIBLE COMPLICATIONS

- Chronic disease—severe degenerative joint disease
- Recurrence of infection
- Limited joint range of motion
- Generalized sepsis
- Osteomyelitis

EXPECTED COURSE AND PROGNOSIS

- Acutely diagnosed disease (within 24–48 hours) responds well to antibiotic therapy.
- Delayed diagnosis or resistant or highly virulent organisms—guarded to poor prognosis.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Infectious arthritis
- Joint ill

SEE ALSO

- Osteomyelitis
- Polyarthritis, Immune-mediated

ABBREVIATION

NSAIDs = nonsteroidal anti-inflammatory drugs

INTERNET RESOURCES

N/A

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Client Education Handout
available online



BASICS

DEFINITION

The escape of fluid, either transudate or exudate, into the abdominal cavity between the parietal and visceral peritoneum.

PATHOPHYSIOLOGY

- Ascites can be caused by the following:
 - CHF and associated interference in venous return
 - Depletion of plasma proteins associated with inappropriate loss of protein from renal or gastrointestinal disease—protein-losing nephropathy or enteropathy, respectively
 - Obstruction of the vena cava or portal vein, or lymphatic drainage due to neoplastic occlusion
 - Overt neoplastic effusion
 - Peritonitis—infective or inflammatory
 - Electrolyte imbalance, especially hypernatremia
 - Liver cirrhosis.

SYSTEMS AFFECTED

- Cardiovascular
- Gastrointestinal
- Hemic/Lymph/Immune
- Renal/Urologic

SIGNALMENT

- Dogs and cats
- No species or breed predisposition

SIGNS

- Episodic weakness
- Lethargy
- Abdominal fullness
- Abdominal discomfort when palpated
- Dyspnea from abdominal distension or associated pleural effusion
- Anorexia
- Vomiting
- Weight gain
- Scrotal or penile edema
- Groaning when lying down

CAUSES

- Nephrotic syndrome
- Cirrhosis of liver
- Right-sided CHF
- Hypoproteinemia
- Ruptured bladder
- Peritonitis
- Abdominal neoplasia
- Abdominal hemorrhage

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiating Abdominal Distension without Effusion

- Organomegaly—hepatomegaly, splenomegaly, renomegaly, and hydrometra.
- Abdominal neoplasia.
- Pregnancy.
- Bladder distension.
- Obesity.
- Gastric dilatation.

Differentiating Diseases

- Transudate—nephrotic syndrome, cirrhosis of liver, right-sided CHF, hypoproteinemia, and ruptured bladder.
- Exudate—peritonitis, abdominal neoplasia, and hemorrhage.

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilic leukocytosis occurs in patients with systemic infection.
- Albumin is low in patients with impaired liver synthesis, gastrointestinal loss, or renal loss.
- Cholesterol is low in patients with impaired liver synthesis.

Liver Enzymes

- Low to normal in patients with impaired liver synthesis.
- High in patients with liver inflammation, hyperadrenocorticism, gallbladder obstruction, and chronic passive congestion.

Total and Direct Bilirubin

- Low to normal in patients with impaired liver synthesis.
- High in patients with biliary obstruction caused by tumor, gallbladder distension, or obstruction.

BUN and Creatinine

- High in patients with renal failure.
- BUN low in patients with impaired liver synthesis or hyperadrenocorticism.

Glucose

Low in patients with impaired liver synthesis.

OTHER LABORATORY TESTS

- To detect hypoproteinemia—protein electrophoresis and immune profile.
- To detect proteinuria—urinary protein:creatinine ratio (normal < 0.5:1).
- To detect liver ascites—analysis of serum ascites albumin gradient.

IMAGING

- Thoracic and abdominal radiography is sometimes helpful.
- Ultrasonography of the liver, spleen, pancreas, kidney, bladder, and abdomen can often determine cause.
- Stages of ascites:
 - Stage I: minimal ascites. Detected by ultrasound only.
 - Stage II: moderate ascites. Abdominal distention visible and/or noted on ballottement.
 - Stage III: significant ascites. Marked abdominal distention. Patient uncomfortable, possibly with labored breathing.

DIAGNOSTIC PROCEDURES

Ascitic Fluid Evaluation

Exfoliative cytologic examination and bacterial culture and antibiotic sensitivity—remove approximately 3–5 mL of abdominal fluid via aseptic technique.

Transudate

- Clear and colorless.
- Protein < 2.5 g/dL.
- Specific gravity < 1.018.
- Cells < 1,000/mm³—neutrophils and mesothelial cells.

Modified Transudate

- Red or pink; may be slightly cloudy.
- Protein 2.5–5 g/dL.
- Specific gravity > 1.018.
- Cells < 5,000/mm³—neutrophils, mesothelial cells, erythrocytes, and lymphocytes.

Exudate (Non-septic)

- Pink or white; cloudy.
- Protein 2.5–5 g/dL.
- Specific gravity > 1.018.
- Cells 5,000–50,000/mm³—neutrophils, mesothelial cells, macrophages, erythrocytes, and lymphocytes.

Exudate (Septic)

- Red, white, or yellow; cloudy.
- Protein > 4.0 g/dL.
- Specific gravity > 1.018.
- Cells 5,000–100,000/mm³—neutrophils, mesothelial cells, macrophages, erythrocytes, lymphocytes, and bacteria.

Hemorrhage

- Red; spun supernatant clear and sediment red.
- Protein > 5.5 g/dL.
- Specific gravity 1.007–1.027.
- Cells consistent with peripheral blood.
- Does not clot.

Chyle

- Pink, straw, or white.
- Protein 2.5–7 g/dL.
- Specific gravity 1.007–> 1.040.
- Cells <10,000/mm³—neutrophils, mesothelial cells, and large population of small lymphocytes.
- Other—fluid in tube separates into cream-like layer when refrigerated; fat droplets stain with Sudan III.

Pseudochyle

- White.
- Protein > 2.5 g/dL.
- Specific gravity 1.007–1.040.
- Cells <10,000/mm³—neutrophils, mesothelial cells, and small lymphocytes.
- Other—fluid in tube does not separate into cream-like layer when refrigerated; does not stain with Sudan III.

Urine

- Clear to pale yellow.
- Protein > 2.5 g/dL.
- Specific gravity 1–> 1.040.
- Cells 5,000–50,000/mm³—neutrophils, erythrocytes, lymphocytes, and macrophages.
- Other—if the urinary bladder ruptured < 12 hours before, urinary glucose and protein could be negative; if bladder ruptured > 12 hours before, urine becomes a dialysis medium with ultrafiltrate of plasma, and urine contains glucose and protein.

Bile

- Slightly cloudy and yellow.
- Protein > 2.5 g/dL.
- Specific gravity > 1.018.
- Cells 5,000–750,000/mm³—neutrophils, erythrocytes, macrophages, and lymphocytes.
- Other—bilirubin confirmed by urine dipstick; non-icteric patient may have gallbladder rupture, biliary tree leakage, or rupture in the proximal bowel.

**TREATMENT**

- Can design treatment on an outpatient basis, with follow-up or inpatient care, depending on physical condition and underlying cause.
- If patients are markedly uncomfortable when lying down or become more dyspneic with stress, consider removing enough ascites to reverse these signs.
- Dietary salt restriction may help control transudate fluid accumulation due to CHF, cirrhosis, or hypoproteinemia.
- For exudate ascites control, address the underlying cause; corrective surgery is often indicated, followed by specific therapeutic

management (e.g., patient with splenic tumor: tumor removed, abdominal bleeding controlled, blood transfusion administered).

LARGE-VOLUME PARACENTESIS

- Stage III treatment.
- Pretreat patient with hetastarch (6%) @ 1–2 mL/kg for 2 hours.
- Abdominal tap (paracentesis), until drainage slows.
- Post-treat patient with hetastarch (6%) @ 1–2 mL/kg for 4 hours.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Patients with liver insufficiency or CHF—restrict sodium and give a diuretic combination of hydrochlorothiazide (2–4 mg/kg q12h PO) and spironolactone (1–2 mg/kg q12h PO); if control is inadequate, furosemide (1–2 mg/kg q8h PO) can be substituted for the thiazide with spironolactone continued; must monitor serum potassium concentration to prevent potassium imbalances.
- Patients with hypoproteinemia, nephrotic syndrome, and associated ascitic fluid accumulation—can treat as above with the addition of hetastarch (6% hetastarch in 0.9% NaCl); administer an IV bolus (dogs, 20 mL/kg; cats, 10–15 mL/kg) slowly over ~ 1 hour; hetastarch increases plasma oncotic pressure and pulls fluid into the intravascular space for up to 24–48 hours.
- Systemic antibiotic therapy is dictated by bacterial identification and sensitivity testing in patients with septic exudate ascites.

**FOLLOW-UP****PATIENT MONITORING**

- Varies with the underlying cause.
- Check sodium, potassium, BUN, creatinine, and weight fluctuations periodically if the patient is maintained on a diuretic.

POSSIBLE COMPLICATIONS

Aggressive diuretic administration may cause hypokalemia, which could predispose to metabolic alkalosis and exacerbation of hepatic encephalopathy in patients with underlying liver disease; alkalosis causes a shift from NH₄ to NH₃.

**MISCELLANEOUS****AGE-RELATED FACTORS**

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

Abdominal effusion

SEE ALSO

- Cirrhosis and Fibrosis of the Liver
- Congestive Heart Failure, Right-Sided
- Hypoalbuminemia
- Nephrotic Syndrome

ABBREVIATIONS

CHF = congestive heart failure

Suggested Reading

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**Client Education Handout
available online**



BASICS

DEFINITION

- Nasal disease caused by *Aspergillus* spp., primarily *A. fumigatus*. • Saprophytic fungus that is ubiquitous in the environment.
- Opportunistic pathogen.

PATOPHYSIOLOGY

- Inhalation of fungus leads to disease in the nasal cavity and frontal sinus with destruction of turbinates, formation of plaque lesions, and overproduction of mucus causing clinical signs of nasal disease.
- Rarely may be associated with underlying foreign body or previous trauma.
- Causes a locally aggressive and invasive disease but does not result in systemic mycosis.
- Confined to nasal cavity and frontal sinus—sinonasal form (most common in dogs).
- Can result in sino-nasal or sino-orbital disease in cats.

SYSTEMS AFFECTED

Respiratory—nasal cavity, sinus, orbit (cats, rare in dogs)

GENETICS

Unknown

INCIDENCE/PREVALENCE

Unknown, but a common diagnosis in dogs with nasal discharge in many locations.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog and cat (less common)

Breed Predilections

- Dogs—dolichocephalic and mesocephalic breeds
- Cats—brachycephalic breeds may be overrepresented

Mean Age and Range

- Dogs—predominantly young to middle-aged
- Cats—no predilection

Predominant Sex

None identified

SIGNS

Historical Findings

- Unilateral or bilateral nasal discharge—typically mucoïd, mucopurulent, or serosanguinous but may be primarily epistaxis.
- Sneezing.
- Typically chronic signs—several months.
- Many patients will have been treated with antibiotics for a possible bacterial infection before presentation with variable response.

Physical Examination Findings

- Unilateral or bilateral nasal discharge.
- Increased nasal airflow on the affected side.
- Depigmentation with ulceration of the nasal planum—~40% of dogs.
- Facial pain.
- Ipsilateral mandibular lymphadenopathy.
- Stertor, exophthalmos, hard palate

ulceration, facial asymmetry, loss of nasal airflow—sino-orbital disease in cats.

CAUSES

- No underlying cause identified, although preexisting foreign body or trauma is occasionally implicated.
- Likely due to inhalation of a large bolus of fungus that is ubiquitous in the environment.
- Species—most commonly *A. fumigatus* in dogs, *A. felis* in cats others—*A. niger*, *A. flavus*.

RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Foreign body
- Oronasal fistula
- Lymphoplasmacytic rhinitis
- Neoplasia
- Nasopharyngeal polyp, nasal tumor, or cryptococcus—cats only

CBC/BIOCHEMISTRY/URINALYSIS

- Often normal
- Possible inflammatory leukogram

OTHER LABORATORY TESTS

Serology

- Detects fungi-specific serum antibodies.
- AGID—commercially available; 98% specificity, 67% sensitivity in dogs; 43% sensitivity in cats. Serial serology does not appear to correlate with clinical status.
- ELISA—88% sensitivity, 97% specificity in dogs, 90% sensitivity in cats.
- Counter-immunoelectrophoresis—85% specificity in dogs.
- Serum galactomannan—unreliable.

Culture

- Tissue fungal culture of affected area; visualized biopsy sample taken from a region of suspected fungal growth showed 100% specificity, 81% sensitivity in dogs.
- Culture of nasal discharge is less specific and insensitive.

IMAGING

Computed Tomography

- Imaging method of choice.
- Cavitated turbinate lysis.
- Thickening of the mucosa along the nasal turbinates.
- Frontal sinus proliferative mass effect.
- Soft tissue mass in the choana or nasopharynx—cats.
- Necessary for evaluation of the cribriform plate before topical antifungal treatment.

Skull Radiography

- Intraoral dorsoventral radiograph of the nasal cavity shows turbinate lysis.
- Rostrocaudal or skyline frontal sinus view may show increased soft tissue density in the frontal sinus.
- Cannot evaluate cribriform plate.

DIAGNOSTIC PROCEDURES

Rhinoscopy

- Flexible rhinoscopy in dogs allows examination of the nasopharynx and possibly

the frontal sinus if the opening of the nasofrontal duct is destroyed by fungal infection.

- Rigid rhinoscopy—examination of the nasal cavity alone; good visualization is possible due to large airspaces caused by turbinate lysis; excessive mucus and bleeding can make full examination difficult.

- Visualization of fungal plaques (white, yellow, black, or light-green) on the mucosa of the nasal cavity and/or frontal sinus confirms fungal infection.
- Sinuscopy—may be required to confirm the diagnosis in dogs that lack nasal plaques.

PATHOLOGIC FINDINGS

- Biopsies obtained of affected area under direct rhinoscopic visualization using cup biopsy instruments.
- Samples immersion-fixed in buffered 10% formalin, routinely processed.
- Evidence supportive of a diagnosis of aspergillosis—identification of septate, branching hyphae and conidia on histopathology. Surrounding inflammation is commonly neutrophilic or lymphoplasmacytic, rarely eosinophilic.
- Blind biopsies in an unaffected area of the nasal cavity can result in a false diagnosis of inflammation.



TREATMENT

APPROPRIATE HEALTH CARE

Overnight hospitalization advised after topical treatment or surgery.

NURSING CARE

Maintain the nares free of nasal discharge.

ACTIVITY

Restriction of activity is not required if no bleeding is documented.

DIET

N/A

CLIENT EDUCATION

- Dogs—inform client that multiple topical treatments are usually necessary to cure the disease; follow-up with rhinoscopy is highly recommended to ensure resolution.
- No established protocols for treatment in cats.

SURGICAL CONSIDERATIONS

Endoscopic Debridement

- Extensive curettage and removal of fungal material from the nose and frontal sinus are essential to allow efficacy of topical medication.

Trehipination of the Frontal Sinus

- Can be required for dogs with frontal sinus involvement.
- Performed using a Jacob's chuck and intramedullary pin.
- Allows direct visualization of the frontal sinus with a rigid rhinoscope and local debridement of fungal plaques.
- Allows for lavage and topical treatment of the area using a red rubber catheter.

ASPERGILLOSIS, NASAL

(CONTINUED)

Surgical Debridement and Exenteration

- Used in some cats with sino-orbital disease.

**MEDICATIONS****DRUG(S) OF CHOICE*****Topical Clotrimazole or Enilconazole Therapy***

- 1-hour infusion into nasal cavity under anesthesia.
- Treatment is usually performed during the same anesthesia as diagnostics.
- Treatment of choice in dogs; reported efficacy 85–89% with multiple treatments.
- Foley catheters are used to occlude the nares and nasopharynx.
- Dose—Clotrimazole: 1 gram in 100 mL of polyethylene glycol 200 (1% solution) evenly divided between two 60 mL syringes slowly infused over 1 hour into each side for large dogs; if trephination is used, divide the amount between the nasal cavity and sinus on the same side; less volume in smaller dogs.
- Enilconazole: 100 mL of 1%, 2%, or 5% solution.
- Dog is placed in dorsal recumbency with head turned to each side every 15 minutes during the infusion.
- Dog is placed in sternal recumbency with head down at the end of the procedure to drain all medication from the nasal cavity.
- Has been used in cats without orbital involvement in combination with oral antifungal therapy with varying success.

Systemic Therapy

- Antifungal triazole drugs should be considered if the cribriform plate is not intact; also used as primary therapy in some cats.
- Can also be used in combination with topical therapy.
- May be cost-prohibitive.
- Itraconazole 5 mg/kg PO q12h in dogs with a reported efficacy of 60–70%; 10 mg/kg PO q24h in cats.
- Voriconazole 5 mg/kg PO q12h; efficacy as sole therapy has not been established, neurotoxicity in cats.
- Posaconazole: dogs, 5–10 mg/kg PO q12–24h, cats, 5 mg/kg PO q24h or divided q12h; efficacy as sole therapy has not been established.
- Fluconazole is not recommended due to resistance.

CONTRAINdications

- Breach in the cribriform plate can allow contact of antifungal medication with brain resulting in neurologic signs and possible death.
- Sino-orbital disease necessitates the use of systemic therapy. Amphotericin B should be considered.

PRECAUTIONS

- Topical clotrimazole and enilconazole are caustic to all mucosal surfaces—protective gear (gloves, goggles) should be worn by all staff that are in close contact.
- Enilconazole can be associated with tissue swelling and upper airway obstruction.

ALTERNATIVE DRUG(S)***Enilconazole***

- Also active in the vapor phase.

Combined Clotrimazole Irrigation and Depot Therapy

- Clotrimazole (1%) is flushed through a trephine hole in the frontal sinus over 5 minutes; 50 mL in each side in dogs > 10 kg; 25 mL in each side in dogs < 10 kg.
- Clotrimazole cream (1%) is then introduced into the front sinuses; 20 g in each side in dogs > 10 kg, 10 g in each side in dogs < 10 kg.
- Reported efficacy similar to topical clotrimazole or enilconazole alone (86%).

**FOLLOW-UP****PATIENT MONITORING*****Dogs***

- Monitor clinical signs, although reduction of clinical signs does not establish resolution of disease.
- Follow-up rhinoscopy is recommended in all cases to establish response to treatment, regardless of clinical signs—histopathology and culture can help establish response.
- Serial serology (AGID) appears not to correlate with clinical status.
- Repeat CT scan should be considered for reassessment of the cribriform plate before repeat topical treatment if a worsening clinical signs are seen.
- Monitor liver enzymes in animals on triazole therapy.
- Monitor renal parameters in animals on Amphotericin B.

Cats

- Monitor clinical signs for improvement or resolution.
- Monitor liver enzymes in animals on triazole therapy.
- Monitor renal parameters in animals on Amphotericin B.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Topical therapy—monitor after treatment for any complications such as swelling of oropharynx, neurologic signs, infection/swelling of trephine site.
- Triazoles can cause anorexia and can be hepatotoxic.
- Amphotericin B can be nephrotoxic.

EXPECTED COURSE AND PROGNOSIS

- Studies have shown an 87% response rate to topical therapy in dogs after one to three treatments.
- A newer study showed that recurrence or reinfection is more common

than previously thought and can occur years after supposedly successful therapy.

- The prognosis for cats with sinonasal aspergillosis is better than with the sino-orbital form.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

ZOONOTIC POTENTIAL

There are no documented cases of human infection from an affected dog or cat.

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

None

ABBREVIATIONS

- AGID = agar gel immunodiffusion
- CT = computed tomography
- ELISA = enzyme-linked immunosorbent assay

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Author Jill S. Pomrantz

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BASICS

OVERVIEW

- Opportunistic fungal infection caused by *Aspergillus* spp., common molds that are ubiquitous in the environment, forming numerous spores in dust, straw, grass clippings, and hay.
- Disseminated disease does not appear to be related to the nasal form of the disease, although one report of a dog developing fungal osteomyelitis 6 months after treatment for nasal aspergillosis raises the possibility.
- Disseminated disease—usually *A. terreus* or *A. deflectus*,
- Portal of entry not definitively established but possibly through the respiratory tract or gastrointestinal tract, with subsequent hematogenous spread.
- Most commonly affects intervertebral discs, bones, thoracic lymph nodes, lung and renal pelvis. May affect respiratory (bronchopulmonary) only, or rarely, cornea or ear canal only.

SIGNALMENT

Dogs

- More common in dogs than in cats.
- German shepherds, and less so Rhodesian ridgebacks, overrepresented but reported sporadically in many breeds; average age 3 years (range 2–8 years); females three times more likely to develop disease as males.

Cats

- Persians—marginally increased incidence.
- Disseminated cases mostly affect the lungs and/or gastrointestinal tract.

SIGNS

Dogs

- May develop acutely or slowly over a period of several months, usually terminally ill when first presenting.
- Lameness—fungal osteomyelitis causing pronounced swelling and discharging, fistulous tracts.
- Neurologic—fungal discospondylitis causing paraparesis, paraplegia, spinal pain. Central signs—vestibular signs, seizures, hemiparesis, mental dullness, ataxia, vision impairment, circling.
- Renal involvement—polyuria/polydipsia, hematuria.
- Respiratory—cough, hemoptysis, increased respiratory effort.
- Reproduction—pyometra.
- Cardiac—pericarditis, ascites due to right sided failure, arrhythmias.
- Gastrointestinal—abdominal distension, anorexia.
- Ocular—uveitis, chorioretinitis, hyphema, panophthalmitis.
- Nonspecific—fever, weight loss, weakness, vomiting, and lymphadenopathy.

Cats

- Usually nonspecific signs (e.g., lethargy, depression, vomiting, and diarrhea).
- Ocular—exophthalmos.

CAUSES & RISK FACTORS

- Caused by *Aspergillus* species, most commonly *A. terreus* or *A. deflectus*, *A. fumigatus*, *A. niger*, *A. flavipes*, and *A. alabamensis* also associated. *A. felis* recently reported to cause fungal rhinosinusitis in cats, disseminated disease in dogs, and pulmonary aspergillosis in humans.
- German shepherds and immunosuppressed animals at higher risk.
- Geographic/environmental conditions—may be a factor, as some regions have a higher incidence (e.g., California, Louisiana, Michigan, Georgia, Florida, and Virginia in the United States; Western Australia; Barcelona; and Milan).
- Cats—associated with FIP, FePLV, FeLV, FIV, diabetes mellitus, and immunosuppressant use.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Bacterial osteomyelitis/discospondylitis; spinal neoplasia; intervertebral disc disease; skeletal neoplasia; bacterial pyelonephritis; bacterial pneumonia; other causes of vestibular signs/seizures; other causes of uveitis (see Anterior Uveitis—Cats, Anterior Uveitis—Dogs).

CBC/BIOCHEMISTRY/URINALYSIS

- Nonspecific.
- Dogs—mature neutrophilic leukocytosis with eosinophilia and monocytosis. One third have normocytic, normochromic nonregenerative anemia. Cats—may have nonregenerative anemia and leukopenia.
- Biochemistry—may see high globulins, ALP, ALT, amylase, creatinine, phosphate, BUN, and calcium.
- Urinalysis—may see isosthenuria, hematuria, pyuria, and possible fungal hyphae in the sediment; detection of the fungal hyphae can be improved by allowing the sample to incubate at room temperature for 24–48 hours; sediment samples may be examined unstained as wet preparations or may be air dried and stained with Diff-Quick (the hyphae branch at 45° and stain purple).

OTHER LABORATORY TESTS

- Methods of detection include: cytology, culture and histopathology.
- Definitive diagnosis by fungal culture from normally sterile body fluids and tissues, e.g., urine, bone, CSF, blood, lymph node, pleural effusions, intervertebral disc aspirates, kidney, spleen. Urine culture positive in approximately 50% of dogs.

- Culture on Sabouraud's dextrose agar (requires 5–7 days).

• Antibody serology (agar gel immunodiffusion, and ELISA) support the diagnosis but is insensitive for diagnosis of disseminated aspergillosis.

- Galactomannan antigen ELISA (urine or serum) good sensitivity (89%) and specificity (89%) in one small study. Pulmonary and ocular infections have lower sensitivity. False positive in dogs treated with Plasmalyte or with other mycotic infections (*Penicillium*, *Paecilomyces*, *Cladosporidium*, *Geotrichum*, *Histoplasma*, *Cryptococcus*).
- Cats—test for FeLV and FIV.

IMAGING

Radiographic Findings

- Spinal views may show end-plate lysis, attempted bony intervertebral bridging, and lysis of vertebral bodies consistent with discospondylitis; productive and destructive lesions of the vertebral bodies.
- Bony proliferation, lysis and periosteal reaction typical of osteomyelitis of the diaphyseal region of long bones.
- Pulmonary involvement rare, mixed interstitial/alveolar pattern, enlarged sternal and/or tracheobronchial lymph nodes, pleural effusion; productive and destructive lesions of sternabrae. Pulmonary cavitary lesions in dogs with chronic pulmonary localization.

Ultrasonographic Findings

- Kidneys—most common site to detect changes; changes seen include renal pelvis dilation ± echogenic debris within pelvis; loss of corticomedullary distinction; renal distortion and mottled appearance of the parenchyma; dilation of proximal ureter; renalomegaly; nodules or masses; hydronephrosis.
- Spleen—hypoechoic, lacy, sharply demarcated areas with no doppler signal suggestive of infarct are most significant finding in spleen; other findings include nodules/masses, mottled parenchyma, splenic venous thrombosis.
- Other—abdominal lymphadenomegaly; diffuse hepatic hypoechogenicity, ascites, or evidence of venous thrombosis.

MRI Findings

Useful for further defining brain lesions in animals with CNS signs; changes similar to other infectious and non-infectious inflammatory brain diseases. May help to identify subtle vertebral lesions in dogs with discospondylitis.

DIAGNOSTIC PROCEDURES

Area to collect sample relies on clinical presentation but may include CSF tap, joint aspirates, intervertebral disc space aspirates, abdominocentesis/thoracocentesis, aspirate of various organs (spleen, liver, kidney) or lymph nodes.

PATHOLOGIC FINDINGS

- Hyphae usually visualized; special stains assist organism detection.
- Focal osteomyelitis with multiple pale granulomas in kidneys, spleen, lymph node, myocardium, pancreas, and liver.
- Microscopic granulomas can be found in lungs, eyes, thyroid, uterus, brain, and prostate and contain numbers of septate, branching hyphae that may have characteristic lateral branching aleuriospores.
- Occasionally pulmonary congestion or GI mucosal reddening and erosions.
- Best visualized with periodic acid-Schiff, Gomori's methenamine silver, or Crocott's stain.

**TREATMENT****DOGS**

- Treatment rarely curative; severely ill dogs are recognized to have poor prognosis. May halt progression of clinical signs.
- Fluid therapy—indicated by the degree of renal compromise and azotemia.
- Pulmonary lobectomy followed by systemic antifungals has been successful in dogs with cavitary lesions without evidence of dissemination.

CATS

Disseminated—likely difficult to treat; limited data.

**MEDICATIONS****DRUG(S)**

- Combination itraconazole 5–10 mg/kg PO q24h (can be divided) and amphotericin B (dogs, 2–3 mg/kg IV 3 days per week for a total of 9–12 treatments, to cumulative dose of 24–27 mg/kg)—treatment of choice.
- Itraconazole as monotherapy has achieved long-term remission in a small number of dogs.

- New triazoles: voriconazole, posaconazole and ravuconazole all have activity against *Aspergillus*. Some dogs treated with voriconazole or posaconazole have gone into remission for many months. *Aspergillus* spp. resistant to fluconazole.
- Terbinfine (5–10 mg/kg PO q24h) used alone or in combination with triazoles has been used to treat resistant infections in humans.
- β -glucan synthase inhibitors caspofungin, micafungin, anidulafungin—limited clinical information in dogs but efficacious in invasive aspergillosis in humans.
- Combination therapy with flucytosine (dogs, 25–50 mg/kg PO q6h) and amphotericin B may prove successful, but no published reports.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Amphotericin B—contraindicated in dogs with pre-existing renal compromise or failure; amphotericin B lipid complex significantly reduced nephrotoxicity.
- Oral azoles—nausea, intermittent anorexia, liver enzyme elevation.
- Combination of flucytosine and amphotericin B—cutaneous drug eruptions in dogs.
- Avoid midazolam and cisapride with azoles—fatal drug reactions noted in humans.
- Hepatotoxicity and ulcerative dermatitis more likely to occur at doses of 10 mg/kg/day or higher. Discontinue itraconazole if adverse effects occur. May be able to reinstitute at lower dose once side effects have resolved.

**FOLLOW-UP**

Disseminated—monitor serial radiographs every 1–2 months, renal function, and urine cultures; prognosis poor, especially in German shepherds.

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

None

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine transaminase
- BUN = blood urea nitrogen
- CSF = cerebrospinal fluid
- ELISA = enzyme-linked immunosorbent assay
- FeLV = feline leukemia virus
- FePLV = feline panleukopenia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- MRI = magnetic resonance imaging

Suggested Reading

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Client Education Handout available online



BASICS

OVERVIEW

- Given for its antipyretic, analgesic, anti-inflammatory, and antiplatelet effects.
- Aspirin inhibits cyclooxygenase, reducing the synthesis of prostaglandins and thromboxanes.
- Gastric irritation and hemorrhage can occur; dogs are especially sensitive.
- Repeated doses can produce gastrointestinal ulceration and perforation.
- Toxic hepatitis, metabolic acidosis, and anemia can occur, especially in cats.

SIGNALMENT

Cats and less commonly dogs

SIGNS

- Depression
- Anorexia
- Vomiting—vomit may be blood-tinged
- Tachypnea
- Hyperthermia
- Muscular weakness and ataxia
- Ataxia, coma, seizures, and death in 1 or more days

CAUSES & RISK FACTORS

- Owners employing human dosage guidelines to medicate cats and dogs.
- Cats have a decreased ability to conjugate salicylate with glycine and glucuronic acid due to a deficiency in glucuronidyl transferase.
- Half-life increases with dosage—cats, 22–27 hours for 5–12 mg/kg and approximately 44 hours for 25 mg/kg; dogs, 7.5 hours; responsible for higher risk in cats. Elimination is slower in neonatal and geriatric patients.
- Patients with hypoalbuminemia may be at higher risk of toxicity because aspirin is highly protein bound to plasma albumin.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Ethylene glycol or alcohol
- Anticoagulant rodenticides

- Other causes of liver failure, including acetaminophen, iron, metaldehyde, and blue-green algae

CBC/BIOCHEMISTRY/URINALYSIS

- Cats—prone to Heinz body formation
- Hyponatremia and hypokalemia
- Anemia, hypoproteinemia, elevated liver enzymes, elevated white blood cell count

OTHER LABORATORY TESTS

- Initial respiratory alkalosis followed by metabolic acidosis
- High ketones and pyruvic, lactic, and amino acid levels
- Decreased sulfuric and phosphoric acid renal clearance

DIAGNOSTIC PROCEDURES

Salicylic acid concentrations in serum or urine



TREATMENT

- Inpatient—following general principles of poisoning management
- Induced gastric emptying—gastric lavage or induced emesis
- Correction of acid-base balance—continuous intravenous fluids; assisted ventilation and supplemental oxygen for severely-affected animals
- Whole blood transfusions for severe cases of hemorrhage and hypotension
- Peritoneal dialysis, hemodialysis, or charcoal hemoperfusion—advanced procedures



MEDICATIONS

DRUG(S)

- No specific antidote available.
- Activated charcoal—1–2 g/kg PO.
- Sodium bicarbonate 1 mEq/kg IV alkalinizes urine; must closely monitor acid-base status.
- Gastrointestinal protectants—sucralfate and a H₂ blocker or proton pump inhibitor; misoprostol for patients at higher risk for gastrointestinal hemorrhage.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- Maintaining renal function and acid-base balance is vital.
- Severe acid-base disturbances, severe dehydration, toxic hepatitis, bone marrow depression, and coma are poor prognostic indicators.



MISCELLANEOUS

- Be sure that history of “aspirin” medication does not refer to other available pain medications.
- Question owner about any pre-existing painful condition that may have prompted the aspirin administration.

Suggested Reading

Plumb DC. Aspirin. In: Plumb DC, ed., Plumb's Veterinary Drug Handbook, 7th ed. Ames, IA: Wiley-Blackwell, 2011, pp. 83–87.

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ASTHMA, BRONCHITIS—CATS



BASICS

DEFINITION

- Chronic bronchitis—inflammation in the airways (bronchi and bronchioles) lacking a specific etiology; chronic daily cough of greater than 2 months in duration.
- Asthma—acute or chronic airway inflammation associated with increased airway responsiveness to various stimuli, airway narrowing due to smooth muscle hypertrophy or constriction, reversibility of airway constriction, and presence of eosinophils, lymphocytes, and mast cells within the airways. • Bronchitis is thought to result in airflow obstruction due to airway remodeling while asthma is associated with airway constriction; however, clinically the two disease processes can appear similar. No physical examination findings or biomarkers can distinguish between the two syndromes, although reversal of airflow obstruction following administration of a beta-agonist is suggestive of the asthmatic form of disease.

PATOPHYSIOLOGY

- Lower airway inflammation likely results from inhalation of irritant substances.
- Bronchiolar smooth muscle constriction—reversible spontaneously or with treatment.
- Increase in mucosal goblet cells, mucus production, and edema of bronchial wall associated with inflammation. • Excessive mucus can cause bronchiolar obstruction, atelectasis, or bronchiectasis. • Smooth muscle hypertrophy implies chronicity—usually not reversible. • Chronic inflammation leads to airway remodeling and irreversible airflow obstruction.

SYSTEMS AFFECTED

- Respiratory • Cardiac—pulmonary hypertension rarely

GEOGRAPHIC DISTRIBUTION

Worldwide.

SIGNALMENT

Species

Cat

Breed Predilections

Siamese overrepresented

Mean Age and Range

Any age; more common between 2 and 8 years

Predominant Sex

One study showed females overrepresented

SIGNS

Historical Findings

- Coughing, tachypnea, labored breathing or wheezing. • Signs are typically episodic and can be acute or chronic.

Physical Examination Findings

- Severely affected cats present with open-mouth breathing, tachypnea, and cyanosis. • Increased tracheal sensitivity is common. • Chest auscultation may reveal crackles and/or expiratory wheezes, but can be normal. • Labored breathing with an abdominal push on expiration, increase in expiratory effort.

CAUSES

Triggers of airway inflammation unknown

RISK FACTORS

- Cigarette smoke, poor environmental hygiene, dusty cat litter, hair sprays, and air fresheners can exacerbate disease. • Use of potassium bromide—implicated in causing signs of bronchitis/asthma in some cats.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Rule out infectious pneumonia (*Mycoplasma*, *Toxoplasma*, bacterial or fungal pneumonia). • Consider *Dirofilaria immitis* and primary lung parasites (*Aelurostrongylus abstrusus*, *Capillaria aerophilus*, *Paragonimus kellicotti*). More common in southern and midwest US, and in outdoor and hunting cats in some geographic regions. • Primary or metastatic neoplasia can have similar clinical and radiographic appearance. • Clinical presentation of idiopathic pulmonary fibrosis may appear similar to feline bronchitis.

CBC/BIOCHEMISTRY/URINALYSIS

Frequently normal, ~40% of cats with bronchial disease have peripheral eosinophilia.

OTHER LABORATORY TESTS

- Fecal exams—flotation for *Capillaria*, sedimentation for *Paragonimus*, Baermann for *Aelurostrongylus*. False-negative tests common.
- Heartworm antigen and antibody testing, particularly if coughing occurs in conjunction with vomiting. • Radioallergosorbent testing or intradermal skin testing—no correlation between skin allergies and respiratory disease currently documented.

IMAGING

Radiography

- Classically, diffuse bronchial wall thickening; interstitial or patchy alveolar patterns also possible. • Severity of radiographic changes does not necessarily correlate with clinical severity or duration, and normal radiographs can be found.
- Hyperinflation of lung fields—flattened and caudally displaced diaphragm, increased distance between the heart and diaphragm, extension of lungs to the first lumbar vertebrae thought to reflect bronchoconstriction. • Collapse of right middle lung lobe due to mucus plugging and atelectasis reported in 11% of cases.

- Pulmonary lobar arterial enlargement is suspicious for heartworm disease.

Echocardiography

Useful to document heartworm disease or secondary pulmonary hypertension.

DIAGNOSTIC PROCEDURES

Transoral Tracheal Wash

Use a sterile endotracheal tube and polypropylene catheter to collect airway fluids at the level of the carina.

Bronchoscopy

• Allows visualization of trachea and bronchi. Excessive amounts of thick mucus are common with bronchitis. Mucosa of the airways is typically hyperemic and edematous.

Cytology of TOTW or BAL

- Eosinophils and neutrophils are most prominent cell types. • Up to 20% eosinophils on BAL cytology can be found in normal cats. • A mixed inflammatory cell population occurs in about 21% of cats.

Bacterial Cultures

- Quantitated cultures recommended; positive cultures frequently encountered but bacterial colony counts > 100–300 cfu/mL uncommon with bronchitis. • Specific *Mycoplasma* culture often needed.

Biopsy

Keyhole biopsy—can differentiate between idiopathic pulmonary fibrosis, neoplasia and bronchitis if needed.

PATHOLOGIC FINDINGS

Hyperplasia/hypertrophy of goblet cells, hypertrophy of airway smooth muscle, epithelial erosion, and infiltrates.



TREATMENT

APPROPRIATE HEALTH CARE

- Remove patient from environment that exacerbates disease. • Hospitalize for acute respiratory distress.

NURSING CARE

Oxygen therapy, bronchodilators, and sedatives in an acute crisis. Minimize manipulation in order to lessen stress and oxygen needs of the animal.

ACTIVITY

Usually self-limited by patient.

DIET

Calorie restriction for obese cats.

CLIENT EDUCATION

- Most causes are chronic and progressive.
- Do not discontinue medical therapy when clinical signs have resolved—subclinical inflammation is common and can lead to progression of disease. Lifelong medication and environmental changes usually necessary.
- Some clients can be taught to give

(CONTINUED)

ASTHMA, BRONCHITIS—CATS

A

terbutaline subcutaneously and corticosteroid injections at home for a crisis situation.

**MEDICATIONS****DRUG(S) OF CHOICE*****Emergency Treatment***

- Oxygen and a parenteral bronchodilator. Injectable terbutaline (0.01 mg/kg IV or SC); repeat if no clinical improvement (decrease in respiratory rate or effort) in 20–30 minutes.
- A sedative can aid in decreasing anxiety (butorphanol tartrate at 0.2–0.4 mg/kg IV or IM, buprenorphine at 0.01 mg/kg IV or IM, or acepromazine at 0.01–0.05 mg/kg SC).
- A short-acting parenteral corticosteroid may also be required. Dexamethasone sodium phosphate (0.1–0.25 mg/kg, IV or SC). Can repeat if no improvement noted within 20–30 minutes.

Long-Term Management**Corticosteroids**

- Decrease inflammation.
- Oral treatment is preferred over injectable for closer monitoring of dose and duration.
- Prednisolone: 0.5–1 mg/kg PO q12h. Begin to taper dose (50% each week) after 1–2 weeks if clinical signs have improved. Maintenance therapy = 0.5–1 mg/kg PO q24–48h.
- Longer-acting parenteral steroids (Vetalog or Depomedrol) should be reserved only for situations where owners are unable to administer oral or inhaled medication on a routine basis.

Inhaled Corticosteroids

- Requires a form-fitting facemask, spacer, and metered-dose inhaler (MDI). Veterinary brand: Aerokat (Trudell Medical).
- The most common corticosteroid used as an MDI is fluticasone propionate (Flovent). 110- μ g Flovent MDI is recommended (1–2 actuations, 7–10 breaths q12h). In one study, use of 44- μ g Flovent decreased BAL eosinophil counts in cats with experimentally induced lower airway disease.
- Flovent is used for long-term control of airway inflammation. Takes 10–14 days to reach peak effect; use oral steroids concurrently during this time.
- Results in some suppression of the hypothalamic-pituitary axis but systemic side effects appear to be limited.

Bronchodilators

- Methylxanthines: sustained-release theophylline formulations recommended, and pharmacokinetics can vary greatly. Only generic currently available. Dose at 15–20 mg/kg PO once daily in the evening.
- Beta-2 agonists (terbutaline, albuterol)—reverse smooth muscle constriction. Oral terbutaline dose is 1/4 of a 2.5 mg tablet

q12h. Initial albuterol dose is 20 μ g/kg PO q12h; can increase to 50 μ g/kg PO q8h.

Inhaled Bronchodilators

- Albuterol—preferred inhalant bronchodilator, effect lasts less than 4 hours. Long-term use of traditional racemic form of inhaled albuterol (R and S-enantiomers) has been associated with worsened airway inflammation. Enantiomer specific R-albuterol should be used if the drug is needed in moderately to severely affected cats (q12–24h) or during respiratory distress.

Anthelmintics

- Empirical therapy is indicated for cats with clinical signs of bronchial disease and eosinophilic airway cytology in an appropriate geographic location.
- Consider fenbendazole, ivermectin, or praziquantel.

Antibiotics

Use based on a positive quantitative culture and susceptibility testing or *Mycoplasma* isolation.

CONTRAINDICATIONS

Beta-2 antagonists (e.g., propranolol) are contraindicated because of their ability to block sympathetically mediated bronchodilation.

PRECAUTIONS

- Long-term use of steroids increases risk of development of diabetes mellitus and predisposes to immunosuppression. • Use of corticosteroids in cats may precipitate congestive heart failure. • Beta agonists could cause tachycardia and exacerbate underlying cardiac disease.

ALTERNATIVE DRUG(S)

Leukotriene receptor blockers and inhibitors of generation: no evidence to support use. Anti-serotonin and antihistamine drugs: no evidence to support use. Immunotherapy: no clinical evidence to support use at this time.

**FOLLOW-UP****PATIENT MONITORING**

- Owners should report any increase in coughing, sneezing, wheezing, or respiratory distress. Medications should be increased appropriately or additional therapy initiated if clinical signs worsen. • Follow-up radiographs may be helpful to detect onset of new disease.
- Owner should watch for signs of PU/PD that could indicate diabetes mellitus or renal disease. Monitor blood glucose and urine cultures.

PREVENTION/AVOIDANCE

Eliminate any environmental factors that can trigger a crisis situation (see "Risk Factors").

Change furnace and air-conditioner filters on a regular basis. Consider dust-free litters.

POSSIBLE COMPLICATIONS

- Acute episodes can be life-threatening.
- Right-sided heart disease rarely develops as a result of long-term bronchitis.

EXPECTED COURSE AND PROGNOSIS

- Long-term therapy should be expected.
- Most cats do well if recurrence of clinical signs is carefully monitored and medical therapy appropriately adjusted. • A few cats will be refractory to treatment; these carry a much worse prognosis.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Cat pulmonale can be a sequela to chronic lower airway disease.

PREGNANCY/FERTILITY/BREEDING

Glucocorticoids are contraindicated in the pregnant animal. Bronchodilators should be used with caution.

SYNONYMS

Allergic bronchitis, asthmatic bronchitis, feline lower airway disease, extrinsic asthma, eosinophilic bronchitis.

SEE ALSO

- Heartworm Disease—Cats • Respiratory Parasites

ABBREVIATIONS

- BAL = bronchoscopy/bronchoalveolar lavage • MDI = metered-dose inhaler
- PU/PD = polyuria/polydipsia

INTERNET RESOURCES

- www.Aerokat.com: for ordering facemasks and spacers for inhalant therapy.
- www.fritzthebrave.com: source for clients to research use of inhaled medications.

Suggested Reading

- Cohn LA, DeClue AE, Cohen RL, Reiner CR. Effects of fluticasone propionate dosage in an experimental model of feline asthma. J Feline Med Surg 2010, 12(2):91–96.
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Authors Carrie J. Miller and Lynelle R. Johnson
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Client Education Handout
available online

ASTROCYTOMA



BASICS

OVERVIEW

- Glial cell neoplasm, most commonly affecting the brain and rarely the spinal cord.
- Neoplastic cells are of astrocytic origin. • It is the most common intra-axial (situated inside of the brain parenchyma) intracranial neoplasm of dogs but is rarely diagnosed in cats. • Tumors are often located in the pyriform area of the temporal lobe, the cerebral hemispheres, the thalamus, hypothalamus, or midbrain. • Biologic behavior of this tumor is dictated by the histopathologic grade (I–IV, from best to worst prognosis) and anatomic involvement.
- Tumors typically do not penetrate the ventricular system or metastasize outside of the cranial vault.

SIGNALMENT

- Dog—often brachycephalic breeds > 5 years of age; no sex predilection reported.
- Cat—usually > 9 years; no sex or breed predilection reported.

SIGNS

- Location and growth kinetic dependent
- Seizures • Behavioural changes • Apathy towards normal activities including eating, playing, and societal interactions
- Disorientation • Loss of conscious proprioception • Cranial nerve abnormalities
- Head muscle atrophy • Upper motor neuron tetraparesis



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other primary tumors arising from tissues of the central nervous system • Metastatic neoplasia with brain tropism such as hemangiosarcoma • Granulomatous meningoencephalitis • Trauma
- Cerebrovascular infarction • Meningitis

CBC/BIOCHEMISTRY/URINALYSIS

Usually unremarkable

OTHER LABORATORY TESTS

CSF analysis may show albumin-cytologic dissociation (high protein with low number of nucleated cells). The CSF analysis is indicated to exclude infectious etiology, not to diagnose astrocytoma.

IMAGING

- MRI of brain is ideal for mass lesion confirmation, as it is superior to CT scanning for detecting lesions in the middle and caudal fossae. Additionally, MRI is more sensitive than CT for detection infarcts, bleeding, and edema. • Brain MRI may be useful in establishing a tentative differential diagnosis of a glial tumor, based on tumor

characteristics highlighted in specific sequences.

DIAGNOSTIC PROCEDURES

- Neurologic exam. • Ophthalmic exam.
- MRI. • CSF analysis. • Tumor biopsy for definitive diagnosis, when specific antineoplastic treatment is sought (surgery, curative-intent radiation therapy, experimental therapies).



TREATMENT

- Surgery. • Radiation therapy can be very effective in improving neurologic signs.
- Chemotherapy with lomustine, procarbazine, or temozolamide might exert cytoreductive activities. • Anti-inflammatory dosing with corticosteroids to reduce peritumoral edema. • Consultation with a neurosurgeon and a radiation oncologist is essential for the appropriate patient management.



MEDICATIONS

DRUG(S)

Seizure Control

- Status epilepticus—diazepam (0.5–1 mg/kg IV, up to three times to achieve effect); if no response to diazepam, use pentobarbital (5–15 mg/kg IV slowly to effect).
- Long-term management—phenobarbital (1–4 mg/kg PO q12h) with or without adjuvant potassium bromide (20 mg/kg PO q24h).

Tumor Control

- Timely consultation with a neurosurgeon is of paramount importance for the appropriate management of the patient. • Radiation therapy may be effective, and consultation with a radiation oncologist is recommended. Stereotactic radiosurgery or intensity modulated radiation therapy may be considered as first-line treatment options.
- Chemotherapy may be effective for treating dogs. Potential drugs that may exert measurable anticancer effects include CCNU (60–70 mg/m² PO every 3 weeks) or temozolamide (100–120 mg/m² PO q24h for 5 days every 3 weeks). • Prednisone (1 mg/kg q24h), may be effective in reducing peritumoral edema and improving the neurologic signs. Patients may need to be on steroids long term, even after the definitive treatment of the tumor.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Prednisone and phenobarbital may cause polyphagia, polydipsia, and polyuria.
- Phenobarbital may cause sedation for up to 2 weeks after initiation of treatment, and

increase in hepatic enzymes on serum biochemical panel. • CBC and platelet count is recommended 7–10 days after chemotherapy and immediately before each dose of chemotherapy to monitor myelosuppression. • Chemotherapy has the potential to be synergistic with radiation therapy. Timely specialty to a referral center with neurosurgery, radiation therapy, and medical oncology capabilities is important for patients seeking more than palliative care.



FOLLOW-UP

PATIENT MONITORING

- Blood phenobarbital concentration should be assessed after 7–10 days of treatment, with modifications to dosages for achieving target plasma concentrations. • Serial MRIs should be considered for documenting response if multimodality therapy is used. • Serial CBC and platelet counts should be performed to monitor myelotoxicity associated with chemotherapy.

EXPECTED COURSE AND PROGNOSIS

- Long-term prognosis—guarded. • Median survival after chemotherapy plus medical management may be up to 7 months.
- Median survival after radiation therapy has been reported to be as high as 12 months.



MISCELLANEOUS

SEE ALSO

- Seizures (Convulsions, Status Epilepticus)—Cats • Seizures (Convulsions, Status Epilepticus)—Dogs

ABBREVIATIONS

- CSF = cerebrospinal fluid • CT = computed tomography • MRI = magnetic resonance imaging

Suggested Reading

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Stoica G, Levine J, Wolff J, Murphy K. Canine astrocytic tumors: a comparative review. Vet Pathol 2011, 48(1):266–275.

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BASICS

OVERVIEW

An uncommon intestinal viral infection characterized by enteritis and diarrhea.

SIGNALMENT

- Cats
- No known breed, sex, or age predilection

SIGNS

- Small bowel diarrhea often green and watery.
- Kittens show more severe signs.
- May be severe and acute enough to cause dehydration and anorexia.

CAUSES & RISK FACTORS

- A small, non-enveloped, RNA virus of the genus *Astrovirus*.
- Details of the incidence, prevalence, and predisposing factors unknown.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Many causes of gastroenteritis
- Food allergy
- Toxin ingestion
- Inflammatory bowel disease
- Neoplasia
- Intestinal parasites
- Viral infections—panleukopenia, rotavirus, enteric coronavirus, enteric calicivirus
- Bacterial infections—salmonellosis, coliforms
- Protozoal infections—*Giardia*, cryptosporidiosis

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

- Electron microscopy of feces—identify astrovirus particles.
- Difficult to isolate in the laboratory.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

None

PATHOLOGIC FINDINGS

None described; similar to mild enteritis, rotavirus, or coronavirus enteritis.



TREATMENT

- Control diarrhea.
- Reestablish fluid and electrolyte balance.



MEDICATIONS

DRUG(S)

No specific antiviral drugs.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

None



FOLLOW-UP

PATIENT MONITORING

Monitor fluid and electrolytes.

PREVENTION/AVOIDANCE

Isolate infected cats during acute disease.

POSSIBLE COMPLICATIONS

Secondary intestinal viral and bacterial infections.

EXPECTED COURSE AND PROGNOSIS

- Illness usually < 1 week.
- Mortality—appears low.
- Prognosis—good.
- If diarrhea persists, investigate other causes.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Sequence analysis of human and animal astroviruses suggests human-to-animal transmission does not occur.

Suggested Reading

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Lukashov VV, Goudsmit J. Evolutionary relationships among Astroviridae. J Gen Virol 2002, 83:1397–1405.

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ATAXIA



BASICS

DEFINITION

- A sign of sensory dysfunction that produces incoordination of the limbs, head, and/or trunk.
- Three clinical types—sensory (proprioceptive), vestibular, and cerebellar; all produce changes in limb coordination, but vestibular and cerebellar ataxia also produce changes in head and neck movement.

PATHOPHYSIOLOGY

Sensory (Proprioceptive)

- Proprioceptive pathways in the spinal cord (i.e., fasciculus gracilis, fasciculus cuneatus, and spinocerebellar tracts) relay limb and trunk position to the brain.
- When the spinal cord is slowly compressed, proprioceptive deficits are usually the first signs observed, because these pathways are located more superficially in the white matter and their larger sized axons are more susceptible to compression than are other tracts.
- Generally accompanied by weakness owing to early concomitant upper motor neuron involvement; weakness not always obvious early in the course of the disease.
- Ataxia can occur with spinal cord, brainstem, and cerebral lesions; mild to absent with unilateral brainstem lesions, and subtle to absent with unilateral cerebral lesion.

Vestibular

- Changes in head and neck position are relayed through the vestibulo-cochlear nerve to the brainstem.
- Vestibular receptors or the nerve in the inner ear are considered part of the peripheral nervous system, whereas nuclei in the brainstem are part of the central nervous system.
- Localize the vestibular signs to peripheral or central vestibular nervous system because prognosis and rule-outs differ for these two locations.
- Both locations of vestibular disease cause various degrees of disequilibrium with ensuing vestibular ataxia.
- Affected animal leans, tips, falls, or even rolls toward the side of the lesion; accompanied by head tilt.
- Central vestibular signs usually have changing types of nystagmus or vertical nystagmus; somnolence, stupor, or coma (due to involvement of the nearby ascending reticular activating system); multiple cranial nerve signs; proprioceptive deficits and quadriplegia or hemiparesis.
- Peripheral vestibular signs do not include changes in mental status, vertical nystagmus, proprioceptive deficits, quadriplegia or hemiparesis.

- Bilateral vestibular involvement, peripheral or central in origin, has characteristic exaggerated head motion with often poor to absent physiologic nystagmus.

Cerebellar

- The cerebellum regulates, coordinates, and modulates motor activity.
- Proprioception is normal because the ascending proprioceptive pathways to the cortex are intact; weakness does not occur because the upper motor neurons are intact.
- Inadequacy in the performance of motor activity; strength preservation; no proprioceptive deficits.
- Affected animal shows uncoordinated motor activity of limbs, head, and neck; hypermetria; dysmetria; head tremors; intention tremors; and truncal sway. Menace responses may be absent without visual dysfunction.

SYSTEMS AFFECTED

Nervous—spinal cord (and brainstem and cortex), cerebellum, vestibular system.

SIGNALMENT

Any age, breed, or sex

SIGNS

- Important to define the type of ataxia to localize the problem.
- Only one limb involved—consider a lameness problem.
- Only hind limbs affected—likely a spinal cord disorder affecting the spinocerebellar tracts.
- All or both ipsilateral limbs affected—cervical spinal cord, or cerebellar localization.
- Head tilt and/or nystagmus—vestibular localization.

CAUSES

Neurologic

Cerebellar

- Degenerative—abiotrophy (Kerry blue terrier, Gordon setter, rough-coated collie, Australian kelpie, Airedale, Bernese mountain dog, Finnish harrier, Brittany spaniel, border collie, beagle, Samoyed, wirehaired fox terrier, Labrador retriever, Great Dane, chow chow, Rhodesian ridgeback, domestic shorthair cats); storage diseases often have cerebellomedullary involvement.
- Anomalous—hypoplasia secondary to perinatal infection with panleukopenia virus (cats); malformed cerebellum due to herpesvirus infection (newborn puppies); arachnoid or epidermoid cyst located near fourth ventricle.
- Neoplastic—any CNS tumor (primary or secondary) localized to the cerebellum.
- Infectious—canine distemper virus; FIP; and any other CNS infection affecting the cerebellum.
- Inflammatory, idiopathic, immune-mediated—granulomatous meningoencephalomyelitis.
- Toxic—metronidazole.

Vestibular—Central Nervous System

- Infectious—FIP; canine distemper virus; rickettsial diseases.
- Inflammatory, idiopathic, immune-mediated—granulomatous meningoencephalomyelitis, meningoencephalomyelitis of unknown origin.
- Nutritional—thiamine deficiency.
- Toxic—metronidazole.

Vestibular—Peripheral Nervous System

- Infectious—otitis media interna; *Cryptococcus* granuloma (cats).
- Inflammatory—nasopharyngeal (middle ear) polyps (cats).
- Idiopathic—geriatric vestibular disease (dogs); idiopathic vestibular syndrome (cats).
- Metabolic—hypothyroidism.
- Neoplastic—squamous cell carcinoma, bone tumors.
- Traumatic.

Spinal Cord

- Degenerative—degenerative myelopathy (old German shepherd, Welsh corgi).
- Vascular—fibrocartilaginous embolic myelopathy.
- Anomalous—hemivertebrae; dens hypoplasia with atlantoaxial subluxation-luxation; Chiari-like malformation; cervical spondylomyelopathy; spinal sub-arachnoid diverticulum; other spinal cord and vertebral malformation.
- Neoplastic—primary bone tumors; multiple myeloma and metastatic tumors that infiltrate the vertebral body; meningioma; others.
- Infectious—discospondylitis; myelitis.
- Traumatic—intervertebral disc herniation; fracture or luxation; atlantoaxial subluxation-luxation.

Metabolic

- Anemia
- Polycythemia
- Electrolyte disturbances—especially hypokalemia, hypocalcemia, and hypoglycemia

Miscellaneous

- Drugs—acepromazine; antihistamines; antiepileptic drugs
- Respiratory compromise
- Cardiac compromise—reverse PDA, aortic thromboembolism

RISK FACTORS

- Intervertebral disc disease—dachshund, poodle, cocker spaniel, and beagle.
- Cervical spondylomyelopathy—Doberman pinscher and Great Dane.
- Fibrocartilaginous embolism—young, large-breed dogs and miniature schnauzers.
- Dens hypoplasia and atlantoaxial luxation—small-breed dogs, poodles.
- Chiari-like malformation—Cavalier King Charles spaniel, small-breed dogs.

(CONTINUED)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Differentiate the types of ataxia.
- Differentiate from other disease processes that can affect gait—musculoskeletal, metabolic, cardiovascular, respiratory.
- Musculoskeletal disorders—typically produce lameness, pain, and a reluctance to move; degenerative joint disease signs often improve with increased movements.
- Systemic illness and endocrine, cardiovascular, and metabolic disorders—can cause intermittent ataxia, especially of the pelvic limbs; with fever, weight loss, murmurs, arrhythmias, hair loss, or collapse with exercise, suspect a non-neurologic cause; obtain minimum data from hemogram, biochemistry, and urinalysis.
- Head tilt or nystagmus—likely vestibular localization.
- Intention tremors of the head or hypermetria—likely cerebellar localization.
- All four limbs affected—lesion is in the cervical spinal cord, cerebellum or is multifocal to diffuse.
- Only pelvic limbs affected—lesion is anywhere below the second thoracic vertebra.

CBC/BIOCHEMISTRY/URINALYSIS

Normal unless metabolic cause (e.g., hypoglycemia, electrolyte imbalance, anemia, polycythemia).

OTHER LABORATORY TESTS

- Hypoglycemia—determine serum insulin concentration on sample that has low glucose value; low glucose and higher than expected insulin value suggest insulin-secreting tumor.
- Anemia—differentiate as nonregenerative or regenerative on the basis of the reticulocyte count.
- Electrolyte imbalance—correct the problem; see if ataxia resolves.
- Antiepileptic drugs—if being administered, evaluate serum concentration for toxicity.

IMAGING

- Spinal radiography, myelography, CT or MRI—if spinal cord dysfunction suspected.
- Bullae radiography—if peripheral vestibular disease suspected; CT or MRI superior; for inner ear disease, MRI superior to CT.
- Thoracic radiography—for older patients and patients suspected to have neoplasia or systemic fungal infection.

- CT or MRI—if cerebellar disease suspected; MRI superior to CT.
- Abdominal ultrasonography—if hepatic, renal, adrenal, or pancreatic dysfunction suspected.

DIAGNOSTIC PROCEDURES

Cerebrospinal fluid—helps confirm nervous system etiology.



TREATMENT

- Usually outpatient, depending on severity and acuteness of clinical signs.
- Exercise—decrease or restrict if ataxia originates from spinal cord disease.
- Client should monitor gait for increasing dysfunction or weakness; if paresis worsens or paralysis develops, other testing is warranted.
- Avoid drugs that could contribute to the problem; may not be possible in patients on antiepileptic drugs for seizures.



MEDICATIONS

DRUG(S) OF CHOICE

Not recommended until the source or cause of the problem is identified.



FOLLOW-UP

PATIENT MONITORING

Periodic neurologic examinations to assess condition.

POSSIBLE COMPLICATIONS

- Spinal cord—progression to weakness and possibly paralysis
- Hypoglycemia—seizures
- Cerebellar disease—head tremors and bobbing
- Brainstem disease—stupor, coma, death



MISCELLANEOUS

AGE-RELATED FACTORS

N/A

SEE ALSO

- See specific causes
- Cerebellar Degeneration
- Head Tilt
- Paralysis

ABBREVIATIONS

- CNS = central nervous system
- CT = computed tomography
- FIP = feline infectious peritonitis
- MRI = magnetic resonance imaging

INTERNET RESOURCES

https://www.vetlearn.com/_preview?_cms.fe.previewId=1f98fff0-caa9-11e1-aa85-005056ad4736&WT.mc_id=newsletter%3BPV07111

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Client Education Handout
available online

ATHEROSCLEROSIS



BASICS

OVERVIEW

Thickening of the inner arterial wall in association with lipid deposits. Chronic arterial change characterized by loss of elasticity, luminal narrowing, and proliferating and degenerative lesions of the intima and media.

SIGNALMENT

- Rare in dogs.
- Not described in cats.
- Higher prevalence in miniature schnauzer, Doberman pinscher, poodle, and Labrador retriever.
- Geriatric patients (> 9 years).

SIGNS

Historical Findings

- None in some animals
- Lethargy
- Anorexia
- Weakness
- Dyspnea
- Collapse
- Vomiting
- Diarrhea

Physical Examination Findings

- Dyspnea
- Irregular rhythm
- Heart failure
- Disorientation
- Blindness
- Circling
- Coma
- Episodic lameness

CAUSES & RISK FACTORS

- Severe hypothyroidism
- Increasing age
- Hyperlipidemia in miniature schnauzers
- Male gender (male dogs may have predisposition)
- High total cholesterol
- Diabetes
- Glomerulonephritis



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Arteriosclerosis

CBC/BIOCHEMISTRY/URINALYSIS

- Hypercholesterolemia
- Hyperlipidemia
- High BUN and creatinine
- High liver enzymes

OTHER LABORATORY TESTS

- Low T₃ and T₄.
- High values for alpha-2 and beta fractions on protein electrophoresis.

IMAGING

Radiography

Thoracic and abdominal radiographs may reveal cardiomegaly and hepatomegaly.

DIAGNOSTIC PROCEDURES

Electrocardiography

- Conduction abnormalities and notched QRS complexes.
- Atrial fibrillation.
- ST segment elevation or depression with myocardial infarction.



TREATMENT

- Treat the underlying disorder and clinical signs (e.g., dyspnea if congestive heart failure develops).
- Diet—low-fat diet, weight loss program, and high soluble fiber intake to control hyperlipidemia.



MEDICATIONS

DRUG(S)

- Treat conduction disturbances and arrhythmias if clinically indicated.
- Thyroid replacement if hypothyroidism is confirmed.
- Antihypertensive therapy if hypertension is documented.
- Blood cholesterol-reducing medications if hyperlipidemic.
- Treat diabetes.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- Monitor T₄ concentration 4–6 hours post-administration after the first 6 weeks of treatment and adjust dosage accordingly.
- Monitor blood triglyceride and cholesterol levels.
- Monitor ECG for conduction disturbances and ST segment changes.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Hypothyroidism
- Diabetes
- Mitral valve disease (myxomatous)
- Glomerulonephritis

AGE-RELATED FACTORS

Geriatric patients (> 9 years)

SEE ALSO

Myocardial Infarction

INTERNET RESOURCES

www.vetgo.com/cardio

Suggested Reading

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BASICS

OVERVIEW

- Results from malformation or disruption of the articulation between the first and second cervical vertebrae (atlas and axis, respectively); causes spinal cord compression.
- AA instability can result in spinal cord trauma or compression at the junction between the atlas and axis—may cause neck pain and/or varying degrees of general proprioceptive (GP) ataxia /upper motor neuron (UMN) tetraparesis, tetraplegia (with or without nociception), and death from respiratory arrest.

Etiology

- Congenital: anomaly of the dens (aplasia, hypoplasia, or malformation [dorsal angulation] of the dens) and its ligamentous attachments.
- Acquired: may be a consequence of traumatic injury.

SIGNALMENT

- Congenital—toy-breed dogs (Yorkshire terrier, miniature or toy poodle, Chihuahua, Pekingese, and Pomeranian).
- Age at onset—usually before 12 months of age.
- Uncommon in larger-breed dogs, dogs > 1 year old, and cats.
- No sex predilection.

SIGNS

- Intermittent or progressive ambulatory tetraparesis, usually with neck pain—most common.
- Neurologic signs vary from mild to moderate GP/UMN ambulatory tetraparesis to non-ambulatory GP/UMN tetraparesis, or tetraplegia depending on degree of spinal cord compression and secondary pathology (i.e., edema, hemorrhage, or gliosis).
- Animals may have only neck pain without concurrent neurologic deficits.
- Episodes of collapse secondary to weakness.
- Abnormal postural reactions with spinal reflexes that are normal to exaggerated with normal to increased muscle tone in all four limbs.
- Acute death may occur when accompanied by trauma and respiratory arrest (uncommon).

CAUSES & RISK FACTORS

- Usually caused by abnormal development of the dens and/or ligamentous support structures, resulting in subluxation of the atlantoaxial joint.
- Fracture of the axis.
- Clinical signs often occur as a result of mild or insignificant trauma (e.g., jumping or playing).
- Clinical signs may be exacerbated by activity such as flexion of the neck.

- Toy-breed dogs—at risk for congenital malformation of the dens.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Differential diagnoses are consistent with various causes of cervical myelopathies, including:
 - Other congenital malformation.
 - Trauma.
 - Meningitis or meningoencephalitis (i.e., infectious or non-infectious [granulomatous meningoencephalomyelitis]).
 - Fibrocartilaginous embolic myelopathy.
 - Disk herniation.
 - Neoplasia.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

IMAGING

- Plain radiography of the cervical vertebral column:
 - Lateral view—caudal and dorsal displacement of the axis in relationship to the atlas, resulting in an increased distance between vertebrae.
 - Ventral dorsal or oblique view—may reveal absence, hypoplasia, or malformation (dorsal angulation) of the dens.
- Cross-sectional imaging:
 - MRI.
 - Diagnosis based on observation of caudal and dorsal displacement of the axis in relationship to the atlas as evidenced by the following features of the atlantoaxial articulation: (1) Dorsal: displacement of the spinous process of the axis; (2) Ventral: increased size of the occipito-atlas-axis joint cavity.
 - Allows identification of spinal cord compression.
 - Allows recognition of secondary spinal cord pathology such as edema, hemorrhage, or gliosis, which may impact prognosis.
- Computed tomography:
 - May provide detailed visualization of bony structures, which allows for the creation of three-dimensional reconstructed image to help surgical planning.
- Precautions:
 - Proper positioning will require sedation or general anesthesia.
 - Sedation or general anesthesia carries significant risk for iatrogenic trauma.
 - Care needs to be exercised when positioning animals.
 - AVOID EXCESSIVE FLEXION OF THE NECK!
 - Flexion may exacerbate compression, which may worsen clinical signs or cause death due to spinal cord trauma.
 - To protect against neck flexion during recovery, affected animals should be closely monitored until they are capable of maintaining normal head and neck carriage.



TREATMENT

- Prior to treatment, consultation with a board-certified neurologist or surgeon should be pursued.
- Improper treatment can lead to irreversible deterioration in neurologic function.

MEDICAL

- Neck brace (splint) to stabilize the cervical vertebral column in extension.
 - Fiberglass cast material is positioned ventrally from the rostral aspect of mandible to the xiphoid and incorporated into bandage material, which immobilizes the head and neck.
 - Strict exercise restriction (cage confinement) for a minimum of 8 weeks.
 - Frequent bandage/splint changes are needed.
- Adjunctive medication (see below).

Overall Prognosis

- Successful outcome observed in 62.5% of dogs.
- Improved prognosis was associated with an acute onset and short duration of clinical signs (< 30 days).
- Surgery is recommended to treat animals that fail to improve or experience recurrence of signs following medical treatment.

SURGERY

- Treatment of choice in the majority of cases.
- Surgical approach; **ventral method is preferred.**
 - Ventral approach—variety of methods:
 - Transarticular pinning or lag screw technique; ventral tips of the pins incorporated in polymethylmethacrylate to prevent pin migration.
 - Transarticular pinning and ventral cortical screws or K-wires in the bodies of the atlas and axis ± K-wires applied longitudinally and wired to the screws; screw heads and K-wires are incorporated in polymethylmethacrylate to provide fixation.
 - Dorsal approach—use wire or synthetic suture material to fix the spinous process of the axis to the dorsal arch of the atlas; provides less rigid fixation and may be associated with greater implant failure.
 - Strict exercise restriction is required for the first month postoperatively, followed by a gradual return to activity over an additional month.
 - Adjunctive medication (see below).
- Overall prognosis ranges from 63% to 91% success: improved prognosis was associated with young (< 24 months) dogs, duration of clinical signs < 10 months, and mild neurologic deficits.

ATLANTOAXIAL INSTABILITY

(CONTINUED)

- Complications:
 - Failure to improve/worsening of neurologic deficits.
 - Implant failure/infection.
 - Respiratory—respiratory arrest, dyspnea, cough, and aspiration pneumonia.
 - Death.



MEDICATIONS

DRUG(S)

- Anti-inflammatory medication:
 - Corticosteroids: prednisone 0.5–1.0 mg/kg PO divided twice daily for 2 weeks, followed by a tapering regime. Suggested protocol following initial dose: 0.5 mg/kg PO daily for 5 days, followed by 0.5 mg/kg PO every other day for 5 days.
 - NSAID: 1- to 4-week course.
- Analgesia:
 - Tramadol 2.0–4.0 mg/kg PO q6–8h.
 - Gabapentin 10–20 mg/kg PO q6–8h.
 - Pregabalin 3–4 mg/kg (begin with 2 mg/kg) PO q8–12h.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Corticosteroid—use caution when given in conjunction with medical treatment; may reduce pain, resulting in increased activity and spinal cord trauma.
- Avoid NSAIDs in combination with corticosteroids in all patients—increases risk of life-threatening gastrointestinal hemorrhage.



FOLLOW-UP

- Dogs treated medically require frequent (weekly) bandage changes for associated soft tissue trauma.

- All dogs should be reevaluated at 1 and 3 months (postoperatively or after neck brace removal) and monthly until neurologic deficits resolve or remain static over 2–3 months.
- More frequent rechecks may be needed for dogs experiencing complications or recurrence of signs.
- Untreated animals may experience deterioration in neurologic function, catastrophic acute spinal cord trauma, respiratory arrest, and death.



MISCELLANEOUS

- Rehabilitation may play a significant role in the ultimate neurologic functional level of the patient.
- Rehabilitation should only be considered in dogs > 30 days postoperatively or after neck brace (splint) removal.

ABBREVIATIONS

- GP = general proprioceptive
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug
- UMN = upper motor neuron

INTERNET RESOURCES

<http://www.acvs.org/AnimalOwners/HealthConditions/SmallAnimalTopics/AtlantoaxialInstability/>

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BASICS

DEFINITION

- A genetically predisposed hypersensitivity reaction to normally innocuous substances.
- Manifests as an inflammatory, chronically relapsing, non-contagious and pruritic skin disease.

PATOPHYSIOLOGY

- Atopic dermatitis (AD) has a multifactorial etiology involving genetic, structural, and immunologic factors. • Classical theory describes the pathway through which susceptible animals become sensitized to environmental allergens producing allergen-specific IgE, followed by mast cell degranulation upon re-exposure to allergens via epicutaneous absorption (extrinsic AD).
- A subset of AD patients does not have increased allergen-specific IgE (intrinsic AD).
- Current focus on the pathogenesis of AD includes abnormalities in barrier function and T-cell dysregulation or imbalance. • Barrier function impairment, shown as increased transepidermal water loss and decreased filagrin expression, in affected dogs has been demonstrated. • Acute lesions of AD are characterized by increased $T_{H}2$ lymphocyte activity while $T_{H}1$ cytokines predominate in chronic lesions. Thus a $T_{H}2:T_{H}1$ imbalance in AD has been proposed. • Recently, aberrant regulatory T-cell function has been reported.
- Following repeat epicutaneous absorption of allergens, mast cell degranulation results in the release of histamine, proteolytic enzymes, cytokines, chemokines, and other chemical mediators. • Bacterial superantigens, auto-antigens released via keratinocyte damage, and *Malassezia* may play a role in perpetuating the inflammation.

SYSTEMS AFFECTED

- Ophthalmic • Respiratory • Skin/Exocrine

GENETICS

- Dogs— inherited predisposition; polygenic with environmental influences important for disease development.
- Cats— inherited predisposition less clear.

INCIDENCE/PREVALENCE

- Canine—true prevalence is unknown; estimated at 3–15% of the canine population.
- Feline—unknown; generally believed to be lower than that for dogs.

GEOGRAPHIC DISTRIBUTION

Canine—recognized worldwide; local environmental factors (temperature, humidity, and flora) influence the seasonality, severity, and duration of signs.

SIGNALMENT

Species

Dogs and cats

Breed Predilections

- Canine—any breed, including mongrels; recognized more frequently in certain breeds or families (can vary geographically). • United States—Boston terrier, boxer, cairn terrier, Chinese Shar-Pei, cocker spaniel, Dalmatian, English bulldog, English and Irish setter, French bulldog, American pit bull terrier, Lhasa apso, miniature schnauzer, pug, Sealyham terrier, Scottish terrier, West Highland white terrier, wirehaired fox terrier, Labrador retriever, and golden retriever.
- Feline—none reported.

Mean Age and Range

- Canine—mean age at onset 1–3 years; range 3 months–6 years; signs may be mild the first year but usually progress and become clinically apparent before 3 years of age.
- Feline—6 months to 2 years.

Predominant Sex

None reported

SIGNS

General Comments

- Pruritus—itching, scratching, rubbing, licking. • Most cutaneous changes caused by self-induced trauma; primary lesions usually unrecognized.

Historical Findings

- Facial, pedal, or axillary pruritus • Early age of onset • History in related individuals
- May be initially seasonal • Recurring skin or ear infection • Temporary response to glucocorticosteroids • Symptoms progressively worsen with time • Feline—face and neck pruritus

Physical Examination Findings

- Areas most commonly affected—interdigital spaces, carpal and tarsal areas, muzzle, periocular region, axillae, groin, and pinnae.
- Lesions—vary from none to broken hairs or salivary discoloration to erythema, papules, and, alopecia, to crusts, hyperpigmentation, lichenification. The skin may become excessively oily or dry seborrhea, and hyperhidrotic (apocrine sweating).
- Secondary bacterial and yeast skin infections (common). • Chronic relapsing otitis externa.
- Conjunctivitis, blepharitis, and rhinitis may occur.

CAUSES

- Pollens (grasses, weeds, and trees) • Mold spores (indoor and outdoor) • *Malassezia*
- House dust and storage mites • Animal dander • Insects

RISK FACTORS

- Temperate environments with long allergy seasons and high pollen and mold spore levels. • Concurrent pruritic dermatoses, such as flea bite hypersensitivity and adverse food reaction (summation effect).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Adverse food reaction—may cause identical symptoms; may occur concurrently with atopic dermatitis; differentiation is made by noting response to hypoallergenic diet. • Flea bite different lesion distribution and response to flea control. • Sarcoptic mange—causes severe pruritus of the ventral chest, lateral elbows, lateral hocks, and pinna margins; differentiation by multiple skin scrapings and/or complete response to a trial of miticidal therapy. • Secondary pyoderma—follicular papules, pustules, crusts, and epidermal collarettes. • Secondary yeast infections—erythematous, scaly, crusty, greasy, and malodorous body folds and intertriginous areas; differentiation by demonstration of numerous budding yeast organisms on skin cytology. • Contact dermatitis (allergic or irritant)—severe erythema and pruritus of the feet and thinly haired areas of the flank and axillae.

CBC/BIOCHEMISTRY/URINALYSIS

Eosinophilia—rare in dogs without concurrent flea infestations; common in cats.

DIAGNOSTIC PROCEDURES

- Diagnosis of AD is made by history, physical examination, and ruling out of differential diagnoses; not by either serologic or intradermal allergy testing. • Greatest treatment success noted when immunotherapy is based on results of both serum and intradermal testing.

Serologic Allergy Tests

- Measures the amount of allergen-specific IgE antibody in the patient's serum.
- Advantages over IDT—availability; hair coat does not require clipping; sedation is not required. • Disadvantages—cannot distinguish between allergic and normal patients; frequent false-positive or false-negative reactions; limited number of allergens tested; inconsistent assay validation, quality control, and reliability (may vary with the laboratory used); a subset of AD patients does not have elevated levels of circulating allergen-specific IgE.

Intradermal Test (Preferred)

- Small amounts of test allergen are injected intradermally causing localized reactions; wheal formation is measured and evaluated subjectively. • Advantages—more physiologically-appropriate determination of allergens for immunotherapy; potentially higher success rate of immunotherapy versus allergens chosen based on serum testing.
- Disadvantages—results more difficult to interpret in cats owing to the relatively small wheals produced; requires sedation and clipping a small patch of hair coat; false

ATOPIC DERMATITIS

(CONTINUED)

positive and false negative reactions may occur.

PATHOLOGIC FINDINGS

Skin biopsy—rule out other differential diagnoses; results not pathognomonic; acanthosis, mixed mononuclear superficial perivascular dermatitis, sebaceous gland metaplasia, with secondary superficial bacterial folliculitis.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient

ACTIVITY

Avoid offending allergens when possible

DIET

Diets rich in essential fatty acids may be beneficial

CLIENT EDUCATION

- Explain the inheritable and progressive nature of the condition.
- Rarely goes into remission and cannot be cured.
- Ongoing therapy may be necessary to maintain quality of life.



MEDICATIONS

DRUG(S) OF CHOICE

Immunotherapy (Hyposensitization)

- Subcutaneous or sublingual administration of gradually increasing doses of the causative allergens to reduce sensitivity.
- Allergen selection—based on allergy test results, patient history, and/or knowledge of local exposure.
- Immunotherapy formulation procedures and administration protocols are not standardized and vary widely between clinicians.
- Preferred treatment in most cases; especially indicated when it is desirable to avoid or reduce the amount of corticosteroids required to control signs, when signs last longer than 4–6 months per year, or when non-steroid forms of therapy are ineffective.
- Successfully reduces pruritus in 60–80% of dogs and cats.
- Response is slow, requiring at least 3 months and up to 1 year for full effect.

Cyclosporine

- Cyclosporine, modified (name brand preferred—Atopica 5 mg/kg/day) effective in controlling pruritus associated with chronic atopic dermatitis.
- Response is similar to that of glucocorticosteroids.
- Slow onset of activity (1–4 weeks).
- Many patients can be adequately controlled with less frequent dosing (every 2–4 days).
- Patient monitoring is recommended.
- Drug blood level monitoring recommended in cats.

Corticosteroids

- May be given for short-term relief and to break the itch-scratch cycle.
- Should be

tapered to the lowest dosage that adequately controls pruritus.

- Prednisolone (0.25–0.5 mg/kg PO q48h).
- Cats—oral steroids or very infrequent methylprednisolone acetate by injection (2–4 mg/kg).

Antihistamines

- Less effective than corticosteroids.
- Dogs—hydroxyzine (1–2 mg/kg PO q12h), chlorpheniramine (0.2–0.4 mg/kg PO q12h), diphenhydramine (2.2 mg/kg PO q12h), fexofenadine (2–5 mg/kg PO q12–24h), and clemastine (0.04–0.10 mg/kg PO q12h).
- Cats—chlorpheniramine (0.5 mg/kg PO q12h); efficacy estimated at 10–50%.

Oclacitinib

Oclacitinib Apoquel (0.4–0.6 mg/kg q12h for 14 days then q24h). Dogs—effective in controlling pruritus associated with chronic atopic dermatitis. Onset time and response similar to glucocorticoids. Long-term safety and efficacy undetermined.

PRECAUTIONS

- Cyclosporine—may affect glucose homeostasis; may increase incidence of urinary tract infection.
- Corticosteroids—use judiciously in dogs to avoid iatrogenic hyperglucocorticism and associated problems, aggravation of pyoderma, and induction of demodicosis.
- Antihistamines—can produce drowsiness, and rarely anorexia, vomiting, diarrhea, increased pruritus; use with caution in patients with cardiac arrhythmias.
- Oclacitinib—not for use in dogs under 1 year of age; insufficient long-term experience.

POSSIBLE INTERACTIONS

Concurrent use of cyclosporine and ketoconazole permits a 50% dose reduction of each drug

ALTERNATIVE DRUG(S)

- Frequent bathing (once to twice weekly) in cool water with antipruritic shampoos is very beneficial and should be strongly encouraged.
- Fatty acids: ω -3 (eicosapentaenoic acid 66 mg/kg/day) may be more effective than ω -6 (linoleic acid 130 mg/kg/day) fatty acids.
- Tricyclic antidepressants: dog—doxepin 1–2 mg/kg PO q12h; or amitriptyline 1–2 mg/kg PO q12h; overall effectiveness is unclear; not extensively studied in the cat.
- Gabapentin (dogs, 10–30 mg/kg q6–12h; cats, 3–8 mg/kg q6–8h).
- Pentoxifylline 10 mg/kg q8–12h.
- Topical triamcinolone spray 0.015% can be used over large body surfaces to control pruritus with minimal side effects.



FOLLOW-UP

PATIENT MONITORING

- Examine patient every 2–8 weeks when a new course of therapy is started.
- Monitor

pruritus, self-trauma, development of bacterial folliculitis, and possible adverse drug reactions.

- Once an acceptable level of control is achieved, examine patient every 3–12 months.
- CBC, serum chemistry profile, and urinalysis with culture—recommended every 3–12 months for patients on chronic corticosteroid, cyclosporine or Oclacitinib therapy.

PREVENTION/AVOIDANCE

- If offending allergens have been identified through allergy testing, avoidance may help to reduce the level of pruritus; this is seldom possible.
- Minimizing other sources of pruritus (e.g., flea infestation, adverse food reaction, and secondary skin infection) permits better response to therapy.

POSSIBLE COMPLICATIONS

- Secondary bacterial folliculitis or *Malassezia* dermatitis.
- Concurrent flea bite hypersensitivity and/or adverse food reaction.

EXPECTED COURSE AND PROGNOSIS

- Not life-threatening unless intractable pruritus results in euthanasia.
- Degree of pruritus usually worsens and the duration of signs last longer each year without intervention.
- Some cases spontaneously resolve.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Flea bite hypersensitivity
- Adverse food reaction/food hypersensitivity
- Bacterial folliculitis
- Malassezia* dermatitis
- Otitis externa

AGE-RELATED FACTORS

Severity worsens with age

PREGNANCY/FERTILITY/BREEDING

- Corticosteroids—contraindicated during pregnancy.
- Affected animals should not be used for breeding.

SYNOMYMS

- Atopy
- Canine atopic disease

SEE ALSO

- Flea Bite Hypersensitivity and Flea Control
- Food Reactions, Dermatologic
- Otitis Externa and Media
- Pyoderma

ABBREVIATION

IDT = intradermal test

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Consulting Editor Alexander H. Werner



Client Education Handout
available online

ATRIAL FIBRILLATION AND ATRIAL FLUTTER



BASICS

DEFINITION

- Atrial fibrillation—rapid, irregularly irregular supraventricular rhythm. Two forms recognized: primary atrial fibrillation, an uncommon disease that occurs mostly in large dogs with no underlying cardiac disease, and secondary atrial fibrillation, which occurs in dogs and cats secondary to underlying cardiac disease.
- Atrial flutter is similar to atrial fibrillation, but the atrial rate is generally slower and is characterized by saw-toothed flutter waves in the baseline of the ECG. The ventricular response is generally rapid but may be regular or irregular.

ECG FEATURES

Atrial Flutter

- Atrial rhythm usually regular; rate approximately 300–400 bpm.
- P waves usually discerned as either discrete P waves or a “saw-toothed” baseline.
- Ventricular rhythm and rate generally depend on the atrial rate and AV nodal conduction, but are generally regular or regularly irregular and rapid.
- Conduction pattern to the ventricles is variable—in some cases every other atrial depolarization produces a ventricular depolarization (2:1 conduction ratio), giving a regular ventricular rhythm; other times the conduction pattern appears random, giving an irregular ventricular rhythm that can mimic atrial fibrillation.

Secondary Atrial Fibrillation

- No P waves present—baseline may be flat or may have small irregular undulations (“f” waves); some undulations may look like P waves.
- Ventricular rate high—usually 180–240 bpm in dogs and > 220 bpm in cats.
- Interval between QRS complexes is irregularly irregular; QRS complexes usually appear normal.

Primary Atrial Fibrillation

Similar to secondary atrial fibrillation except ventricular rate usually in the normal range.

PATHOPHYSIOLOGY

- Atrial fibrillation—caused by numerous small reentrant pathways creating a rapid (> 500 depolarizations/minute) and disorganized depolarization pattern in the atria that results in cessation of atrial contraction. Depolarizations continuously bombard the AV nodal tissue, which acts as a filter and does not allow all depolarizations to conduct to the ventricles. Many atrial depolarizations activate only a part of the atria because the rapid rate renders portions of the atria refractory, and thus they cannot reach the AV junction. Other atrial impulses penetrate into the AV junctional tissue but are not robust enough to penetrate the entire length. Blocked impulses affect the

conduction properties of the AV junctional tissue and alter conduction of subsequent electrical impulses; electrical impulses are conducted through the AV junction irregularly, producing an irregular ventricular rhythm.

- Atrial flutter—probably originates from one site of reentry that moves continuously throughout the atrial myocardium and frequently and regularly stimulates the AV node. When the atrial rate becomes sufficiently fast, the refractory period of the AV node exceeds the cycle length (P to P interval) of the SVT, and some atrial depolarizations are blocked from traversing the AV node (functional second-degree AV block).

SYSTEMS AFFECTED

Cardiovascular

Loss of atrial contraction may result in decreased stroke volume and cardiac output depending on heart rate; high heart rate may result in deterioration in myocardial function (tachycardia-induced myocardial failure).

GENETICS

No breeding studies available

SIGNALMENT

Species

Dog and cat

Breed Predilections

Large- and giant-breed dogs are more prone to primary atrial fibrillation.

Mean Age and Range

N/A

Predominant Sex

N/A

SIGNS

General Comments

- Generally relate to the underlying disease process and/or CHF rather than the arrhythmia itself, but previously stable animals may decompensate.
- Patients with primary atrial fibrillation are generally asymptomatic but may demonstrate mild exercise intolerance.

Historical Findings

- Coughing/dyspnea/tachypnea.
- Exercise intolerance.
- Rarely syncope.
- Dogs with primary atrial fibrillation are typically asymptomatic.

Physical Examination Findings

- On auscultation, patients with atrial fibrillation have an erratic heart rhythm that sounds like “tennis shoes in a dryer.”
- First heart sound intensity in atrial fibrillation is variable; second heart sound only heard on beats with effective ejection, not on every beat.
- Third heart sounds (gallop sounds) may be present.
- Patients with atrial fibrillation have pulse deficits and variable pulse quality.
- Signs of CHF often present (e.g., cough, dyspnea, cyanosis).

CAUSES

- Chronic valvular disease • Cardiomyopathy
- Congenital heart disease • Digoxin toxicity
- Idiopathic • Ventricular preexcitation (atrial flutter)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Frequent atrial (supraventricular) premature depolarizations
- Supraventricular tachycardia with AV block
- Multifocal atrial tachycardia (irregular)

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

- Echocardiography and radiography may characterize type and severity of the underlying cardiac disease; moderate to severe left atrial enlargement common.
- Typically normal in patients with primary atrial fibrillation, although mild left atrial enlargement may accompany the hemodynamic alterations imposed by the arrhythmia.

DIAGNOSTIC PROCEDURES

A baseline 24-hour Holter is recommended to determine if the arrhythmia is chronic or paroxysmal. If it is chronic, drug therapy is indicated.



TREATMENT

APPROPRIATE HEALTH CARE

- Patients with fast (secondary) atrial fibrillation are treated medically to slow the ventricular rate. Converting the atrial fibrillation to sinus rhythm would be ideal, but such attempts in patients with severe underlying heart disease or left atrial enlargement are generally futile because of a low success rate and high rate of recurrence. Consider electrical cardioversion to sinus rhythm for a dog with primary atrial fibrillation and only mild structural heart disease.
- Patients with primary atrial fibrillation may be converted back to normal sinus rhythm. The success rate depends on chronicity. Patients that have been in atrial fibrillation for > 4 months generally have a lower success rate and a higher rate of recurrence. In these patients, rate control, if necessary, is the recommended treatment.
- Electrical (DC) cardioversion—application of a transthoracic electrical shock at a specific time in the cardiac cycle; requires special equipment, trained personnel, and general anesthesia. Using a monophasic defibrillator: Start with 4 J/kg; if no conversion occurs,

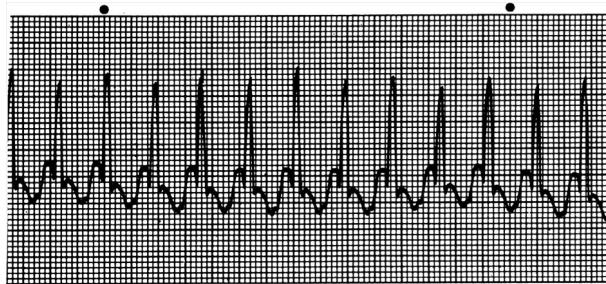


Figure 1.

Atrial flutter with 2:1 conduction at ventricular rate of 330/minute in a dog with an atrial septal defect. This supraventricular tachycardia was associated with a Wolff-Parkinson-White pattern. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

increase dose by 50 J and repeat until a max of 360 J. Using a biphasic defibrillator: Start with 1 to 2 J/kg; if no cardioversion occurs, increase dose by 50 J and repeat until max of 360 J. • For atrial flutter, conversion to sinus rhythm can be done by drug therapy, electrical cardioversion, or rapid atrial pacing (transvenous pacing electrode).

NURSING CARE

As indicated for CHF.

ACTIVITY

Restrict activity until tachycardia is controlled.

DIET

Mild to moderate sodium restriction if CHF.

CLIENT EDUCATION

- Secondary atrial fibrillation and atrial flutter is usually associated with severe underlying heart disease; goal of therapy is to lower heart rate and control clinical signs. • Sustained conversion to sinus rhythm is unlikely with secondary atrial fibrillation.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

- Digoxin, β -adrenergic blockers, esmolol, and calcium channel blockers (diltiazem) are frequently used to slow conduction through the AV node; definition of an adequate heart rate response varies among clinicians, but in dogs is generally 140–160 bpm.
- For atrial flutter, therapy is aimed at suppressing the atrial re-entry circuit using sotalol, amiodarone, or procainamide.

Dogs

- Digoxin—maintenance oral dose 0.005–0.01 mg/kg PO q12h; to achieve a therapeutic serum concentration more rapidly, the maintenance dose can be doubled for the first day. If digoxin is administered alone and

the heart rate remains high, check the digoxin level and adjust the dose to bring the level into the therapeutic range. If the heart rate remains high, consider adding a calcium channel blocker or a β -adrenergic blocker.

- Diltiazem—initially administered at a dose of 0.5 mg/kg PO q8h, then titrated up to a maximum of 1.5 mg/kg PO q8h or until an adequate response is obtained.
- Therapy for atrial fibrillation is aimed at suppressing the atrial reentry circuit using sotalol, amiodarone, or procainamide. The conversion to normal sinus rhythm is usually unsuccessful.

Cats

- Diltiazem (1–2.5 mg/kg PO q8h) or atenolol (6.25–12.5 mg/cat PO q12–24h) are the drugs of choice in most cats.
- If the heart rate is not sufficiently slowed with these drugs or if myocardial failure is present, digoxin (5 μ g/kg PO q24–48h) can be added.

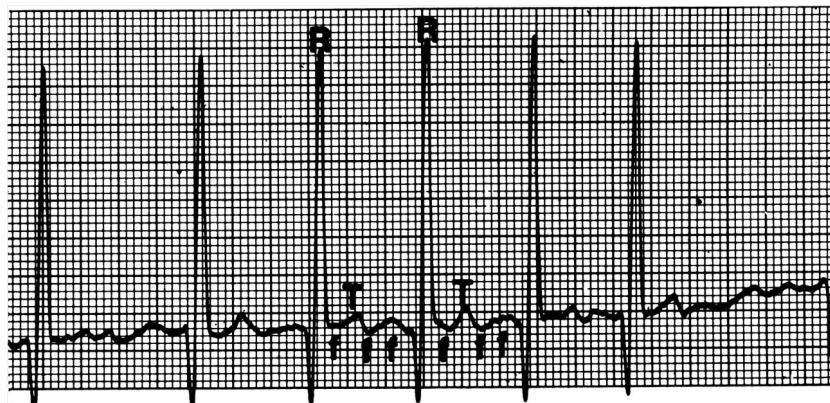


Figure 2.

“Coarse” atrial fibrillation in a dog with patent ductus arteriosus. The f waves are prominent. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

(CONTINUED)

ATRIAL FIBRILLATION AND ATRIAL FLUTTER

A

CONTRAINDICATIONS

- Digoxin, diltiazem, propranolol, and atenolol should not be used in patients with preexisting AV block.
- Use of calcium channel blockers in combination with beta blockers should be avoided because clinically significant bradyarrhythmias and/or AV block can develop.

PRECAUTIONS

- Calcium channel blockers and β -adrenergic blockers, both negative inotropes, should be used cautiously in animals with myocardial failure.
- Using high-dose oral quinidine for conversion into sinus rhythm carries a risk of quinidine toxicity (e.g., hypotension, weakness, ataxia, and seizures)—administration of diazepam intravenously controls seizures; other signs abate within several hours of discontinuing quinidine administration.

POSSIBLE INTERACTIONS

Quinidine raises the digoxin level, generally necessitating a digoxin dose reduction.

**FOLLOW-UP****PATIENT MONITORING**

- Monitor heart rate and ECG closely.
- As heart rates in the hospital and those measured on the surface ECG may be inaccurate (due to patient anxiety and other environmental factors), Holter monitoring provides a more

accurate means for assessing the need for heart rate control and/or the efficacy of medical therapy for heart rate control.

POSSIBLE COMPLICATIONS

Worsening of cardiac function with onset of arrhythmia.

EXPECTED COURSE AND PROGNOSIS

- Secondary atrial fibrillation—associated with severe heart disease, so a guarded-to-poor prognosis.
- Primary atrial fibrillation with normal ultrasound findings—generally a good prognosis.

**MISCELLANEOUS****ABBREVIATIONS**

- AV = atrioventricular
- CHF = congestive heart failure
- ECG = electrocardiogram
- SVT = supraventricular tachycardia

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Client Education Handout available online

ATRIAL PREMATURE COMPLEXES



BASICS

DEFINITION

Premature atrial beats that originate outside the sinoatrial node and disrupt the normal sinus rhythm for 1 or more beats

ECG FEATURES

- Heart rate usually normal; rhythm irregular due to the premature P wave (called a P' wave) that disrupts the normal P wave rhythm (Figure 1).
- Ectopic P' wave—premature; configuration differs from that of the sinus P waves and may be negative, positive, biphasic, or superimposed on the previous T wave.
- QRS complex—premature; configuration usually normal (same as that of the sinus complexes). If the P' wave occurs during the refractory period of the AV node, ventricular conduction does not occur (non-conducted APCs), so no QRS complex follows the P' wave. If there is partial recovery in the AV node or intraventricular conduction systems, the P' wave is conducted with a long P'-R interval or with an abnormal QRS configuration (aberrant conduction). The more premature the complex, the more marked the aberration.
- In the P–QRS relationship, the P'-R interval is usually as long as, or longer than, the sinus P'-R interval.
- A non-compensatory pause—when the R–R interval of the two normal sinus complexes enclosing an APC is less than the R–R intervals of three consecutive sinus complexes—usually follows an APC (Figure 2). The ectopic atrial impulse discharges the sinus node and resets the cycle.

PATHOPHYSIOLOGY

- Mechanisms—an increase in automaticity of atrial myocardial fibers or a single reentrant circuit.
- May be normal finding in aged dogs; commonly seen in dogs with atrial enlargement secondary to chronic mitral

valvular insufficiency; may also be observed in dogs or cats with any atrial disease.

- May not cause hemodynamic problems; the clinical significance relates to their frequency, timing relative to other complexes, and the underlying clinical problems.
- Can presage more serious rhythm disturbances (e.g., atrial fibrillation, atrial flutter, or atrial tachycardia).

SYSTEMS AFFECTED

Cardiovascular

GENETICS

N/A

INCIDENCE/PREVALENCE

Not documented

SIGNALMENT

Species

Dog and cat

Breed Predilections

Small-breed dogs

Mean Age and Range

Geriatric animals, except those with congenital heart disease

SIGNS

Historical Findings

- No signs
- CHF
- Coughing and dyspnea
- Exercise intolerance
- Syncope

Physical Examination Findings

- Irregular heart rhythm
- Cardiac murmur
- Gallop rhythm
- Signs of CHF

CAUSES & RISK FACTORS

- Chronic valvular disease
- Congenital heart disease
- Cardiomyopathy
- Atrial myocarditis
- Electrolyte disorders
- Neoplasia
- Hyperthyroidism

- Toxemias
- Drug toxicity (e.g., digitalis)
- Normal variation in aged animals



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Marked sinus arrhythmia.
- Ventricular premature complexes when aberrant ventricular conduction follows an APC.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

Echocardiography and Doppler ultrasound may reveal the type and severity of the underlying heart disease.

DIAGNOSTIC PROCEDURES

- Electrocardiography
- Holter monitor to quantify APC frequency and event monitor/Holter ECG to correlate symptoms with rhythm.

PATHOLOGIC FINDINGS

Atrial enlargement; other features vary depending on underlying cause.



TREATMENT

APPROPRIATE HEALTH CARE

- Treat animal as inpatient or outpatient.
- Treat the underlying CHF, cardiac disease, or other causes.

NURSING CARE

Usually not necessary; varies with underlying cause.

ACTIVITY

Restrict if symptomatic.

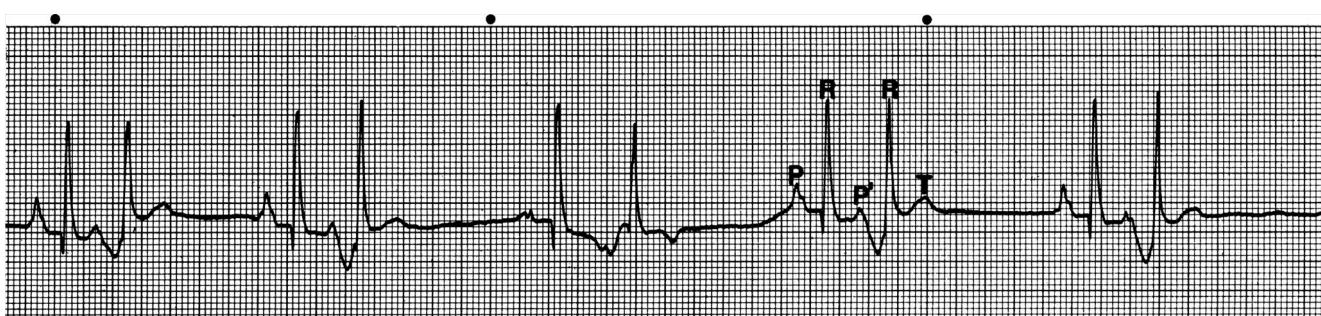


Figure 1.

APCs in a dog. P' represents the premature complex. The premature QRS resembles the basic QRS. The upright P' wave is superimposed on the T wave of the preceding complex. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Blackwell Publishing, 1992, with permission.)

(CONTINUED)

ATRIAL PREMATURE COMPLEXES

A

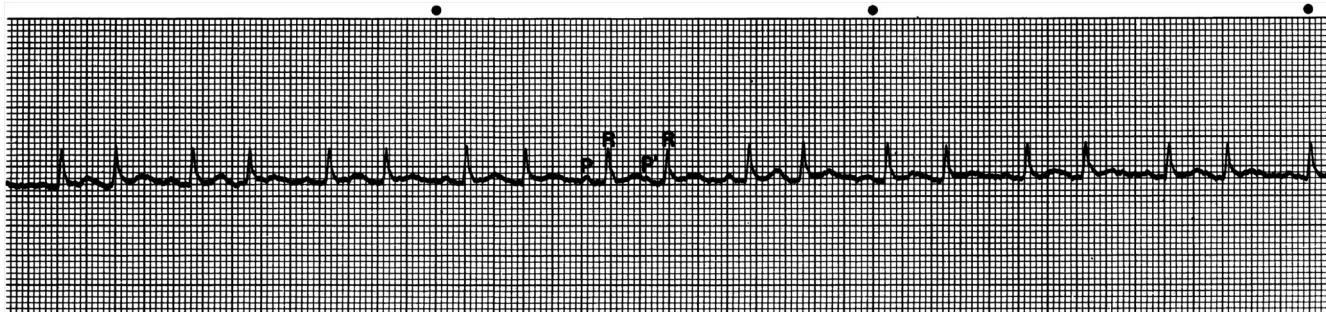


Figure 2.

APCs in bigeminy in a cat under general anesthesia. The second complex of each pair is an APC, where the first is a sinus complex. The abnormality in rhythm disappeared after the anesthetic was stopped. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Blackwell Publishing, 1992, with permission.)

DIET

No modifications unless required for management of underlying condition (i.e., low-salt diet).

CLIENT EDUCATION

APCs may not cause hemodynamic abnormalities; may be precursors of serious arrhythmias.

SURGICAL CONSIDERATIONS

N/A

**MEDICATIONS****DRUG(S) OF CHOICE**

Treat CHF and correct any electrolyte or acid/base imbalances.

Dogs

- Digoxin (0.005–0.01 mg/kg PO q12h, maintenance dosage), diltiazem (0.5–1.5 mg/kg PO q8h), or atenolol (0.25–1 mg/kg PO q12h) are used to treat clinically significant arrhythmias.
- Digoxin—treatment of choice; also indicated to treat the cardiac decompensation that is usually present.
- CHF is treated with appropriate dosage of diuretic, angiotensin converting enzyme inhibitor, and pimobendan; appropriate management of CHF may reduce APC frequency.

Cats

- Cats with hypertrophic cardiomyopathy—diltiazem (1–2.5 mg/kg PO q8h) or atenolol (6.25–12.5 mg PO q12–24h).
- Cats with dilated cardiomyopathy—digoxin (one-fourth of a 0.125 mg digoxin tablet q24h or q48h).

CONTRAINDICATIONS

Negative inotropic agents (e.g., propranolol) should be avoided in animals with CHF.

PRECAUTIONS

Use digoxin, diltiazem, atenolol, or propranolol cautiously in animals with underlying atrioventricular block or hypotension.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

Monitor heart rate and rhythm with serial ECG.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Frequent APCs may further diminish cardiac output in patients with underlying heart disease and worsen clinical symptoms.

EXPECTED COURSE AND PROGNOSIS

Even with optimal antiarrhythmic drug therapy some animals have an increased frequency of APCs or deteriorate to more severe arrhythmia as the underlying disease progresses.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

None

AGE-RELATED FACTORS

Typically occurs in geriatric dogs

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYS

Atrial extrasystoles, atrial premature contractions, atrial premature impulses

SEE ALSO

Supraventricular Tachycardia

ABBREVIATIONS

- APC = atrial premature complex
- AV = atrioventricular
- CHF = congestive heart failure

INTERNET RESOURCES

www.vetgo.com/cardio.

Suggested Reading

Jackson BL, Lehmkohl LB, Adin DB. Heart rate and arrhythmia frequency of normal cats compared to cats with asymptomatic hypertrophic cardiomyopathy. *J Vet Cardiology* 2014; 16:215–225.

Keene B, Smith FWK, Tilley LP, Hansen B. *Rapid Interpretation of Heart Sounds, Murmurs, Arrhythmias, and Lung Sounds: A Guide to Cardiac Auscultation in Dogs and Cats*. 3rd ed. CD-ROM and Manual. Philadelphia: Elsevier, 2015.

Tilley LP, Smith FWK, Jr. *Electrocardiography*. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., *Manual of Canine and Feline Cardiology*, 5th ed. St. Louis, MO: Saunders Elsevier, 2015 (in press).

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Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

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Client Education Handout
available online

ATRIAL SEPTAL DEFECT



BASICS

OVERVIEW

- Congenital defect in which the interatrial septum fails to develop normally, resulting in communication between the atria. Unknown cause; genetic basis suspected. Acquired ASD secondary to atrial rupture reported in dogs with degenerative mitral valve disease.
- Comprises 0.7–3.7% of congenital heart defects in dogs and < 10% of congenital heart defects in cats. Significantly higher incidence (37.7%) noted in a more recent study.
- 3 major types of ASD classified based on the location of the defect within the interatrial septum: ostium primum ASD (most apical portion of septum, adjacent to the atrioventricular valves), ostium secundum ASD (central portion of the septum, region of fossa ovalis), and sinus venosus ASD (upper portion of septum, junction of cranial vena cava).
- Secundum ASD with left-to-right shunting is most common (98.7% in one study of dogs and cats).
- Ostium primum ASDs typically large; may be component of atrioventricular (AV) canal defect.
- Sinus venosus ASDs typically located at the junction of the cranial vena cava (less commonly the caudal vena cava) and right atrium. Right pulmonary veins may be directed at the right atrium through the defect. May be associated with anomalous pulmonary venous connections of some or all pulmonary veins.
- Isolated ASDs typically shunt left-to-right. Magnitude of flow dependent on size (ostium) of defect, relative systemic and pulmonary resistance, and relative compliance of the ventricles. Small defects allowing atria to maintain normal differential pressure are termed restrictive. Large defects more likely to cause significant left-to-right shunting and volume overload to the right heart and pulmonary vessels. Development of secondary pulmonary hypertension can lead to reverse (right-to-left) shunting, termed Eisenmenger's physiology. ASDs may occur with concurrent defects; conditions increasing right atrial pressure (i.e., pulmonic stenosis, tricuspid valve dysplasia, tricuspid valve stenosis) can also cause balanced or reverse shunting.

SIGNALMENT

- Dog and cat
- Various breeds affected; higher prevalence in boxer and standard poodle
- No sex predisposition

SIGNS

General Comments

- Most commonly asymptomatic (73.7% in one study).
- Severe cases may present with signs of CHF.

- Signs related to generalized cyanosis may occur with right-to-left shunting.

Historical Findings

Clinical signs related to concurrent heart disease or cyanosis; exercise intolerance, syncope, cough, and dyspnea.

Physical Examination Findings

- Soft systolic murmur over the pulmonic valve due to relative pulmonic stenosis (increased blood flow across a normal pulmonic valve).
- Rarely a diastolic murmur over the tricuspid valve due to relative tricuspid stenosis.
- Split S2 (fixed) due to delayed closure of the pulmonic valve.
- Cyanosis with right-to-left shunting.
- Ascites and jugular vein distension with right heart failure.



DIAGNOSIS

CBC/BIOCHEMISTRY/URINALYSIS

- Typically normal.
- Polycythemia in some patients with right-to-left shunting.

IMAGING

Radiographic Findings

- None with small defects.
- Right-sided heart enlargement and pulmonary overcirculation with significant shunting.

Echocardiographic Findings

- Right atrial and/or right ventricular dilation
- Septal dropout (not artifactual septal dropout in the region of the fossa ovalis)
- Shunting across ASD by color-flow or spectral Doppler
- Increased pulmonic flow velocity
- Dilation of the pulmonary trunk

OTHER

Electrocardiography

- Usually normal.
- Right atrial and ventricular enlargement (tall P wave, right axis deviation, deep S waves in lead II).
- Arrhythmias and intraventricular conduction disturbances possible.



TREATMENT

GENERAL

- Long-term prognosis for small ASDs is good; treatment is not typically required.
- Large ASDs with hemodynamically significant shunting and right-sided enlargement warrant closure.

MEDICAL THERAPY

- Standard treatment of CHF (furosemide, pimobendan, ACE inhibitor).

- Treatment of polycythemia (right-to-left shunting) if clinically indicated.

SURGICAL THERAPY

- Open heart surgery under cardiopulmonary bypass- direct surgical closure using patch graft.

- Pulmonary artery banding as palliative measure to limit left-to-right shunting.

CATHETER-BASED THERAPY

- Amplatzer® atrial septal occluder (ASO) device delivered percutaneously through the jugular vein for secundum-type defects; requires adequate atrial diameter, ostium diameter, ASD rim tissue, and vessel size for venous access.
- Hybrid procedure involving surgical access to right atrium, transatrial delivery of ASO device, and active device fixation under inflow occlusion reported.



FOLLOW-UP

PATIENT MONITORING

Recheck when decompensation or other clinical signs develop.

EXPECTED COURSE AND PROGNOSIS

- Dependent on defect size and co-existing abnormalities.
- Small, isolated defects unlikely to cause clinical signs.
- Defects > 12 mm more likely to cause heart failure.



MISCELLANEOUS

ABBREVIATIONS

- ASD = atrial septal defect
- CHF = congestive heart failure

Suggested Reading

Bonagura JD, Lehmkohl LB. Congenital heart disease. In: Fox PR, Sisson D, Moise ND, eds., Textbook of Canine and Feline Cardiology, 2nd ed. Philadelphia: Saunders 1999, pp. 471–535.

Chetboul V, Charles V, Nicolle A, et al. Retrospective study of 156 atrial septal defects in dogs and cats (2001–2005). J Vet Med Assoc 2006, 53(4):179–184.

Gordon SG, Miller MW, Roland RM, et al. Transcatheter atrial septal defect closure with the Amplatzer atrial septal occluder in 13 dogs: short- and mid-term outcome. J Vet Intern Med 2009, 23(5):995–1002.

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BASICS

DEFINITION

ECG rhythm characterized by absence of P waves; condition can be temporary (e.g., associated with hyperkalemia or drug-induced), terminal (e.g., associated with severe hyperkalemia or dying heart), or persistent.

ECG Features

Persistent Atrial Standstill

- P waves absent.
- Heart rate usually slow (< 60 bpm).
- Rhythm regular with supraventricular type QRS complexes.
- Heart rate does not increase with atropine administration.

Hyperkalemic Atrial Standstill

- Heart rate normal or slow.
- Rhythm regular or irregular.
- QRS complexes tend to be wide and become wider as the potassium level rises; with severe hyperkalemia (potassium > 10 mEq/L), the QRS complexes are replaced by a smooth biphasic curve.
- Heart rate may increase slightly with atropine.

PATHOPHYSIOLOGY

Persistent Atrial Standstill

Caused by an atrial muscular dystrophy; skeletal muscle involvement common.

Hyperkalemic Atrial Standstill

Generally occurs with serum potassium levels > 8.5 mEq/L; value influenced by serum sodium and calcium levels and acid-base status. Hyperkalemic patients with atrial standstill have sinus node function, but impulses do not activate atrial myocytes; thus, the associated rhythm is termed a sinoventricular rhythm. Since the sinus node is functional, an irregular rhythm may be due to sinus arrhythmia.

SYSTEMS AFFECTED

Cardiovascular

GENETICS

None

INCIDENCE/PREVALENCE

Rare rhythm disturbance

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dog and cat

Breed Predilections

Persistent atrial standstill—most common in English Springer spaniels; other breeds occasionally affected.

Mean Age and Range

Most animals with persistent atrial standstill are young; animals with hypoadrenocorticism are usually young to middle-aged.

Predominant Sex

Hypoadrenocorticism more common in females (69%).

SIGNS

Historical Findings

- Vary with underlying cause.
- Lethargy common; syncope may occur.
- Patients with persistent atrial standstill may show signs of congestive heart failure.

Physical Examination Findings

- Vary with underlying cause.
- Bradycardia common.
- Patients with persistent atrial standstill may have skeletal muscle wasting of the antebrachium and scapula.

CAUSES

- Hyperkalemia.
- Atrial disease, often associated with atrial distension (e.g., cats with cardiomyopathy).
- Atrial myopathy (persistent atrial standstill).

RISK FACTORS

- Hyperkalemic atrial standstill
- Hypoadrenocorticism
- Conditions leading to obstruction or rupture of the urinary tract
- Oliguric or anuric renal failure



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Slow atrial fibrillation
- Sinus bradycardia with small P waves lost in the baseline

CBC/BIOCHEMISTRY/URINALYSIS

Persistent Atrial Standstill

Normal

Hyperkalemic Atrial Standstill

- Hyperkalemia.
- Hyponatremia and sodium:potassium ratio < 27 if atrial standstill secondary to hypoadrenocorticism.
- Azotemia and hyperphosphatemia with hypoadrenocorticism, renal failure, and rupture or obstruction of the urinary tract.

OTHER LABORATORY TESTS

ACTH stimulation test if hypoadrenocorticism suspected

IMAGING

Echocardiogram and electromyography if persistent atrial standstill suspected—cardiomegaly and depressed contractility may be seen.

DIAGNOSTIC PROCEDURES

Skeletal muscle biopsy in animals with persistent atrial standstill.

PATHOLOGIC FINDINGS

Persistent Atrial Standstill

- Greatly enlarged and paper-thin atria; usually biatrial involvement, although one case of only left atrial involvement was reported.
- Severe scapular and brachial muscle wasting in some dogs.
- Marked fibrosis, fibroelastosis, chronic mononuclear cell inflammation, and steatosis throughout the atria and interatrial septum.



TREATMENT

APPROPRIATE HEALTH CARE

Persistent Atrial Standstill

Not life-threatening condition; animal can be treated as an outpatient.

Hyperkalemic Atrial Standstill

Potentially life-threatening; often requires aggressive treatment.

NURSING CARE

Aggressive fluid therapy with 0.9% saline often required to correct hypovolemia and lower serum potassium levels (see Hyperkalemia) in patients with hyperkalemic atrial standstill.

ACTIVITY

Restrict activity in patients with persistent atrial standstill and signs of CHF or syncope.

DIET

N/A

CLIENT EDUCATION

Persistent Atrial Standstill

Clinical signs generally improve after pacemaker implantation; signs of CHF may develop, and weakness and lethargy may persist even after heart rate and rhythm are corrected with the pacemaker.

SURGICAL CONSIDERATIONS

Persistent Atrial Standstill

Implant permanent ventricular pacemaker to regulate rate and rhythm.

Hyperkalemic Atrial Standstill

Hyperkalemia secondary to urinary tract obstruction or rupture may require surgery.



MEDICATIONS

DRUG(S) OF CHOICE

Persistent Atrial Standstill

Treat with diuretics and ACE inhibitor (e.g., enalapril or benazepril) if CHF develops.

Hyperkalemic Atrial Standstill

- Treat the underlying cause (e.g., oliguric renal failure, hypoadrenocorticism).
- Aggressive fluid therapy with 0.9% saline and possibly sodium bicarbonate or insulin

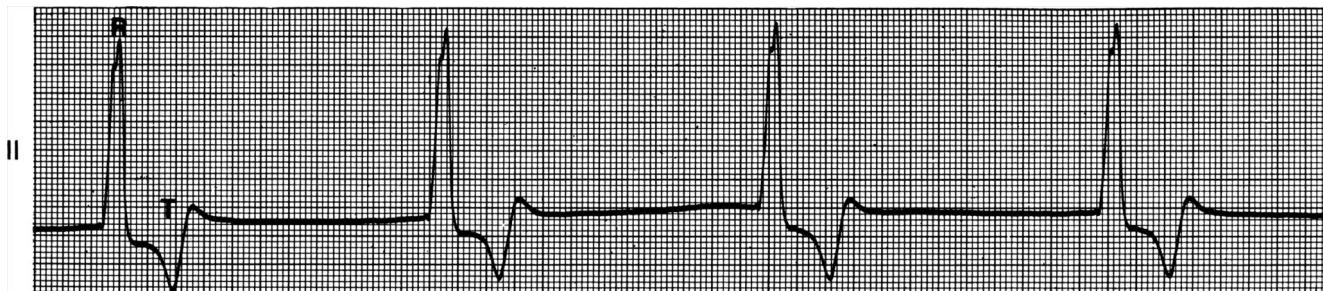


Figure 1.

Atrial stand still in a dog with a potassium of 9 mEq/L. Note the absence of P waves and wide QRS complexes.

with dextrose as discussed under Hyperkalemia.

- Calcium gluconate—counters the cardiac effects of hyperkalemia; can be used in life-threatening situations to reestablish a sinus rhythm while instituting treatment to lower potassium concentration.

CONTRAINDICATIONS

Avoid potassium-containing fluids or medications that increase potassium concentration in hyperkalemic patients.

PRECAUTIONS

Diuretics lower preload and may worsen weakness in dogs with persistent atrial standstill and CHF unless a pacemaker has been implanted.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Monitor ECG during treatment of hyperkalemia and periodically in animals with a permanent ventricular pacemaker.
- Monitor electrolytes in patients with hyperkalemic atrial standstill.
- Monitor patients with persistent atrial standstill for signs of CHF.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

CHF in patients with persistent atrial standstill

EXPECTED COURSE AND PROGNOSIS

Persistent Atrial Standstill

Clinical signs generally improve after pacemaker implantation. Signs of CHF may develop, and weakness and lethargy persist even after heart rate and rhythm are corrected with the pacemaker. There may be persistence of signs related to muscular dystrophy.

Hyperkalemic Atrial Standstill

Long-term prognosis is excellent if underlying cause can be corrected and hyperkalemia reversed.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Diseases causing hyperkalemia (e.g., hypoadrenocorticism, urethral obstruction or urinary tract tear, acidosis, and drugs).

AGE-RELATED FACTORS

Persistent atrial standstill—usually diagnosed in young animals; hypoadrenocorticism—usually diagnosed in young to middle-aged animals.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYS

Silent atrial

SEE ALSO

- Digoxin Toxicity
- Hyperkalemia
- Hypoadrenocorticism (Addison's Disease)
- Urinary Tract Obstruction

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- ACTH = adrenocorticotropic hormone
- CHF = congestive heart failure
- ECG = electrocardiogram

Suggested Reading

Kittleson MD. Electrocardiography. In: Kittleson MD, Kienle RD, eds., Small Animal Cardiovascular Medicine. St. Louis, MO: Mosby, 1998, pp. 72–94.

Kraus MS, Gelzer ARM, Moise S. Treatment of cardiac arrhythmias and conduction disturbances. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., Manual of Canine and Feline Cardiology, 5th ed. St. Louis, MO: Saunders Elsevier, 2015 (in press).

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Client Education Handout
available online



BASICS

DEFINITION

• Endocardial splitting is a linear defect limited to the endocardial layer of the atrium (typically the left atrium) resulting from distension of the atrial wall beyond its elastic limits. • An atrial tear may result if the split extends through the myocardium and epicardium, resulting in a full thickness defect in the atrial wall and hemorrhage into the pericardial space.

PATHOPHYSIOLOGY

• Endocardial splitting typically results from increased left atrial volume and pressure secondary to severe mitral regurgitation and mechanical trauma from the regurgitant jet; primary endocardial degeneration may also play a role. • If the split is incomplete, fibrin may seal the defect temporarily; this either heals as a linear depression in the endocardial surface or subsequently extends through the myocardium resulting in a complete left atrial tear. • A left atrial tear results in peracute bleeding into the pericardial sac and severe, life-threatening hemodynamic compromise secondary to acute cardiac tamponade. • If a tear occurs in the interatrial septum, an acquired atrial septal defect may form. • Tearing of either atrium may also rarely occur secondary to blunt trauma, or iatrogenically during pericardiocentesis.

SYSTEMS AFFECTED

- Cardiovascular • Respiratory

INCIDENCE/PREVALENCE

Atrial tear is a rare cause of hemorrhagic pericardial effusion in the dog encompassing approximately 2% of pericardial effusion cases.

SIGNALMENT

Species

Dog; uncommon in cat

Breed Predilections

- Same as endocardiosis breeds; more common in small- to medium-sized dogs.
- Poodle, dachshund, cocker spaniel, and Shetland sheepdog may be overrepresented.
- If trauma is the cause, any breed may be represented.

Mean Age and Range

Middle-aged to older dogs are predisposed.

SIGNS

Historical Findings

- Acute onset of weakness and collapse that may progress quickly to respiratory or cardiopulmonary arrest; episode may follow a period of increased excitement or activity.
- History of long-standing cardiac disease with signs of CHF described in most patients.
- Acute worsening of cough or dyspnea are

commonly observed. • Possible history of blunt trauma.

Physical Examination Findings

- Collapse. • Tachycardia. • Weak arterial pulses or pulsus paradoxus. • Pale, muddy, or ashen mucous membranes; prolonged CRT.
- Other signs of significant cardiac disease (e.g., murmur, gallop rhythm, arrhythmia, cough, or dyspnea) are typically present.
- Signs of right heart failure (e.g., ascites and jugular venous distension) may also be seen in some patients. • Heart sounds may be muffled, or if a murmur was heard before the atrial wall tear occurred, it may be reduced in intensity.

CAUSES

- Mitral valve endocardiosis • Chordae tendinae rupture • Cardiac neoplasia, most commonly hemangiosarcoma • Chest trauma • Cardiac catheterization

RISK FACTORS

- Severe mitral regurgitation, left atrial enlargement. • May be precipitated by an episode of excitement, stress, or activity.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of acute cardiovascular collapse or syncope • Pericardial effusion from other causes (e.g., neoplastic and idiopathic)
- Heart failure • Severe cardiac arrhythmias

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia is uncommon unless pericardiocentesis is performed since volume of blood loss is relatively small.
- Hypoproteinemia is common. • Elevations in serum lactate, metabolic acidosis.
- Increased ALT, AST in some patients.
- Prerenal azotemia; hyponatremia or other electrolyte derangements may be seen.

OTHER LABORATORY TESTS

NT-proBNP and TnI levels may be elevated.

IMAGING

Radiographic Findings

- Moderate to severe left atrial enlargement is expected. • Comparison with previous thoracic radiographs may show rounding and further enlargement of cardiac silhouette; characteristic globoid cardiac silhouette associated with pericardial effusion may be more obvious on the DV view. • Interstitial to alveolar pulmonary infiltrates if concomitant left-sided CHF is present. • Small volume pleural effusion, ascites, hepatomegaly, and large caudal vena cava may be seen due to right-sided CHF.

Echocardiographic Findings

- Pericardial effusion is evidenced by a hypoechoic space between the heart and pericardial sac; the volume of pericardial

effusion identified may be relatively small as the pericardium remains inelastic due to the acute nature of the bleed; a characteristic linear, hyperechoic blood clot may be seen within the pericardial sac. • The actual tear is often not identified though an associated thrombus is occasionally visualized within the left atrium. • Cardiac tamponade is evidenced by diastolic collapse of the right atrium and/or ventricle. • Signs of advanced mitral endocardiosis, including mitral valve thickening and prolapse, moderate to severe mitral regurgitation, moderate to severe left atrial enlargement and often one or more ruptured chordae tendinae.

DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

- Sinus tachycardia • Atrial or ventricular arrhythmias • Possible dampened QRS complexes • Electrical alternans • ST-segment abnormalities • Possible left ventricular or left atrial enlargement pattern

PATHOLOGIC FINDINGS

- Endocardial splitting is noted grossly as a pale linear depression in the atrial endocardium. • Atrial wall tears appear as full thickness defects extending through the atrial endocardium, myocardium and epicardium; an associated thrombus may or may not be present. The caudolateral aspect of the left atrium is most commonly affected, with many tears occurring at the atrio-auricular junction.
- Hemorrhagic pericardial effusion or pericardial thrombus are seen with acute tears.
- Mitral endocardiosis characterized by thickened mitral valve leaflets with rolled edges; chordae tendinae rupture may be seen; atrial jet lesions are possible. • Cardiomegaly with severe left atrial enlargement expected.



TREATMENT

APPROPRIATE HEALTH CARE

- If a left atrial tear is strongly suspected, perform pericardiocentesis only if the effusion is causing symptomatic, life-threatening cardiac tamponade, since further hemorrhage into the pericardial sac or exsanguination may occur once pericardial fluid is removed. • If pericardiocentesis is performed, remove only enough fluid to improve clinical signs.
- Pericardiocentesis will likely be difficult given the small volume of effusion typically identified, severe cardiac enlargement, and the small size of most dogs with left atrial rupture; ultrasound guidance and continuous ECG monitoring are highly recommended. • Best practices for management of left atrial tears have not been clearly established; however, aggressive medical management to lower left atrial pressure using afterload and preload reducers is recommended based on the author's clinical experience. • If a fibrin clot

ATRIAL WALL TEAR

(CONTINUED)

forms over the defect, the patient may stabilize and recover.

NURSING CARE

- Administer oxygen to dogs with dyspnea or signs of hemodynamic instability.
- Administer IV fluids or blood products only if evidence of hypovolemia is present; most dogs remain in a volume overloaded state and further intravascular volume expansion will increase left atrial pressure and potentially worsen tamponade.

ACTIVITY

Strict cage rest in the acute period should be followed by chronic exercise restriction.

CLIENT EDUCATION

Left atrial tear typically accompanies advanced cardiac disease and chronic medical therapy will be necessary; though the prognosis is guarded for surviving the acute event some dogs with left atrial tear have lived more than a year after the incident.

SURGICAL CONSIDERATIONS

- Exploratory thoracotomy may be considered if hemorrhage persists or recurs but should be undertaken cautiously given the advanced state of cardiac disease typically present.
- Transcatheter septal puncture and balloon tear of the fossa ovalis may also be considered to decompress the left atrium; however, right heart failure or hypoxemia due to right-to-left shunting may result.



MEDICATIONS

DRUG(S) OF CHOICE

- Atrial tears occur secondary to elevated left atrial pressure; thus medical therapy should be focused on lowering of left atrial pressures in order to reduce continued hemorrhage into the pericardial space and permit fibrin clot formation at the site of the tear; this may be accomplished with preload (e.g., diuretics, nitroglycerin paste) and/or afterload reducers (arterial vasodilators).
- Preload and afterload reduction must be undertaken cautiously to avoid worsening of hemodynamic compromise.
- Afterload reduction may be achieved by conservative doses of sodium nitroprusside; a low starting CRI dose of 0.5–1 µg/kg/min is recommended to achieve a decrease in LA pressure without precipitating significant hypotension; blood pressure monitoring is recommended and the dose may be uptitrated as necessary every 15–30 minutes up to a maximum of 10 µg/kg/min to achieve an improvement in clinical signs and/or a reduction in blood pressure of 10–15 mmHg.
- Alternatively, amlodipine may be started at 0.1–0.2 mg/kg PO q24h; chronic amlodipine therapy may be implemented in normotensive

or hypertensive animals to reduce regurgitant fraction and lower left atrial pressure.

- Diuretics should be used cautiously if needed to treat dyspnea associated with concomitant congestive heart failure (e.g., 1–2 mg/kg of furosemide IV as needed); signs of left-sided congestive heart failure may worsen as cardiac tamponade resolves due to augmentation of preload; more aggressive diuretic therapy may then be required.
- Pimobendan (0.2–0.3 mg/kg PO q12h) may result in a further reduction in left atrial pressure though studies have not specifically examined its use in the setting of left atrial rupture and the author typically delays starting inotropes for several days so as not to disrupt stability of the fibrin clot.
- Once the patient is stable, ACE inhibitors (e.g., enalapril 0.5 mg/kg q12–24h) should be implemented for chronic management of accompanying heart failure.

PRECAUTIONS

- Aggressive fluid therapy is not warranted in these patients; further volume expansion may increase left atrial pressure, worsen cardiac tamponade, and contribute to hemodynamic compromise.
- Best practices for management of left atrial tear have not been clearly established; the choice of whether to perform pericardiocentesis, and whether to administer preload and/or afterload reducers should be made based on assessment of the volume status, blood pressure and clinical stability of the patient.

POSSIBLE INTERACTIONS

Sodium nitroprusside should never be administered concurrently with phosphodiesterase-V inhibitors (e.g., sildenafil or tadalafil) due to the potential for life-threatening systemic hypotension.



FOLLOW-UP

PATIENT MONITORING

- Recommend close monitoring of respiratory rate and effort, mucous membrane color and CRT, pulse quality, and heart rate; blood pressure monitoring is recommended if arterial vasodilators are implemented.
- Follow-up examination with echocardiography helps determine resolution of pericardial effusion and resorption of an atrial or pericardial clot.
- Close follow-up every 2–3 months thereafter is recommended for repeat pericardial fluid checks and medication adjustments as deemed appropriate.

PREVENTION/AVOIDANCE

Recommend avoidance of strenuous physical activity and excitement.

POSSIBLE COMPLICATIONS

- Even if the tear seals, the patient is prone to further tears because of underlying cardiac disease.
- Most dogs have or will develop concurrent CHF.

EXPECTED COURSE AND PROGNOSIS

Prognosis for survival is guarded to poor; however, some animals can do well for several months or longer with close monitoring, exercise restriction and optimal medical management of cardiac disease.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Chronic valvular disease
- CHF
- Mainstem bronchial compression

SYNOMYMS

- Atrial rupture
- Atrial splitting

SEE ALSO

- Atrial Septal Defect
- Atrioventricular Valve (Myxomatous) Disease
- Congestive Heart Failure
- Pericardial Effusion
- Syncope

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- CHF = Congestive heart failure

INTERNET RESOURCES

James Buchanan Cardiology Library:
<http://www.vin.com/MEMBERS/CMS/Misc/Default.aspx?id=7703>.

Suggested Reading

Peddle GD, Buchanan JW. Acquired atrial septal defects secondary to rupture of the atrial septum in dogs with degenerative mitral valve disease. J Vet Cardiol 2010, 12:129–134.

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Sadanaga KK, MacDonald MJ, Buchanan JW. Echocardiography and surgery in a dog with left atrial rupture and hemopericardium. J Vet Intern Med 1990, 4:216–221.

Author Suzanne M. Cunningham
Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

atrioventricular block, complete (third degree)

A



BASICS

DEFINITION

- All atrial impulses are blocked at the AV junction; atria and ventricles beat independently. A secondary “escape” pacemaker site (junctional or ventricular) stimulates the ventricles.
- Atrial rate normal.
- Idioventricular escape rhythm slow.

ECG Features

- Ventricular rate slower than the atrial rate (more P waves than QRS complexes)—ventricular escape rhythm (idioventricular) usually < 40 bpm; junctional escape rhythm (idiojunctional) 40–60 bpm in dogs and 60–100 bpm in cats.
- P waves—usually normal configuration (Figure 1).
- QRS complex—wide and bizarre when pacemaker located in the ventricle, or in the lower AV junction in a patient with bundle branch block; normal when escape pacemaker in the lower AV junction (above the bifurcation of the bundle of His) in a patient without bundle branch block.
- No conduction between the atria and the ventricles; P waves have no constant relationship with QRS complexes; P-P and R-R intervals relatively constant (except for a sinus arrhythmia).

PATHOPHYSIOLOGY

Slow ventricular escape rhythms (< 40 bpm) result in low cardiac output and eventual heart failure, often when animal is excited or exercised, since demand for greater cardiac output is not satisfied. As the heart fails, signs increase with mild activity.

SYSTEMS AFFECTED

Cardiovascular

GENETICS

Can be an isolated congenital defect

INCIDENCE/PREVALENCE

Not documented

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT**Species**

Dog and cat

Breed Predilections

- Cocker spaniel—can have idiopathic fibrosis.
- Pug and Doberman pinscher—can have associated sudden death, AV conduction defects, and bundle of His lesions.

Mean Age and Range

Geriatric animals, except congenital heart disease patients. Median age for cats—14 years.

Predominant Sex

Intact female dogs

SIGNS**Historical Findings**

- Exercise intolerance
- Weakness or syncope
- Occasionally, CHF

Physical Examination Findings

- Bradycardia
- Variable third and fourth heart sounds
- Variation in intensity of the first heart sounds
- Signs of CHF
- Intermittent “cannon” A waves in jugular venous pulses

CAUSES & RISK FACTORS

Isolated congenital defect

- Idiopathic fibrosis
- Infiltrative cardiomyopathy (amyloidosis or neoplasia)
- Hypertrophic cardiomyopathy in cats
- Digitalis toxicity
- Hyperthyroidism in cats
- Myocarditis
- Endocarditis
- Electrolyte disorder
- Myocardial infarction

- Other congenital heart defects
- Lyme disease
- Chagas disease



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Advanced second-degree AV block
- Atrial standstill
- Accelerated idioventricular rhythm

CBC/BIOCHEMISTRY/URINALYSIS

- Abnormal serum electrolytes (e.g., hyperkalemia, hypokalemia) possible.
- High WBC with left shift in animals with bacterial endocarditis.

OTHER LABORATORY TESTS

- High serum digoxin concentration if AV block is due to digoxin toxicity.
- Lyme titer and accompanying clinical signs if AV block due to Lyme disease.

IMAGING

Echocardiography and Doppler ultrasound to assess cardiac structure and function.

DIAGNOSTIC PROCEDURES

- Electrocardiography
- His bundle electrogram to determine the site of the AV block.
- Long-term (Holter) ambulatory recording if AV block is intermittent.

PATHOLOGIC FINDINGS

Degeneration or fibrosis of the AV node and its bundle branches, associated with endocardial and myocardial fibrosis and organized endomyocarditis.



TREATMENT

APPROPRIATE HEALTH CARE

- Temporary or permanent cardiac pacemaker—only effective treatment in symptomatic patients.

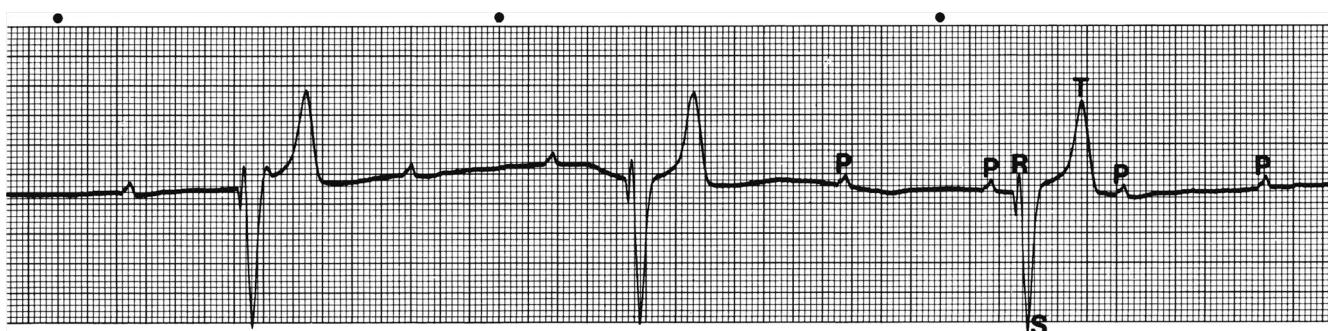


Figure 1.

Complete heart block. The P waves occur at a rate of 120, independent of the ventricular rate of 50. The QRS configuration is a right bundle branch block pattern. The regular rate and stable QRS indicate that the rescuing focus is probably near the AV junction. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Blackwell Publishing, 1992, with permission.)

ATRIOVENTRICULAR BLOCK, COMPLETE (THIRD DEGREE) (CONTINUED)

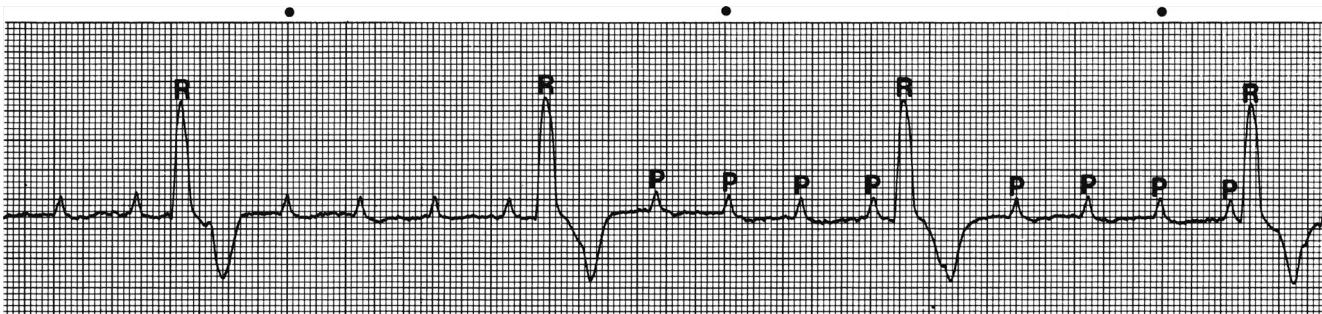


Figure 2.

Complete heart block in a cat. The P waves rate is 240/minute, independent of the ventricular rate of 48/minute. QRS configuration is a left bundle branch block pattern. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Blackwell Publishing, 1992, with permission.)

- Carefully monitor asymptomatic patients without a pacemaker for development of clinical signs.

NURSING CARE

Cage rest prior to pacemaker implantation; when the pulse generator is put into a subcutaneous pocket, a non-constricting bandage is required around the ventral neck or abdomen for 3–5 days to prevent seroma formation or pacemaker movement.

ACTIVITY

Restrict if symptomatic

DIET

No modifications unless required to manage underlying condition (e.g., low-salt diet).

CLIENT EDUCATION

- Temporary or permanent cardiac pacemaker—only effective treatment in symptomatic patients.
- Asymptomatic patients without a pacemaker—must be carefully monitored for development of clinical signs.

SURGICAL CONSIDERATIONS

- Most patients—at high anesthetic cardiopulmonary risk; usually paced preoperatively with a temporary external pacemaker system.
- The small size of cats makes pacemaker implantation more difficult than in dogs.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Treatment with drugs—usually of no value. Traditionally used to treat complete AV block: atropine, isoproterenol, corticosteroids, and dobutamine.
- Intravenous isoproterenol infusion may help increase the rate of the ventricular escape rhythm to stabilize hemodynamics.
- If CHF—diuretic and vasodilator therapy may be needed before pacemaker implantation.

CONTRAINDICATIONS

Avoid digoxin, xylazine, acepromazine, beta blockers (e.g., propranolol and atenolol), and calcium channel blockers (e.g., verapamil and diltiazem); ventricular antiarrhythmic agents are dangerous because they suppress lower escape foci.

PRECAUTIONS

Vasodilators—may cause hypotension in animals with complete AV block; monitor closely if used, especially prior to pacemaker implantation.

**FOLLOW-UP****PATIENT MONITORING**

- Monitor—pacemaker function with serial ECGs.
- Radiographs—following pacemaker implantation, to confirm the position of the lead and generator.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Pulse generators—broad range of clinical life; pacemaker replacement necessary when battery is depleted, pulse generator malfunction occurs, or exit block develops; pacemaker leads can become dislodged and infected.

EXPECTED COURSE AND PROGNOSIS

Poor long-term prognosis if no cardiac pacemaker implanted, especially when the animal has clinical signs. Cats can sometimes survive > 1 year.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

None

ABBREVIATIONS

- AV = atrioventricular
- CHF = congestive heart failure
- ECG = electrocardiogram
- WBC = white blood cell

INTERNET RESOURCES

www.vetgo.com/cardio

Suggested Reading

Bright JM. Pacemaker therapy. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., Manual of Canine and Feline Cardiology, 5th ed. St. Louis, MO: Saunders Elsevier, 2015 (in press). Kellum HB, Stepien RL. Third-degree atrioventricular block in 21 cats (1997–2004). J Vet Intern Med 2006, 20:97–103.

Schrope DP, Kelch WJ. Signalment, clinical signs, and prognostic indicators associated with high-grade second or third-degree atrioventricular block in dogs: 124 cases (January 1, 1997–December 31, 1997). J Am Vet Med Assoc 2006, 228:1710–1717.

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Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

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Client Education Handout
available online

ATROVENTRICULAR BLOCK, FIRST DEGREE



BASICS

DEFINITION

Refers to a delay in conduction that occurs between atrial and ventricular activation.

ECG Features

- Rate and rhythm—usually normal.
- Usually there are regularly occurring normal P waves and QRS complexes (Figures 1 and 2).
- Prolonged, consistent PR intervals—dogs, > 0.13 sec; cats, > 0.09 sec (Figures 1 and 2).

PATHOPHYSIOLOGY

- Virtually never causes clinical signs.
- May become a more severe AV conduction disturbance in some animals.
- Normally the PR interval tends to shorten with rapid heart rates.
- May be the result of intra-atrial conduction delay (prolongation of the PA interval on surface ECG and simultaneous His bundle electrogram) or delay of conduction within the AV node itself (prolongation of the AH interval on His bundle electrogram).

SYSTEMS AFFECTED

Cardiovascular

GENETICS

N/A

INCIDENCE/PREVALENCE

Common

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dog and cat

Breed Predilections

American cocker spaniel, dachshund, brachycephalic dogs, Persian cats

Mean Age and Range

- May occur in young, otherwise healthy dogs as a manifestation of high vagal tone.
- Intra-atrial conduction delay involving the right atrium may be seen with congenital heart disease, especially atrioventricular septal defects.
- May be noted in aged patients with degenerative conduction system disease, particularly cocker spaniels and dachshunds.
- Persian cats of any age with high vagal tone and in cats of any age with hypertrophic cardiomyopathy.

SIGNS

Historical Findings

- Most animals are asymptomatic.
- If drug-induced, may have a history of clinical signs related to drug toxicity—anorexia, vomiting, and diarrhea with digoxin; weakness with calcium channel blockers or β -adrenergic antagonists.

Physical Examination Findings

- Normal—unless also signs of more generalized myocardial disease, drug toxicity, or non-cardiac disease.

CAUSES

- May occur in normal animals.
- Enhanced vagal stimulation resulting from non-cardiac diseases—usually accompanied by sinus arrhythmia, sinus arrest, and/or Mobitz type I second-degree AV block.
- Pharmacologic agents (e.g., digoxin, β -adrenergic antagonists, calcium channel blocking agents, propafenone, amiodarone, α_2 -adrenergic agonists, parasympathomimetic agents [bethanechol, physostigmine, pilocarpine] and severe procainamide or quinidine toxicity).
- Degenerative disease of the conduction system.
- Hypertrophic cardiomyopathy.

- Myocarditis (especially *Trypanosoma cruzi*, *Borrelia burgdorferi*, *Rickettsia rickettsii*).
- Infiltrative diseases (tumors, amyloid).
- Atropine administered intravenously may briefly prolong the PR interval.

RISK FACTORS

Any condition or intervention that raises vagal tone



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

P waves superimposed upon preceding T waves because of first-degree AV block should be differentiated from bifid T waves.

CBC/BIOCHEMISTRY/URINALYSIS

- Serum electrolytes—hypokalemia and hyperkalemia may predispose to AV conduction disturbances.
- Leukocytosis—may be noted with bacterial endocarditis or myocarditis.

OTHER LABORATORY TESTS

- Serum digoxin concentration—may be high.
- *T. cruzi*, *B. burgdorferi*, *R. rickettsii* titers—may be high.
- T_4 —may be high in cats if associated with thyrotoxic myocardial disease.

IMAGING

Echocardiographic examination—may reveal hypertrophic or infiltrative myocardial disorder.

DIAGNOSTIC PROCEDURES

May be needed to identify causes of high vagal tone—upper airway disease, cervical and thoracic masses, gastrointestinal disorders, and high intraocular pressure.

PATHOLOGIC FINDINGS

Variable—depend on underlying cause

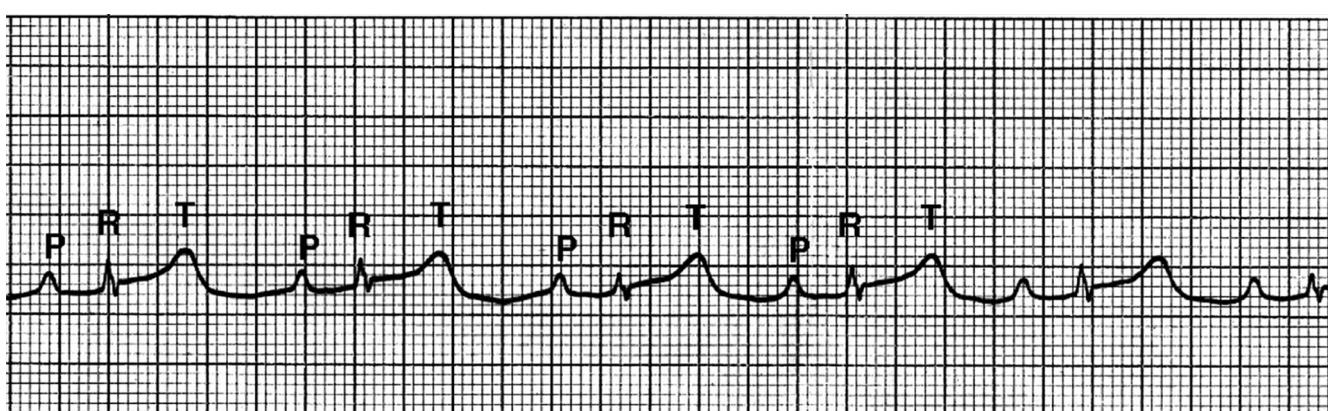


Figure 1.

Lead II ECG rhythm strip recorded from a cat with hypertrophic cardiomyopathy. There is sinus bradycardia (120 bpm) and first-degree atrioventricular conduction block. The PR interval is 0.12 second (paper speed = 50 mm/s).

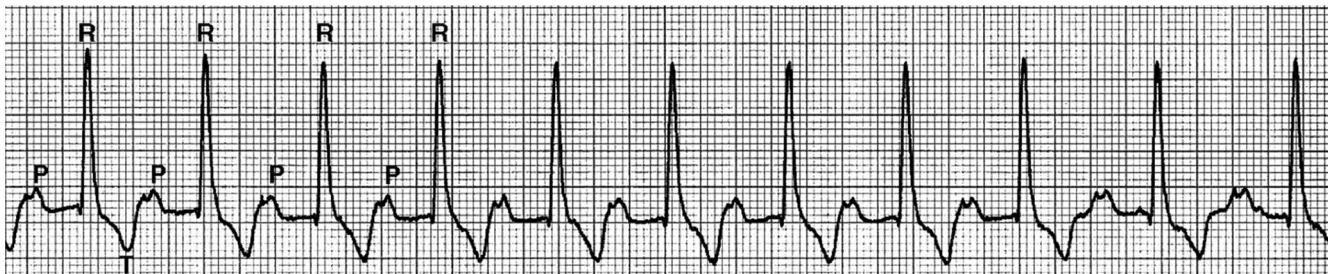


Figure 2.

Lead II ECG rhythm strip recorded from a dog showing sinus tachycardia (175 bpm) and first-degree atrioventricular conduction block. Because the heart rate is rapid, P waves are superimposed on the downslope of the preceding T waves. The PR interval exceeds 0.16 second (paper speed = 50 mm/s).



TREATMENT

APPROPRIATE HEALTH CARE

- Remove or treat underlying cause(s).
- Hospitalization may be necessary to manage the underlying cause (e.g., cardiomyopathy, gastrointestinal disease, airway disease).

NURSING CARE

N/A

ACTIVITY

Unrestricted; unless restriction required for an underlying condition.

DIET

No modifications or restrictions unless required to manage an underlying condition.

CLIENT EDUCATION

Generally unnecessary

SURGICAL CONSIDERATIONS

None unless required to manage an underlying condition.



MEDICATIONS

DRUG(S) OF CHOICE

Medications used only if needed to manage an underlying condition.

CONTRAINDICATIONS

- Avoid hypokalemia—increases sensitivity to vagal tone; may potentiate AV conduction delay.
- Avoid drugs likely to impair impulse conduction further (calcium channel blocking agents, β -adrenergic antagonists, α_2 -adrenergic agonists, amiodarone, propafenone).

PRECAUTIONS

Drugs with vagomimetic action (e.g., digoxin, bethanechol, physostigmine, pilocarpine) may potentiate first-degree block.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

Except in healthy young animals, monitor ECG to detect any progression in conduction disturbance.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

- Depends on underlying cause.
- Prognosis usually excellent if no significant underlying disease is present.



MISCELLANEOUS

ASSOCIATED CONDITIONS

None

AGE-RELATED FACTORS

PR interval—tends to lengthen with advancing age

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Atrioventricular Block, Complete (Third Degree)
- Atrioventricular Block, Second Degree—Mobitz I
- Atrioventricular Block, Second Degree—Mobitz II

ABBREVIATIONS

- AV = atrioventricular
- ECG = electrocardiogram
- T_4 = thyroxine

Suggested Reading

Kittleson MD. Electrocardiography. In: Kittleson MD, Kienle RD, eds., Small Animal Cardiovascular Medicine. St. Louis, MO: Mosby, 1998, pp. 72–94.

Miller MS, Tilley LP, Smith FWK, Fox PR. Electrocardiography. In: Fox PR, Sisson D, Moise NS, eds., Textbook of Canine and Feline Cardiology. Philadelphia: Saunders, 1999, pp. 67–106.

Tilley LP, Smith FWK, Jr. Electrocardiography. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., Manual of Canine and Feline Cardiology, 5th ed. St. Louis, MO: Saunders Elsevier, 2015 (in press).

Authors Francis W.K. Smith, Jr and Larry P. Tilley

Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.



Client Education Handout
available online

ATRIOVENTRICULAR BLOCK, SECOND DEGREE—MOBITZ I

A

**BASICS****DEFINITION**

Second-degree AV block refers to failure of one or more P waves but not all P waves to be conducted. Mobitz Type I second-degree AV block occurs when AV transmission is progressively delayed prior to a blocked P wave.

ECG Features

- PR interval—becomes progressively longer prior to the appearance of a P wave that is not followed by a QRS complex (Figure 1).
- Heart rate and QRS morphology—usually normal.
- Often cyclical.

PATHOPHYSIOLOGY

- Frequently associated with high resting vagal tone and sinus arrhythmia in dogs.
- Generally not pathologic or hemodynamically significant.
- This type of AV block usually results from conduction delay within the AV node itself (rather than delay in other segments of the AV conducting system) and is characterized by a progressive increase in AH interval with eventual block between the A and H deflections on a His bundle recording.

SYSTEMS AFFECTED

Cardiovascular

GENETICS

N/A

INCIDENCE/PREVALENCE

Radiotelemetry studies have shown that this arrhythmia occurs in 64% of healthy adult dogs and 100% of healthy puppies 8–12 weeks of age.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT**Species**

Dog; uncommon in cat

Breed Predilections

N/A

Mean Age and Range

- Usually occurs in young, otherwise healthy dogs as a manifestation of high vagal tone.
- Occasionally occurs in older dogs with abnormally strong vagal tone.
- Rarely noted in old dogs with degenerative conduction system disease.

SIGNS**Historical Findings**

- Most animals are asymptomatic.
- If drug-induced, owner may report signs of drug toxicity—anorexia, vomiting, and diarrhea with digoxin; weakness with calcium channel blockers or β -adrenergic antagonists.
- If heart rate is abnormally slow, syncope or weakness may occur.

Physical Examination Findings

- May be normal unless signs of more-generalized myocardial disease or non-cardiac disease are present.
- Intermittent pauses in the cardiac rhythm.
- First heart sound may become progressively softer, followed by a pause.
- An audible S4 may be heard unaccompanied by S1 and S2 when block occurs.

CAUSES

- Occasionally noted in normal animals.
- Enhanced vagal stimulation resulting from non-cardiac diseases—usually accompanied by sinus arrhythmia, sinus arrest.
- Pharmacologic agents—digoxin, β -adrenergic antagonists, calcium channel blocking agents, propafenone, amiodarone, α_2 -adrenergic agonists, opioids.

RISK FACTORS

Any condition or intervention that enhances vagal tone.

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- Non-conducted P waves from supraventricular premature impulses or supraventricular tachycardias should be distinguished from second-degree AV block.

- Type II second-degree AV block (no variation in PR intervals).

CBC/BIOCHEMISTRY/URINALYSIS

Hypokalemia may predispose to AV conduction disturbances

OTHER LABORATORY TESTS

Serum digoxin concentration—may be high

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- May be necessary to identify specific causes of enhanced vagal tone (e.g., upper airway disease, cervical and thoracic masses, gastrointestinal disorders, and high intraocular pressure).
- Atropine response test—administer 0.04 mg/kg atropine IM and repeat ECG in 20–30 minutes; may be used to determine whether AV block is due to vagal tone; resolution of AV block with atropine supports vagal cause.
- Electrophysiologic studies are generally unnecessary but will confirm this type of second-degree AV block if surface ECG is equivocal.

PATHOLOGIC FINDINGS

Generally, no gross or histopathologic findings

**TREATMENT****APPROPRIATE HEALTH CARE**

- Treatment usually unnecessary
- Treat or remove underlying cause(s)

NURSING CARE

Generally unnecessary

ACTIVITY

Unrestricted

DIET

Modifications or restrictions only to manage an underlying condition.

CLIENT EDUCATION

Explain that any treatment is directed toward reversing or eliminating an underlying cause.

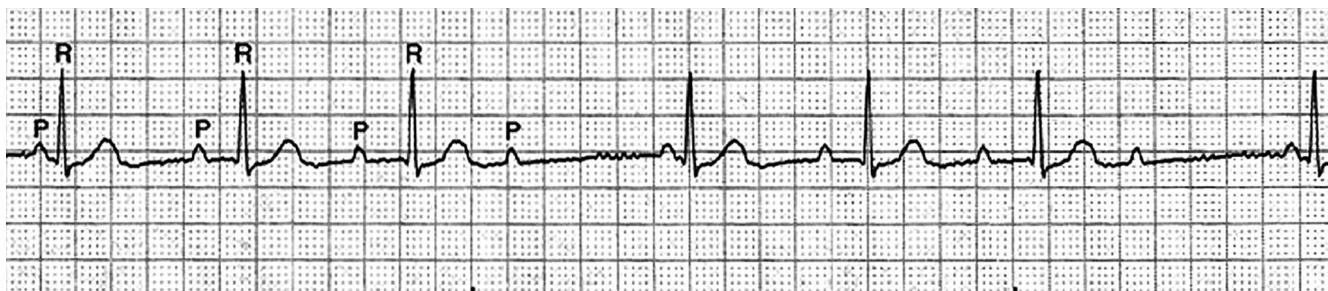


Figure 1.

Lead II ECG strip recorded from a dog with Mobitz type I, second-degree AV block. The PR intervals become progressively longer with the longest PR intervals preceding non-conducted P waves (typical Wenckebach phenomenon) (paper speed = 50 mm/s).

atrioventricular block, second degree—Mobitz I (Continued)

SURGICAL CONSIDERATIONS

N/A except to manage an underlying condition

**MEDICATIONS****DRUG(S)**

Only as needed to manage an underlying condition

CONTRAINDICATIONS

Drugs with vagomimetic action (e.g., digoxin, bethanechol, physostigmine, pilocarpine) may potentiate block.

PRECAUTIONS

Hypokalemia increases the sensitivity to vagal tone and may potentiate AV conduction delay.

POSSIBLE INTERACTIONS

N/A

**FOLLOW-UP****PATIENT MONITORING**

Typically not necessary

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

N/A

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Wenckebach periodicity
- Wenckebach phenomenon

SEE ALSO

- Atrioventricular Block, Complete (Third Degree)
- Atrioventricular Block, First Degree
- Atrioventricular Block, Second Degree—Mobitz II

ABBREVIATIONS

- AV = atrioventricular
- ECG = electrocardiogram

Suggested Reading

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Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

Acknowledgment The authors and editors acknowledge the prior contribution of Janice McIntosh Bright.



Client Education Handout available online

atrioventricular block, second degree—Mobitz II

A

**BASICS****DEFINITION**

Second-degree AV block refers to failure of one or more P waves but not all P waves to be conducted. Mobitz Type II second-degree AV block occurs when one or more P waves are blocked without a preceding progressive delay in AV transmission.

ECG Features

- One or more P waves not followed by a QRS complex; PR interval is constant but may be either normal or consistently prolonged (Figure 1).
- Ventricular rate—usually slow.
- Fixed ratio of P waves to QRS complexes may occur (e.g., 2:1, 3:1, 4:1 AV block).
- High-grade (advanced) second-degree AV block is characterized by two or more consecutive blocked P waves.
- In second-degree AV block with a 2:1 conduction ratio or higher, it is impossible to observe prolongation of the PR interval before the block, so a designation of Mobitz is not appropriate.
- QRS complexes may appear normal but may also be wide or have an abnormal morphology due to aberrant intraventricular conduction or to ventricular enlargement.
- Abnormally wide QRS complexes may indicate serious, extensive cardiac disease.

PATHOPHYSIOLOGY

- Rare in healthy animals.
- May be hemodynamically important when ventricular rate is abnormally slow.
- Frequently progresses to complete AV block, particularly when accompanied by wide QRS complexes.
- Typically this type of AV block results from conduction delay within the AV node itself (rather than delay in another segment of the AV conducting system) that is characterized by normal or prolonged AH intervals with intermittent block between A and H deflections on a His bundle electrogram).

SYSTEMS AFFECTED

- Cardiovascular.
- Central nervous or musculoskeletal systems if inadequate cardiac output.

GENETICS

May be heritable in pugs

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT*Species*

Dog and cat

Breed Predilections

American cocker spaniel, pug, dachshund, Airedale terrier, Doberman pinscher.

Mean Age and Range

Generally occurs in older animals

Predominant Sex

N/A

SIGNS*Historical Findings*

- Presenting complaint may be syncope, collapse, weakness, or lethargy.
- Some animals are asymptomatic.
- Animals may show signs of the underlying disease process.

Physical Examination Findings

- \pm weakness.
- Bradycardia common.
- May be intermittent pauses in the cardiac rhythm.
- An S4 may be audible in lieu of the normally expected heart sounds (i.e., S1, S2) when the block occurs.
- If associated with digoxin intoxication, there may be vomiting, anorexia, and diarrhea.
- May be other abnormalities reflecting the underlying etiology.

CAUSES

- Heritable in pugs.
- Enhanced vagal stimulation from non-cardiac diseases.

- Degenerative change within the cardiac conduction system—replacement of AV nodal cells and/or Purkinje fibers by fibrotic and adipose tissue in old cats and dogs.

- Pharmacologic agents (e.g., digoxin, β -adrenergic antagonists, calcium channel blocking agents, propafenone, α_2 -adrenergic agonists, muscarinic cholinergic agonists, or severe procainamide or quinidine toxicity).
- Infiltrative myocardial disorders (neoplasia, amyloid).

- Endocarditis (particularly involving the aortic valve).
- Myocarditis (viral, bacterial, parasitic, idiopathic).
- Cardiomyopathy (especially in cats).
- Trauma.
- Atropine administered intravenously may cause a brief period of first- or second-degree heart block before increasing the heart rate.

RISK FACTORS

Any condition or intervention that enhances vagal tone

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- High-grade (advanced) form must be distinguished from complete AV block.
- Non-conducted P waves arising from refractoriness of the conduction system during supraventricular tachycardias must be differentiated from pathologic conduction block.

CBC/BIOCHEMISTRY/URINALYSIS

- Serum electrolytes—hypokalemia and hyperkalemia may predispose to AV.
- Conduction disturbances.
- Leukocytosis—may be noted with bacterial endocarditis or myocarditis.
- Electrolyte abnormalities (e.g., severe hypokalemia, hyperkalemia, or hypercalcemia) may predispose to AV block.



Figure 1.

Lead II ECG rhythm strip recorded from a dog with both first- and second-degree atrioventricular block. The second-degree AV block is high grade with both 2:1 and 3:1 block resulting in variation in the RR intervals. The PR interval for the conducted beats is prolonged but constant (0.28 second) (paper speed = 25 mm/s).

ATRIOVENTRICULAR BLOCK, SECOND DEGREE—MOBITZ II (CONTINUED)

OTHER LABORATORY TESTS

- Serum digoxin concentration—may be high.
- High T₄ in cats—if associated with hyperthyroidism.
- High arterial blood pressure—if associated with hypertensive heart disease.
- Positive *Borrelia*, *Rickettsia*, or *Trypanosoma cruzi* titers—if associated with one of these infectious agents.
- Blood cultures may be positive in patients with vegetative endocarditis.

IMAGING

Echocardiographic examination may reveal structural heart disease (e.g., endocarditis, neoplasia, or cardiomyopathy).

DIAGNOSTIC PROCEDURES

- Atropine response test—administer 0.04 mg/kg atropine IM and repeat ECG in 20–30 minutes; may be used to determine whether AV block is due to high vagal tone.
- Electrophysiologic testing is generally unnecessary but can be done to confirm this type of AV block if surface ECG findings are equivocal.

PATHOLOGIC FINDINGS

- Variable—depend on underlying cause.
- Old animals with degenerative change of the conduction system may have focal mineralization of the interventricular septal crest visible grossly; chondroid metaplasia of the central fibrous body and increased fibrous connective tissue in the AV bundle is noted histopathologically.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Treatment—may be unnecessary if heart rate maintains adequate cardiac output.
- Positive dromotropic interventions are indicated for symptomatic patients.
- Treat or remove underlying cause(s).

NURSING CARE

Generally unnecessary

ACTIVITY

Cage rest advised for symptomatic patients.

DIET

Modifications or restrictions only to manage an underlying condition.

CLIENT EDUCATION

- Need to seek and specifically treat underlying cause.
- Pharmacologic agents may not be effective long term.

SURGICAL CONSIDERATIONS

Permanent pacemaker may be required for long-term management of symptomatic patients.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Atropine (0.02–0.04 mg/kg IV, IM) or glycopyrrolate (5–10 µg/kg IV, IM) may be used short term if positive atropine response.
- Chronic anticholinergic therapy (propantheline 0.5–2 mg/kg PO q8–12h or hyoscyamine 3–6 µg/kg q8h)—indicated for symptomatic patients if improved AV conduction with atropine response test.
- Isoproterenol (0.04–0.09 µg/kg/minute IV to effect) or dopamine (2–5 µg/kg/minute IV to effect) may be administered in acute, life-threatening situations to enhance AV conduction and/or accelerate an escape focus.

CONTRAINdications

- Drugs with vagomimetic action (e.g., digoxin, bethanechol, physostigmine, pilocarpine) may potentiate block.
- Avoid drugs likely to impair impulse conduction further or depress a ventricular escape focus (e.g., procainamide, quinidine, lidocaine, calcium channel blocking agents, β-adrenergic blocking agents).

PRECAUTIONS

Hypokalemia—increases sensitivity to vagal tone and may potentiate AV conduction delay.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

Frequent ECG because often progresses to complete (third-degree) AV block.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Prolonged bradycardia may cause secondary congestive heart failure or inadequate renal perfusion.

EXPECTED COURSE AND PROGNOSIS

Variable—depends on cause. If degenerative disease of the cardiac conduction system, often progresses to complete (third-degree) AV block.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

May be noted in cats with primary or secondary myocardial disease.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Atrioventricular Block, Complete (Third Degree)
- Atrioventricular Block, Second Degree—Mobitz I

ABBREVIATIONS

- AV = atrioventricular
- ECG = electrocardiogram
- T₄ = thyroxine

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Client Education Handout
available online

ATRIOVENTRICULAR VALVE DYSPLASIA

A



BASICS

DEFINITION

A congenital malformation of the mitral or tricuspid valve apparatus.

PATHOPHYSIOLOGY

- Atrioventricular valve dysplasia can result in valvular insufficiency, valvular stenosis, or dynamic outflow tract obstruction, depending on the anatomic abnormality. AVVD may occur alone or in association with abnormalities of the ipsilateral outflow tract (e.g., valvular or subvalvular aortic or pulmonic stenosis). It is not uncommon for mitral and tricuspid valve dysplasia to occur together in the same patient.
- Valvular insufficiency results in dilation of the ipsilateral atrium, eccentric hypertrophy of the associated ventricle, and, if sufficiently severe, signs of CHF. Cardiomyopathy of chronic volume overload and elevated atrial pressures are the end result culminating in pulmonary congestion if the mitral valve is affected and systemic congestion if the tricuspid valve is affected.
- Valvular stenosis results in atrial dilation and hypertrophy and, when severe, hypoplasia of the receiving ventricle. Tricuspid valve stenosis results in elevated right atrial pressure and systemic congestion if pressures exceed 15–20 mmHg. Right-to-left shunting may occur if there is an atrial septal defect or patent foramen ovale. Mitral valve stenosis results in elevated pulmonary capillary pressure and pulmonary edema if pressures exceed 25–30 mmHg. Pulmonary hypertension is a common complicating condition in animals with mitral valve stenosis.
- Outflow tract obstruction may develop from defects that translocate the anterior leaflet to a position closer to the interventricular septum. Concentric left ventricular hypertrophy develops in proportion to the severity of the obstruction.

SYSTEMS AFFECTED

- Cardiovascular—inflow obstruction due to valvular stenosis and chronic volume overload from valvular insufficiency result in elevated pulmonary (left AV valve) or systemic (right AV valve) venous pressures. Signs of low cardiac output develop if the lesion is sufficiently severe. Concentric left ventricular hypertrophy develops secondary to dynamic outflow obstruction.
- Respiratory—pulmonary edema may develop secondary to mitral stenosis or mitral valve insufficiency. Pulmonary hypertension is a common complication in animals with mitral stenosis.
- Neurologic—collapse and loss of consciousness, most often during physical exertion, may occur with severe disease due to low cardiac output and hypotension. Collapse in animals with dynamic outflow obstruction is most often due to ventricular arrhythmia.

GENETICS

Tricuspid valve dysplasia is inherited as an autosomal recessive trait in Labrador retrievers. Heritability and pattern of inheritance not established in other breeds.

INCIDENCE/PREVALENCE

These are common congenital cardiac anomalies in cats (17% of reported congenital cardiac defects in one study). Less frequently diagnosed in dogs.

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Tricuspid valve dysplasia—increased risk for Labrador retriever, German shepherd dog, Great Pyrenees, possibly Old English sheepdog. Also common in cat.
- Mitral valve dysplasia—increased risk in bull terrier, Newfoundland, Labrador retriever, Great Dane, golden retriever, Dalmatian, and Siamese cat. Perhaps the most common congenital heart defects of cats. Mitral valve malformations often are noted in cats with hypertrophic cardiomyopathy.

Mean Age and Range

Variable; signs are most often manifest within the first few years after birth.

Predominant Sex

Males are more likely to evidence heart failure.

SIGNS

Historical Findings

- Exercise intolerance is the most common problem in dogs and cats with AV valve dysplasia.
- Abdominal distention, weight loss, and stunting may be observed with severe tricuspid valve dysplasia.
- Labored respiration is common in dogs or cats with mitral valve dysplasia.
- Syncope and collapse if critical mitral or tricuspid valve stenosis, severe outflow tract obstruction, an associated arrhythmia, or heart failure from AV valvular insufficiency.

Physical Examination Findings

Mitral Valve Dysplasia

- A holosystolic murmur is heard over the cardiac apex on the left. With severe disease the murmur is accompanied by a thrill or gallop heart sounds. A soft diastolic murmur may be present in the same location in animals with mitral stenosis but many affected animals have no audible murmur. A systolic ejection murmur that intensifies with exercise or excitement is audible in animals with dynamic outflow tract obstructions.
- Evidence of left heart failure—tachypnea, increased respiratory efforts, pulmonary crackles, and cyanosis in animals with severe defects.

Tricuspid Valve Dysplasia

- A holosystolic murmur is heard over the cardiac apex on the right. With severe disease the murmur is accompanied by a thrill or

gallop heart sounds. Silent tricuspid regurgitation is well documented in cats and is attributable to a large regurgitant orifice and laminar regurgitant flow. Distention and pulsation of the external jugular veins may be evident.

- Evidence of right heart failure—ascites and, more rarely, peripheral edema with severe malformations.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- With the noted exception of the age of onset, congenital AV valvular insufficiency resembles acquired degenerative AV valve insufficiency with respect to historical findings, physical examination abnormalities, and clinical sequelae.
- The right-sided murmur of tricuspid insufficiency is sometimes confused with the right-sided murmur of a ventricular septal defect.
- Ascites caused by silent tricuspid regurgitation or tricuspid valve stenosis is often attributed to pericardial effusion, hepatic disease, or obstruction of the caudal vena cava.
- Dogs and cats with cor triatriatum share many of the clinical features of AV valve stenosis.
- There is no certain way to distinguish mitral valve dysplasia producing outflow tract obstruction and the obstructive form of cardiomyopathy. If the obstruction can be abolished with a beta blocker and left ventricular hypertrophy resolves, it is likely that the primary abnormality was mitral valve dysplasia.

IMAGING

Radiographic Findings

Mitral Valve Dysplasia

- Left atrial and left ventricular enlargement with valvular insufficiency. Isolated left atrial enlargement with valvular stenosis. Mild left atrial enlargement with dynamic outflow obstruction.
- Evidence of left heart failure—distended pulmonary veins, interstitial or alveolar edema in severe cases.

Tricuspid Valve Dysplasia

- Right atrial and right ventricular enlargement with valvular insufficiency. Cardiac silhouette may appear globoid with pronounced enlargement. Isolated right atrial enlargement with valvular stenosis.
- Evidence of right heart failure—dilated caudal vena cava, hepatosplenomegaly, or ascites in severe cases.

Echocardiography

Mitral Valve Dysplasia

- Valvular insufficiency results in left atrial dilation and eccentric hypertrophy of the left ventricle. The papillary muscles are typically flattened and displaced dorsally. Chordae tendineae are often short and thickened. Doppler echocardiography demonstrates a high velocity retrograde systolic transmitral jet

ATRIOVENTRICULAR VALVE DYSPLASIA

(CONTINUED)

and modestly increased transmural inflow velocities. • Mitral stenosis results in left atrial dilation while the left ventricular dimensions are normal or small. The valve leaflets are often thickened, relatively immobile, and often fused. Doppler echocardiography demonstrates a high velocity transmural diastolic jet with a reduced EF slope. There may also be evidence of concurrent mitral insufficiency and/or secondary pulmonary hypertension. Exclude the possibility of cor triatriatum sinister. • Dynamic left ventricular outflow obstruction is characterized by systolic motion of the anterior mitral valve leaflet toward the interventricular septum, increased LV outflow tract velocities, and concentric left ventricular hypertrophy.

Tricuspid Valve Dysplasia

• Valvular insufficiency results in right atrial dilation and eccentric hypertrophy of the right ventricle. The papillary muscles and chordae tendineae may be fused, creating a curtain-like appearance of the tricuspid valve. Doppler echocardiography demonstrates a high velocity retrograde systolic trans-tricuspid jet and modestly increased transtricuspid inflow velocities. • Tricuspid stenosis results in right atrial dilation with normal or small right ventricular dimensions. The valve leaflets do not open completely. Doppler echocardiography demonstrates a high velocity diastolic trans-tricuspid jet with a reduced EF slope. There may be evidence of concurrent tricuspid valve insufficiency and/or right-to-left shunting across a patent foramen ovale or associated atrial septal defect. Exclude the possibility of cor triatriatum dexter.

Cardiac Catheterization

• Indicated only in those cases in which the diagnosis cannot be confirmed by echocardiography or if surgical correction is anticipated. • Mitral dysplasia—hemodynamic measurements should include left ventricular pressures, pulmonary capillary wedge pressure or direct measurement of LA pressure, pulmonary artery pressures, and, in cases of dynamic obstruction, simultaneous recording of aortic and left ventricular pressures with medical provocation. Contrast studies are best accomplished with a left ventricular injection in cases of valvular insufficiency, and direct left atrial injection via trans-septal catheterization in cases of valvular stenosis. • Tricuspid dysplasia—hemodynamic measurements should include right ventricular and right atrial pressures. Contrast studies are best accomplished with a right ventricular injection in cases of valvular insufficiency, and right atrial injection in cases of valvular stenosis.

DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

- Usually reflect pattern of chamber enlargement. • Severe defects may be

accompanied by a variety of arrhythmias, particularly atrial premature beats, supraventricular tachycardia, or atrial fibrillation.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient treatment required for CHF.

CLIENT EDUCATION

Owners should be informed of heritability and advised against breeding.

DIET

Sodium-restricted if overt or pending CHF.

SURGICAL CONSIDERATIONS

- Valve repair or replacement is available in a few centers. • Balloon valvuloplasty is sometimes effective for valvular stenosis.



MEDICATIONS

DRUG(S) OF CHOICE

- Mitral or tricuspid dysplasia with insufficiency—diuretics, angiotensin converting enzyme inhibitors, and pimobendan (0.3 mg/kg q12h) for patients with imminent or overt congestive heart failure. Furosemide (2–4 mg/kg q12–24h), enalapril (0.5 mg/kg q12h) are used to control congestion. Digoxin (2–4 µg/kg q12h) is used to control supraventricular tachyarrhythmias.
- Mitral or tricuspid stenosis—diuretics to control edema. Furosemide (2–4 mg/kg q12–24h) dose adjusted to resolve congestion. Heart rate should be maintained near 150 bpm using digoxin (2–4 µg/kg q12h), a calcium channel blocker such as diltiazem (1–1.5 mg/kg q8h), or a beta-receptor blocking drug, such as atenolol (0.5–1.5 mg/kg q12–24h).
- Dynamic outflow tract obstruction—titrate a beta-receptor blocking drug, such as atenolol (0.5–1.5 mg/kg q12–24h), to abolish or diminish severity of outflow obstruction.

PRECAUTIONS

Standard patient monitoring for cardiac medication side effects (e.g., digitalis toxicity, azotemia).



FOLLOW-UP

PATIENT MONITORING

- Recheck yearly if no signs of heart failure.
- Recheck at a minimum of every 3 months if signs of CHF (thoracic radiographs, ECG, and echocardiography advisable).

PREVENTION/AVOIDANCE

Do not breed affected animals.

POSSIBLE COMPLICATIONS

- Congestive heart failure—left-sided with mitral valve dysplasia; right-sided with tricuspid valve dysplasia. • Collapse or syncope with exercise. • Paroxysmal supraventricular tachycardia or atrial fibrillation with severe disease.

EXPECTED COURSE AND PROGNOSIS

- Depends on severity of underlying defect
- Guarded to poor with serious defects



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Mitral valve dysplasia commonly accompanies valvular or subvalvular aortic stenosis as well as TVD. • Tricuspid valve dysplasia commonly accompanies pulmonic stenosis as well as MVD.

PREGNANCY/FERTILITY/BREEDING

Should be avoided—heritable defect and possibility of causing decompensated or worsening heart failure.

SEE ALSO

- Congestive Heart Failure, Left-Sided
- Congestive Heart Failure, Right-Sided

ABBREVIATIONS

- AV = atrioventricular • AVVD = atrioventricular valve dysplasia • CHF = congestive heart failure • ECG = electrocardiogram • MVD = mitral valve dysplasia • TVD = tricuspid valve dysplasia

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Client Education Handout
available online

ATRIOVENTRICULAR VALVE (MYXOMATOUS) DISEASE



BASICS

DEFINITION

Myxomatous mitral valve disease is characterized by progressive myxomatous degeneration, which refers to a characteristic pathologic weakening and disturbance in the organization of the connective tissue of the AV valve (mitral and tricuspid) apparatus.

PATHOPHYSIOLOGY

- Lesions characterized by pathologic weakening and disorganization of valvular connective tissue, in which the spongiosa component is unusually prominent with accumulation of mucopolysaccharides and glycosaminoglycans.
- The valve leaflets become thickened and elongated with disease progression.
- Degenerative changes in the chordae tendineae lead to thickening and elongation of these structures; thereby contributing to systolic atrial displacement of the valve leaflets (valve prolapse).
- With progression, the valve lesions cause insufficient coaptation of the leaflets during systole, leading to backward regurgitation of blood from the ventricle into the atrium.
- Severity and progression of AV valve regurgitation depends on severity and progression of valve lesions (leaflets and/or tendinous chords).
- Compensatory mechanisms include cardiac dilatation and eccentric hypertrophy, increased force of contraction, increased heart rate, increased pulmonary lymphatic drainage (left-sided AV valve regurgitation), fluid retention, and neurohormonal modulation of cardiovascular function.
- With progression, the valvular regurgitation can no longer be compensated, leading to reduced cardiac output and increased venous pressures (leading to pulmonary edema if left-sided congestive heart failure [CHF] and to ascites if right-sided). With atrial tear, acute cardiac tamponade may result.

SYSTEMS AFFECTED

- Cardiovascular—both AV valves are commonly affected, but semilunar valves less commonly affected.
- Hepatobiliary—passive congestion.
- Renal/Urologic—prerenal azotemia.
- Respiratory—if edema and/or pulmonary hypertension develops.

GENETICS

Etiology currently unknown, but the current leading scientific hypothesis is that a genetically determined dystrophic process initiates the valve degeneration. The age at which the disease develops is inherited as a polygenic threshold trait (i.e., multiple genes influence the trait and a certain threshold has to be reached before the disease develops).

INCIDENCE/PREVALENCE

The most common cardiac disease in dogs. The prevalence is strongly influenced by age. It is uncommon in young individuals but common in old dogs. The prevalence reaches > 90% in some affected dog breeds > 10 years.

SIGNALMENT

Species

Mainly dogs. Extremely rare in cats.

Breed Predilections

Typically small breeds (< 20 kg but may be encountered in larger dogs), such as Cavalier King Charles spaniels, Chihuahuas, Miniature schnauzers, Maltese, Pomeranians, Cocker spaniels, Pekingese, Poodles, and others.

Mean Age and Range

Murmur may be detected from 2 years of age with a peak incidence at 6–8 years in affected breeds, such as Cavalier King Charles spaniels. Onset of CHF from 8–12 years.

Predominant Sex

Males develop the disease at a younger age than females, which means a higher prevalence at a given age in males.

SIGNS

Signs depend on the stage of disease. The descriptions here align with the grading system described in the ACVIM consensus statement on myxomatous mitral valve disease.

Clinically Healthy Patients but Belonging to a Risk Group (ACVIM Stage A)

No abnormal findings

Patients Without Overt Clinical Signs (ACVIM Stage B)

- Systolic click (early stage).
- Systolic murmur best heard over the mitral or tricuspid areas.
- Murmurs may range from being of soft, low intensity to loud holosystolic. With progression, the murmur typically gets louder and radiates more widely.
- Initially patients have no obvious radiographic or echocardiographic changes in cardiac chamber size (ACVIM stage B1). As the disease progresses, evidence of cardiomegaly will be seen (ACVIM stage B2), often before obvious clinical signs of heart failure are recognized.

Patients with Overt Clinical Signs or Stabilized by CHF Therapy (ACVIM stages C and D)

- Usually loud heart murmur.
- Tachycardia and loss of respiratory sinus arrhythmia.
- Arrhythmia and pulse deficit may be present, most commonly supraventricular premature beats or atrial fibrillation.
- Weak femoral pulse, prolonged capillary refill time and pale mucous membranes in case of low output failure.

- Tachypnea/dyspnea/orthopnea in case of decompensated CHF.
- Respiratory crackles/rales in case of decompensated CHF.
- Pink froth, i.e., pulmonary edema may be evident in the nostrils and oropharynx in cases with severe decompensated CHF.
- Ascites if right-sided CHF.
- Diagnostic imaging invariably shows left atrial (LA) and ventricular (LV) dilatation and eccentric hypertrophy, sometimes bilateral enlargement, and evidence of pulmonary congestion/edema.

CAUSES

Primary (inciting) factor unknown, but the disease is influenced by genetic factors in affected breeds.

RISK FACTORS

- Breed
- Sex (males have an earlier onset)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Dilated cardiomyopathy
- Congenital heart disease
- Bacterial endocarditis
- Chronic airway or interstitial lung disease
- Pneumonia
- Pulmonary embolism
- Pulmonary neoplasia
- Heartworm disease

CBC/BIOCHEMISTRY/URINALYSIS

- CBC/Biochemistry usually unremarkable unless severe disease and ongoing CHF therapy
- Prerenal azotemia secondary to impaired renal perfusion; urinary specific gravity is high unless complicated by underlying renal disease or previous diuretic administration.
- High liver enzyme activity in many patients with right-sided CHF.

OTHER LABORATORY TESTS

- Natriuretic peptides—concentrations are often unremarkable unless moderate to severe disease.
- Serum troponin I—concentrations unremarkable unless severe disease.

IMAGING

Radiographic Findings

- Heart size ranges from normal to left-sided or generalized cardiomegaly.
- LA enlargement is usually the earliest finding.
- Left-sided CHF—pulmonary congestion; increased interstitial pattern ± air bronchograms; initially, congestion and edema are perihilar, with all lung fields eventually showing changes.

Echocardiographic Findings

- Thickening and distortion of the AV valve leaflets.

ATRIOVENTRICULAR VALVE (MYXOMATOUS) DISEASE

(CONTINUED)

- Elongation and rupture of the chordae tendineae, causing mitral valve prolapse.
- Atrial dilatation (uni- or bilaterally).
- The LV might be distended and is hyperdynamic if the regurgitant flow is high and myocardial function intact; as the ventricle becomes more grossly distended, it may become normo- or, less commonly, hypodynamic because of myocardial failure.
- Pericardial effusion (usually mild) is rarely seen.
- Doppler studies document a jet of regurgitation into the left atrium.
- Doppler evaluation for the presence of pulmonary hypertension should be routinely performed.

DIAGNOSTIC PROCEDURES

- Systemic blood pressure should be monitored in patients with severe disease or receiving diuretics to check for hypotension. Hypertension is not common.
- Arterial/venous blood gases can be used to quantify hypoxemia and monitor treatment response.
- Abdominocentesis/Pleurocentesis—a modified transudate is characteristic of CHF.

Electrocardiographic Findings

- Sinus tachycardia is common in patients with CHF.
- May show evidence of LA enlargement (P mitrale) or LV enlargement (tall and wide R waves).
- Supraventricular, most commonly atrial fibrillation, or ventricular arrhythmias may develop in severe disease.

PATHOLOGIC FINDINGS

- Gross valvular changes range from only a few discrete nodules at the line of closure to gross distortion of the valve by gray-white nodules and plaques causing contraction of the cusps and rolling of the free edge; the chordae are irregularly thickened, with regions of tapering and rupture.
- Mild disease—normal cardiac size. More progressed cases—LA and LV dilation. Degree of right-sided dilatation variable.
- The degree of LV hypertrophy may be apparent only on weighing the heart.
- Jet lesions—irregular thickening and opacity of the atrial endocardium.
- Recent and healed LA splits or tears in some patients.
- Small thrombi in the LA are rarely seen.

**TREATMENT****APPROPRIATE HEALTH CARE**

Treat patients that need oxygen support as inpatients; if stable, patients may be managed at home.

NURSING CARE

Oxygen therapy as needed for hypoxemia.

ACTIVITY

- Absolute exercise restriction for symptomatic patients.
- Stable patients receiving medical treatment—avoid strenuous exercise.

DIET

- Prevent cardiac cachexia by ensuring adequate calorie intake.
- Avoid food with high sodium content.

CLIENT EDUCATION

- Discuss the progressive nature of the disease.
- Mild disease severity is suggestive of a long period without clinical signs; moderate to severe indicates a shorter period.
- If the client is a breeder, inform him/her about the genetics of the disease and impact of the finding on future breeding.
- Appropriate level of exercise, but at the same time maintain quality of life.
- Common signs of CHF listed above.
- How to medicate (if indicated)—consistent dosing and that doses of diuretics should be adjusted in collaboration with the veterinarian.
- Possible adverse side reactions of medications.
- How to monitor resting/sleeping respiratory rates at home, and at which rate new contact with the clinician should be initiated.
- Diet (if indicated)—emphasize the importance of avoiding cardiac cachexia by paying close attention to appetite and using an appropriate diet.

SURGICAL CONSIDERATIONS

Surgical valve replacement and purse-string suture techniques to reduce the area of the mitral valve orifice have been used; experience with these techniques and access usually limited.

**MEDICATIONS****DRUG(S) OF CHOICE**

Recommended treatment depends on the stage of the disease; these recommendations follow the guidelines set by the consensus statement developed by the ACVIM.

Patients Without Overt Clinical Signs (ACVIM Stage B)

- If no cardiac enlargement, no treatment is currently recommended.
- Administering ACE inhibitors to Stage B2 patients is of unproven efficacy (despite two clinical trials). Administration of pimobendan to Stage B2 patients is of unknown value at this time.

Patients Showing Overt Clinical Signs (ACVIM stage C and D)***Signs of Acute CHF (Often Treated as Inpatient)***

- Furosemide IV, SC, IM, or PO. Dose is dependent on severity of CHF.

- Mild to moderate CHF: 2–4 mg/kg q8–24h.

- Severe or fulminant CHF: 4–8 mg/kg q2–6h, preferably IV, IM, or SC.

- Monitor outcome of treatment by respiratory rate and general clinical status. Dosages can often be reduced when the patient has stabilized.

- Oxygen supplementation and cage rest to patients with significant dyspnea. 40% in O₂ cage (can go as high as 100%) up to 24 hours; nasal O₂ in may be used in large-breed dogs, 50–100 mL/kg/minute through humidifier.

- Pimobendan at 0.25 mg/kg q12h PO.

- Additional options in cases with severe fulminant CHF:

- Nitroglycerin: ointment (one-fourth inch/5 kg up to 2 inches percutaneously) or injectable (1–5 µg/kg/minute CRI).

- Arterial vasodilator to decrease afterload rapidly, such as hydralazine at 0.5 mg/kg q12h titrated up to 2 mg/kg if necessary), or sodium nitroprusside at 1–10 µg/kg/minute. Both drugs require blood pressure monitoring and should be considered only in hospitalized dogs when monitored by a specialist.

- Dobutamine (dogs, 1–10 µg/kg/minute; cats, 1–5 µg/kg/minute).

- Dopamine (1–10 µg/kg/minute).

- Antiarrhythmics—as needed.

- Severe ascites may require abdominal paracentesis.

Chronic CHF (Typically Treated as Outpatient)

- Exact composition of medical therapy depends on disease severity and clinical signs. All dogs with CHF require life-long treatment with a diuretic, such as furosemide.

- Mild to moderate CHF: 1 mg/kg q24h to 3–4 mg/kg q8h PO.

- Moderate to severe CHF: 2–3 mg/kg q12h or higher.

- Pimobendan at 0.25 mg/kg q12h PO.

- ACEI (i.e., enalapril, benazepril, ramipril). Dose and dose interval dependent on ACE inhibitor used (enalapril [0.5 mg/kg q12–24h], benazepril [0.25–0.5 mg/kg q24h]).

- Spironolactone at 2 mg/kg q12–24h PO and/or hydrochlorothiazide at 2–4 mg/kg q12h PO.

- Digoxin at 0.22 mg/m² q12h PO, or lower.

- Adequate antiarrhythmic treatment if significant arrhythmia is present.

- Sildenafil at 0.5–2 mg/kg in case of pulmonary hypertension.

PRECAUTIONS

- Use digoxin, diuretics, and ACE inhibitors with caution in patients with renal disease.

- Nitrate tolerance may develop if appropriate 12-hour nitrate-free intervals are omitted from the dosing schedule.

- Beta-blockers are negative inotropes and may have an acute adverse effect on myocardial function and clinical status.

(CONTINUED)

ATRIOVENTRICULAR VALVE (MYXOMATOUS) DISEASE

A

POSSIBLE INTERACTIONS

- Furosemide potentiates the effects of an ACE-inhibitor, spironolactone, or a thiazide.
- Nonsteroidal anti-inflammatory drugs should be used with caution in patients receiving furosemide and ACEI.

ALTERNATIVE DRUG(S)

- Diuretics—add thiazide and/or potassium sparing diuretic (e.g., spironolactone) in refractory animals.
- Torsemide and bumetanide are alternatives to furosemide.
- Vasodilators—isosorbide dinitrate can be used in place of nitroglycerin ointment in patients requiring long-term nitrate administration.

**FOLLOW-UP****PATIENT MONITORING**

- Frequency of reexaminations depends on severity of myxomatous valve disease and severity of CHF (if present).
- Dogs without signs of CHF:
 - Slight to moderate disease severity: Perform echocardiography when a murmur is first detected and every 6–12 months thereafter to document progressive cardiomegaly. A baseline radiograph may be useful.
 - Moderate to severe disease severity may require more frequent monitoring.
- Dogs with signs of CHF:
 - Once acute CHF has been successfully treated, dogs can be treated at home.
 - Reexamination after 1 to 2 weeks of therapy (check for signs of decompensated CHF, dehydration, electrolyte imbalance, renal dysfunction, and presence of a complication). Moderate to severe disease severity may require more frequent monitoring.

◦ Thereafter once every 3–6 months if the patient is stable on the medication. More severe cases may require more frequent monitoring.

• Monitor BUN and creatinine when diuretics and ACE inhibitors are used in combination. Monitor potassium levels, especially when combinations of spironolactone, ACE inhibitors and digoxin are used.

POSSIBLE COMPLICATIONS

- Asymptomatic patients may develop CHF
- Recurrent CHF in patients stabilized by medical therapy
- Pulmonary hypertension
- Biventricular CHF in patients with initial left-sided CHF
- Mild pleural and/or pericardial effusion
- Arrhythmia, most commonly atrial fibrillation
- Rupture of first-order tendinous chord(s), leading to a flail valve leaflet
- Atrial tear leading to acquired atrial septal defect or cardiac tamponade
- Formation of intracardiac thrombus and/or myocardial infarction.

EXPECTED COURSE AND PROGNOSIS

The lesions on the AV valves are progressive in nature and myocardial function may worsen, necessitating increasing drug dosages; long-term prognosis depends on response to treatment and stage of heart failure.

**MISCELLANEOUS****SYNOMYMS**

- Chronic valvular disease (CVD)
- Chronic mitral valve disease
- Degenerative valvular disease
- Degenerative mitral valve disease (DMVD)
- Myxomatous mitral valve disease (MMVD)
- Endocardiosis

SEE ALSO

- Atrial Wall Tear
- Congestive Heart Failure, Left-Sided
- Congestive Heart Failure, Right-Sided

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- AV = atrioventricular
- CHF = congestive heart failure
- LA = left atrium
- LV = left ventricle
- MAVD = myxomatous mitral valve disease

Suggested Reading

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**Client Education Handout
available online**

ATRIOVENTRICULAR VALVULAR STENOSIS



BASICS

DEFINITION

Atrioventricular valvular stenosis is a pathologic narrowing of the mitral or tricuspid valve orifice due to valvular dysplasia or an obstructive, supravalvular ring.

PATHOPHYSIOLOGY

- Atrioventricular stenosis increases the resistance to ventricular filling.
- Ventricular filling in clinically significant disease requires a persistent diastolic pressure gradient between atrium and ventricle.
- Concomitant valvular regurgitation is common.
- The increased atrial pressure leads to atrial dilation, venous congestion, and often to CHF. Pulmonary edema occurs with mitral stenosis; whereas ascites, pleural effusion and chylothorax can develop in cases of severe tricuspid stenosis.
- The foramen ovale can remain patent (PFO) in patients with tricuspid stenosis, allowing right-to-left shunting with signs of cyanotic heart disease.
- Partial atrioventricular septal defect (primum ASD and abnormal atrioventricular valve) is observed in some cats with supravalvular mitral (ring) stenosis.
- Cardiac output and therefore exercise capacity are limited with atrioventricular valvular stenosis.
- The atrial pressure increases disproportionately with faster heart rates, thereby creating the risk for "flash" pulmonary edema in dogs or cats with mitral stenosis.
- Development of atrial tachyarrhythmias, especially atrial fibrillation, is associated with cardiac decompensation.
- Pulmonary hypertension can develop consequent to MS, leading to exercise intolerance and right ventricular hypertrophy. This can be severe, especially in cats with mitral stenosis.

SYSTEMS AFFECTED

- Respiratory—with MS—bronchial compression from enlarged left atrium, pulmonary edema from left heart failure; potential for hemoptysis due to rupture of pulmonary venous-bronchial venous connections; pleural effusion with atelectasis in tricuspid stenosis or in long-standing MS complicated by pulmonary hypertension or atrial fibrillation.
- Hepatobiliary—with TS—hepatic congestion, ascites.

GENETICS

- Uncertain in most cases.
- Tricuspid valve dysplasia in Labrador retrievers has been localized to a defect in dog chromosome 9 inherited as an autosomal dominant trait with reduced penetrance.

INCIDENCE/PREVALENCE

Rare

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog and cat

Breed Predilections

- MS is overrepresented in bull terriers and Newfoundlands, and in Siamese cats.
- TS has been reported most often in Old English sheepdogs and Labrador retrievers.

Mean Age and Range

Most patients are presented at a young age, although exceptions occur, especially in cats.

Predominant Sex

N/A

SIGNS

Historical Findings

- Exercise intolerance
- Syncope
- Exertional dyspnea or tachypnea
- Cough—MS
- Cyanosis
- Abdominal distention—TS
- Acute posterior paresis—cats with MS and arterial thromboembolism
- Stunted growth
- Hemoptysis from rupture of intrapulmonary vessels—MS

Physical Examination Findings

- Soft diastolic murmur with point of maximal intensity over the left apex (MS) or right hemithorax (TS).
- Holosystolic murmur of mitral or tricuspid regurgitation is more often detected.
- Tachypnea, dyspnea from pulmonary edema or pleural effusion.
- Crackles from pulmonary edema.
- Jugular distention, jugular pulses, ascites, hepatomegaly with TS or biventricular CHF associated with pulmonary hypertension and atrial fibrillation in chronic MS.
- Cyanosis from right to left shunting with TS or from venous admixture and pulmonary edema with MS.

CAUSES

- Usually due to congenital dysplasia of the mitral or tricuspid valve.
- Supravalvular obstructing rings of tissue have been associated with atrioventricular stenosis; this is especially important in cats.
- Infective endocarditis, intracardiac neoplasia, and hypertrophic cardiomyopathy with scarring are rare causes of acquired AV valve stenosis.
- Acquired tricuspid stenosis has been observed due to fibrous scarring of the tricuspid valve in dogs with transvenous pacing leads.

RISK FACTORS

Breed predispositions (see above); see "Risk Factors" for Endocarditis, Infective; permanent transvenous pacing.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Atrioventricular valvular stenosis must be differentiated from the more common causes of mitral and tricuspid regurgitation in the absence of stenosis. These include both congenital and acquired lesions of the atrioventricular valves and support apparatus. Acquired lesions that obstruct the inflow tracts (see "Causes"). Cor triatriatum dexter and cor triatriatum sinister can mimic some of the clinical findings of pure tricuspid and mitral valve stenosis, respectively.

CBC/BIOCHEMISTRY/URINALYSIS

May be normal or reflect changes related to CHF or drug therapy for CHF.

IMAGING

Thoracic Radiography

- Atrial enlargement is the most consistent and outstanding feature; may see generalized cardiomegaly, especially with atrioventricular valve regurgitation.
- MS—may see pulmonary venous congestion and pulmonary edema; intrapulmonary hemorrhage can be misinterpreted as pneumonia or another parenchymal disease.
- TS—may see hepatomegaly; increased diameter of caudal vena cava.

Echocardiography

- Diagnostic test of choice.
- Two-dimensional echocardiography reveals a markedly dilated atrium and attenuated valve excursion during diastole, often with thickened, irregular AV valve leaflets; valve leaflets may appear to "dome" during diastole. A supravalvular obstructing ring also may be evident as well as other lesions (see "Causes" above).
- M-mode studies show an enlarged atrium and discordant motion of the AV valve leaflets indicating commissural fusion; the E-to-F slope is decreased.
- Color-flow imaging reveals a turbulent diastolic jet that originates proximal to the stenotic valve and projects toward the apex of the ventricle; AV valve regurgitation is often present.
- Spectral Doppler studies show increased diastolic transvalvular flow velocities; prolonged calculated pressure half-time is a hallmark feature; E-wave/A-wave amplitude reversal is often evident in cases still in normal sinus rhythm.
- Right-sided chamber enlargements in MS with pulmonary hypertension or with chronic atrial fibrillation.

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ATRIOVENTRICULAR VALVULAR STENOSIS

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- Concurrent defects such as patent foramen ovale, ASD, or bridging septal leaflet.

Angiography

- Right atrium: injection demonstrates a markedly dilated atrium in TS; with concurrent PFO or ASD, opacification of the left atrium is also observed following right atrial injection.
- Might visualize thickened, irregular valve leaflets or a stenotic valve funnel.
- Ventricular injection often reveal valvular regurgitation.
- There can be delayed opacification of the ventricles and great vessels.

Cardiac Catheterization

- A diastolic pressure gradient is identified between the atrium and ventricle. A large "A" wave is common if atrial function is preserved.
- High left atrial, pulmonary capillary wedge, and pulmonary artery pressures occur in MS.
- High right atrial and central venous pressures are present in TS.
- Ventricular pressure may be normal in the absence of concurrent defects.

DIAGNOSTIC PROCEDURES**Electrocardiography**

- Variable enlargement and ventricular conduction patterns are observed. Widened or tall P-waves are commonly observed.
- Splintered R-waves are present in some dogs with tricuspid dysplasia.
- Axis deviation due to hypertrophy or ventricular conduction disturbances is relatively common in cats with mitral valve malformation.
- Ectopic rhythms, especially of atrial origin, are often observed. Atrial fibrillation is the most important rhythm disturbance as atrial contribution to filling is lost and the R to R intervals vary with short cycles increasing the mean diastolic gradient.

PATHOLOGIC FINDINGS

- The atrioventricular valve is abnormal, with thickened leaflets and fused commissures. Other lesions may be identified such as a supra-mitral ring (see "Causes").
- Many cases also have abnormal chordae tendineae and papillary muscles.
- Atrial dilation and hypertrophy are common.
- Patent foramen ovale with TS or partial atrioventricular septal defect (primum ASD and bridging septal leaflet) with supravalvular mitral (ring) stenosis.

**TREATMENT****APPROPRIATE HEALTH CARE**

Patients in overt CHF should be treated with inpatient medical management. Surgical or catheter-based interventions can be considered once heart failure has been stabilized. Control of heart rhythm

disturbances, especially AF, is also important. These patients are typically complicated and consultation with a cardiologist is highly recommended. Electrocadioversion of atrial fibrillation should be considered but advanced atrial disease can render the procedure less effective or limit the duration of sinus rhythm.

NURSING CARE

Sedation with butorphanol is appropriate for dyspneic patients. Oxygen therapy should be administered to the patient with dyspnea or hypoxemia from left-sided congestive heart failure. Fluid therapy is typically contraindicated in the patient with overt CHF except in cases of moderate to severe azotemia, renal compromise, or severe dehydration. Therapeutic paracentesis may be considered in the patient with pleural effusions or tympanic ascites.

ACTIVITY

Exercise restriction is important recommended for any animal with this condition because tachycardia increases the mean gradient across the stenotic valve predisposing to pulmonary edema or venous congestion. Cage rest for patients with CHF.

DIET

Feed a sodium-restricted diet to patients in CHF.

CLIENT EDUCATION

The client must be advised of symptoms associated with CHF and the urgency of treatment, particularly with left-sided CHF. The likelihood of recurrent bouts of CHF should also be discussed. Development of atrial fibrillation can lead to marked decompensation.

SURGICAL CONSIDERATIONS

- Surgical valve replacement or repair requires cardiopulmonary bypass or hypothermia; cost, availability, and high complication and mortality rates are greatly limiting factors.
- Balloon valvuloplasty is an alternative referral treatment and has been used successfully for managing some cases of AV stenosis.

**MEDICATIONS****DRUG(S) OF CHOICE****CHF**

- Furosemide—dogs, 2–6 mg/kg IV, IM, SC, PO q8–24h; cats, 1–4 mg/kg IV, IM, SC, PO q8–24h.
- ACE inhibitor—enalapril—dogs, 0.25–0.5 mg/kg PO q12h; cats, 0.25–0.5 mg/kg PO q12–24h; see below under "Follow-Up" for patient monitoring.
- Nitroglycerin paste (1/4 to 1 inch topically q12h) to reduce pulmonary venous pressures, but this has not been evaluated critically.

Atrial Tachyarrhythmias

- Digoxin—dogs, 3–5 µg/kg PO q12h; cats, one-fourth of a 0.125-mg tablet PO q24–48h; adjust dosage based on serum concentrations.
- Beta-blockers such as atenolol or the calcium channel blocker diltiazem for suppression of frequent atrial premature complexes and for heart rate control in atrial tachycardia/flutter/fibrillation. Beware: using these drugs in uncontrolled CHF.
- Typical atenolol dosages: dogs, 0.25–1.0 mg/kg q12h; cats, 6.25–12.5 mg/cat q12–24h; start low and titrate to effect.
- Diltiazem dosages: dogs, 2–6 mg/kg daily in two (long-acting diltiazem) or three divided dosages; start low and titrate to effect; cats, 7.5 mg diltiazem HCl PO q8h.. Higher dosages are sometimes needed.
- Sotalol for intractable/recurrent arrhythmias—dogs, 1–2 mg/kg PO q12h; cats, 10–20 mg/cat q12h.
- Dogs can be referred for electrocardioversion to convert AF to sinus rhythm (with follow-up therapy with sotalol or amiodarone); however, reversion back to AF is common owing to marked atrial dilatation.

Pulmonary Hypertension

- Sildenafil—dogs, 0.5–3 mg/kg PO q8–12 hours.

PRECAUTIONS

- As a general rule pimobendan is relatively contraindicated in pure valvular stenosis; however, many dogs and cats with advanced CHF have been treated with this drug with apparent success, especially when there is combined stenosis/regurgitation of the valve.
- Use ACE inhibitors or other vasodilators judiciously in patients with CHF; cardiac output is limited and vasodilation may induce hypotension. Monitor arterial blood pressure and renal function.

POSSIBLE INTERACTIONS

- Furosemide and ACE inhibitors can affect kidney function, alter blood electrolytes, and reduce blood pressure; these parameters should be monitored.
- Sildenafil can also reduce systemic blood pressure and should not be used with nitroglycerin paste or other nitrates.

ALTERNATIVE DRUG(S)

Spironolactone (2 mg/kg PO q12–24h) should be considered as an ancillary diuretic and for its antifibrotic benefit (as an aldosterone antagonist).

**FOLLOW-UP****PATIENT MONITORING**

- Thoracic radiographs for pulmonary edema or pleural effusion.

atrioventricular valvular stenosis

(CONTINUED)

- Echocardiography with Doppler studies—to estimate pulmonary pressures and subjectively assess right heart function if on sildenafil.
- Digoxin level—check 7–10 days following institution of therapy; 8- to 12-hour trough should be 0.8–1.5 ng/mL.
- Renal function, electrolyte status, and arterial blood pressure when on diuretic and/or ACE inhibitor.
- Standard rhythm ECG or Holter (ambulatory ECG) if arrhythmias are present.

POSSIBLE COMPLICATIONS

- CHF
- Atrial fibrillation
- Syncope
- Arterial thromboembolism—cats with MS
- Pulmonary hemorrhage with MS

EXPECTED COURSE AND PROGNOSIS

- Morbidity is high; except for mild cases, prognosis is generally poor once an animal becomes symptomatic. However, some animals will live for many years even with relatively severe stenosis of the mitral or tricuspid valve.
- Surgical intervention or balloon valvuloplasty might alter course of disease, but data are limited.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Concurrent congenital defects are common (e.g., subaortic stenosis in MS, PFO in TS; primum ASD in cats with supravalvular mitral (ring) stenosis).

PREGNANCY/FERTILITY/BREEDING

The possibility that this may be a heritable defect must be considered in assessing suitability of the animal for breeding, particularly in breeds with a predilection for this defect. The additional hemodynamic burden of gestation may be poorly tolerated by an already compromised heart. In general breeding is strongly discouraged.

SYNOMYS

Atrioventricular valve dysplasia with stenosis; supravalvular mitral ring.

SEE ALSO

- Atrioventricular Valve Dysplasia
- Endocarditis, Infective

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- AF = atrial fibrillation
- AV = atrioventricular
- CHF = congestive heart failure
- ECG = electrocardiogram
- MS = mitral stenosis
- PFO = patent foramen ovale
- TS = tricuspid stenosis

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- Authors** Lora S. Hitchcock and John D. Bonagura
- Consulting Editors** Larry P. Tilley and Francis W.K. Smith, Jr.



BASICS

DEFINITION

- Azotemia is an excess of urea, creatinine, or other non-protein nitrogenous substances in blood, plasma, or serum.
- Uremia is the polysystemic toxic syndrome that results from marked loss in kidney functions. Uremia occurs simultaneously in animals with increased quantities of urine constituents in blood (azotemia), but azotemia may occur in the absence of uremia.

PATHOPHYSIOLOGY

- Azotemia can be caused by (1) increased production of non-protein nitrogenous substances, (2) decreased glomerular filtration rate, or (3) reabsorption of urine that has escaped from the urinary tract into the bloodstream. High production of non-protein nitrogenous waste substances may result from high intake of protein (diet or gastrointestinal bleeding) or accelerated catabolism of endogenous proteins. Glomerular filtration rate may decline because of reduced renal perfusion (prerenal azotemia), acute or chronic kidney disease (renal azotemia), or urinary obstruction (post-renal azotemia). Reabsorption of urine into the systemic circulation may also result from leakage of urine from the excretory pathways (also a form of post-renal azotemia).
- Pathophysiology of uremia—incompletely understood; may be related to (1) metabolic and toxic systemic effects of waste products retained because of renal excretory failure, (2) deranged renal regulation of fluids, electrolytes, and acid-base balance, and (3) impaired renal production and degradation of hormones and other substances (e.g., erythropoietin and 1,25-dihydroxycholecalciferol).

SYSTEMS AFFECTED

- Uremia affects virtually every body system.
- Cardiovascular—arterial hypertension, left ventricular hypertrophy, heart murmur, cardiomegaly, cardiac rhythm disturbances.
- Endocrine/Metabolic—renal secondary hyperparathyroidism, inadequate production of 1,25-dihydroxycholecalciferol (calcitriol) and erythropoietin, hypergastrinemia, weight loss.
- Gastrointestinal—anorexia, nausea, vomiting, diarrhea, uremic stomatitis, xerostomia, uremic breath, constipation.
- Hemic/Lymph/Immune—anemia and immunodeficiency.
- Neuromuscular—dullness, drowsiness, lethargy, fatigue, irritability, tremors, gait imbalance, flaccid muscle weakness, myoclonus, behavioral changes, dementia, isolated cranial nerve deficits, seizures, stupor,

coma, impaired thermoregulation (hypothermia).

- Ophthalmic—scleral and conjunctival injection, retinopathy, acute-onset blindness.
- Respiratory—dyspnea.
- Skin/Exocrine—pallor, bruising, increased shedding, unkempt appearance, loss of normal sheen to coat.

SIGNALMENT

Dog and cat

SIGNS

General Comments

Azotemia may not be associated with historical or physical abnormalities. Unless patient has uremia, clinical findings are limited to the disease responsible for azotemia. Findings described here are those of uremia.

Historical Findings

- Weight loss
- Declining appetite or anorexia
- Reduced activity
- Depression
- Fatigue
- Weakness
- Vomiting
- Diarrhea
- Halitosis
- Constipation
- Polyuria
- Changes in urine volume (increase or decrease)
- Poor haircoat or unkempt appearance

Physical Examination Findings

- Muscle wasting: sarcopenia/cachexia
- Mental depression
- Dehydration
- Weakness
- Pallor
- Petechiae and ecchymoses
- Dull and unkempt haircoat
- Uremic breath
- Uremic stomatitis (including oral ulcers, infarctions of the tongue)
- Scleral and conjunctival injection
- Relative hypothermia

CAUSES

Prerenal Azotemia

- Reduced renal perfusion due to low blood volume or low blood pressure.
- Accelerated production of nitrogenous waste products because of enhanced catabolism of tissues in association with infection, fever, trauma, corticosteroid excess, or burns.
- Increased gastrointestinal digestion and absorption of protein sources (diet or gastrointestinal hemorrhage).

Renal Azotemia

Acute or chronic kidney diseases (primary kidney disease affecting glomeruli, renal tubules, renal interstitium, and/or renal vasculature) that impair at least 75% of kidney function (glomerular filtration rate).

Post-renal Azotemia

Urinary obstruction; rupture of the excretory pathway.

RISK FACTORS

- Medical conditions—kidney disease, hypoadrenocorticism, low cardiac output, hypotension, fever, sepsis, polyuria, liver disease, pyometra, hypoalbuminemia, dehydration, acidosis, exposure to nephrotoxic chemicals, gastrointestinal hemorrhage, urolithiasis, urethral plugs in cats, urethral trauma, and neoplasia.
- Advanced age may be a risk factor.
- Drugs—potentially nephrotoxic drugs, nonsteroidal anti-inflammatory drugs, diuretics, antihypertensive medications; failure to adjust dosage of drugs primarily eliminated by the kidneys to correspond with decline in renal function.
- Toxins—ethylene glycol, grapes (dogs), lilies (cats).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Dehydration, poor peripheral perfusion, low cardiac output, history of recent fluid loss, high protein diet, or black, tarry stools—rule out prerenal azotemia.
- Recent onset of altered urine output (high or low), clinical signs consistent with uremia, exposure to possible nephrotoxicants or ischemic renal injury, or kidney size normal or enlarged—rule out acute renal failure.
- Progressive weight loss, polyuria, polydipsia, small kidneys, disparate kidney size (cats—big kidney and little kidney), pallor, and signs of uremia that have developed over several weeks to months—rule out chronic renal failure.
- Abrupt decline in urine output and onset of signs of uremia; disparate kidney size (cats—big kidney and little kidney), occasionally dysuria, stranguria, and hematuria; large urinary bladder or fluid-filled abdomen—rule out post-renal azotemia.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Nonregenerative anemia (normocytic, normochromic)—often present with chronic renal failure.
- Hemoconcentration—often present with prerenal azotemia; can also be seen with acute renal failure and post-renal azotemia.

Biochemistry

- Serial determinations of serum urea nitrogen and creatinine concentrations may help differentiate the cause of azotemia. Appropriate therapy to restore renal perfusion typically yields a dramatic reduction in azotemia in patients with prerenal azotemia (typically within 24–48 hours). Correcting

obstruction to urine flow or a rent in the excretory pathway typically is followed by a rapid reduction in the magnitude of azotemia.

- Concurrent hyperkalemia may be consistent with post-renal azotemia, primary renal azotemia due to oliguric renal failure, or prerenal azotemia associated with hypoadrenocorticism.
- Increased serum albumin and globulin concentration suggest prerenal azotemia or a prerenal component.^s

Urinalysis

- A urine specific gravity value ≥ 1.030 in dogs and ≥ 1.035 in cats supports a diagnosis of prerenal azotemia. Administration of fluid therapy before urine collection may interfere with interpretation of low specific gravity values.
- Azotemic patients that have not been treated with fluids and have urine specific gravity < 1.030 in dogs and < 1.035 in cats typically have primary renal azotemia. A notable exception to this rule is dogs and cats with glomerular disease. Glomerulopathy is sometimes characterized by glomerulotubular imbalance in which adequate urine-concentrating ability may persist despite sufficient renal glomerular damage to cause primary renal azotemia; these patients are recognized by moderate to marked proteinuria in the absence of hematuria and pyuria.
- Urine specific gravity is not useful in identifying post-renal azotemia.

OTHER LABORATORY TESTS

Endogenous or exogenous creatinine, iohexol, or inulin clearance tests or other specific tests of glomerular filtration rate may be used to confirm that azotemia is caused by reduced glomerular filtration rate.

IMAGING

- Abdominal radiographs—used to determine kidney size (small kidneys consistent with chronic kidney disease; mild-to-moderate enlargement of kidneys may be consistent with acute renal failure or urinary obstruction) and to rule out urinary obstruction (marked dilation of the urinary bladder or mineral densities within the excretory pathway).
- Ultrasonography—may detect changes in echogenicity of the renal parenchyma and size and shape of kidneys that support a diagnosis of primary renal azotemia; useful to rule out post-renal azotemia characterized by distension of the excretory pathway and uroliths or masses within or impinging on the excretory pathway and intra-abdominal fluid accumulation (with rupture of the excretory pathway).
- Excretory urography, pyelography, or cystourethrography—may help establish the diagnosis of post-renal azotemia due to

urinary obstruction or rupture of the excretory pathway.

DIAGNOSTIC PROCEDURES

Renal biopsy can be used to confirm the diagnosis of primary kidney disease, to differentiate acute from chronic kidney disease, and to attempt to establish the underlying disease process responsible for primary kidney disease.



TREATMENT

- Prerenal azotemia caused by impaired renal perfusion—correct the underlying cause of renal hypoperfusion; aggressiveness of treatment depends on the severity of the underlying condition and the probability that persistent renal hypoperfusion will lead to primary renal injury or failure.
- Primary renal azotemia and associated uremia—(1) specific therapy directed at halting or reversing the primary disease process affecting the kidneys, and (2) symptomatic, supportive, and palliative therapies that ameliorate clinical signs of uremia; minimize the clinical impact of deficits and excesses in fluid, electrolyte, acid-base balances; minimize the effects of inadequate renal biosynthesis of hormones and other substances, and maintain adequate nutrition.
- Post-renal azotemia—eliminate urinary obstruction or repair rents in the excretory pathway; supplemental fluid administration is often required to prevent dehydration that may develop during the solute diuresis that follows correction of post-renal azotemia.
- Fluid therapy—indicated for most azotemic patients; preferred fluids include 0.9% saline or lactated Ringer's solution. Determine fluid volume to administer on the basis of severity of dehydration or volume depletion. If no clinical dehydration is evident, cautiously assume that the patient is less than 5% dehydrated and administer a corresponding volume of fluid. Generally provide 25% of calculated fluid deficit in the first hour. Thereafter, serially monitor perfusion (capillary refill time, pulse pressure, heart rate, and temperature of feet), blood pressure and urine output to assess adequacy of fluid therapy. If perfusion has not improved, additional fluid should be administered. Provide the remaining fluid deficit over the next 12–24 hours. Fluid therapy should be cautiously administered to patients with overt or suspected cardiac failure and patients that are oliguric or anuric.
- Treat patients in shock appropriately.
- Consider feeding diets formulated for kidney disease to reduce the magnitude of azotemia, hyperphosphatemia, and acidosis.



MEDICATIONS

DRUG(S) OF CHOICE

- Symptomatic therapy may be indicated for uremia in patients with kidney disease.
- Famotidine (0.5–1.0 mg/kg PO, SC, IM, IV q12–24h) or other H₂-receptor antagonists may be used to reduce gastric hyperacidity and nausea (dogs).
- Antiemetics such as maropitant (1 mg/kg q24h PO or SC for 5 days) are indicated for vomiting.

CONTRAINdications

Administration of nephrotoxic drugs

PRECAUTIONS

- Use caution when administering drugs requiring renal excretion. Consult appropriate references concerning dose-reduction schedules or adjustments of maintenance intervals.
- Use caution in administering fluids to patients that are oliguric or anuric. Monitor urine production rates and body weight during fluid therapy to minimize the likelihood of inducing overhydration.
- Stop fluid therapy in overhydrated oliguric/anuric patients. Use caution in administering drugs that may promote hypovolemia or hypotension (e.g., diuretics); carefully monitor the response to such drugs by assessing hydration status, peripheral perfusion, and blood pressure, with serial evaluation of renal function tests.
- Corticosteroids may worsen azotemia by increasing catabolism of endogenous proteins.

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

Serum urea nitrogen and creatinine concentrations 24 hours after initiating fluid administration; also urine production, body weight, and hydration status.

POSSIBLE COMPLICATIONS

- Failure to correct prerenal azotemia caused by renal hypoperfusion rapidly could result in ischemic primary kidney disease.
- Primary renal azotemia can progress to uremia.
- Failure to restore normal urine flow in patients with post-renal azotemia can result in progressive renal damage or death due to hyperkalemia and uremia.

(CONTINUED)

AZOTEMIA AND UREMIA**A****MISCELLANEOUS****ASSOCIATED CONDITIONS**

An association may exist between hypokalemia and azotemia in cats. Preliminary findings suggest that hypokalemia may be associated with functional or structural renal changes leading to azotemia.

AGE-RELATED FACTORS

Primary renal failure may occur in animals of any age, but geriatric dogs and cats appear to be at substantially higher risk for both acute and chronic kidney disease. However, do not assume that azotemia in geriatric dogs and cats indicates primary kidney disease; these

patients are also at higher risk for prerenal and post-renal causes for azotemia.

ZOONOTIC POTENTIAL

Leptospirosis

PREGNANCY/FERTILITY/BREEDING

- Data on azotemia and pregnancy in dogs and cats are very limited. Humans may tolerate minimal renal disease well during pregnancy; however, ability to sustain a viable pregnancy declines as renal function declines.
- Pregnant azotemic animals—pharmacologic agents excreted by non-renal pathways are preferred.

SEE ALSO

- Chapters on acute and chronic kidney disease
- Urinary Tract Obstruction

INTERNET RESOURCES

International Renal Interest Society (IRIS): www.iris-kidney.com.

Suggested Reading

Polzin D. Chronic kidney disease. In: Ettinger SJ, Feldman EC, eds., *Textbook of Veterinary Internal Medicine*, 7th ed. Philadelphia: Saunders, 2010, pp. 2036–2067.

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Author David J. Polzin

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BABESIOSIS



BASICS

OVERVIEW

- Babesiosis is the disease caused by the protozoal parasites of the genus *Babesia*. Merozoites or piroplasms are the stage that infects mammalian red blood cells.
 - *B. canis*—a large (4–7 µm) piroplasm that infects dogs; *B. canis* is distributed worldwide, and there are three subspecies based on genetic, biologic, and geographic data.
 - B. canis vogeli* has been reported in the United States, Africa, Asia, and Australia. *B. canis rossi* is the most virulent and is present in Africa.
 - B. canis canis* has been reported in Europe.
 - Some have proposed that these organisms are indeed three distinct species: *B. vogeli*, *B. rossi*, and *B. canis*.
 - Recent studies have identified at least three genetically distinct small (2–5 µm) piroplasms that can infect dogs:
 - *B. gibsoni* (a.k.a. *B. gibsoni* [Asia])—small piroplasm that infects dogs; worldwide distribution; emerging disease in the United States.
 - *B. conradi* (a.k.a. *B. gibsoni* [United States/California])—small piroplasm that infects dogs; only reported in California.
 - *Babesia (Theileria) annae* (a.k.a. Spanish dog piroplasm and *B. microti*-like parasite)—small piroplasm that infects dogs; reported in Spain, other parts of Europe, and most recently in the United States.
 - *Babesia* sp. (Coco)—large piroplasm identified in splenectomized and immune-suppressed dogs in the United States.
 - Several other single-case reports of novel *Babesia* sp. and other piroplasms (i.e., *T. equi*) have been published.
 - *B. felis*—small (2–5 µm) piroplasm that infects cats; reported in Africa.
 - *Cytauxzoon felis*—small piroplasm that infects cats; reported in the United States.
 - Infection may occur either by tick transmission, direct transmission via blood transfer during dog bites, blood transfusions, or transplacental transmission.
 - Incubation period averages about 2 weeks, but some cases are not clinically diagnosed for months to years.
 - Piroplasms infect and replicate in red blood cells, resulting in both direct and immune-mediated hemolytic anemia.
 - Immune-mediated hemolytic anemia is likely to be more clinically important than parasite-induced RBC destruction, since the severity of signs does not depend on the degree of parasitemia.
- SYSTEMS AFFECTED**
- Hemic/Lymphatic/Immune—anemia, thrombocytopenia (bleeding tendencies appear rare), fever, splenomegaly,

lymphadenomegaly, vasculitis (experimental only).

- Hepatobiliary—increased liver enzymes (mild-moderate, not the sole abnormality detected).
- Nervous—cerebral babesiosis, weakness, disorientation, collapse (most common with *B. canis rossi*).
- Renal/Urologic—renal failure (*B. canis rossi* and *B. annae*).

SIGNALMENT

- Any age or breed of dog can be infected.
- *B. canis* infections are more prevalent in greyhounds.
- *B. gibsoni* (Asia) infections are more prevalent in American pit bull terriers.
- Any age or breed of cat can be infected, but to date, only *C. felis* has been reported in the United States.

SIGNS

- Signs are similar in dogs and cats.
- Signs can be peracute, acute, or chronic.
- Some carrier animals have no detectable clinical signs.
- Dogs—lethargy, anorexia, pale mucous membranes, fever, splenomegaly, lymphadenomegaly, pigmenturia, icterus, weight loss, discolored stool.
- Cats—lethargy, anorexia, pale mucous membranes, icterus.

CAUSES & RISK FACTORS

- History of tick attachment.
- Splenectomized animals develop more severe clinical disease.
- History of splenectomy or chemotherapy appear to be risk factors for *Babesia* sp. (Coco).
- Immune suppression may cause clinical signs and increased parasitemia in chronically infected dogs.
- History of a recent dog-bite wound is a risk for *B. gibsoni* (Asia) infection.
- Recent blood transfusion from a subclinically infected donor.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Any cause of immune-mediated hemolytic anemia or thrombocytopenia, including idiopathic immune-mediated hemolytic anemia or thrombocytopenia, ehrlichiosis, Rocky Mountain spotted fever, systemic lupus erythematosus, neoplasia, endocarditis, hemotrophic mycoplasmosis (haemobartonellosis), and cytauxzoonosis
- A positive Coombs' test does not rule out babesiosis since many animals with babesiosis are also Coombs' positive.
- Non-immune-mediated hemolytic anemia, including microangiopathic anemia, caval syndrome, splenic torsion, DIC, Heinz body

anemia, pyruvate kinase deficiency, phosphofructokinase deficiency.

- Hepatic and post-hepatic jaundice.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia—absent to severe; usually regenerative (reticulocytosis) unless signs are very acute; anemia can be severe in some cases (PCV < 10%), anemia is not present in all cases.
- Thrombocytopenia—usually moderate to severe; some animals have thrombocytopenia without anemia. Thrombocytopenia is the most common hematologic abnormality.
- Leukocyte responses are variable, with both leukocytosis and leukopenia reported.
- Hyperbilirubinemia may be present depending on the rate of hemolysis.
- Hyperglobulinemia is common in chronic infections and may be the only biochemical abnormality in some animals.
- Mildly elevated liver enzymes from anemia/hypoxia.
- Proteinuria and hypoalbuminemia (protein-losing nephropathy) may occur
- Azotemia and metabolic acidosis secondary to renal failure have been reported with *B. canis rossi* and *B. annae*.
- Bilirubinuria is common.
- Hemoglobinuria is detected less commonly in the United States than in Africa.

OTHER LABORATORY TESTS

- Microscopic examination of stained thin or thick blood smears—can provide a definitive diagnosis; sensitivity depends on microscopist experience and staining technique; most success using a quick modified Wright stain; capillary blood may enhance sensitivity; microscopy may not accurately differentiate the species or subspecies.
- IFA—tests for antibodies in serum that react with *Babesia* organisms; cross-reactive antibodies can prevent the differentiation of species and subspecies; some infected animals, particularly young dogs, may have no detectable antibodies.
- PCR—tests for the presence of *Babesia* DNA in a biologic sample (usually EDTA anticoagulated whole blood); can differentiate subspecies and species; more sensitive than microscopy.



TREATMENT

- May require inpatient or outpatient care, depending on the severity of disease.
- Hypovolemic animals should receive aggressive fluid therapy.
- Severely anemic animals may require blood transfusion.

(CONTINUED)

BABESIOSIS**B****MEDICATIONS****DRUG(S) OF CHOICE**

- Imidocarb dipropionate (FDA approved; 6.6 mg/kg SC or IM every 1–2 weeks) and diminazine acetarate (not FDA approved; 3.5–7 mg/kg SC or IM every 1–2 weeks) decrease morbidity and mortality in affected animals. They may completely clear *B. canis* infections but not *B. gibsoni* (Asia).
- Combination therapy of azithromycin (10 mg/kg PO q24h for 10 days) and atovaquone (13.5 mg/kg PO q8h for 10 days) is the treatment of choice and the only treatment that can potentially clear *B. gibsoni* (Asia) infections in dogs. In a controlled study, 85% of dogs cleared the infection after treatment.
- A combination of clindamycin (25 mg/kg PO q12h), metronidazole (15 mg/kg PO q12h), and doxycycline (5 mg/kg PO q12h) had been associated with elimination or reduction of the parasite below the limit of detection of PCR testing. Unfortunately a well-defined treatment course has not been established, with treatment times ranging from 24 to 92 days.
- A combination of doxycycline (7–10 mg/kg PO q24h), enrofloxacin (2–2.5 mg/kg PO q12h) and metronidazole (5–15 mg/kg PO q12h) for 6 weeks was associated with clinical remission in 85% of dogs but PCR was not performed to assess its effect on parasitemia.
- Metronidazole (25–50 mg/kg PO q24h for 7 days), clindamycin (12.5–25 mg/kg PO q12h for 7–10 days), or doxycycline (10 mg/kg PO q12h for 7–10 days) alone each have been reported to decrease clinical signs but not to clear infections.
- Primaquine phosphate (1 mg/kg IM, single injection) is the treatment of choice for *B. felis*.

- Since the anemia and thrombocytopenia are often immune mediated, immunosuppressive agents, such as prednisone (2.2 mg/kg/day PO), may be indicated in some cases that are not responding to anti-protozoal treatments alone. Prolonged immune suppressive therapy BEFORE specific antiprotozoal therapy is contraindicated.
- Antibabesial drugs (imidocarb and diminazene) can cause cholinergic signs that can be minimized by administering atropine (0.02 mg/kg SC, 30 minutes prior to imidocarb or diminazine administration).

CONTRAINdications

High doses of antibabesial drugs (imidocarb and diminazene) have resulted in liver and kidney failure.

**FOLLOW-UP**

- Recheck the CBC and biochemistry as needed to monitor for resolution of anemia, thrombocytopenia, icterus, and other signs.
- Most patients have a clinical response within 1–2 weeks of treatment.
- 2–3 consecutive negative PCR tests beginning 2 months post-treatment should be performed to rule out treatment failure and persistent parasitemia. IFA titers are not recommended for follow-up because titers may persist for years.
- Long-term follow-up of *B. conradae*, *B. annae*, or *B. felis* after treatment has not been reported.
- When a dog housed in a multi-dog kennel is diagnosed with babesiosis, all dogs in that kennel should be screened since there is a high percentage of carrier animals in kennel situations.
- Co-infection with other vector-transmitted pathogens (e.g., *Ehrlichia*, hemotropic *Mycoplasma*, *Leishmania*) should be considered, especially in animals that fail to respond to treatment.

PREVENTION/AVOIDANCE

Vaccines for *B. canis canis* and *B. canis rossi* are available in Europe, but these vaccines may not confer protection against other *Babesia* spp.

Tick control is important for disease prevention. Some recent studies suggest that using acaracides can prevent infection with *Babesia* spp. All attached ticks should be removed as soon as possible.

**MISCELLANEOUS**

All potential blood donors should test negative for the disease (preferably by 2–3 consecutive PCR tests) prior to use as a donor animal.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Transplacental transmission

ABBREVIATIONS

- DIC = disseminated intravascular coagulation
- EDTA = ethylenediaminetetra-acetic acid
- FDA = US Food and Drug Administration
- IFA = indirect fluorescent antibody
- PCR = polymerase chain reaction
- PCV = packed cell volume
- RBC = red blood cell

Suggested Reading

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Breitschwerdt EB. Geographic distribution of babesiosis among dogs in the United States and association with dog bites: 150 cases (2000–2003). J Am Vet Med Assoc 2005, 227(6):942–947.

Solano-Gallego L, Baneth G. Babesiosis in dogs and cats—expanding parasitological and clinical spectra. Vet Parasitol 2011, 181(1):48–60.

Author Adam J. Birkenheuer**Consulting Editor** Stephen C. Barr

BACLOFEN TOXICOSIS

B



BASICS

OVERVIEW

• Baclofen is a central acting skeletal muscle relaxant used to prevent spasticity in people with multiple sclerosis, cerebral palsy, and spinal disorders. • It binds to gamma-aminobutyric acid (GABA) receptors and prevents the release of inhibitory neurotransmitters and substance P. • It has been used extra-label in dogs to reduce urethral resistance (1–2 mg/kg, PO, q8h) but is rarely recommended due to its narrow margin of safety. Use in cats is not recommended. • Doses as low as 1.3 mg/kg in dogs have caused vomiting, depression, and vocalization. • Death has been documented in dogs at 8–16 mg/kg.

The following organ systems are predominantly affected:

- Cardiovascular
- Gastrointestinal
- Musculoskeletal
- Nervous
- Respiratory

SIGNALMENT

• Accidental exposure in dogs is more frequently reported than in cats but any animal may be at risk for poisoning. • Cats are extremely sensitive to baclofen.

SIGNS

- Signs begin within 15 minutes of ingestion but, rarely, may be delayed several hours.
- Common signs: vocalization, vomiting, ataxia, disorientation, hypersalivation, depression, weakness, coma, flaccid paralysis, recumbency, seizures, and hypothermia.
- Life-threatening signs: dyspnea, respiratory depression and arrest secondary to diaphragmatic/intercostal muscle paralysis.

CAUSES & RISK FACTORS

Pet owners with medical conditions such as multiple sclerosis, cerebral palsy, and spinal disorders are more likely to have baclofen in the home.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Toxic: benzodiazepines, depressants, ethanol, ethylene glycol, illicit drugs (marijuana, LSD, phencyclidine [PCP], hallucinogenic mushrooms), methanol, opioids, propylene glycol, tranquilizers, xylitol
- Lower motor neuron disease (e.g., botulism, *Neospora*, tick bite paralysis, *Toxoplasma*)
- Metabolic (e.g., hepatic encephalopathy, hypoglycemia, etc.)

CBC/BIOCHEMISTRY/URINALYSIS

No specific abnormalities expected but should be used to rule out other causes.

OTHER LABORATORY TESTS

- Arterial blood gas analysis (hypoxemia, oxygenation, and ventilation)
- Pulse

oximetry (hypoxemia) • End tidal CO₂ (hypercapnia or hypoventilation)

IMAGING

Thoracic radiographs (aspiration pneumonia)

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Many cases quickly become serious and referral to a 24 hour critical care center should be considered. • Treatment is focused on decontamination and supportive care.
- Induce emesis following recent (< 1 hour) ingestion in asymptomatic patients only if they have not already vomited. Consider gastric lavage for very large ingestions. • One dose of activated charcoal. • IV fluid crystalloids at 1.5–2.5 × maintenance to support organ perfusion and enhance elimination. • Monitor for cardiac arrhythmias, hypoventilation, and aspiration pneumonia. • Oxygen if respiratory depression; ventilator support if severe respiratory depression/failure. • Monitor body temperature and provide warming/cooling measures as needed. • Hemodialysis and hemoperfusion have successfully shortened the elimination half-life and lead to full recovery.



MEDICATIONS

DRUG(S)

- Atropine for bradycardia (0.02–0.04 mg/kg IM, IV, or SQ PRN for dogs or cats).
- Antiemetics as needed (e.g., maropitant 1 mg/kg SQ q24h). • Diazepam for seizures (0.25–0.5 mg/kg IV, to effect, PRN for dogs or cats). Use the lowest effective dose as sedation is caused by baclofen. • For refractory seizures use propofol (1–8 mg/kg IV, to effect, PRN, followed by CRI dose of 0.1–0.6 mg/kg IV for dogs or cats) or general anesthesia. • Agitation may be treated with acepromazine (0.05–0.2 mg/kg IV, IM, or SQ PRN for cats or dogs), diazepam, or midazolam. • Cyproheptadine for vocalization/disorientation (dogs, 1.1 mg/kg PO or rectally q4–6h; cats, 2–4 mg total dose q4–6h). • Intravenous lipid emulsion (ILE) is a relatively new treatment for fat-soluble drugs and has successfully treated dogs suffering from baclofen intoxication. It should be reserved for critical cases. Doses vary. Using 20% emulsion, give 1.5 mL/kg IV bolus followed by a CRI of 0.25 mL/kg/min for 30–60 min up to 8 mL/kg daily. If the initial bolus fails to produce the desired effect, consider additional doses of 1.5 mL/kg IV q4–6h for the initial 24 hours. If after 3–5

boluses no clinical response is seen, discontinue use.

CONTRAINDICATIONS / POSSIBLE INTERACTIONS

- Use acepromazine cautiously due to risk of hypotension. • Use all sedatives cautiously as baclofen also causes sedation. • Avoid drugs that cause respiratory depression (e.g., phenobarbital).



FOLLOW-UP

PATIENT MONITORING

- Serious cases require intense, consistent patient monitoring including vital signs, blood pressure, blood gas analysis, pulse oximetry, and end tidal CO₂. • Nursing care should include turning/repositioning q6h, ocular lubrication, keeping patient dry/clean, passive range of motion of limbs, and soft bedding.

PREVENTION/AVOIDANCE

Educate pet owners about the risks of leaving prescription drugs accessible to pets.

POSSIBLE COMPLICATIONS

Aspiration pneumonia due to combination of vomiting, sedation, seizures, and paralysis of diaphragm/intercostal muscles.

EXPECTED COURSE AND PROGNOSIS

- Patients suffering serious intoxications may take 5–7 days to fully recover. • Recovery often occurs with no residual effects.
- Prognosis is good with early and appropriate care but becomes poor if medical care is delayed. Seizures and aspiration pneumonia are associated with a guarded prognosis.



MISCELLANEOUS

ABBREVIATIONS

- CNS (central nervous system)
- GABA (gamma-aminobutyric acid)
- ILE (intravenous lipid emulsion)
- LSD (lysergic acid diethylamide)
- PCP (phencyclidine)

INTERNET RESOURCES

- <http://www.petpoisonhelpline.com/poison/baclofen/>
- http://www.aspapro.org/sites/pro/files/g-toxbrief_0504.pdf

Suggested Reading

Khorzad R, Lee JA, Whelan M, et al. Baclofen toxicosis in dogs and cats: 145 cases (2004–2010). J Am Vet Med Assoc 2012, 241(8):1059–1064.

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Consulting Editor Lynn R. Hovda



Client Education Handout
available online

BARTONELLOSIS

B



BASICS

OVERVIEW

- Emerging infectious agents that are highly adapted to preferential reservoir hosts, where they establish chronic intraerythrocytic bacteremia.
- Agents—small, curved, facultative fastidious intracellular argyrophilic, hemotrophic Gram-negative rod (bacilli) bacteria.
- Vector transmitted (fleas, ticks).
- Human syndrome—wide variety of clinical syndromes, including, most commonly, cat scratch disease, typified by regional lymphadenopathy after a cat scratch or bite distal to the involved lymph node; worldwide occurrence; estimated > 25,000 cases/year in United States; > 2,000 cases require hospitalization; almost no fatalities.
- Cats—usually asymptomatic.
- Dogs—emerging clinical syndrome.
- Seasonal; more cases reported between July and January.

SIGNALMENT

- Dogs and cats.
- Majority of human patients (80%) < 21 years of age; more males than females (1.2:1).

SIGNS

Human

- Erythematous papule at inoculation site (scratch, bite); then unilateral regional lymphadenopathy (painful, often suppurative) in 3–10 days (> 90% of cases).
- Mild fever.
- Chills—infrequent.
- Malaise.
- Anorexia.
- Myalgia.
- Nausea.
- Atypical manifestations (in up to 25% of cases)—encephalopathy (1–7%); palpebral conjunctivitis (3–5%); meningitis; optic neuritis; osteolytic lesions; granulomatous hepatitis; granulomatous splenitis; pneumonia; endocarditis.

Cats

- No signs of illness.
- Between 5 and 60% seropositive, depending on geographical area.
- Lymphoid hyperplasia (sometimes), uveitis, endocarditis (rare), self-limiting fever.

Dogs

Expanding spectrum of disease including endocarditis, myocarditis, granulomatous lymphadenitis, rhinitis, vasculitis, uveitis, choriorretinitis, arthritis, meningoencephalitis, anemia, thrombocytopenia.

CAUSES & RISK FACTORS

- Contact with domestic kittens and cats (> 90%), particularly young cats with fleas.
- Scratched by cat—up to 83%.
- Up to 95% of cats residing in households of affected humans are seropositive.
- Localized infections in immunocompetent; systemic infection in immunocompromised.
- Dogs: risk factors include tick and flea exposure and rural environment.
- Bartonella include: *Bartonella henselae*, *B. claridgeiae*, *B. koehlerae*, *B. bovis*, *B. quintana*.
- Canine

bartonella include: *B. vinsonii* ssp. *berkhoffii*, *B. henselae*, *B. claridgeiae*, *B. washoensis*, *B. quintana*, *B. rochalimae*, *B. elizabethae*.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Benign adenopathy in human children and young adults—most common cause.
- History of contact with a cat.
- Formation of a papule at the site of primary inoculation (scratch or bite).
- Compatible clinical picture—unilateral regional lymphadenitis.
- Exclusion of other identifiable causes.
- Characteristic histopathologic findings.
- Serologic tests—indirect fluorescent antibody for *B. henselae*.
- Positive skin test no longer used.
- Other causes of lymphadenopathy—lymphogranuloma venereum; syphilis; typical or atypical tuberculosis; other forms of bacterial adenitis; sporotrichosis; tularemia; brucellosis; histoplasmosis; sarcoidosis; toxoplasmosis; infectious mononucleosis; and benign or malignant tumors.
- Dogs: co-infections with other tick-borne diseases (*Ehrlichia*, *Babesia*).

CBC/BIOCHEMISTRY/URINALYSIS

Non-contributory

OTHER LABORATORY TESTS

- Indirect fluorescent antibody test.
- Enzyme immunoassay—IgG antibodies to *B. henselae* (Quest Diagnostics Nichols Institute Laboratory, Valencia, CA).
- Culture—on enriched (blood-containing) media in presence of 5% carbon dioxide at 35–37°C; fastidious and slow growing; requires 14–30 days.
- PCR amplification of bacterial DNA from lesions (Galaxy Diagnostics, Research Triangle Park, NC).

PATHOLOGIC FINDINGS

- Histopathology of lymph nodes—non-specific inflammatory reaction, including granuloma, microabscess, and necrosis.
- Warthin-Starry silver stain—bacilli.



TREATMENT

- Supportive treatment—bed rest; heat on swollen lymph nodes; needle aspiration of suppurative nodes.
- Thoroughly cleanse all cat scratches or bites.
- Prevent cats from contacting open wounds.



MEDICATIONS

DRUG(S)

- Specific antimicrobials—not efficacious.
- Most cases spontaneously resolve in a few weeks or months.

- Severe cases—antibiotic therapy (gentamicin, doxycycline, erythromycin, azithromycin) based on the antimicrobial susceptibility of *B. henselae* may be appropriate.

- Dogs—optimal therapy not established but likely long-term (4–6 weeks) antibiotics consisting of macrolides (erythromycin, azithromycin).



FOLLOW-UP

PREVENTION/AVOIDANCE

Immunocompromised people should avoid young cats.

POSSIBLE COMPLICATIONS

Uncommon



MISCELLANEOUS

- One episode appears to confer life-long immunity.
- Bacillary angiomatosis—vascular proliferative disease of the skin; may also be caused by *B. henselae*; responds to antimicrobial drugs (bartonellosis rarely does).
- Natural host of *B. henselae* is unknown but may be the cat; a related species, *B. quintana*, is spread by lice and causes trench fever in humans.

ZOONOTIC POTENTIAL

The risk of transfer of organisms from infected dogs and cats to people is unknown, although infected cats probably serve as a source of organisms for fleas that are thought to transmit the infection to humans by way of contaminating wounds with infected flea feces (i.e., cat scratch disease).

- Dogs may also serve as chronically infected blood reservoirs for *Bartonella* species, which may be spread by arthropod vectors to people.

ABBREVIATIONS

- PCR = polymerase chain reaction

Suggested Reading

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Pennisi MG, Marsilio F, Hartmann K, et al. *Bartonella* species infection in cats: ABCD guidelines on prevention and management. J Feline Med Surg 2013, 15:563–569.

Zangwell KM. Cat scratch disease and other *Bartonella* infections. Adv Exp Med Biol 2013, 764:159–166.

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Consulting Editor Stephen C. Barr

BASAL CELL TUMOR

B



BASICS

OVERVIEW

- Originates from the basal epithelium of the skin.
- Includes benign (e.g., basal cell epithelioma and basaloïd tumor) and malignant (e.g., basal cell carcinoma) tumors.
- Metastasis is rare with the benign forms, and uncommon with malignant.

SIGNALMENT

- Most common skin tumor in cats (15–26%) and second to third most common skin tumor in dogs (4–12%).
- Median age—dogs, 6–9 years; cats, 10–11 years.
- Breed predilections includes cocker spaniels, poodles, and Siamese cats.

SIGNS

- Solitary, well-circumscribed, firm, often hairless, intradermal raised mass, typically located on the head, neck, or shoulders.
- Can vary greatly in size from a few millimeters to many centimeters in diameter.
- Feline basal cell tumors are frequently heavily pigmented, and occasionally cystic or ulcerated.

CAUSES & RISK FACTORS

- Breed (see "Signalment").
- Contrary to human basal cell tumors, chronic ultraviolet exposure does not appear to play a role in pets.
- Possible association with canine papillomavirus exposure.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other skin tumors including mast cell tumor, extramedullary plasmacytoma, melanoma, hemangioma, hemangiosarcoma, histiocytoma.
- Melanoma is an especially important differential with the pigmented feline basal cell tumors.
- Intradermal cysts.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Cytologic evaluation of fine-needle aspiration sample reveals round cells with basophilic cytoplasm; mitoses are not uncommon despite benign nature.
- When clinically indicated, fine-needle aspiration of draining lymph nodes to confirm or deny the presence of regional metastases.
- Histopathologic examination required for definitive diagnosis. When highly pigmented, immunohistochemistry occasionally required to differentiate from melanoma.

PATHOLOGIC FINDINGS

- Histologic cellular patterns vary from solid to cystic to ribbon appearance.
- Tumor cells may contain melanin pigmentation; may have a fine eosinophilic stroma.
- Nuclear criteria might help predict risk of local recurrence in feline basal cell carcinomas.



TREATMENT

- Surgical excision treatment of choice and generally curative for fully resectable tumors.
- Cryosurgery or plesiotherapy with strontium-90 can be used for smaller, superficial lesions (< 1 cm).



MEDICATIONS

DRUG(S)

N/A

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- Complete surgical excision is usually curative and associated with an excellent prognosis.
- Majority of tumors are locally confined and non-metastatic. Long-term follow-up is generally unnecessary.



MISCELLANEOUS

Suggested Reading

Carpenter JL, Andrews LK, Holzworth J. Tumors and tumor-like lesions. In: Holzworth J, ed., Diseases of the Cat: Medicine and Surgery. Philadelphia: Saunders, 1987, pp. 406–596.

Cowell RL, Tyler RD, Meinkoth JH. Diagnostic Cytology and Hematology of the Dog and Cat. St Louis: Mosby, 1999, pp. 40–42.

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Simeonov R, Simeonova G. Nucleomorphometric analysis of feline basal cell carcinomas. Res Vet Sci 2008; 84:440–443.

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Consulting Editor Timothy M. Fan



BASICS

OVERVIEW

- Alkaline/Acid-based batteries—ulcers to the gastrointestinal tract from leaking contents, oral injury from chewing on casing and rarely heavy metal toxicity from break down of casing in the GI tract.
- Disc/Button/Lithium Ion batteries—rapid necrosis to the esophagus and stomach due to electric current from the battery. Significant necrosis can occur 15 minutes after contact.

SIGNALMENT

Dogs, cats, birds and small mammals. Young animals are more commonly affected.

SIGNS

- Historical: finding chewed-up electronic equipment without the battery, a chewed or mangled battery, or battery packaging.
- Physical:
 - Oral ulcerations
 - Oral injury from chewing on battery casing
 - Loss of appetite, drooling, regurgitation, vomiting, diarrhea, melena, progressive weakness, dyspnea, coughing, stridor, pleuritis, pyothorax, and pneumo-mediastinum.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

History, complete oral exam and full (esophagus and abdominal gastrointestinal tract) survey radiographs of the digestive tract enable diagnosis. Black debris in the oral cavity is evidence of leaked battery contents from a dry cell battery. Distinguish from exposure to other corrosive compounds (cleaning agents, drain cleaners, pool shocking agents, essential oils, and mechanical injury from chewing).

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia—secondary to bleeding gastrointestinal ulceration.
- Leukocytosis—inflammation and secondary infection.
- Elevated total proteins/prerenal azotemia—secondary to dehydration.
- Elevated liver enzymes secondary to heavy metal toxicity from break down of casing.

IMAGING

- Full survey radiographs—determine if a battery was swallowed, assess location and condition of battery and casing, look for evidence of perforation and/or obstruction.

- Endoscopy—pending severity of signs, evaluate extent of damage to the esophagus. May be able to remove the battery or casing. Use caution and do not damage the esophagus.



TREATMENT

- Lavage the oral cavity for 10–15 minutes for alkaline batteries; for disc batteries give 10–20 mL of water every 15 minutes until battery is out of the esophagus.
- Do NOT induce vomiting as this may expose the esophagus to further injury.
- NPO or slurry feeding for 24–48 hours if oral ulcerations are present.
- Ulceration may not be visible in the oral cavity until 48 hours post exposure.
- Wear gloves when cleaning up any battery debris as leaked acid could cause injury to the hands.
- Small, intact dry cell batteries in the stomach should pass within 48 hours. Evaluate all stools and if the battery has not passed the pylorus in 48 hours it should be surgically removed.
- Punctured dry cell batteries and disc/button/lithium ion batteries should be immediately removed by endoscopy or surgery.



MEDICATIONS

- Analgesics—ulcerations can be very painful.
 - Dogs—tramadol 2–5 mg/kg PO q6–8h.
 - Cats—buprenorphine 0.01–0.03 mg/kg buccal, IV or IM.
- H2 Blocker—to aid in the healing of gastric ulcerations.
 - Famotidine 0.5 mg/kg PO or SQ q12h.
- Sucralfate 0.25–1 gram PO q8h on an empty stomach.
- Antibiotics—to prevent secondary infection when ulcers are present.
 - Metronidazole 10–30 mg/kg PO q12–24h.
 - Enrofloxacin: cats, 5 mg/kg PO q24h; dogs, 5–10 mg/kg PO q12h.

CONTRAINdicATIONS

- Emetics—emesis should not be performed as it may worsen damage to the esophagus.
- Steroids—may reduce risk of esophageal stricture but expected to slow healing time.
- NSAIDs—aid in pain management and swelling reduction but may increase risk of gastric ulceration/perforation.



FOLLOW-UP

PATIENT MONITORING

Consider endoscopy 2 weeks post exposure to assess esophagus.

POSSIBLE COMPLICATIONS

Esophageal perforation, esophageal stricture, gastrointestinal obstruction, heavy metal toxicity.

EXPECTED COURSE AND PROGNOSIS

- Non-ruptured dry cell battery: excellent, most pets pass on own within 48 hours.
- Ruptured dry cell battery: guarded, pending location of corrosive exposure and amount of time before removal. Esophageal injury worsens prognosis.
- Disc/button/lithium ion battery: guarded, rapid removal is needed. Significant injury, including esophageal or gastric perforation, can occur within 15 minutes of the ingestion.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Heavy metal toxicity, esophagitis, esophageal stricture, esophageal perforation, gastrointestinal obstruction.

Suggested Reading

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Yamashita M, Saito S, Koyama K, et al. Esophageal electrochemical burn by button-type alkaline batteries in dogs. *Vet Hum Toxicol* 1987, 29:226–230.

Author Catherine A. Angle

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Client Education Handout
available online

BAYLISASCARIASIS

B



BASICS

OVERVIEW

- Two forms of baylisascariasis have been reported in dogs: an intestinal infection occurring in adults and visceral disease caused by larval migration to puppies.
- The disease is caused by the raccoon roundworm *Baylisascaris procyonis*. Infection of raccoons occurs by ingestion of eggs or by ingestion of larvae in tissues of mammalian paratenic hosts.
- Dogs are infected by the ingestion of infective eggs or paratenic hosts from which they develop patent infections with adult worms in their small intestine. Puppies, probably infected by the ingestion of eggs, develop visceral disease like most other mammals.
- Dogs with intestinal infection are typically without signs. Puppies with larval baylisascariasis show signs of neurologic disease.

SIGNALMENT

- Dogs.
- Intestinal form—reported from adult animals.
- Larval form—reported in two puppies; suspected that only severe cases have been reported: infection with only a few larvae probably does not cause severe disease in most puppies.

SIGNS

- Intestinal form—none.
- Larval form—weakness, ataxia, dysphagia, circling, recumbency.

CAUSES & RISK FACTORS

Sharing space with areas frequented by raccoons.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Intestinal form—eggs in feces can be distinguished from those of either *Toxocara* or *Toxascaris*.
- Larval form—rabies, canine distemper, congenital neurologic defect.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

N/A

IMAGING

Larval form—based on lesions of toxocariasis or baylisascariasis in humans, lesions may appear on abdominal ultrasound or CT scans as small, single or multiple ill-defined, oval or elongated, low-attenuating lesions in the liver parenchyma. In neurologic lesions, MRI reveals diffuse periventricular white matter disease with atrophy.

DIAGNOSTIC PROCEDURES

- Intestinal form—direct fecal smear or fecal flotation.
- Larval form—ophthalmoscopic examination may show migratory tracks in retina, may use imaging methods to visualize lesions in soft tissue or brain.



TREATMENT

- Intestinal form—may want to treat as inpatient to prevent environmental contamination with eggs and to ensure proper disposal (as biohazard) or destruction (incineration) of fecal material and worms after treatment.
- Larval form—no treatment to date.

CLIENT EDUCATION

Alert owner of potential risk to people who may frequent similar habitats as raccoons.



MEDICATIONS

DRUG(S)

Intestinal Form

- Pyrantel pamoate (5 mg/kg).
- Febantel (25–35 mg/kg), pyrantel pamoate (5–7 mg/kg), praziquantel (5–7 mg/kg) (Drontal Plus).
- Ivermectin (5 µg/kg), pyrantel pamoate (5 mg/kg) (Heartgard Plus).
- Milbemycin (0.5 mg/kg), lufenuron (10 mg/kg) (Sentinel).

Larval Form

Corticosteroids and long-term albendazole (25–50 mg/kg/day for 10 days) may prove beneficial.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- Intestinal form—check feces 2 weeks after deworming and again 1 month later.
- Larval form—disease has proven fatal.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Intestinal form—eggs are not infectious when passed but can develop in the environment in several days; ingestion of eggs containing infective larvae by humans can cause severe disease, i.e., larval baylisascariasis.
- Larval form—infected puppies pose no zoonotic threat; puppy in one case represented the typical presentation of larval baylisascariasis wherein animals are held in areas that have previously housed a raccoon.
- Alert owner of potential risk to people who may frequent similar habitats as raccoons.

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging

Suggested Reading

Chang S, Lim JH, Choi D, et al. Hepatic visceral larva migrans of *Toxocara canis*: CT and sonographic findings. Am J Roentgenology 2006, 187:W622–W629.

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BENIGN PROSTATIC HYPERPLASIA (BPH)

B



BASICS

OVERVIEW

- Age-related pathologic change in the prostate gland making it non-painfully large.
- Occurs in two phases, glandular and complex.
- Glandular phase characterized by high number of large prostatic cells and a symmetrically large prostate gland.
- Complex phase characterized by glandular hyperplasia, glandular atrophy, small cyst formation, chronic inflammation, and squamous metaplasia of epithelium.

SIGNALMENT

- Observed initially in intact male dogs 1–2 years old.
- Prevalence increases with age; 60% of intact male dogs are affected by 6 years of age and 95% of intact male dogs are affected by 9 years of age.

SIGNS

Historical Findings

- None in most dogs
- Bloody urethral discharge
- Hematuria
- Dysuria
- Blood in ejaculate
- Straining to defecate
- Ribbon-like stools

Physical Examination Findings

- Symmetric, non-painfully enlarged prostate gland.
- Prostatic pain in dogs with complication of bacterial infection or prostatic carcinoma.

CAUSES & RISK FACTORS

- Testosterone and 5- α -dihydrotestosterone
- Estrogens
- Aging
- Risk eliminated by castration



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute bacterial prostatitis—typically associated with fever, depression, pain on rectal palpation, neutrophilia, pyuria, and bacteriuria; may occur concurrently in dogs with benign prostatic hyperplasia.
- Chronic bacterial prostatitis—typically associated with recurrent lower urinary tract infections and subfertility; may occur concurrently in dogs with benign prostatic hyperplasia.
- Prostatic adenocarcinoma—typically associated with poor appetite, weight loss, hind limb weakness, dysuria, hematuria, and

dyschezia; may see carcinoma cells in urine sediment.

- Prostatic and paraprostatic cysts—can cause palpable abdominal cystic mass filled with yellow to orange fluid.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC and biochemistry—normal. If abnormalities detected, see “Differential Diagnosis” above.
- Urinalysis—may be normal or reveal hematuria; pyuria and bacteriuria are absent unless dog has concurrent bacterial infection; see “Differential Diagnosis” above.

OTHER LABORATORY TESTS

- Prostatic fluid obtained by ejaculation or prostatic massage may be clear or hemorrhagic; RBC count high; WBC count normal; culture reveals < 100,000 colony forming units of bacteria/mL unless the dog has concurrent bacterial infection.
- Serum concentration of prostatic esterase is high in some dogs.

IMAGING

Radiography

- Abdominal radiographs reveal prostatomegaly.
- Retrograde urethrocystography may be normal or reveal narrowing of prostatic urethra and/or reflux of contrast media into the prostate gland.

Ultrasonography

- Reveals enlarged prostate gland with uniform prostatic parenchymal echogenicity; small, fluid-filled cysts in some dogs.
- Ultrasound-guided fine-needle aspirate can be used to correctly diagnose prostatic disease in 80% of cases.

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Not required if asymptomatic.
- Castration—most effective and prevents recurrence; if benign prostatic hyperplasia is complicated by acute bacterial prostatitis, delay surgery until the infection is resolved.



MEDICATIONS

DRUG(S)

- If castration is not acceptable, the following drugs may temporarily shrink the prostate gland:
 - Finasteride (0.1–0.5 mg/kg/day for up to 4 months)

◦ Megestrol acetate (0.11 mg/kg PO daily for 3 weeks)

- Medroxyprogesterone (3–4 mg/kg SC with subsequent doses administered at no less than 10-week intervals).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Avoid estrogens because of possible hematologic toxicity and development of squamous metaplasia of the prostate.
- Long-term administration of megestrol acetate or medroxyprogesterone may result in development of diabetes mellitus.



FOLLOW-UP

- Castration will result in rapid involution of the enlarged prostate. The prostate decreases in volume by 50% within 3 weeks following castration.
- Treatment with finasteride not associated with decline in libido, decline in semen quality, or induction of birth defects. BPH will recur after withdrawal of finasteride; time until clinical signs recur is variable.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Bacterial prostatitis and prostatic carcinoma.
- Prostatomegaly in a castrated dog strongly suggests prostatic carcinoma.

SEE ALSO

- Prostatic Cysts
- Prostatitis and Prostatic Abscess
- Prostatomegaly

ABBREVIATIONS

- BPH = benign prostatic hyperplasia/hypertrophy
- RBC = red blood cell
- WBC = white blood cell

SUGGESTED READING

Johnston SD, Root Kustritz MV, Olson PN. Disorders of the canine prostate. In: Canine and Feline Theriogenology. Philadelphia: Saunders, 2001, pp. 337–355.

Smith J. Canine prostatic disease: A review of anatomy, pathology, diagnosis, and treatment. Theriogenology 2008, 70:375–383.

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BENZODIAZEPINE AND OTHER SLEEP AIDS TOXICOSIS



BASICS

DEFINITION

- Toxicosis due to ingestion of sleep aids or antianxiety medications commonly used in human and veterinary medicine.
- Benzodiazepine class—alprazolam (Xanax), clonazepam (Klonopin), diazepam (Valium), lorazepam (Ativan), midazolam (Versed), and many more.
- Imidazopyridine class—eszopiclone (Lunesta), zaleplon (Sonata), and zolpidem (Ambien, Ambien CR, Intermezzo).

PATHOPHYSIOLOGY

- Benzodiazepines and imidazopyridines bind to receptors near the gamma-aminobutyric acid (GABA) receptor/chloride channel on neurons; they potentiate GABA's effect, which increases the opening of the chloride channel, leading to hyperpolarization of the nerve and decreased excitation.
- Imidazopyridines bind near the receptor subset that is responsible for sedation, while benzodiazepines bind to all receptor subsets and so not only mediate sedation but are also anticonvulsant and anxiolytic.
- Paradoxical reactions can occur and are typically described as excitement, irritability, and aberrant demeanor in cats and excitement in dogs, when the expected effect is seizure control or sedation.
- Both classes are well absorbed orally and have rapid onset of actions, often less than 30 minutes.
- Duration of action depends on the drug and may last for hours to days.
- Both classes have wide margins of safety; lethal exposures are rare if a single agent is involved.
- Benzodiazepines—signs can be seen at therapeutic doses; however, the drugs have a wide margin of safety, with the minimal lethal dose being approximately 1,000 times the therapeutic dose. Cats may develop idiosyncratic hepatic failure with chronic oral dosing of diazepam and clonazepam.
- Zaleplon—based on a review of the ASPCA APCC Antox database: In dogs, doses > 0.11 mg/kg have been associated with restlessness and hyperactivity; in cats, doses of > 1.25 mg/kg caused paradoxical reactions.
- Zolpidem—based on a review of the ASPCA APCC Antox database: In dogs, dosages > 0.2 mg/kg can cause mild sedation and ataxia; doses > 0.6 mg/kg can cause paradoxical reactions. In cats, signs of paradoxical reactions were seen at 0.34 mg/kg or greater.

SYSTEMS AFFECTED

- Gastrointestinal—vomiting
- Hepatic—acute necrosis and failure in cats with diazepam and clonazepam
- Nervous—CNS depression and/or paradoxical reactions, ataxia, coma
- Respiratory—depression

GENETICS

N/A

INCIDENCE/PREVALENCE

Commonly prescribed drugs so exposure is common

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dogs and cats—acute toxicity; cats—idiosyncratic hepatic failure with chronic oral dosing of diazepam or clonazepam possible.

Breed Predilections

None

Mean Age and Range

None

Predominant Sex

None

SIGNS

General Comments

- Benzodiazepines can cause sedation with virtually any exposure (even at therapeutic doses).
- Imidazopyridines cause sedation at low doses but likelihood of paradoxical reaction increases with increasing dose, especially in dogs.

Historical Findings

- Evidence of accidental ingestion of medication
- Therapeutic use of drug
- Lethargy
- Ataxia
- Sedation
- Agitation

Physical Examination Findings

- Depression
- Ataxia
- Sedation
- Hypothermia
- Agitation
- Hyperthermia (secondary to agitation)
- Tachycardia
- Icterus (in cats with idiopathic liver failure)

CAUSES

Accidental exposure, inappropriate administration, or therapeutic use

RISK FACTORS

- Younger and older animals
- Animals with preexisting conditions



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- CNS depression—barbiturates, ivermectin, ethylene glycol, alcohols (e.g., ethanol, methanol), marijuana, opioids, and antidepressants (low doses).
- Paradoxical reactions—amphetamines, pseudoephedrine, methylxanthines, cocaine, phenylpropanolamine, and serotonin syndrome (secondary to antidepressants).

CBC/BIOCHEMISTRY/URINALYSIS

- No abnormalities expected in acute overdoses.
- In cats with idiopathic liver failure, elevated liver enzymes and bilirubin.

OTHER LABORATORY TESTS

- Benzodiazepines can be detected in blood, urine, and liver; OTC drug-testing kits may be used to confirm exposure.
- Imidazopyridines can be detected in blood and urine; OTC drug-testing kits are not yet readily available.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

No gross or histologic changes are expected.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—most mildly affected animals can be managed at home with confinement (to avoid injury due to falls) and minimizing stimulation.
- Inpatient—animals who are comatose or showing paradoxical reactions.

NURSING CARE

- Intravenous fluids.
- Monitor and control body temperature.
- Good bedding and frequent turning for recumbent patients.
- Minimize sensory stimulation, especially with paradoxical reactions.

ACTIVITY

Restrict until recovered to avoid injury.

DIET

Cats with liver failure may require forced or tube feeding for support.

CLIENT EDUCATION

- Make all clients aware of proper storage of all medications.

(CONTINUED)

BENZODIAZEPINE AND OTHER SLEEP AIDS TOXICOSIS**B**

- If prescribing diazepam or clonazepam to cats, have owner closely monitor the cat for the first week.

SURGICAL CONSIDERATIONS

N/A

**MEDICATIONS****DRUG(S) OF CHOICE**

- Acpromazine 0.025–0.05 mg/kg IV/IM as needed to control paradoxical reactions.
- Cyproheptadine 1.1 mg/kg PO or rectally for dogs; 2–4 mg/cat for control of paradoxical reactions.
- Flumazenil—a benzodiazepine reversal agent—0.01 mg/kg IV q1–2h as needed.
 - It can be used to reverse both excessive sedation and paradoxical reaction.
 - However, flumazenil can cause seizures so its use is generally restricted to life-threatening situations.

CONTRAINdications

Do not give other benzodiazepines to control paradoxical reactions.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

Care when using other depressant medications (e.g., barbiturates, phenothiazines), as these can potentiate the depressant effects of these drugs.

**FOLLOW-UP****PATIENT MONITORING**

TPR, blood pressure, respiratory effort

PREVENTION/AVOIDANCE

Secure medications out of reach of dogs and cats

POSSIBLE COMPLICATIONS

No long-term complications expected

EXPECTED COURSE AND PROGNOSIS

- Prognosis for acute overdose is excellent with symptomatic care.
- Prognosis for acute hepatic failure in cats with diazepam is poor.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

- Young animals and those with preexisting liver disease may have prolonged signs due to reduced ability to clear the drugs.
- Younger animals may be more prone to paradoxical reactions.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Benzodiazepines are considered teratogenic

SEE ALSO

- Amphetamine Toxicosis
- Antidepressant Toxicosis—SSRIs and SNRIs
- Antidepressant Toxicosis—Tricyclic
- Ethanol Toxicosis
- Ethylene Glycol Toxicosis
- Ivermectin and other Macrocytic Lactones Toxicosis

ABBREVIATIONS

- ASPCA APCC = American Society for the Prevention of Cruelty to Animals Animal Poison Control Center

- CNS = central nervous system
- GABA = gamma-aminobutyric acid
- OTC = over-the-counter

INTERNET RESOURCES

- <http://www.aspca.org/pet-care/animal-poison-control>
- <http://www.petpoisonhelpline.com/poison/lunesta/>

Suggested Reading

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BETA BLOCKER TOXICOSIS

B



BASICS

OVERVIEW

• Beta receptor antagonists are class II antidysrhythmics used to treat hypertrophic or hypertrophic obstructive cardiomyopathy in cats and hypertension and tachydysrhythmias in dogs and cats. • β_1 receptors are primarily located in the heart, eye, and kidney. Blockage may result in significant bradycardia. • β_2 receptors are primarily located in bronchial smooth muscle, gastro-intestinal tract, pancreas, liver, skeletal muscle, vascular smooth muscle, and endothelium. Blockage results in bronchospasm and vasodilation. • Systems affected include: ◦ Cardiovascular—bradycardia, hypotension ◦ Respiratory—bronchospasm ◦ Nervous—decreased mentation, seizures ◦ Endocrine/metabolic—hypoglycemia, metabolic acidosis secondary to hypoperfusion.

SIGNALMENT

Dogs and cats equally affected with no breed, age, or sex predilection.

SIGNS

- Bradycardia • Hypotension • AV block
- Decreased mentation • Respiratory distress/bronchospasm • Seizures • Coma • Death

CAUSES AND RISK FACTORS

Ingestion of medication or inadvertent overdose of beta adrenergic antagonists



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Calcium channel blocker overdose • Cardiac disease with secondary bradycardia
- Cardiovascular drug overdose (e.g. clonidine, digoxin toxicosis) • Sedative overdose (e.g. opioid or baclofen toxicosis)
- Sick sinus syndrome • Hyperkalemia
- Decompensated shock/sepsis

CBC/CHEMISTRY/URINALYSIS

- Hypoglycemia • Hypokalemia • Azotemia and elevated liver enzymes with prolonged hypoperfusion

OTHER LABORATORY TESTS

Blood gas—metabolic acidosis secondary to hypoperfusion

DIAGNOSTIC PROCEDURES

- ECG—1st, 2nd, and 3rd degree AV block; prolonged PR, QRS and QT intervals
- Echocardiogram—negative inotropy, decreased cardiac output



TREATMENT

- Emesis if asymptomatic and recent (< 2 hours) ingestion. • Consider gastric lavage if decreased mental status or large number of pills ingested. • Whole bowel irrigation considered for extended (ER) or sustained release (SR) medications. • Central line placement for CVP monitoring, frequent glucose monitoring and dextrose administration during high dose insulin (HDI) therapy. • Volume resuscitation with IV fluid bolus for hypotension:
 - 10–20 mL/kg for cats over 15–30 minutes
 - 20–30 mL/kg for dogs over 15–30 minutes.



MEDICATIONS

DRUGS

- Activated charcoal (1–2 g/kg) administered within 2 hours post-exposure. • Atropine (0.02–0.04 mg/kg IV) may be used for sinus bradycardia. • Intravenous fat emulsion (IFE): ◦ Used to treat lipid-soluble drug intoxication ◦ Three possible mechanisms:
 - (1) Provide a lipid sink for fat soluble drugs;
 - (2) Supply a fatty acid source for cardiac performance;
 - (3) Increase intracellular calcium (Ca) via activation of voltage gated Ca channels to improve myocyte function.
- IFE dose: 1.5 mL/kg IV bolus of a 20% solution over 1 minute. Follow with a CRI of 0.25 mL/kg/min for 30–60 minutes. Can repeat bolus every 3–5 minutes as needed up to 3 mL/kg, not to exceed a total dose of 8 mL/kg. • HDI/glucose administration:
 - The exact mechanism of HDI is unknown but appears to promote uptake and utilization of carbohydrates as an energy source. May increase myocardial cell cytosolic Ca levels to increase cardiac contractility and cardiac output.
 - HDI increases cardiac output through positive inotropic effects but does not increase systemic vascular resistance. Blood pressure may not improve significantly even though clinical signs and perfusion may improve.
- Recommended treatment:
 - (1) Check blood glucose (BG) concentration and administer dextrose if BG is < 100 mg/dL for dogs and < 200 mg/dL in cats.
 - (2) Administer regular insulin at 1 unit/kg IV. Follow with a CRI IV of regular insulin at 2 units/kg/h. Increase every 10 minutes as needed up to a maximum dose of 10 units/kg/h. When clinical signs resolve, decrease insulin by 1–2 units/kg/h.
 - (3) Monitor BG every 10 minutes while titrating insulin dosing. Once insulin dosing is stabilized, check BG every 30–60 minutes. Dextrose supplementation IV will be needed to maintain BG concentrations. May need to continue dextrose supplementation up to 24 hours after discontinuation of the insulin

therapy. (4) Monitor potassium concentration every hour. Administer potassium chloride to keep potassium concentrations in the low therapeutic range. • 10% calcium chloride or gluconate for hypotension and may increase efficacy of HDI therapy. • 10% Ca chloride 0.2 mL/kg or Ca gluconate 0.6 mL/kg IV bolus to maintain ionized Ca at 1–2 X therapeutic levels. • Glucagon: increases inotropy by increasing myocardial cAMP levels. May not be as effective as HDI or ILE. Dose recommended is 0.05–0.2 mg/kg slow IV bolus followed by a CRI of 0.1–0.15 mg/kg/h.

CONTRAINDICATION/POSSIBLE INTERACTIONS

Vasopressors: Literature suggests that vasopressors are not as effective as other therapies (IFE and HDI) and may make patients less responsive to other therapy.



FOLLOW-UP

PATIENT MONITORING

- Monitor for 8 hours with immediate release preparations and up to 24 hours for ER preparations
- Heart rate/ECG
- Blood pressure
- Potassium levels
- Blood glucose

POSSIBLE COMPLICATIONS

Organ damage (especially kidney and liver damage) can occur secondary to prolonged hypoperfusion.

EXPECTED COURSE AND PROGNOSIS

- Ingestion of immediate release preparations typically result in clinical signs in 6 hours.
- SR or ER preparations may take up to 24 hours for clinical signs to develop.
- Prognosis depends on the dose ingested and response to therapy. • Toxicosis normally results in bradycardia, hypotension and in severe cases decreased mental status, coma and apnea.



MISCELLANEOUS

ABBREVIATIONS

- BG = blood glucose • Ca = calcium
- CRI = continuous rate infusion • ECG = electrocardiogram • ER = extended release
- HDI = high dose insulin • ILE = IV lipid emulsion • IV = intravenous • SR = sustained release

Suggested Reading

Engebretsen KM, Kaczmarek KM, Morgan J, Holger JS. High dose insulin therapy in beta-blocker and calcium channel-blocker poisoning. Clin Toxicol 2011, 49(4):277–283.

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**Client Education Handout
available online**

BETA-2 AGONIST INHALER TOXICOSIS

B



BASICS

OVERVIEW

• Beta-2 agonist inhaler toxicosis occurs when dogs chew and puncture pressurized inhalers containing albuterol (salbutamol), levalbuterol, or salmeterol. • Loss of beta-2 adrenergic selectivity with overdose results in beta-1 stimulation (sinus tachycardia). Failure of the myocardium to effectively oxygenate during extreme periods of tachycardia can result in other tachyarrhythmias such as VPCs and ventricular tachycardia. • Generalized adrenergic stimulation releases catecholamines which exacerbate CV stimulation, stimulate the CNS and respiratory systems, and can result in significant intracellular translocation of potassium and phosphorus. • Propellants are now hydrofluoroalkanes (HFAs) and are expected to sensitize the myocardium less to catecholamines than older chlorofluorocarbon propellants.

SYSTEMS AFFECTED

- Behavioral—hyperactivity, apprehension, nervousness, restlessness.
- Cardiovascular—sinus tachycardia, other tachyarrhythmias.
- Endocrine/Metabolic—hypokalemia, hypophosphatemia.
- Gastrointestinal—mild vomiting.
- Musculoskeletal—tremors, weakness with catecholamine depletion.
- Nervous—anxiety, apprehension initially, depression with catecholamine depletion.
- Neuromuscular—tremors.
- Respiratory—tachypnea.

SIGNALMENT

Young dogs are overrepresented due to their predilection for dietary indiscretion.

SIGNS

- Tachycardia, other tachyarrhythmias
- Lethargy, weakness, depression
- Hyperactivity, apprehension, nervousness, restlessness
- Tachypnea
- Vomiting
- Tremors

CAUSES & RISK FACTORS

- Puncture of inhalers containing beta-2 agonists
- Pets prone to dietary indiscretion with access to inhalers



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Amphetamines and related drugs such as those used for attention deficit hyperactivity disorder (ADHD) (e.g., Adderall, Adipex, Concerta, Cylert, Daytrana, Fastin, Focalin, Ionamin, Metadate, Methylin, Obermine, Quillivant, Phentrol, Ritalin, Straterra, Termene, Vyvanse) and street drugs

- Sympathomimetics (e.g., phenylpropanolamine, pseudoephedrine, phenylephrine, ephedrine)
- Methylxanthines (e.g., caffeine, theobromine)
- Metaldehyde
- Thyroxine
- Tremorgenic mycotoxins
- Hops (*Humulus lupulus*)
- Nicotine

CBC/BIOCHEMISTRY/URINALYSIS

- Hypokalemia
- Hypophosphatemia

DIAGNOSTIC PROCEDURES

ECG to confirm, monitor for arrhythmias.



TREATMENT

- Inpatient treatment—initiate medical management and emergency care as soon as possible following exposure.
- Nursing care required—fluid support.
- Altered activity—cage rest, quiet environment.
- NPO if vomiting.
- Discuss with owner the timing of presentation relative to exposure; patients that have a delayed presentation and prolonged, untreated CNS and CV stimulation may be at greater risk for more serious arrhythmias and slower recovery due to catecholamine depletion.
- No surgical or anesthetic considerations.



MEDICATIONS

DRUG(S)

- Benzodiazepines PRN for anxiety, nervousness, tremors:
 - Diazepam: 0.5 mg/kg IV or 1 mg/kg rectally, repeat PRN.
 - Midazolam: 0.25 mg/kg IV, repeat PRN.
- Beta blockers for severe tachycardia (HR > 160 in large dogs; > 200 in miniature breeds), hypokalemia:
 - Propranolol (preferred, nonspecific blocker): dogs, 0.02–0.06 mg/kg IV to effect.
 - Esmolol (blocks beta-1 only; ultra-short acting): dogs, 0.25–0.5 mg/kg IV as a slow bolus then a CRI of 0.01–0.2 mg/kg/min.
- Potassium chloride supplementation:
 - Up to 0.5 mEq potassium/kg/h IV maximum, based on degree of hypokalemia.
 - Potassium phosphate if phosphorus < 1 mg/dL:
 - 0.01–0.03 mM/kg/h IV.
- Lidocaine for ventricular arrhythmias:
 - Dogs, 2–4 mg/kg IV (maximum of 8 mg/kg over 10 minutes) followed by a CRI of 40–80 µg/kg/min.
 - Cats, 0.25–0.5 mg/kg IV slowly (caution in this species due to predilection for CNS and CV toxicity).

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Electrolytes (potassium, phosphorus) q12h or PRN if ECG changes, weakness (potassium), hemolysis (phosphorus). *Note:* Monitor for rebound hyperkalemia upon recovery if aggressively supplemented.
- Electrocardiography.
- Mentation.

POSSIBLE COMPLICATIONS

- Rarely fatal. Persistent, severe tachycardia can result in myocardial hypoxia and more serious arrhythmias or other cardiac sequelae, especially if preexisting cardiac disease is present.
- Catecholamine depletion can result in weakness and depression once the stimulatory effects wane.

EXPECTED COURSE AND PROGNOSIS

Excellent prognosis with prompt and appropriate treatment in an otherwise healthy patient.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

- Albuterol crosses the placenta. Overdose effects are expected to be similar for the fetus. Hypoxia with cardiac compromise in the bitch may harm the fetus.
- No adverse effects expected with regard to fertility.

ABBREVIATIONS

- ADHD = attention deficit hyperactivity disorder
- CNS = central nervous system
- CRI = constant rate infusion
- CV = cardiovascular
- ECG = electrocardiogram
- HFA = hydrofluoroalkane
- VPCs = ventricular premature contractions

INTERNET RESOURCES

N/A

Suggested Reading

Babski DM, Brainard BM. Albuterol. In: Osweiler GD et al., eds., Blackwell's Five-Minute Veterinary Consultant: Clinical Companion, Small Animal Toxicology. Ames, IA: Wiley-Blackwell, 2011, pp. 119–124.

Menschling D, Volmer PA. Breathe with ease when managing beta-2 agonist inhaler toxicoses in dogs. Vet Med, June 2007, 369–373.

Author Donna Mensching

Consulting Editor Lynn R. Hovda

BILE DUCT CARCINOMA

B



BASICS

OVERVIEW

- Epithelial neoplasia that arises from the cells lining the biliary duct or gallbladder.
- Second most common malignant hepatic tumor in dogs, representing 22–41% of all malignant canine liver tumors. • Most common malignant hepatobiliary tumor in cats, but less common than benign biliary cystadenoma. • Benign biliary cystadenomas may undergo malignant transformation into cystadenocarcinomas. • Common metastatic sites include the lungs, regional lymph nodes, and peritoneum (carcinomatosis). • Other metastatic sites include intestine, pancreas, heart, spleen, kidney, spinal cord, urinary bladder, and bone. • Paraneoplastic alopecia has been associated with feline biliary carcinoma.

SIGNALMENT

- Dog and cat • Possible predilection for Labrador retrievers • Affected animals typically > 10 years of age • Possible predisposition for female dogs

SIGNS

Historical Findings

- Anorexia • Lethargy • Weight loss
- Vomiting • Polydipsia and polyuria
- Icterus • Abdominal distension

Physical Examination Findings

- Hepatomegaly (\pm palpable abdominal mass)
- Ascites • Icterus

CAUSES & RISK FACTORS

- Potential association between canine cholangiocarcinoma and trematode (hookworms, whipworms) infection.
- Carcinoma of the canine biliary tract has been experimentally induced by N-ethyl-N'-nitro-N-nitrosoguanidine.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Imaging and gross pathology—Hepatocellular adenoma (hepatoma), hepatocellular adenocarcinoma, biliary adenoma and cystadenoma, nodular hyperplasia, cirrhosis, chronic active hepatitis, hepatic myelolipoma, carcinoids, hepatic abscess. • Histopathology – Will distinguish from hepatocellular adenocarcinoma based on morphology, however immunohistochemistry (hepatocyte paraffin-1) and Claudin-7 can be used to distinguish between hepatocellular and biliary neoplasms.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia. • Leukocytosis. • Elevated serum enzyme (e.g., ALP, GGT, ALT, AST) activity

is often present but not specific for neoplastic disease. • Hyperbilirubinemia possible.

OTHER LABORATORY TESTS

- α -Fetoprotein (an oncofetal glycoprotein) is elevated in 55% of dogs with bile duct carcinoma and may help differentiate neoplastic from non-neoplastic lesions in dogs. • Coagulation profile (PT, PTT) should be performed before biopsy or surgical procedures.

IMAGING

Abdominal Radiography

May localize a mass to the liver or may demonstrate displacement of the stomach or loss of detail in patients with ascites.

Abdominal Ultrasonography

Can be used to assess location and character of lesion, detect and sample peritoneal effusion, and to guide tumor biopsy.

Thoracic Radiography

Should be used to screen for pulmonary metastasis.

CT and MRI

More sensitive techniques that can discriminate histologic tumor type in humans and are more likely to detect smaller lesions not visible on ultrasound.

DIAGNOSTIC PROCEDURES

- Abdominocentesis and cytologic evaluation of peritoneal fluid, if present. • Cytology or needle core (Tru-Cut) biopsy samples can be obtained via ultrasound guidance.
- Laparoscopy or laparotomy may be needed to obtain larger sample for definitive diagnosis.

PATHOLOGIC FINDINGS

- Gross findings—Morphologic types include massive (37–46%), nodular (0–21%), or diffuse (17–54%). • Can be intrahepatic (most common in dogs), extrahepatic, or within the gall bladder (rare). • Malignant lesions often involve multiple lobes, whereas benign (adenomas/cystadenomas) tend to be solitary. • Histopathology findings—Histologic subtypes include solid (cholangiocarcinoma) and cystic (biliary cystadenocarcinoma) forms. Histologic classification (solid vs. cystic) is not prognostic.



TREATMENT

- Surgical excision is treatment of choice, if complete resection is feasible. • Up to 80% of the liver can be resected if the remaining liver tissue is functional. • No effective surgical treatment exists for nodular or diffuse forms.
- Interventional techniques (chemoembolization) may be utilized for nonresectable solitary tumors.



MEDICATIONS

DRUG(S)

Chemotherapy—no effective protocol identified.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Medications requiring metabolism by the liver or rely upon enterohepatic should be used with caution if evidence of hepatic dysfunction is noted.



FOLLOW-UP

PATIENT MONITORING

Physical examination, lab work (especially liver enzymes), abdominal ultrasonography, and thoracic radiography every 3 months after tumor resection.

PREVENTION/AVOIDANCE

Anthelmintic therapy is warranted due to the potential association between canine bile duct carcinoma and infection with hookworms or whipworms.

POSSIBLE COMPLICATIONS

- Tumor rupture/hemorrhage, especially if the massive form. • Biliary obstruction.

EXPECTED COURSE AND PROGNOSIS

- Aggressive tumor; guarded to poor prognosis, especially if nonresectable. • High rate of metastasis (up to 88%) in both dogs and cats. Widespread intraperitoneal carcinomatosis common in cats. • Most patients die within 6 months of surgery due to local recurrence or metastasis.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Chemotherapy drugs may be carcinogenic and mutagenic.

ABBREVIATIONS

- CT = computed tomography • MRI = magnetic resonance imaging • PT = Prothrombin time • PTT = Partial thromboplastin time

Suggested Reading

Liptak JM. Hepatobiliary Tumors. In Withrow SJ, Vail DM, eds. Small Animal Clinical Oncology, 5th ed. St. Louis, MO: Saunders Elsevier, 2013, pp. 405–410.

Authors Craig A. Clifford and Christine Mullin

Consulting Editor Timothy M. Fan

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BILE DUCT OBSTRUCTION (EXTRAHEPATIC)



BASICS

DEFINITION

Cholestasis caused by biliary tree obstruction at the level of the common bile duct (CBD) causing extrahepatic bile duct obstruction (EHBDO) or at the level of the hepatic ducts; may involve one, several, or all hepatic ducts.

PATHOPHYSIOLOGY

- Serious hepatobiliary injury—follows within weeks of duct obstruction secondary to accumulation of inflammatory mediators, neutrophils, noxious bile acids and other bile constituents accumulating in the periductal area, mechanical effect of duct distention (hydrostatic pressure), and oxidative injury.
- Gallbladder (GB) bile—may become colorless (white bile) if cystic duct obstruction impairs influx of canalicular green hepatic bile (contains bilirubin pigments).
- White bile—reflects increased mucin production, bilirubin exclusion, and sometimes, suppurative inflammation.
- Bacterial infection of bile—increased risk with stasis of bile flow (normal clearance of splanchnic-derived bacteria in the portal circulation).

SYSTEMS AFFECTED

Hepatobiliary

SIGNALMENT

Species

Dog and cat

Breed Predilection

- Animals predisposed to pancreatitis and choleliths: e.g., GB mucocele (GBM)—hyperlipidemic breeds (e.g., miniature Schnauzer, Shetland sheepdog).
- Animals with large duct ductal plate malformation (DPM) phenotype (Caroli's malformation) predisposed to infection and cholelithiasis.
- Choleliths appear more common in small-breed dogs and cats.

Mean Age and Range

Middle-aged to old animals with acquired disease; younger animals with DPM.

Predominant Sex

None

SIGNS

Historical Findings

- Depend on underlying disorder and “completeness” of EHBDO.
- Progressive lethargy and vague illness.
- Progressive jaundice.
- Pale (acholic) stools: complete EHBDO.
- Polyphagia: complete EHBDO causes nutrient malassimilation (fat).
- Bleeding tendencies: within 10 days of complete EHBDO, more severe/overt in cats.

Physical Examination Findings

- Depend on underlying cause

- Weight loss
- Severe jaundice
- Hepatomegaly unless biliary cirrhosis
- Cranial mass effect—extrahepatic biliary structures (small dogs and cats)
- Vague cranial abdominal discomfort
- Acholic feces—unless enteric bleeding (hemoglobin provides pigment)
- Bleeding tendencies—chronic EHBDO
- Orange urine: severe bilirubinuria

CAUSES

- Diverse primary disorders
- Cholelithiasis
- Choledochitis
- Neoplasia
- Bile duct malformations: choledochal cysts, polycystic hepatobiliary disease, DPM, Caroli's malformation, cystadenoma encroaching on porta hepatis (cats)
- Parasitic infestation: flukes (cats)
- Extrinsic compression: lymph nodes, neoplasia, pancreatitis, CBD entrapment in diaphragmatic hernia; foreign body obstruction of sphincter of Oddi in duodenum
- Duct fibrosis: trauma, peritonitis, pancreatitis; major duct involvement in feline cholangitis/cholangiohepatitis
- Duct stricture: blunt trauma, iatrogenic surgical manipulations

RISK FACTORS

See “Causes”



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Mass lesions—primary or metastatic hepatobiliary neoplasia; in adjacent viscera
- Diffuse infiltrative liver disease—neoplastic, inflammatory, HL (cats, canalicular compression), amyloid (rare)
- Infectious hepatitis—bacterial, viral, flukes
- Decompensated chronic hepatitis
- Copper-associated hepatopathy
- Severe hepatic fibrosis/cirrhosis
- Fulminant hepatic failure
- Biliary cysts—choledochal (cats), cystadenoma, polycystic liver disease (cats) compressing CBD at porta hepatis; choledochal cyst (cats), DPM
- Pancreatitis: CBD stenosis, stricture
- Hepatic lipidosis (HL)—cats: canalicular collapse causes jaundice.
- Cholangitis/cholangiohepatitis—cats, esp. sclerosing or destructive cholangitis form.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Anemia—mild non-regenerative (chronic disease) or regenerative (enteric bleeding due to hypertensive splanchnic vasculopathy, ulcerations, coagulopathy due to portal hypertension)
- Microcytosis—uncommon

- Leukogram—variable, neutrophilic leukocytosis, left-shifted leukogram with sepsis
- Plasma—markedly jaundiced

Biochemistry

- Liver enzymes—variable; marked increases in ALP and GGT reflect ductal injury; high ALT and AST reflect hepatocyte injury.
- Total bilirubin—moderate to markedly high; less than observed with hemolysis or HL; bilirubin fractionation—overlaps with hemolytic and sepsis associated jaundice.
- Albumin—variable, usually normal except when EHBDO > 6 weeks (biliary cirrhosis); low albumin reflects synthetic failure.
- Globulins—normal or increased.
- Glucose—normal or low if biliary cirrhosis or sepsis; high if diabetes with pancreatitis.
- Hypercholesterolemia—common.

Urinalysis

- Bilirubinuria and bilirubin crystals.
- Absence of urobilinogen—unless enteric bleeding; unreliable definitive test for EHBDO.

OTHER LABORATORY TESTS

- Serum bile acids—always markedly increased; superfluous test if hepatobiliary jaundice already suspected.
- Coagulation abnormalities—within 10 days of EHBDO develop vitamin K deficiency (PIVKA and PT clotting times most sensitive); may develop DIC; cats more dramatic effect.
- Fecal examination—acholic stools suggest EHBDO; masked by small-volume melena; trematode eggs if fluke infestation.

IMAGING

- Abdominal radiography—hepatomegaly; variable mass lesion in area of gallbladder, pancreatitis pattern, mineralized cholelith(s).
- Cholecystography—rarely provides additional practical information.
- Abdominal ultrasonography—evidence of obstruction within 72–96h (distended, tortuous CBD, cystic duct, and intrahepatic bile ducts); may disclose underlying or primary disorder (e.g., pancreatitis, cystic lesions, mass lesions, choleliths). **Caution:** GB bile “sludge” and a full GB are common in anorectic or fasted patients—do not mistake for EHBDO.
- **Caution:** Feline CBC is serpiginous compared to the dog—always inspect liver image for distended intrahepatic bile ducts and confirm “tubes” are ducts rather than vasculature with color flow Doppler.

DIAGNOSTIC PROCEDURES

- Hepatic aspiration cytology—used to rule in HL (cats) or sample mass lesions; avoid aspiration of obstructed biliary structures as this may cause bile leakage and peritonitis.
- US guided-needle biopsy—strongly contraindicated; may cause iatrogenic bile peritonitis.

BILE DUCT OBSTRUCTION (EXTRAHEPATIC)

(CONTINUED)

B

- Laparotomy—best approach; allows tissue biopsy; biliary decompression; mass excision: cholelith or inspissated bile removal; creation of biliary-enteric anastomosis; stent insertion.

PATHOLOGIC FINDINGS

- Gross—distended, tortuous bile duct, distended GB: cause often grossly apparent; obstruction > 2 weeks: large, dark green or mahogany-colored liver; chronic complete obstruction of cystic duct associates with white or clear GB bile.
- Microscopic—early: biliary epithelial hyperplasia and bile ductule proliferation and dilation with intraluminal biliary debris (mucin, inflammatory cells, usually neutrophils) and periductular edema, and early fibrosis; chronic distention of biliary structures: leads to devitalized biliary epithelium with necrotic debris, intraluminal suppurative debris, mixed periportal inflammatory infiltrates, periductal edema with thick laminating circumferential fibrosis, multifocal parenchymal necrosis.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient—surgical intervention for EHBDO unless the cause is pancreatitis with prospect for resolution with supportive care.

NURSING CARE

- Fluid therapy—depends on underlying conditions (see Pancreatitis); rehydrate and provide maintenance fluids before general anesthesia and surgical interventions; supplement polyionic fluids with potassium chloride and phosphate; judicious electrolyte adjustments based on electrolyte status.
- Water-soluble vitamins—in intravenous fluids; B complex (2 mL/L polyionic fluids).
- Initiate antibiotic therapy before surgery: see “Drugs of Choice.”
- Vitamin K₁: parenteral administration if EHBDO > 5–7 days (see “Drugs of Choice”).

ACTIVITY

Depends on patient status and coagulopathy.

NUTRITIONAL SUPPORT

- Maintain nitrogen balance—avoid protein restriction.
- Restrict fat—if overt fat malassimilation caused by lack of enteric bile acids in chronic EHBDO—rare incidence.
- Supplement fat-soluble vitamins: vitamins E and K most urgent; supplementing vitamins D and A can lead to toxicity.
- Water-soluble vitamin E—necessary in chronic EHBDO (see “Drugs of Choice”).

CLIENT EDUCATION

- Inform client that surgical biliary decompression is essential (unless resolvable pancreatitis or cholelith obstruction); EHBDO progresses to biliary cirrhosis within

6 weeks; exception is pancreatitis causing EHBDO that may self-resolve within 2–3 weeks.

- Warn client that surgical success is contingent on underlying cause, results of liver biopsy, infection, and individual variables.

SURGICAL CONSIDERATIONS

- Surgical exploration—imperative for treating and determining underlying cause unless obvious pancreatitis.
- Excise masses, remove choleliths and inspissated bile; ensure common duct patency.
- Resect GB—if necrotizing cholecystitis or GB mucocele.
- Biliary-enteric anastomosis—if irresolvable occlusion, fibrosing pancreatitis, or neoplasia; anastomotic stoma at least 2.5 cm wide. Chronic recurrent infection likely after biliary-enteric anastomosis. Temporary stent instead of biliary enteric anastomosis may be complicated by infection and stent obstruction, esp. in cats.
- Hypotension and bradycardia (vasovagal reflex)—may develop during biliary tree manipulation; ensure availability of emergency drugs (anticholinergics) and ventilatory support for rescue endeavors.
- Ensure IV catheter access and volume expansion—use colloids when necessary, plasma preferred; be prepared for hemorrhage (have blood available for transfusions).
- Surgical biopsies—submit tissue and bile for aerobic and anaerobic bacterial culture; submit tissue for histology.
- Cytology—make preps from tissue and bile; cytology may detect bacterial infections and fluke eggs not recognized in biopsy sections. Bile, biliary debris, and GB wall—more likely to culture organisms. Wright-Giemsa staining to detect bacteria, Gram stain to characterize bacterial morphology; may advise acute antimicrobial selection. Enteric opportunists are most common. *Bacteroides* may promote polymicrobial infection; may not culture all involved bacteria.
- Sclerosing or destructive feline cholangitis (intrahepatic ductopenia) may clinically emulate EHBDO; does not respond to biliary tree decompression; liver biopsy necessary.



MEDICATIONS

DRUG(S) OF CHOICE

Vitamin K₁

Provide 12–36h before surgery (0.5–1.5 mg/kg IM or SC), 3 doses at 12-h intervals. **Caution:** avoid IV, may cause anaphylaxis. If chronic EHBDO irresolvable, parenteral Vit. K₁ given chronically with frequency titrated using PIVKA or PT, too much vit. K₁ causes hemolytic (Heinz body) anemia in cats.

Vitamin E

- If chronic EHBDO irresolvable (rare) use polyethylene glycol alpha tocopherol succinate (TPGS-vitamin E) 10 U/kg/day PO and injectable Vitamin K₁ (see above).
- Treat early to allow response before surgery.

Antibiotics

Before surgery—broad-spectrum antimicrobials for potential biliary infections as surgical manipulations may disseminate bacteremia; initially use antibiotics with wide spectrum as follows—triad of: ticarcillin 25 mg/kg IV q8h, metronidazole 7.5 mg/kg IV or PO q12h, enrofloxacin 5 mg/kg PO q12–24h (24h dose in cats no greater than 5 mg/kg/24h to avoid retinopathy).

Antioxidants

- Vitamin E (α -tocopherol acetate)—10–100 IU/kg; a larger-than-normal (normal = 10 IU/kg /day) oral dose needed in chronic EHBDO because of fat malabsorption (lack of enteric bile acids); use of TPGS-Vitamin E preferred (see previous).
- S-Adenosylmethionine (SAME) with proven bioavailability and efficacy as GSH donor—20 mg/kg/day PO enteric-coated tablet 1–2 hours before feeding; provides numerous additional metabolic benefits.

Ursodeoxycholic Acid

10–15 mg/kg PO per day—AFTER biliary decompression as a choleretic; ensure adequate hydration to achieve choleresis; *inappropriate before* biliary decompression: can accelerate liver injury in EHBDO. Does not facilitate fat assimilation in chronic EHBDO. Beneficial effects: antifibrotic, anti-endotoxic, hepato-protectant, anti-apoptotic, immunomodulator.

Bowel Preparation Before Surgery

- May reduce endotoxemia potentiating perioperative hypotension.
- Mechanical cleansing of colon with water or crystalloid fluids.
- Acutely alter enteric flora to reduce enteric translocation of opportunistic pathogen with medications given either: PO or by high enema; neomycin: 22 mg/kg q8h, lactulose 1–2 mL/kg q8h; metronidazole 7.5 mg/kg q12h; rifaximin 5–10 mg/kg q12h; probiotic bacteria (empirical product dose); enrofloxacin 2.5 mg/kg q12h PO.

Gastrointestinal Protectants

Agents reducing gastric acidity—famotidine (H₂-blocker) or omeprazole (pump inhibitor) combined with sucralfate for local cytoprotection if PO medications tolerated and enteric bleeding recognized; stagger sucralfate administration from other oral medications to avoid drug interactions.

CONTRAINdications

- Provide biliary decompression before institution of ursodeoxycholic acid.
- Take care to reduce drug dosages for medications eliminated in bile if EHBDO.

(CONTINUED)

BILE DUCT OBSTRUCTION (EXTRAHEPATIC)**B****PRECAUTIONS**

See “hypotension and bradycardia (vasovagal reflex)” under “Surgical Considerations.”

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

- Depends on underlying condition—special monitoring for underlying disorders causing EHBDO; see appropriate conditions.
- Total bilirubin values acutely reflect biliary decompression; values normalize within days.
- Liver enzyme activities—decline slowly.
- CBC—repeat q2–3 days initially if septic.
- Bile peritonitis—evaluate abdominal girth, body weight, and fluid accumulation (e.g., by palpation, ultrasonography preferred, abdominocentesis).
- Determine necessity for pancreatic enzyme supplementation based on site of biliary-enteric anastomosis; patients with cholecystojejunostomies may benefit from enzyme supplementation; cannot rely on trypsin-like immunoreactive (TLI) substance to estimate pancreatic exocrine adequacy in this circumstance; evaluate body weight and condition; check feces for steatorrhea (fat malassimilation; suspend feces in water and microscopically examine for lipid globules—only relevant if animal is fed a normal fat-containing diet; if steatorrheic after biliary-enteric anastomosis and non-icteric, reduce dietary fat and supplement with pancreatic enzymes. Pancreatic enzymes can induce oral or esophageal ulcers especially in cats, must be mixed in food and followed by liquid or food to prevent mucosal injury.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Bile peritonitis
- Restenosis of bile duct—if not bypassed
- Stenosis of biliary-enteric anastomosis
- Severe enteric hemorrhage with EHBDO—hypertensive enteric vasculopathy with coagulopathy (vitamin K deficiency)
- Hemorrhage during surgery
- Septic bacteremia or SIRS during or after surgery
- Unresponsive hypotension during surgery
- Vasovagal reflex—biliary tree manipulation

EXPECTED COURSE AND PROGNOSIS

- Depends on underlying disease.
- Prognosis good if fibrosing pancreatitis and pancreatic inflammation resolves; bile duct patency may return.
- Be aware: biliary tree may appear distended on subsequent ultrasounds.
- Permanent peribiliary fibrosis from EHBDO.
- Cats with sclerosing cholangitis can appear to have EHBDO; but show no response to biliary decompression; liver biopsy essential for diagnosis.

CONSIDERATIONS/PRECAUTIONS

- Anticipate bleeding tendencies and vasovagal reflex during surgical procedures.
- Always submit liver and biliary tree biopsies for histology; all tissues and bile for bacterial culture (aerobic, anaerobic).

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- See “Causes”
- Sclerosing or destructive cholangitis (cats) confused with EHBDO

SEE ALSO

- Cholangitis/Cholangiohepatitis Syndrome
- Gallbladder Mucocele
- See “Causes”

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- CBD = common bile duct
- DIC = disseminated intravascular coagulation
- EHBDO = extrahepatic bile duct obstruction
- GB = gallbladder
- GGT = gamma glutamyltransferase
- GSH = glutathione
- HL = hepatic lipidosis
- PIVKA = proteins invoked by vitamin K absence or antagonism
- PT = prothrombin time
- TPGS-Vitamin E = d- α -tocopheryl polyethylene glycol succinate

Suggested Reading

Center SA. Diseases of the gallbladder and biliary tree. *Vet Clin North Am Small Anim Pract* 2009, 39(3):543–598.

Center SA. Interpretation of liver enzymes. *Vet Clin North Am Small Anim Pract* 2007, 37(2):297–333.

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Consulting Editor Sharon A. Center



**Client Education Handout
available online**

BILE PERITONITIS

B



BASICS

OVERVIEW

- Chemical peritonitis due to release of free bile into the abdominal cavity.
- Can involve focal or diffuse peritoneal inflammation depending on chronicity and causal factors, and omental adhesions.

SIGNALMENT

- More common in dog than in cat
- No age, breed, or sex predilection

SIGNS

Historical Findings

- Acute presentation if septic peritonitis
- May have chronic illness if non-septic
- Rare asymptomatic biliary rupture associated with omental encapsulation of leakage
- Abdominal discomfort: vague
- Lethargy
- Gastrointestinal signs: anorexia, vomiting, diarrhea
- Weight loss
- \pm Abdominal distention
- Variable jaundice
- Collapse, if septic

Physical Examination Findings

- Lethargy
- Variable (cranial) abdominal pain
- Jaundice
- Abdominal effusion
- \pm Fever
- \pm Endotoxic shock, if septic

CAUSES & RISK FACTORS

- Limited arterial perfusion (cystic artery) to GB fundus predisposes to ischemic necrosis and GB rupture.
- Trauma to biliary structures—auto-mobile injuries, surgical, animal bites, gunshot wounds, cystic artery laceration during cholecystocentesis.
- Common bile duct (CBD): common site of rupture with blunt trauma.
- Cholecystitis/choledochitis—may derive from GB mucocele (GBM); sepsis more common with necrotizing cholecystitis.
- EHBDO—may derive from neoplasia, cholelithiasis, pancreatitis, duct stricture.
- Focal, small-volume, bile peritonitis—associated with cholecystitis; may reflect omental entrapment of bile or transmural bile leakage without rupture.
- Chemical peritonitis due to bile—predisposes to septic peritonitis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Conditions promoting inflammation/devitalization of biliary structures, e.g.,

cholecystitis, choledochitis, neoplasia, GBM, neoplasia, blunt trauma.

- Conditions causing EHBDO, e.g., neoplasia, choleliths, pancreatitis, duct stricture/fibrosis.
- Sepsis or endotoxemia.
- Ascites: in jaundiced cirrhotic patient.
- Non-hepatic conditions causing abdominal effusion and jaundice.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

Inflammatory leukogram—left shift and toxic neutrophils if necrotizing cholecystitis or sepsis; non-regenerative anemia if chronic inflammation.

Biochemistry

- High liver enzymes, especially ALP; hyperbilirubinemia; \pm hypoalbuminemia; \pm prerenal azotemia
- Electrolyte, fluid, and acid-base disturbances; hyponatremia common.

Urinalysis

Bilirubinuria

OTHER LABORATORY TESTS

Coagulation tests—abnormal if sepsis syndrome, DIC, or chronic EHBDO.

IMAGING

- Abdominal radiography—reduced abdominal detail, generalized or focal in GB area; cranial abdominal mass effect; rare mineralized cholelith or biliary gas (emphysematous cholecystitis).
- Thoracic radiography—rare bicavity effusion (pleural effusion), signs of trauma (e.g., fractured rib, hernia).
- Abdominal ultrasonography—effusion; EHBDO—distended GB or CBD; cholecystitis /choledochitis—thick GB or duct wall; necrotizing cholecystitis—segmental GB wall hyperechogenicity, laminated wall (represents necrosis); pericholecystic fluid; hepatic /pancreatic mass effect: common with bile peritonitis; choleliths or GBM ("kiwifruit sign"); gas in GB or bile ducts (emphysematous inflammation, implicates gas-forming organisms) casting acoustic shadow; ruptured GB may be difficult to image; liver size usually normal; variable parenchymal echogenicity reflects hepatic pathology (e.g., ascending cholangitis, CCHS).

DIAGNOSTIC PROCEDURES

- Abdominocentesis—physicochemical, cytologic, and culture evaluations; ultra-sound guidance optimizes sampling; sample close to biliary structures but avoid structure penetration.
- Cytology—impression smears of GB, liver, and bile (with particulate material) used for immediate detection of infection and neoplasia; modified transudate or exudate, phagocytized/free bile and bilirubin.

- Acellular mucinous material reflects biliary mucin production; GBM material may be free within abdominal cavity.

- Ratio of bilirubin in effusion:serum usually $\geq 2\text{--}3:1$.

- Bacterial aerobic/anaerobic culture and sensitivity—effusion, GB wall, liver, GB contents; Gram-negative enteric opportunists and anaerobes most common; polymicrobial infection possible.

- Exploratory laparotomy—appropriate for definitive diagnosis and treatment; permits cholecystectomy, cholecysto-enterostomy, duct or GB repair.

- Liver biopsy—important, evaluates for antecedent or coexistent disease, sample distant to the GB to avoid artifacts.

PATHOLOGIC FINDINGS

Depend on cause and site of rupture



TREATMENT

- Inpatient—expediency of surgery depends on patient condition: achieve euhydration, correct electrolyte and acid-base status, provide preoperative antimicrobial treatment for best survival.
- Abdominal lavage to reduce peritoneal contamination if surgery delayed; use warm polyionic fluids and aseptic technique.
- Surgical experience important for best outcome: complicated resections and anastomoses may be required.
- Need for cholecystectomy decided at surgery; discolored GB wall indicates ischemic devitalized wall.



MEDICATIONS

DRUG(S)

- Antimicrobials—in all patients, initiate broad-spectrum antimicrobials *before* surgical intervention; enteric Gram-negative and anaerobic organisms most common opportunists (good initial choices: ticarcillin, piperacillin, or third-generation cephalosporins, with enro-floxacin and metronidazole); customized antimicrobial treatment, thereafter based on cultures; continue antimicrobials $\geq 4\text{--}8$ weeks if signs of infection confirmed by culture or on cytology.
- Vitamin K₁ (0.5–1.5 mg/kg IM or SC q12h for up to 3 doses)—all jaundiced patients *before* surgery.
- Prepare for blood component \pm synthetic colloid therapy.
- Antiemetics if patient is vomiting—metoclopramide (0.2–0.5 mg/kg PO, SC q6–8h or 1–2 mg/kg/24h IV by CRI); ondansetron (0.5–1.0 mg/kg q12h, IV or PO, 30 minutes before feeding); maropitant

(CONTINUED)

BILE PERITONITIS**B**

(1.0 mg/kg/day IV, SC, PO, maximum of 5 days).

- H₂-receptor antagonists if gastric bleeding—famotidine (0.5–2.0 mg/kg PO, IV, SC q12–24h); sucralfate (0.25–1.0 g PO q8–12h).
- Ursodeoxycholic acid as choleretic and hepatoprotectant if GBM, choleliths, CCHS, or chronic hepatitis—may administer chronically if GBM or cholelithiasis: 10–15 mg/kg PO daily, divided, with food for best bioavailability.
- Antioxidants—Vitamin E (10 IU/kg/24h); S-adenosylmethionine (SAMe, with proven bioavailability and efficacy; (20 mg/kg PO daily 2h before feeding) until enzymes normalize, indefinitely if chronic hepatitis or CCHS, GBM, inspissated bile syndrome; choleretic influence requires higher dose (40 mg/kg/day).

**FOLLOW-UP****PATIENT MONITORING**

- Sequential hematologic, biochemical, and imaging tests.
- Repeat abdominocentesis to assess continued infection and/or bile leakage as indicated.

POSSIBLE COMPLICATIONS

- Cholangitis/cholangiohepatitis
- Pancreatitis
- Recurrent bacterial cholangitis if biliary-enteric anastomosis required

EXPECTED COURSE AND PROGNOSIS

- High survival rate for dogs with sterile bile peritonitis, if successful surgery, depending on underlying cause.
- Higher mortality in septic bile peritonitis (up to 73%).
- Anticipate slow clinical recovery and normalization of liver enzymes but rapid resolution of hyperbilirubinemia with successful surgery.

**MISCELLANEOUS****SEE ALSO**

- Cholecystitis
- Cholelithiasis
- Gallbladder Mucocele
- Hepatitis, Chronic

ABBREVIATIONS

- ALP = alkaline phosphatase
- CCHS = cholangitis/cholangiohepatitis
- CMD = common bile duct
- CRI = constant rate infusion
- EHBDO = extrahepatic bile duct obstruction
- GB = gallbladder
- GBM = GB mucocele

Suggested Reading

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BILIUS VOMITING SYNDROME

B



BASICS

OVERVIEW

• Clinical entity associated with chronic intermittent vomiting of bile thought to be the result of reflux of intestinal contents (bile) into the stomach. The normal aboral gastric and intestinal motility along with a functional pylorus prevents the reflux of bile and other intestinal contents back into the stomach. When bile is refluxed into the stomach, it is normally rapidly removed by subsequent peristaltic contractions. Bile remaining in the gastric lumen along with the presence of gastric acid and pepsin can subsequently cause gastric mucosal damage. Bilius vomiting syndrome (BVS) is suspected to be secondary to alterations in normal gastrointestinal motility. • Clinical signs often occur early in the morning, suggesting that prolonged fasting or gastric inactivity may modify normal motility patterns, resulting in bile reflux.

SIGNALMENT

- Commonly observed in dogs, rarely in cats
- Most animals are middle-aged or older
- No breed or sex predisposition

SIGNS

- Chronic intermittent vomiting of only bile associated with an empty stomach. Signs generally occur late at night or early in the morning. Signs may occur daily but are usually more intermittent. Between episodes, the animal appears normal in all other respects, and most dogs appear healthy immediately after vomiting episodes.
- Results of physical examination are usually unremarkable.

CAUSES & RISK FACTORS

- Cause is unknown (idiopathic). • Primary gastric hypomotility or abnormal (oral-directed) intestinal peristaltic motility are suspected as the probable underlying causes. • Conditions causing gastritis, duodenitis or intestinal obstructive disease may be responsible for altered proximal gastrointestinal motility and can cause bile reflux. Investigate *Giardia*, inflammatory bowel disease, intestinal neoplasia, or obstructions as possible etiologies. • Previous pyloric opening or resection surgery will also increase the risk of enterogastric reflux.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Any number of gastrointestinal and non-gastrointestinal disorders can cause chronic vomiting. *Giardia* should be excluded

since the signs of this disease may mimic those of idiopathic bilius vomiting.

- Inflammatory bowel disease can result in bile reflux. • Intestinal obstruction or partial obstructions should be ruled out.

CBC/BIOCHEMISTRY/URINALYSIS

Results usually unremarkable

OTHER LABORATORY TESTS

Fecal examination to detect *Giardia* or other parasites

IMAGING

- A barium contrast study may reveal delayed gastric emptying, although must be interpreted with caution in the hospital setting. • Barium given with meals, radiopaque markers, or using special motility capsules (Smartpill) may also demonstrate delayed gastric motility.

DIAGNOSTIC PROCEDURES

- Endoscopic findings are frequently unremarkable and helps rule out underlying gastrointestinal disease. • There may be evidence of bile in the stomach or gastritis in the antral region of the stomach. • Endoscopy is useful to rule out structural or inflammatory disease of the stomach or duodenum.



TREATMENT

- It is generally not a serious debilitating disorder if major conditions such as gastritis, inflammatory bowel disease, or gastrointestinal neoplasia have been ruled out.
- The idiopathic bilius vomiting cases are generally treated symptomatically on an outpatient basis and treatment response supports the suspected diagnosis. • Feeding the animal multiple meals including a late evening meal often resolves clinical signs. Food possibly could act as a buffer to the refluxed bile or may in some way enhance gastrointestinal motility. • If diet modification fails, medical treatment should be considered.



MEDICATIONS

DRUG(S)

- Choices include agents for gastric mucosal protection against the refluxed bile or the use of gastric prokinetic agents to improve motility.
- Often a single evening dose of a medication may be all that is required to prevent clinical signs if the signs occur at night.
- Drugs for gastric mucosal protection include various antacids or sucralfate (1 g/25 kg).
- Drugs that block gastric acid production including famotidine (0.5–1.0 mg/kg q12h), ranitidine (1–2 mg/kg q8–12h), nizatidine (1–5 mg/kg q24h) and omeprazole (0.7–1.5 mg/kg q24h) may be beneficial. Ranitidine and nizatidine also have mild gastric prokinetic effects in vitro and may be beneficial.
- Specific gastric prokinetic agents include metoclopramide (0.2–0.4 mg/kg PO q6–8h) and cisapride (0.5 mg/kg PO q8–12h). Cisapride is only available through compounding pharmacies.
- Erythromycin (0.5–1 mg/kg q8h) given at physiologic doses stimulates gastric motility by activation of motilin receptors and may also resolve signs.

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CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Gastric prokinetic agents should not be administered in patients with gastrointestinal obstruction. • Metoclopramide is contraindicated with concurrent phenothiazine and narcotic administration and in animals with epilepsy. Metoclopramide can cause nervousness, anxiety, or depression.
- Cisapride at higher doses can cause vomiting, diarrhea, or abdominal cramping.
- Erythromycin can cause vomiting.



FOLLOW-UP

- Most patients respond to one of the above treatments and a clinical response supports the diagnosis. • Failure to respond suggests another underlying or causative factor.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Gastroesophageal reflux

SEE ALSO

- Chapters on gastric or gastrointestinal motility disorders • Gastroesophageal Reflux

Suggested Reading

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Bilious vomiting in dogs: retrospective study of 20 cases (2002–2012). J Am Anim Hosp Assoc 2014, (in press).

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BLASTOMYCOSIS

B



BASICS

DEFINITION

A systemic, mycotic infection caused by the dimorphic soil organism *Blastomyces dermatitidis*.

PATHOPHYSIOLOGY

- A small spore (conidia) is shed from the mycelial phase (*Ajellomyces dermatitidis*) of the organism growing in the soil and inhaled, entering the terminal airway.
- At body temperature, the spore transforms to its yeast form, which initiates the infection in the lungs.
- From this focus of mycotic pneumonia, the yeast disseminates hematogenously throughout the body.
- The immune response to the invading organism produces a pyogranulomatous infiltrate to control the organism.

SYSTEMS AFFECTED

- Respiratory—85% of affected dogs have lung disease.
- Eyes, skin, subcutaneous tissues, lymphatic system, testes, CNS, and bones—commonly affected.
- Prostate, mammary gland, nasal cavity, nasopharynx, gums, heart, and vulva—less commonly affected.
- Subclinical infection is uncommon.

INCIDENCE/PREVALENCE

Depends on environmental and soil conditions that favor growth of *Blastomyces*. Growth of the organism requires sandy, acid soil, and a proximity to water.

GEOGRAPHIC DISTRIBUTION

Most common along the Mississippi, Ohio, and Tennessee river basins. Also reported in the area of the Great Lakes and St. Lawrence River, southern Canada, mid-Atlantic states, and has been found outside the endemic area in Colorado.

SIGNALMENT

Species

- Predominantly dog
- Occasionally cat

Breed Predilections

Large-breed dogs weighing ≥ 25 kg, especially sporting breeds; may reflect increased exposure rather than susceptibility.

Mean Age and Range

- Dogs—most common in 1–5 years of age; uncommon after 7 years of age.
- Cats—no age predilection noted for cats.

Predominant Sex

- Dogs—males in most studies.
- Cats—none noted.

SIGNS

Historical Findings

- Weight loss; depressed appetite.
- Cough and dyspnea.
- Eye inflammation and discharge.
- Lameness.
- Draining skin lesions.
- Syncope if cardiac involvement.

Physical Examination Findings

Dogs

- Fever up to 104°F (40°C)—approximately 50% of patients.
- Harsh, dry lung sounds associated with increased respiratory effort—common.
- Generalized or regional lymphadenopathy with or without skin lesions or subcutaneous swellings.
- Uveitis with or without secondary glaucoma and conjunctivitis, ocular exudates, and corneal edema.
- Lameness—bone involvement in up to 30% cases.
- Testicular enlargement and prostatomegaly—occasionally seen.
- Murmur and AV block—with endocarditis and myocarditis.

Cats

- Increased respiratory effort
- Granulomatous skin lesions
- Visual impairment

RISK FACTORS

- Wet environment—banks of rivers, streams, and lakes or in swamps; most affected dogs live within 400 meters of water.
- Exposure to recently excavated areas.
- Blastomycosis has been reported in indoor-only cats.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Respiratory signs—bacterial pneumonia, neoplasia, heart failure, pleural effusion, or other fungal infection.
- Lymph node enlargement—similar to lymphoma.
- The combination of respiratory disease with ocular, bony, or skin/subcutaneous involvement in a young dog suggests the diagnosis.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC changes reflect mild to moderate inflammation; may note mild anemia in chronic cases.
- High serum globulins with borderline low albumin concentrations with chronic infection.
- Hypercalcemia (generally mild) in some dogs secondary to the granulomatous changes.
- *Blastomyces* yeasts may be found in the urine of dogs with prostatic involvement; mild proteinuria consistent with systemic inflammation/disease.

OTHER LABORATORY TESTS

- Urine or serum antigen testing—useful for making a diagnosis if organisms cannot be found on cytology or histopathology; positive test strongly supports diagnosis with a sensitivity of $> 90\%$; greater sensitivity reported with urine antigen test.
- Urine antigen test cross-reacts with some other fungal infections such as histoplasmosis.
- AGID—is not sensitive early in the disease but very specific for fungal infection.

IMAGING

Radiographs

- Lungs—generalized interstitial to nodular infiltrate but can see non-uniform distribution of lesions.
- Tracheobronchial lymphadenopathy—common.
- Changes—consistent with bacterial pneumonia; may resemble metastatic tumors, especially hemangiosarcoma.
- Chylothorax secondary to blastomycosis has been reported in dogs.
- Focal bone lesions—lytic and proliferative; can be mistaken for osteosarcoma.

DIAGNOSTIC PROCEDURES

- Cytology of lymph node aspirates, lung aspirates, tracheal wash fluid, or impression smears of draining skin lesions—best method for diagnosis.
- Histopathology of bone biopsies or enucleated blind eyes—identify the organism.
- Organisms—usually plentiful in the tissues; may be scarce in tracheal washes if there is no productive cough.

PATHOLOGIC FINDINGS

- Lesions—pyogranulomatous with budding yeast $5\text{--}20 \mu\text{m}$ diameter with a thick, refractile, double-contoured cell wall; occasionally very fibrous with few organisms found.
- Lungs with large amounts of inflammatory infiltrate do not collapse when the chest is opened.
- Special fungal stains—facilitate finding the organisms.



TREATMENT

NURSING CARE

Severely dyspneic dogs—require an oxygen cage/support for a protracted period (days to more than a week); about 25% of dogs have worsening of lung disease during the first few days of treatment, attributed to an inflammatory response after the *Blastomyces* organisms die and release their contents.

ACTIVITY

Patients with respiratory compromise must be restricted.

DIET

Palatable and high quality to stimulate the appetite.

CLIENT EDUCATION

- Inform owner that treatment is costly and requires a minimum of 60–90 days.
- Reassure owners that an infected dog is not contagious to other animals or people (although other dogs in the house may have also been environmentally exposed).

SURGICAL CONSIDERATIONS

- Removal of an abscessed lung lobe may be required when medical treatment cannot resolve the infection.
- Blind eyes should be enucleated to remove potential sites of residual infection.

B BLASTOMYCOSIS

(CONTINUED)



MEDICATIONS

DRUG(S) OF CHOICE

Itraconazole

- Dogs—5 mg/kg PO q12h with a fat-rich meal, such as canned dog food, for the first 3 days to achieve a therapeutic blood concentration as soon as possible; then reduce to 5 mg/kg q24h.
- Cats—5 mg/kg PO q12h; open the 100 mg capsules containing pellets and mix with palatable food.
- Avoid antacid drugs. as itraconazole absorption is best in an acidic environment.
- Treat for a minimum of 90 days or for 1 month after all signs of disease have disappeared (whichever is longer).
- Absorption of compounded itraconazole is highly unreliable and the use of compounded itraconazole is not recommended.

Fluconazole

- Dogs—5 mg/kg PO q12h; has been reported as efficacious.
- Cats—50 mg PO q12–24h.
- Cheaper alternative but may require longer treatment duration.

Intravenous Amphotericin B

- Dogs with neurologic signs or life-threatening disease should be treated with AMB.
- 0.5–1.0 mg/kg IV q48h in dogs that cannot take oral medication or that do not respond to azole therapy (see Histoplasmosis); use the lipid complex for dogs with renal dysfunction.

CONTRAINDICATIONS

Corticosteroids—usually contraindicated because the anti-inflammatory effects allow uninhibited proliferation of the organisms; patients with previous steroid therapy require a longer duration of treatment; for dogs with life-threatening dyspnea, dexamethasone (0.1–0.2 mg/kg daily) for 2–3 days may be lifesaving when given in conjunction with itraconazole treatment; taper and discontinue steroids as soon as possible.

PRECAUTIONS

Itraconazole and Fluconazole Toxicity

- Anorexia—most common sign; attributed to liver toxicity; monitor serum ALT monthly for duration of treatment or when anorexia occurs; temporarily discontinue drug for patients with anorexia and moderate ALT elevation; after appetite improves, restart at half the previously used dose.
- Ulcerative dermatitis—seen in some dogs; the result of vasculitis; dose-related condition; temporarily discontinue drug; when ulcers have resolved, restart at half the previously used dose.

Amphotericin B Toxicity

- Only absolute contraindication to therapy is anaphylaxis but the major limiting factor is

cumulative nephrotoxicity. • Monitor creatinine throughout therapy—elevation above normal or 20% greater than baseline is considered significant.



FOLLOW-UP

PATIENT MONITORING

Serum chemistry—monthly to monitor for hepatic toxicity or if anorexia develops.

Thoracic Radiographs

- Determine duration of treatment.
- Considerable permanent pulmonary changes (fibrosis/scarring) may occur after the infection has resolved, making determination of persistent active disease difficult.
- At 90 days of treatment—if active lung disease is seen, continue treatment for an additional 30 days.
- If lungs are normal, stop treatment and repeat radiographs again in 30 days.
- At 120 days of treatment—if the lungs are the same as day 90, changes are residual (fibrosis).
- If better than day 90, continue treatment for 30 more days, if lesions are significantly worse than at 90 days, change treatment to amphotericin B and then repeat radiographs.
- Continue treatment as long as there is improvement in the lungs; if there is no further improvement and no indication of active disease, the lesions are likely the result of scarring.

PREVENTION/AVOIDANCE

- Location of environmental growth of *Blastomycetes* organisms unknown, thus difficult to avoid exposure; exposure to lakes and streams could be restricted but is not very practical.
- Dogs that recover from the infection may be immune to reinfection.

EXPECTED COURSE AND PROGNOSIS

- Death—25% of dogs die during the first week of treatment; early diagnosis improves chance of survival.
- More severe pulmonary disease and invasion into the CNS decrease prognosis.
- Recurrence—about 20% of dogs; usually within 3–6 months after completion of treatment; may occur > 1 year after treatment; a second course of azole treatment cures most patients; drug resistance has not been observed.
- With early detection of blastomycosis, the prognosis in cats appears similar to dogs.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Yeast form is not spread from animals to humans, except through bite wounds; inoculation of organisms from dog bites has occurred.
- Avoid cuts during necropsy of infected dogs and avoid needle sticks when

aspirating lesions.

- Warn clients that blastomycosis is acquired from an environmental source and that they may have been exposed at the same time as the patient; the incidence in dogs is 10 times that in humans.
- Encourage clients with respiratory and skin lesions to inform their physicians that they may have been exposed to blastomycosis.

PREGNANCY/FERTILITY/BREEDING

Azole drugs can have teratogenic effects (embryotoxicity found at high doses) and should ideally be avoided during pregnancy (but the risk of not treating the mother needs to be balanced with the theoretical risk of azole therapy to the fetuses).

ABBREVIATIONS

- AGID = agar gel immunodiffusion
- ALT = alanine transaminase • AMB = amphotericin B • CBC = complete blood count • CNS = central nervous system

INTERNET RESOURCES

Information on antigen testing:
www.miravistalabs.com.

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Client Education Handout
available online

BLEPHARITIS

B



BASICS

DEFINITION

- Inflammation of the outer (skin) and middle (muscle, connective tissue, and glands) portions of the eyelid, usually with secondary inflammation of the palpebral conjunctiva.
- Anterior—most commonly associated with bacterial infection or self-trauma.
- Posterior—disorders of the meibomian glands.

PATOPHYSIOLOGY

- Same as virtually every condition that affects the skin in general.
- Mechanisms of inflammation—immune mediated, infectious, endocrine mediated, self- and external trauma, parasitic, radiation, and nutritional.
- Inflammatory response often exaggerated because eyelid conjunctiva is rich in mast cells and densely vascularized.
- Meibomian gland dysfunction—common; bacterial lipases alter meibomian lipids so they plug the gland; they also produce irritating fatty acids, enhance bacterial growth, and destabilize the tear film.

SYSTEMS AFFECTED

Ophthalmic

SIGNALMENT

See "Causes"

SIGNS

- Serous, mucoid, or mucopurulent ocular discharge.
- Blepharospasm.
- Eyelid hyperemia, edema, and thickening.
- Pruritus.
- Excoriation.
- Depigmentation—skin; hair.
- Alopecia.
- Swollen, cream-colored meibomian glands.
- Elevated, pinpoint meibomian gland orifices.
- Abscesses.
- Scales and crusts.
- Papules or pustules.
- Single or multiple nodular hyperemic swellings.
- Concurrent conjunctivitis and/or keratitis.
- In Siamese-type cats with color points, chronic blepharitis often causes lightening of hair on affected lids due to increased temperature of the skin.

CAUSES

Congenital

- Eyelid abnormalities—may promote self-trauma or moist dermatitis.
- Prominent nasal folds, medial trichiasis, and lower lid entropion—shih tzu, Pekingese, English bulldog, Lhasa apso, pug; Persian and Himalayan cat.
- Distichia—shih tzu, pug, golden retriever, Labrador retriever, poodle, English bulldog.
- Ectopic cilia.
- Lateral lid entropion—shar-pei, chow chow, Labrador retriever, rottweiler; adult cats (rare).
- Lagophthalmos—brachycephalic dogs; Persian, Himalayan, and Burmese cats.
- Deep medial canthal pocket—dolichocephalic dogs.
- Dermoids—rottweiler, dachshund, and others; Burmese cat.

Allergic

- Type I (immediate)—atopy, food, insect bite, inhalant, *Staphylococcus* hypersensitivity.
- Type II (cytotoxic)—pemphigus, pemphigoid, drug eruption.
- Type III (immune complex)—SLE; *Staphylococcus* hypersensitivity; drug eruption.
- Type IV (cell mediated)—contact and flea bite hypersensitivity; drug eruption.

Bacterial

- Hordeolum—localized abscess of eyelid glands, usually staphylococcal; may be external (sty in young dogs, involving glands of Zeis) or internal (in old dogs, involves one or more meibomian glands).
- Generalized bacterial blepharitis and meibomianitis—usually *Staphylococcus* or *Streptococcus*.
- Pyogranulomas.
- *Staphylococcus* hypersensitivity—young and old dogs.

Neoplastic

- Sebaceous adenomas and adenocarcinomas—originate from meibomian gland.
- Squamous cell carcinoma—white cats.
- Mast cell—may masquerade as swollen, hyperemic lesion.

Other

- External trauma—eyelid lacerations; thermal or chemical burns.
- Mycotic—dermatophytosis; systemic fungal granulomas.
- Parasitic—demodicosis; sarcoptic mange; *Cuterebra* and *Notoedres cati*. Note: *Demodex injai* has a propensity for sebaceous glands and can be associated with meibomian gland dysfunction in dogs, including chalazia and granulomatous blepharitis.
- Chalazia (singular, chalazion)—sterile, yellow-white, painless meibomian gland swellings caused by a granulomatous inflammatory response to escape of meibum into surrounding eyelid tissue.
- Nutritional—zinc-responsive dermatosis (Siberian husky, Alaskan malamute, puppies); fatty acid deficiency.
- Endocrine—hypothyroidism (dogs); hyperadrenocorticism (dogs); diabetic dermatosis.
- Viral—chronic blepharitis in cats secondary to FHV-1.
- Irritant—topical ocular drug reaction; nicotine smoke in environment; after parotid duct transposition.
- Familial canine dermatomyositis—collie and Shetland sheepdog.
- Nodular granulomatous episclerokeratitis—fibrous histiocytoma and collie granuloma in collies; may affect the eyelids, cornea, or conjunctiva.
- Eosinophilic granuloma—cats; may affect eyelids, cornea, or conjunctiva.
- Eyelid contact with tear overflow and purulent exudate (tear burn).
- Conjunctivitis.
- Keratitis.
- Dry eye.
- Dacryocystitis.
- Orbital disease.
- Radiotherapy.
- Drug contact irritant—any drug, often neomycin.
- Idiopathic—particularly in cats with chronic idiopathic conjunctivitis (especially Persians and Himalayans).

RISK FACTORS

- Breed predisposition to congenital eyelid abnormalities, e.g., entropion, ectropion, etc.
- Hypothyroidism—may promote chronic bacterial disease in dogs.
- Canine seborrhea—may promote chronic generalized meibomianitis, with predisposition for *Demodex injai* infection.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Clinical signs are diagnostic.

CBC/BIOCHEMISTRY/URINALYSIS

Usually non-diagnostic unless metabolic cause (e.g., diabetic dermatosis).

OTHER LABORATORY TESTS

- Indicated for suspected systemic disorder.
- Consider tests for hypothyroidism.

DIAGNOSTIC PROCEDURES

- If possible, avoid topical anesthetic or fluorescein before obtaining culture.
- Cytology—deep skin scrapings; conjunctival scrapings; expressed exudate from meibomian glands and pustules.
- Dermatophyte culture—deep skin scrapings.
- Wood's light evaluation—skin.
- KOH preparation—skin scrapings.
- Aerobic bacterial culture and sensitivity—exudate from skin; conjunctiva; expressed exudate from meibomian glands and pustules; often will not recover *Staphylococcus* from patients with chronic meibomianitis and suspected *Staphylococcus* hypersensitivity.
- IFA or PCR for FHV-1 and *Chlamydia*—conjunctival scrapings from cats with primary conjunctivitis or keratitis.
- Eye examination—potential inciting cause; corneal ulcer; foreign body; distichia; ectopic cilia; dry eye.
- Ancillary ocular tests—fluorescein application; Schirmer tear test.
- Thorough medical history and dermatologic examination—help identify generalized dermatologic disease.
- Full-thickness wedge biopsy of eyelid—histologic evaluation.
- Direct immunofluorescence for autoimmune disease; intradermal skin testing, RAST, ELISA, and food elimination diet for hypersensitivity-induced disease.
- Do not underestimate the value of referral to a dermatologist for refractory cases, especially when atopy is suspected.

PATHOLOGIC FINDINGS

- Routine histopathology often non-diagnostic in chronic disease.
- Carefully select patients based on history, ophthalmic exam, and response to medical therapy.



TREATMENT

APPROPRIATE HEALTH CARE

See "Nursing Care"

BLEPHARITIS

B

NURSING CARE

- Secondary disease—treat primary disease.
- Suspected self-trauma—Elizabethan collar.
- Topical gentamicin, neomycin, terramycin, and most ointments—may cause an irritant blepharoconjunctivitis (rare); withdrawal of agent may resolve condition.
- Cleanse eyelids—to remove crusts; warm compresses applied for 5–15 minutes 3–4 times daily, avoiding ocular surfaces; saline lactated Ringer's solution, or a commercial ocular cleansing agent (e.g., I-Lid n Lash); must clip periocular hair short.

DIET

Only with food allergy-induced disease.

CLIENT EDUCATION

- In cats with FHV-1-related blepharitis inform client that there is no cure and that clinical signs often recur when the animal is stressed.
- Inform client that there is no cure for FHV-1 and that clinical signs often recur when the animal is stressed.

SURGICAL CONSIDERATIONS

- Temporary everting eyelid sutures—spastic entropion; or in puppies before permanent surgical correction.
- Repair eyelid lacerations.
- Lancing—large abscesses only; lance and curette hordeola that resist medical treatment and chalazia that have hardened and come to a point, causing keratitis; manually express infected meibomian secretions.



MEDICATIONS

DRUG(S)

Antibiotics

- Systemic—generally required for effective treatment of bacterial eyelid infections; may try amoxicillin-clavulanic acid or cephalaxin; 20 mg/kg q8h.
- Topical—may try neomycin, polymyxin B, and bacitracin combination or chloramphenicol.

Congenital

- Topical antibiotic ointment—q6–12h; until surgery is performed to prevent frictional rubbing of eyelid hairs or cilia on the ocular surface.
- Saline, lactated Ringer's solution, or ocular irrigant—regularly flush deep medial canthal pocket debris.

External Trauma

- Topical antibiotic ointment—q6–12h; for spastic entropion secondary to pain and blepharospasm to reduce friction until entropion is surgically relieved.
- Systemic antibiotics indicated.

Allergic

- *Staphylococcus* hypersensitivity blepharitis—systemic broad-spectrum antibiotics and systemic corticosteroids (prednisolone 0.5 mg/kg q12h for 3–5 days, then taper); many patients respond dramatically to systemic corticosteroids alone. Systemic

cyclosporine if refractory to corticosteroids (5 mg/kg PO q24h until remission, then q48–72h).

- Infected meibomian glands—oral tetracycline (15–20 mg/kg PO q8h) or doxycycline (3–5 mg/kg PO q12h) or cephalaxin (22 mg/kg q8h) for at least 3 weeks (the former two are lipophilic and cause decreased production of bacterial lipases and irritating fatty acids); topical polymyxin B and neomycin with 0.1% dexamethasone (q6–8h to the eye) or topical 0.02% tacrolimus compounded ointment (q8–12h).

Note: Some affected dogs might also have concomitant Demodex injai infection and require treatment for demodicosis.

- Failure of treatment—may try injections of commercial *Staphylococcus aureus* bacterin (Staphage Lysate).
- Eyelid lesions associated with puppy strangles—usually benefit from treatment of the generalized condition.
- Atopy (see Atopy); consider Janus kinase inhibitor (oclacitinib; Apoquel) to control pruritus and self-trauma.

Bacterial

- Based on culture and sensitivity testing.
- While results are pending—topical polymyxin B and neomycin with 0.1% dexamethasone ointment (q4–6h); plus a systemic broad-spectrum antibiotic.

Mycotic

- *Microsporum canis* infection—usually self-limiting; treatment includes 2% miconazole cream, 1% clotrimazole cream, or diluted povidone-iodine solution (1 part to 300 parts saline) applied q12–24h for at least 6 weeks; do not use lotions.

Parasitic

- Demodicosis—localized disease: see Demodicosis. Some dogs require systemic treatment with moxidectin, ivermectin, or milbemycin oxime.
- *Notoedres* infection—lime sulfur dips.
- Sarcoptic mange—same as for generalized disease.

Idiopathic

- Clinical signs often controlled with topical polymyxin B and neomycin with 0.1% dexamethasone (q8–24h or as needed); occasionally may also need systemic prednisolone (0.5 mg/kg q12h for 3–5 days, then taper) and/or a systemic antibiotic.

CONTRAINDICATIONS

- Topical corticosteroids—do not use with corneal ulceration.
- Many cats with presumed idiopathic blepharoconjunctivitis have FHV-1 infection; topical and systemic corticosteroids may exacerbate the infection.
- Oral tetracycline and doxycycline—do not use in puppies and kittens.
- Neomycin—avoid topical use if suspect it is causing the blepharitis.

PRECAUTIONS

- Ectoparasitism—wear gloves; do not contact ocular surfaces with a drug topically

applied to skin; apply artificial tear ointment to the eyes for protection.

POSSIBLE INTERACTIONS

Staphylococcal bacterin for *Staphylococcus* hypersensitivity—anaphylactic reaction (rare).



FOLLOW-UP

PATIENT MONITORING

- Depends on cause and mode of therapy.
- Bacterial—treated with systemic and topical treatment for at least 3 weeks; should notice improvement within 10 days.
- Most common causes of treatment failure—use of subinhibitory antibiotic concentrations; failure to correct one or more predisposing factors; stopping medications too soon.

PREVENTION/AVOIDANCE

Depends on cause

POSSIBLE COMPLICATIONS

- Cicatricial lid contracture—results in trichiasis, ectropion, or lagophthalmos.
- Spastic entropion—because of blepharospasm and pain.
- Inability to open eyelids—owing to matting of discharge and hair.
- Qualitative tear film deficiency—result of loss of proper meibum secretion.
- Recurrence of bacterial infection or FHV-1 blepharoconjunctivitis.

EXPECTED COURSE AND PROGNOSIS

Depends on cause



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Dermatophytosis
- Sarcoptic mange

SEE ALSO

- Conjunctivitis—Cats
- Conjunctivitis—Dogs
- Epiphora
- Keratitis, Nonulcerative
- Keratitis, Ulcerative
- Red Eye

ABBREVIATIONS

- ELISA = enzyme-linked immunosorbent assay
- FHV-1 = feline herpesvirus type 1
- IFA = immunofluorescent antibody test
- PCR = polymerase chain reaction
- RAST = radioallergosorbent test
- SLE = systemic lupus erythematosus

Suggested Reading

Maggs D. Eyelids. In: Maggs DJ, Miller PE, Ofri R, Slatter's Fundamentals of Veterinary Ophthalmology, 5th ed. St. Louis, MO: Saunders, 2012, pp. 110–139.

Author Terri L. McCalla

Consulting Editor Paul E. Miller



Client Education Handout
available online



BASICS

DEFINITION

Loss of vision in one or both eyes without ocular vascular injection or other externally apparent signs of ocular inflammation.

PATHOPHYSIOLOGY

Results from abnormalities in focusing images on the retina, the retina detecting an image, optic nerve transmission, or CNS interpretation of images.

SYSTEMS AFFECTED

- Nervous
- Ophthalmic

SIGNALMENT

- Dog and cat
- Any age, breed, or sex
- Many causes (e.g., cataracts and progressive retinal atrophy) have a genetic basis and are often highly breed- and age-specific
- SARDS—tends to occur in older dogs
- Optic nerve hypoplasia—congenital

SIGNS

Historical Findings

- Varies with underlying cause
- Bumping into objects
- Clumsy behavior
- Reluctance to move
- Impaired vision in dim light

Physical Examination Findings

- Varies with underlying cause
- Decreased or absent menace response
- Impaired visual placing responses

CAUSES

- Cataracts—entire lens must become opaque to produce complete blindness; incomplete opacification may reduce performance of visually demanding tasks.
- Loss of focusing power of the lens—rarely completely blinding; substantial hyperopia (far-sightedness) occurs when the optical power of the lens is not replaced after lens extraction or if the lens luxates posteriorly out of the pupillary plane and into the vitreous.
- Retina—SARDs; PRA; retinal detachment; taurine deficiency (cats), enrofloxacin toxicity (cats); ivermectin toxicity (dogs, cats).
- Optic nerve—optic neuritis; neoplasia of the optic nerve or adjacent tissues; trauma; optic nerve hypoplasia; lead toxicity; excessive traction on the optic nerve during enucleation resulting in trauma to the contralateral optic nerve or optic chiasm (especially cats and brachycephalic dogs).
- CNS (amaurosis)—lesions of the optic chiasm or tract; optic radiation; visual cortex. CNS-associated vision loss that occurs at a level higher than the optic chiasm often has vague visual disturbances in which the patient has some vision but clearly does not have normal vision.

RISK FACTORS

- Poorly regulated diabetes mellitus—cataracts.
- Related animals with genetic cataracts or PRA.
- Systemic hypertension—retinal detachment.
- CNS hypoxia—

blindness may become apparent after excessively deep anesthesia or revival from cardiac arrest.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Signs

- Anterior segment inflammation and glaucoma—conjunctiva typically injected.
- Young patients—may lack menace responses but will successfully navigate a maze or visually track hand movements or cotton balls.
- Postictal period—transient vision loss.
- Abnormal mentation—may be difficult to determine whether an animal is visual; other neurologic abnormalities help localize the lesion.

CAUSES

- Optic neuritis, retinal detachment, SARDs, or visual cortex hypoxia—sudden vision loss (over hours to weeks).
- SARDs—often preceded by polyuria, polydipsia, polyphagia, and weight gain.
- PRA—gradual vision loss, especially in dim light; apparently acute vision loss with sudden change in environment.
- Cataract—history of either gradual or rapidly increasing opacification and vision loss in a quiet eye.
- Optic nerve hypoplasia—congenital; may be unilateral or bilateral.
- Optic neuropathy or CNS disease—signs of other neurologic abnormalities.
- Pupillary light responses—usually normal with cataracts or visual cortex lesions; sluggish to absent with retinal or optic nerve diseases.
- Ophthalmoscopy—normal with SARDs, retrobulbar optic neuritis, and higher visual pathway lesions; abnormal with retinal detachment and neuropathies of the optic nerve head.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal, unless underlying systemic disease.
- Hyperglycemia or glucosuria—may note with diabetic cataracts.
- Elevated ALP and changes consistent with hyperadrenocorticism (Cushing's syndrome)—suggest SARDs.
- Retinal detachment secondary to systemic hypertension (cats)—mildly high BUN or serum creatinine; changes consistent with hyperthyroidism.

OTHER LABORATORY TESTS

- Blood lead and serology for deep fungal or viral infections—consider for suspected optic neuritis (see Optic Neuritis and Papilledema).
- LDDST—may help rule out Cushing's syndrome with SARDs.
- Sex hormone abnormalities are common in patients with SARDs.

IMAGING

- Ocular ultrasound—may demonstrate a retinal detachment (especially if the ocular media are opaque) or optic nerve mass lesion.
- Plain skull radiographs—seldom

informative.

- CT or MRI—often helpful with orbital or CNS lesions.

DIAGNOSTIC PROCEDURES

- Ophthalmic examination with a penlight—usually permits diagnosis of cataracts or retinal detachments severe enough to cause blindness.
- Ophthalmoscopy—may reveal PRA or optic nerve disease; normal examination suggests SARDs, retrobulbar optic neuritis, or a CNS lesion.
- Systemic blood pressure—determine in retinal detachments.
- Electrotoretinography—differentiates retinal from optic nerve or CNS disease when the diagnosis is in doubt.
- CSF tap—may be of value with a neurogenic cause of vision loss.



TREATMENT

- Try to obtain a definitive diagnosis on an outpatient basis before initiating treatment.
- Consider referral before attempting empirical therapy.
- Most causes are not fatal, but must perform a workup to rule out potentially fatal diseases.
- Reassure client that most causes of a blind quiet eye are not painful and that blind animals can lead relatively normal and functional lives.
- Warn client that the environment should be examined for potential hazards to a blind animal.
- Advise client that patients with progressive retinal atrophy or genetic cataracts should not be bred and that related animals should be examined.
- Retinal detachment—recommend severely restricted exercise until the retina is firmly reattached.
- Calorie-restricted diet—to prevent obesity; owing to reduced activity level.
- Cats with nutritionally induced retinopathy—ensure diet has adequate levels of taurine.
- SARDs, progressive retinal atrophy, optic nerve atrophy, and optic nerve hypoplasia—no effective treatment.
- Cataracts, luxated lenses, and some forms of retinal detachment—best treated surgically.



MEDICATIONS

DRUG(S) OF CHOICE

- Depends on cause.
- Workup is declined, infectious disease is unlikely, and the likely diagnosis is either SARDs or retrobulbar optic neuritis—consider systemic prednisolone (1–2 mg/kg/day for 7–14 days, then taper); may concurrently administer oral chloramphenicol or other systemic broad-spectrum antibiotic.

CONTRAINdicATIONS

Do not use systemic corticosteroids and other immunosuppressive drugs with optic neuritis and retinal detachments that are infectious in origin.

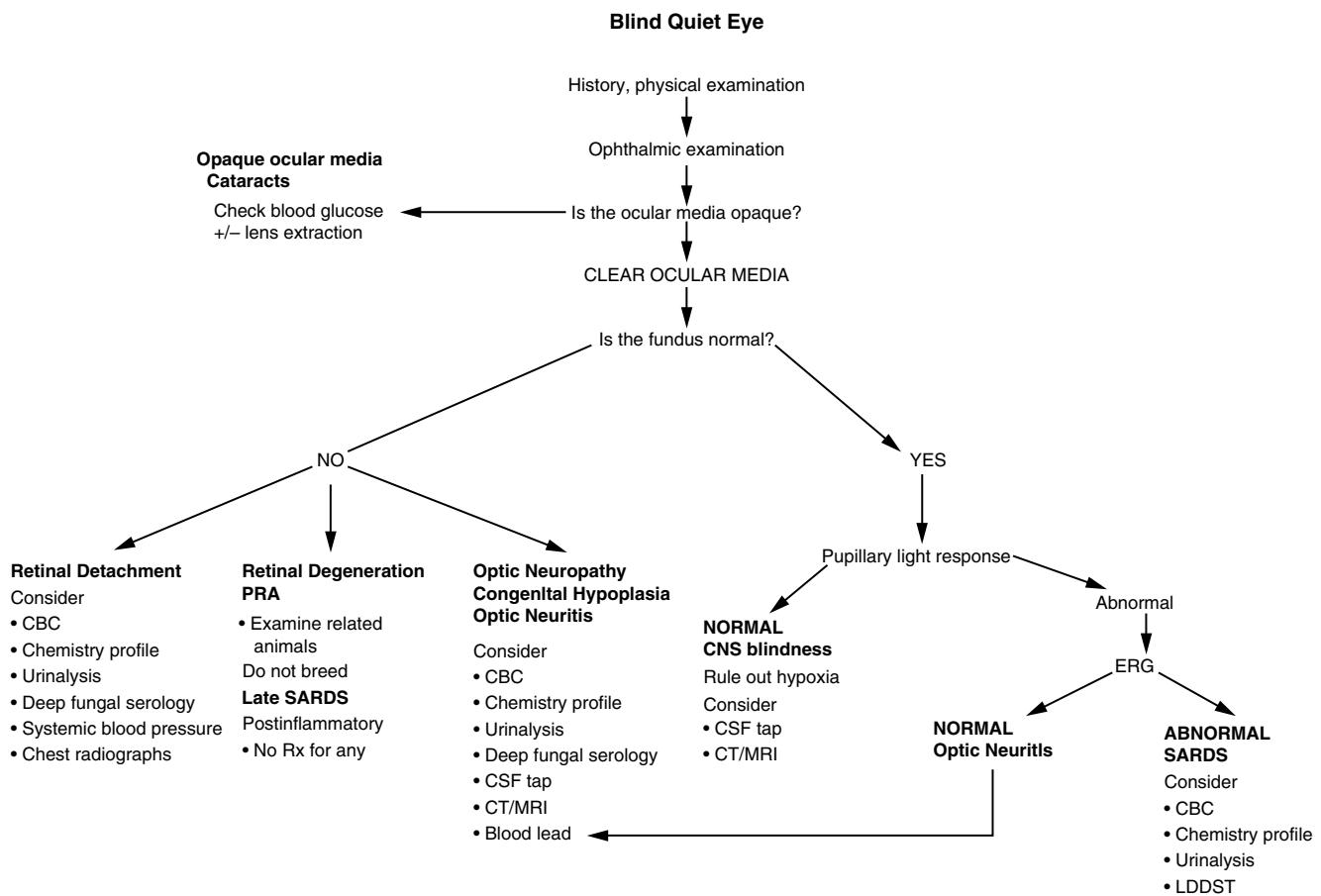


Figure 1.

PRECAUTIONS

Pretreatment with corticosteroids may mimic or mask liver enzyme changes in SARDs.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

• Flunixin meglumine (dogs)—may try a single dose (0.5 mg/kg IV) in place of corticosteroids if infectious causes have not been ruled out. • Oral azathioprine 1–2 mg/kg/day for 3–7 days, then taper; may be used to treat immune-mediated retinal detachments if systemic corticosteroids are not effective; perform a CBC, platelet count, and liver enzyme every 1–2 weeks for the first 8 weeks, then periodically.

**FOLLOW-UP****PATIENT MONITORING**

• Repeat ophthalmic examinations—as required to ensure that ocular inflammation is controlled, and, if possible, vision is maintained. • Recurrence of vision loss—common in optic neuritis; may occur weeks, months, or years after initial presentation.

POSSIBLE COMPLICATIONS

- Death
- Permanent vision loss.
- Loss of the eye
- Chronic ocular inflammation and pain
- Obesity from inactivity or as a sequela of SARDs

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- SARDs (dogs)—signs similar to those of hyperadrenocorticism. • Neurologic disease—may note seizures, behavior or personality changes, circling or other CNS signs. • Cardiomyopathy (cats)—taurine deficiency.

AGE-RELATED FACTORS

- PRA and many cataracts—breed-specific ages of onset. • SARDs—tends to occur in older dogs. • Optic nerve hypoplasia—congenital.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Corticosteroids and immunosuppressive drugs may complicate pregnancy.

ABBREVIATIONS

- ALP = alkaline phosphatase
- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- LDDST = low-dose dexamethasone suppression test
- MRI = magnetic resonance imaging
- PRA = progressive retinal atrophy
- SARDs = sudden acquired retinal degeneration syndrome

INTERNET RESOURCES

- Books: <http://www.petcarebooks.com/>.
- Pepe the Blind Dog: <http://www.pepedog.com/>.
- Unique idea for active blind dogs, the angel vest: <http://angelvest.homestead.com/>

Suggested Reading

- Maggs DJ, Miller PE, Ofri R. Fundamentals of Veterinary Ophthalmology, 5th ed. St Louis, MO: Saunders Elsevier, 2013.
Rubin LF. Inherited Eye Disease in Purebred Dogs. Baltimore, MD: Williams & Wilkins, 1989.

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Client Education Handout available online

BLOOD TRANSFUSION REACTIONS



BASICS

OVERVIEW

- Classified as acute or delayed, immune mediated or not immune mediated.
- Severe reactions usually occur during or shortly after transfusion.
- Can occur with any blood product, including hemoglobin-based oxygen-carrying solutions.

SIGNALMENT

- Dogs and cats
- No sex predilection
- All ages affected

SIGNS

Acute Hemolytic Reaction

- Restlessness
- Fever
- Tachycardia
- Vomiting
- Tremors
- Weakness
- Incontinence
- Collapse
- Shock
- Oliguria
- Loss of transfusion efficacy

Delayed Hemolytic Reaction

Loss of transfusion efficacy—usually no clinical signs.

Acute Non-hemolytic Reaction

- Anaphylactic reaction—fever, urticaria, erythema, angioedema, and pruritus.
- Transfusion of contaminated blood—acute septicemia, fever, and shock.
- Circulatory overload/rapid transfusion—vomiting, distended jugular veins, dyspnea, cough, cyanosis, and congestive heart failure.
- Citrate toxicity—hypocalcemia, myocardial depression, and weakness.
- Hyperammonemia—encephalopathy.
- Hypothermia—shivering and impaired platelet function.

CAUSES & RISK FACTORS

Purebred cats and previously transfused dogs have a higher risk of severe transfusion reaction than other animals.

Acute Hemolysis

- Blood group mismatch.
- Naturally occurring autoantibody (particularly in cats).
- Acquired autoantibody (IHA).
- Transfusion of damaged and hemolyzed RBCs (after inappropriate storage, excessive heating, freezing, or mechanical damage).

Delayed Hemolysis

- Immune reaction to minor red cell antigens; occurs after 3–14 days.

Acute Non-hemolytic Reaction

- Anaphylaxis and immune reaction to donor leukocytes or platelets, major histocompatibility complex antigens, or plasma antigens, resulting in release of inflammatory mediators and pyrogens.
- Transfusion of contaminated blood—lack of aseptic collection and storage conditions.
- Circulatory overload—rapid transfusion; excessive volume of blood in small patients or in patients with heart failure or oliguric renal failure.
- Citrate toxicity—after circulatory overload, particularly in small patients or in

patients with hepatopathy.

- Hyperammonemia—high ammonia concentration in stored blood; important only for animals with hepatopathy.
- Hypothermia—rapid transfusion of refrigerated blood to small or already hypothermic patients.

Delayed Non-hemolytic Reaction

- Transmission of blood-borne disease—use of infected donor (*hemotropic Mycoplasma* spp. DNA found in 10% of active donors in one study).
- Transfusion-associated graft vs. host disease—rare, but > 90% fatal complication of transfusion of blood components that contain immunocompetent donor T-lymphocytes. Has not been clearly reported in canine or feline patients yet.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hemolysis—rule out ongoing fulminant hemolytic disease (IHA, *Babesia*, *Mycoplasma*) and use of hemolyzed blood.
- Fever, hypotension—rule out underlying infectious and inflammatory diseases, bacterial contamination.

CBC/BIOCHEMISTRY/URINALYSIS

Hemoglobinemia, leukocytosis, bilirubinemia, hemoglobinuria, and bilirubinuria.

OTHER LABORATORY TESTS

- Repeat cross-match to confirm incompatibility.
- Bacterial culture or Gram staining of contaminated blood may reveal organism.
- *Mycoplasma* PCR in cats.



TREATMENT

- Immediately discontinue transfusion.
- Administer fluids to maintain blood pressure and renal blood flow; for hypotension, use isotonic crystalloids such as Plasmalyte (50–90 mL/kg/h, give 30% of the dose, then reassess).
- Additional supportive therapy for DIC, shock, or thromboembolism (see Disseminated Intravascular Coagulation; Shock, Septic; Aortic Thromboembolism; Pulmonary Thromboembolism).



MEDICATIONS

DRUG(S)

- For hemolysis—rapid-acting corticosteroid, such as prednisolone sodium succinate (11 mg/kg once) or dexamethasone sodium phosphate (2.2 mg/kg once); heparin (dose still controversial, 300 U/kg SC q6h; not for use in bleeding patients).
- For urticaria,

fever—diphenhydramine (1–2 mg/kg); dexamethasone sodium phosphate (0.2 mg/kg once); continue transfusion afterwards, if clinically indicated.

- For septicemia—broad-spectrum IV antibiotics
- For volume overload—furosemide 2–4 mg/kg IV, oxygen supplementation.



FOLLOW-UP

PATIENT MONITORING

- Check attitude, temperature, vital signs, lung sounds, PCV, total solids, and plasma color before, during, and after transfusion.
- For acute hemolytic reactions or septicemia—monitor CVP and urine output.
- If pulmonary thromboembolism is suspected, check chest radiographs and arterial blood gases frequently.

PREVENTION/AVOIDANCE

- Carefully record any transfusion reaction in the patient's medical file.
- Pretransfusion testing:
 - Screen donors for infectious disease.
 - Blood type donors and recipients.
 - Typing cards/cartridges (DMS, Alvedia, DMS/Agrolabo, DMS/Abaxis).
 - Crossmatching: Gel agglutination or strip tests (Diamed, DMS, Alvedia).
- Adhere to standard transfusion protocols (e.g., use of healthy donors; appropriate blood collection, storage, and administration techniques).
- Initially, transfuse at 0.5 mL/minute.

POSSIBLE COMPLICATIONS

- Fulminant hemolysis may cause acute renal failure, pulmonary thromboembolism, multiorgan thromboembolism, DIC, and cardiac arrhythmias.
- Volume overload may cause heart failure.
- Cardiac arrest.

EXPECTED COURSE AND PROGNOSIS

- Acute course in most animals.
- Prognosis good in stable animals, guarded in severely ill animals or when not recognized early.
- Cats with type B blood receiving mismatched blood have the worst prognosis.



MISCELLANEOUS

ABBREVIATIONS

- CVP = central venous pressure
- DIC = disseminated intravascular coagulation
- IHA = immune hemolytic anemia
- PCR = polymerase chain reaction
- PCV = packed cell volume
- RBC = red blood cell

Suggested Reading

Sullivan L, Hackett TB. Transfusion Medicine: Best Practices. In: Bonagura JD, Twedd DC, eds., Current Veterinary Therapy XV: Elsevier, 2014, pp. 309–313.

Author Jörg Bucheler

Consulting Editor Alan H. Rebar

BLUE-GREEN ALGAE TOXICOSIS

B



BASICS

OVERVIEW

- Cyanobacterial blooms can occur in fresh and brackish waters, and in backyard ponds where algal material is concentrated.
- Nutrient-rich runoff, increased water temperatures, and stagnant water conditions favor toxic bloom formation. • Blue-green algae exposure can lead to an acute hepato- or neurotoxicosis in animals and humans.
- Hepatotoxic blue-green algae poisonings are more frequently reported than neurotoxic algal intoxication. • Toxin-producing cyanobacteria include *Microcystis*, *Anabena*, *Aphanizomenon*, *Oscillatoria*, *Lyngbya*, and *Planktothrix* spp. • Microcystins are hepatotoxic blue-green algae toxins that have been found worldwide. • Anatoxins, which include anatoxin-a and anatoxin-a_s, are neurotoxic blue-green algae toxins.

SIGNALMENT

- Dogs: no breed, sex, or age predilection.
- Cats: no cases reported.

SIGNS

Hepatotoxic

- Diarrhea, weakness, shock. • Rapid progression to depression, coma, and death.

Neurotoxic

- Onset of rigidity and muscle tremors within minutes to a few hours after exposure. • Rapid progression to paralysis, cyanosis, and death.

CAUSES & RISK FACTORS

- Access to and ingestion of toxin-contaminated water and/or algal material.
- Blooms more common in nutrient-rich water in warmer months. • Blooms concentrated through wind or by removal into containers. • Certain algae reside in the benthic zone, e.g., in the sediment. Dogs mouthing material such as rocks from sediment can be at risk.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Hepatotoxic

- Amanitins, xylitol, cycad palms, acetaminophen, manganese, pennyroyal oil, cocklebur. • Other causes of acute liver failure: infectious, metabolic, dietary.

Neurotoxic

- Strychnine, metaldehyde, avitrol, pyrethrins/pyrethroids, zinc phosphide, bromethalin. • Organophosphorus, carbamate, and organochlorine insecticides.
- Penitrem A, methylxanthines. • Poisonous plants (*Brunfelsia* spp., cyanide, oleander, poison hemlock). • Illicit substances (amphetamine & derivatives),

ephedra-containing compounds.

- Neurotoxic mushrooms.

CBC/BIOCHEMISTRY/URINALYSIS

Hepatotoxic

- Elevated serum liver enzymes (ALT, AST, ALP, bilirubin) • Hypoalbuminemia
- Hypoglycemia

Neurotoxic

No specific changes.

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Morphologic algal ID in suspect water, algal material, or stomach content. Positive ID confirms hazard but is not confirmatory for the toxin because toxicity is strain specific.

Hepatotoxic

- Detection of algal material on fur or in stomach contents. • Analysis of stomach contents and water/algal source for microcystins.

Neurotoxic

- Detection of anatoxin-a in gastric contents, urine, bile and suspect source material.
- Depressed blood cholinesterase activity with anatoxin-a_s poisoning.

PATHOLOGIC FINDINGS

Hepatotoxic

- Detection of algal material on fur or in stomach contents. • Enlarged liver.
- Histologic detection of centrilobular hepatocellular necrosis and intrahepatic hemorrhage.

Neurotoxic

- Detection of algal bloom material in GI tract and/or on legs. • Typically no lesions.



TREATMENT

- No antidote available. • Rapid onset typically prevents timely therapeutic intervention. • GI decontamination with activated charcoal can be attempted but efficacy is not known. • Hepatotoxic: supportive care, close monitoring, and case-specific intravenous fluids to correct electrolytes and hypoglycemia, vitamin K1, and plasma transfusions. • Neurotoxic: supportive care and seizure control.



MEDICATIONS

DRUG(S)

- Activated charcoal: 1 g/kg PO q2–6h until 2–3 days post-ingestion. Mix activated charcoal in water at 1 g/5 mL of water.
- Intravenous fluids: maintain hydration, induce diuresis, correct hypoglycemia.
- Dextrose: 50% dextrose 1 mL/kg IV slow

bolus (1–3 min).

- Vitamin K1: 0.5–1.5 mg/kg SC or IM q12h; 1–5 mg/kg PO q24h.
- Blood products: dependent on hemostatic test results.
- Diazepam (2–5 mg/kg IV, repeat in 30 min if necessary) for seizure control.
- Phenobarbital (2–5 mg/kg IV q6–12h) for seizure control.
- Methocarbamol (55–220 mg/kg IV) for muscle relaxation.

ALTERNATIVE DRUGS

- S-adenosylmethionine (SAMe): antioxidant and hepatoprotectant; no data on efficacy in hepatotoxic cyanotoxin toxicosis available. Dose 20 mg/kg PO q24h.
- Ascorbic acid and cimetidine: hepatocyte protectors; no data on efficacy in hepatotoxic cyanotoxin poisoning available.
- N-acetylcysteine (NAC): antioxidant; no data on efficacy in hepatotoxic cyanotoxin toxicosis available.
- Glutathione precursor that can be included in the treatment regimen for acute hepatic failure at 140 mg/kg IV load, followed by 70 mg/kg IV q6h for 7 treatments.

CONTRAINdications/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Hepatotoxic: liver enzymes/function, coagulation status.
- Neurotoxic: thermoregulation, respiratory function, blood gases.

PREVENTION/AVOIDANCE

- Deny access to water with visible algal blooms
- Remove algal blooms from ponds immediately and discard material safely.

POSSIBLE COMPLICATIONS

- Hepatotoxic: hepatic encephalopathy, DIC.
- Neurotoxic: DIC, rhabdomyolysis, myoglobinuria with subsequent renal failure.

EXPECTED COURSE AND PROGNOSIS

- Prognosis is poor to guarded. • Rapid onset and progression. Often lethal.



MISCELLANEOUS

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine transaminase
- AST = aspartate transaminase
- DIC = disseminated intravascular coagulation

INTERNET RESOURCES

<http://www.cdc.gov/nceh/hsb/hab/>

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Client Education Handout
available online



BASICS

OVERVIEW

- Paralytic illness caused by a preformed neurotoxin produced by the bacterium *Clostridium botulinum* (Gram +, anaerobe) contained in uncooked food, carrion, and contaminated or improperly stored silage.
- Most cases in dogs are caused by *Clostridium botulinum* neurotoxin serotype C. The neurotoxin interferes with the release of acetylcholine at the neuromuscular junction, resulting in diffuse lower motor neuron signs.

SIGNALMENT

Dogs (naturally infected) and cats (experimentally infected except for one case report of natural *Clostridium botulinum* type C toxicosis).

SIGNS

Historical Findings

- Signs appear a few hours to 6 days after toxin ingestion
- Other dogs of the household, neighborhood, or kennel may be affected
- Acute progressive weakness develops, starting in the hind limbs and ascending to the trunk, front limbs, neck, and muscles innervated by the cranial nerves. Severe tetraparesis or tetraplegia ensues.

Physical Examination

- Possible increased or decreased heart rate
- In severe cases—diaphragmatic respiration.

Neurologic Examination Findings

- Mental status—normal
- Cranial nerves—may reveal sluggish pupillary light reflexes, diminished palpebral reflexes, decreased jaw tone, decreased gag reflex, salivation, and dysphonia.
- Gait and posture—a stiff, short-stride gait (no ataxia) is initially observed until recumbence develops (usually within 12–24 hours).
- Spinal reflexes—decreased to absent with decreased muscle tone (to atonia) and muscle atrophy
- Autonomic signs—mydriasis with decreased pupillary light reflexes, decreased lacrimation, ileus, and urine retention or frequent voiding of small volumes.
- No hyperesthesia.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Acute canine polyradiculoneuritis (coonhound paralysis), myasthenia gravis, tick bite paralysis, coral snake venom toxicity, dumb form of rabies, lasalocid (growth promoter in ruminants) toxicosis.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

- Definitive diagnosis is based on detection of botulinum toxin in serum, feces, vomitus, or ingested food sample; by a neutralization test in small rodents; or by in vitro test that measures toxin antigenicity rather than toxicity
- Detection of anti-C botulinum neurotoxin antibodies may help support clinical diagnosis.

IMAGING

Thoracic radiographs—possible megaesophagus and/or signs of aspiration pneumonia.

DIAGNOSTIC PROCEDURES

- Electromyography may reveal fibrillation potentials and positive sharp waves in affected muscles.
- Motor nerve conduction velocity may be normal or decreased with reduced amplitude of evoked motor unit potentials.



TREATMENT

- If recent ingestion—gastric lavage, cathartics (avoid agents containing magnesium) or enemas may be useful.
- Mildly affected dogs recover over a period of several days with supportive treatment including passive and active physical therapy, frequent turning, good bedding (to prevent decubital sores), bladder care (expression or catheterization), and feeding from an elevated position (when megaesophagus present).
- Dogs with respiratory difficulties require intensive care monitoring with arterial blood gas, intermittent esophageal suction, alimentation by nasogastric or gastrostomy tube, and eventually ventilatory support.



MEDICATIONS

DRUG(S)

- Type C antitoxin may cause anaphylaxis; not effective when the toxin is already fixed at the nerve ending.
- Ophthalmic ointment prevents exposure corneal ulceration if keratoconjunctivitis sicca.
- Oral antibiotics are not recommended since they might make the disease worse by releasing more toxin through bacterial lysis or by promoting intestinal infection. To be used only if secondary infections (respiratory, urinary) occur.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Aminoglycosides, procaine penicillin, tetracyclines, phenothiazines, antiarrhythmic agents, and magnesium should be avoided

because they have the potential to block neuromuscular transmission.



FOLLOW-UP

PATIENT MONITORING

Monitor patients for respiratory failure, aspiration pneumonia, progressive lower motor neuron signs, urinary tract infection, and ocular complications.

PREVENTION/AVOIDANCE

- Prevent access to carrion and feed dogs cooked food.
- Avoid contact with spoiled raw meat.

POSSIBLE COMPLICATIONS

- Respiratory failure and death in severe cases
- Aspiration pneumonia from megaesophagus and regurgitations
- Keratoconjunctivitis sicca and corneal ulceration
- Prolonged recumbence—pulmonary atelectasia and infection; decubital sores; urine scalding.

EXPECTED COURSE AND PROGNOSIS

- Maximum severity of signs usually reached within 12–24 hours.
- Neurologic signs disappear in reverse order of appearance.
- Complete recovery usually occurs within 1–3 weeks, and requires the formation of new nerve terminals and functional neuromuscular junctions.



MISCELLANEOUS

SEE ALSO

- Coonhound Paralysis (Acute Polyradiculoneuritis)
- Snake Venom Toxicosis—Coral Snakes
- Myasthenia Gravis
- Tick Bite Paralysis

Suggested Reading

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BRACHIAL PLEXUS AVULSION

B



BASICS

OVERVIEW

- Trauma with traction and/or severe abduction of a forelimb causes avulsion of nerve rootlets from their spinal cord attachment.
- Ventral (motor) nerve roots more susceptible than dorsal (sensory) roots.
- Rule out nerve root avulsions in traumatized animals unable to bear weight on a forelimb, especially before surgical repair of orthopedic injuries.

SIGNALMENT

- Dog and cat • No age, sex, or breed predilection

SIGNS

- Depend on the extent and distribution of rootlet damage.
- Motor signs—weakness (partial damage) to paralysis (ventral root avulsion).
- Sensory signs—decreased to absent pain perception (dorsal root avulsion).
- Muscle atrophy—begins within a week of injury.
- Complete avulsion—spinal nerves C5 to T2; most common.
- Cranial avulsion—spinal nerves C5 to C7: atrophy of supraspinatus and infraspinatus muscles, loss of shoulder movements, elbow flexion (dropped elbow), analgesia of the crano-dorsal scapula and medial forearm.
- Hemiplegia of the diaphragm may be seen by fluoroscopy (phrenic nerve roots C5 to C7). If roots C8 to T2 are preserved, weight bearing remains almost normal.
- Caudal avulsion—spinal nerves C7 to T2: inability to bear weight with knuckling over dorsum of paw. If C5 to C7 are spared, the limb is held in a flexed position and there is analgesia distal to the elbow (except for a small area on the medial aspect of forearm).
- T1 to T2 involvement: causes an ipsilateral partial Horner syndrome (anisocoria only) and lack of ipsilateral cutaneous trunci reflex (present contralaterally).
- Bilateral—rarely encountered, caused by significant fall with sternal landing and splaying of limbs.

CAUSES & RISK FACTORS

- Trauma—road accident; hung by foot; dragged; fall



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Brachial plexus trauma without avulsion—rare; temporary deficit owing to root contusion (neurapraxia).
- Brachial plexus tumor—usually chronic, progressive onset.
- Brachial plexus neuritis or neuropathy—acute onset; no trauma; bilateral deficits.
- Fibrocartilaginous embolic myelopathy—deficits of ipsilateral hind limb, and mild deficits of contralateral fore- and hind limbs

usually present. • Pure radial nerve paralysis caused by fracture of humerus or first rib—no nerve root sign. • Lateralized intervertebral disc protrusion—animal painful.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

IMAGING

CT or MRI—visualize lesion; rarely needed for diagnosis

DIAGNOSTIC PROCEDURES

- History—trauma with sudden onset of typical neurologic deficits.
- Spinal nerve root involvement—map motor and sensory deficits; note signs of Horner syndrome; determine if cutaneous trunci reflex present.
- EMG and NCS—denervation in affected muscles, starting 5–7 days post-injury; may help further define deficits and detect signs of recovery.

PATHOLOGIC FINDINGS

- Ventral and dorsal root avulsions—intradurally at the root-spinal cord junction (most fragile area because it lacks protective perineurium).
- Neuroma formation—on pial surface of the spinal cord.



TREATMENT

APPROPRIATE HEALTH CARE

- No specific treatment.
- Outcome depends on initial damage.
- Amputation of limb—may be necessary for patients showing complications (infections/self-mutilation, likely as a result of paresthesia) and no improvement.
- Carpal fusion (arthrodesis) and transposition of the biceps muscle tendon—consider only with adequate function of the triceps and musculocutaneous muscles.

NURSING CARE

- Protective wrap or boot over paw when patient walks on rough surfaces—increased skin fragility and lack of protective reflexes due to sensory deficits can result in severe excoriations from limb dragging.
- Early and sustained physical therapy—to prevent severe muscle atrophy and tendon contraction during recovery of reversible injuries; passive range of motion; massage therapy.
- Monitor non-complicated cases for 4–6 months before considering amputation.



MEDICATIONS

DRUG(S)

Prednisolone (prednisone)—1-week anti-inflammatory course may decrease early edema and favor healing of reversible injuries.



FOLLOW-UP

PREVENTION/AVOIDANCE

Serial clinical and electrophysiologic monitoring to assess improvement/severity.

PREVENTION/AVOIDANCE

Avoid free-roaming.

POSSIBLE COMPLICATIONS

- Skin excoriation and secondary infection—from trauma to unprotected paw.
- Trophic ulcers—thin, traumatized skin, especially over arthrodesis sites.
- Paresthesia may lead to self-mutilation.

EXPECTED COURSE AND PROGNOSIS

- Preserved pain sensation (dorsal roots intact)—suggests less severe injury to ventral nerve roots.
- Cranial avulsion—better prognosis with preserved sensation to distal limb and ability to bear weight.
- Complete avulsion—poor prognosis for recovery, amputation likely.
- Rarely, mild cases may resolve after 2–3 months.



MISCELLANEOUS

SEE ALSO

Polyneuropathies (Peripheral Neuropathies)

ABBREVIATIONS

- CT = computed tomography
- EMG = electromyography
- MRI = magnetic resonance imaging
- NCS = nerve conduction studies

INTERNET RESOURCES

Braund KG. Neuropathic Disorders (6-Feb-2003): http://www.ivis.org/advances/Vite/braund20b/chapter_frm.asp?LA=1#Traumatic_Neuropathy

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BRACHYCEPHALIC AIRWAY SYNDROME

B



BASICS

DEFINITION

Partial upper airway obstruction in brachycephalic breeds of dogs and cats caused by any of the following: stenotic nares, overlong soft palate, everted laryngeal saccules, and laryngeal collapse. Hypoplastic trachea can also be present and worsen respiratory distress.

PATHOPHYSIOLOGY

- In normal dogs, the upper airway accounts for 50–70% of total airway resistance. Brachycephalic breeds have increased upper airway resistance due to stenosis of nares, aberrant formation of nasal conchae, and presence of nasopharyngeal turbinates. Skull bones are shortened in length but normal in width, and soft tissues are not proportionately reduced, resulting in redundant tissue and narrowed air passages.
- Increased airway resistance leads to more negative intra-airway pressures—may result in secondary eversion of laryngeal saccules, further elongation of palate, and laryngeal collapse.
- Recruitment of pharyngeal dilator muscles (sternohyoid) becomes necessary to maintain airway patency. Sleep apnea may occur secondary to relaxation of these muscles.

SYSTEMS AFFECTED

- Respiratory—respiratory distress, hypoxemia, hypercarbia, hyperthermia, aspiration pneumonia, non-cardiogenic pulmonary edema from airway obstruction.
- Cardiovascular—cardiovascular collapse if complete airway obstruction or severe hyperthermia occurs.
- Gastrointestinal—may be reluctant to eat or drink, increased airway resistance can exacerbate hiatal hernia, gastroesophageal reflux, and esophagitis.

GENETICS

- Brachycephalic head shape—inherited defect in development of skull bones perpetuated by selective breeding.

INCIDENCE/PREVALENCE

- Dogs—common in brachycephalic breeds.
- Cats—less commonly severe enough to require treatment.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Dogs—brachycephalic breeds (English bulldogs most common—up to 55% of breed, French bulldog, pug, Boston terrier). Norwich terriers and Cavalier King Charles spaniels affected by a variant of the syndrome.
- Cats—Persians and Himalayans.

Mean Age and Range

- Young adults, most diagnosed by 2–3 years.
- If diagnosed later than 4 years look for concurrent disease or exacerbating circumstances.
- Laryngeal collapse reported in brachycephalic breed puppies as young as 6–7 months.

Predominant Sex

No sex predilection

SIGNS

Historical Findings

- Snoring, stridor, stertorous breathing
- Tachypnea, frequent panting
- Coughing and gagging
- Difficulty eating and swallowing
- Ptyalism, regurgitation, and vomiting
- Syncope and episodes of collapse

Physical Examination Findings

- Stridor and stertorous breathing.
- Stenotic nares—medial collapse of lateral nasal cartilage.
- Increased respiratory effort—retraction of the commissures of lips, open-mouth breathing or constant panting, increased respiratory rate, abduction of forelimbs, increased abdominal component of respiration, recruitment of secondary muscles of respiration.
- In severe distress, may see paradoxical abdominal movement, inward collapse of intercostal muscles during inspiration, orthopnea, and cyanosis.
- Hyperthermia may be present.

CAUSES

- Inherited or congenital defects in conformation.
- Elongated soft palate—> 90% of surgical cases in dogs.
- Stenotic nares—about 50% of dogs. Most common defect in cats.
- Aberrant formation of rostral and caudal nasal conchae.
- Presence of nasopharyngeal turbinates (20% of dogs).
- Laryngeal disease—everted laryngeal saccules (> 50% of dogs) and/or laryngeal collapse (~10% of dogs).

RISK FACTORS

- Breed.
- Obesity—worsens airway obstruction, associated with poorer outcome postoperatively, and may contribute to gastroesophageal reflux resulting in aspiration pneumonia.
- Excitement and/or warm, humid weather—increased panting can lead to airway edema, further compromise of the lumen, and hyperthermia.
- Exercise—dogs are often exercise-intolerant due to airway compromise and hypoxia.
- Sedation—relaxation of muscles of pharynx and palate can cause complete airway obstruction.
- Respiratory infection or concurrent pulmonary disease—will cause further respiratory compromise.
- Endocrine disease (hypothyroidism and hyperadrenocorticism)—could worsen weight gain and cause excessive panting.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Foreign bodies of nasopharynx, larynx, or trachea.
- Infection—upper respiratory infection, nasopharyngeal abscess.
- Neoplasia obstructing the nasopharynx, glottis, larynx, or trachea.
- Laryngeal paralysis.
- Pharyngeal mucocoele.
- Nasopharyngeal polyp or cyst.

CBC/BIOCHEMISTRY/URINALYSIS

CBC—usually normal, but polycythemia can occur with chronic hypoxia, and leukocytosis if concurrent infection or severe stress.

OTHER LABORATORY TESTS

- Arterial blood gas—to diagnose respiratory acidosis and hypoxemia, and response to oxygen supplementation.
- Pulse oximetry—to diagnose hypoxemia.

IMAGING

Radiographic Findings

- If stable, cervical and thoracic radiographs recommended.
- Cervical radiographs may show thickened, elongated soft palate and suggest tracheal hypoplasia.
- Thoracic radiographs can reveal aspiration pneumonia, pulmonary edema, air in esophagus, and hypoplastic trachea (TD/TI = tracheal diameter at the level of thoracic inlet/thoracic inlet distance, which is the distance from the sternum to the ventral surface of TI. A ratio < 0.13 in bulldogs and < 0.16 in other brachycephalic breeds suggests hypoplastic trachea).

Fluoroscopy

Gives information about degree of dynamic pharyngeal obstruction by palate and concurrent disease such as collapsing trachea (uncommon in brachycephalic dogs).

DIAGNOSTIC PROCEDURES

Laryngoscopy/Pharyngoscopy

- Performed under general anesthesia, and because of risk of airway obstruction, owner should be prepared to proceed with surgical intervention if deemed necessary.
- An overlong soft palate extends more than just a few millimeters beyond tip of epiglottis and hangs down into glottis.
- The soft palate is often thickened and inflamed and there may be inflammation and edema of the arytenoid cartilages.
- Everted laryngeal saccules are diagnosed by visualizing two smooth, round, glistening masses in ventral half of laryngeal opening—they often obscure visualization of vocal folds.
- Laryngeal collapse can also be seen.
- Flexible endoscopy with retroflexed view of nasopharynx can detect nasopharyngeal turbinates.

Tracheoscopy

- Can reveal hypoplastic trachea with overlap of dorsal tracheal rings and dorsal tracheal membrane.
- Collapsing trachea can also be diagnosed.

BRACHYCEPHALIC AIRWAY SYNDROME

(CONTINUED)

B

TREATMENT

APPROPRIATE HEALTH CARE

- Surgery recommended for patients with significant clinical signs or to prevent progressive respiratory dysfunction.
- Emergency presentation in severe respiratory distress requires rapid intervention including O₂ supplementation, cautious use of antianxiety medication. • If hyperthermic, cool via convective losses by wetting patient with cool water and placing fan to blow over them. Administer IV fluids, up to a shock rate if extremely hyperthermic (T° > 106°F [41°C]). • If complete airway obstruction, immediate orotracheal intubation and/or temporary tracheostomy is indicated.
- Dexamethasone can be administered (0.1 mg/kg IV) to reduce inflammation.

NURSING CARE

- Patients require 24-hour monitoring because of risk of acute airway obstruction and death.
- Monitor respiratory rate, effort, heart rate, pulse quality, mucous membrane color, capillary refill time, temperature, and other physical parameters before and after surgery.
- Pulse oximetry and arterial blood gases, depending on severity of condition.
- Administer IV fluids at maintenance rate and minimize handling and stress.
- O₂ therapy and cooling as necessary.

ACTIVITY

Usually self-limited

DIET

- If overweight, weight loss is recommended.
- For obese, stable patients, weight loss is recommended prior to surgery.

CLIENT EDUCATION

- Avoidance of risk factors is critical.
- Inform owners that dogs with brachycephalic airway syndrome are at increased anesthetic risk, especially if obese, or have cardiac disease or aspiration pneumonia.
- Inform owners that surgery often improves but does not normalize airway.

SURGICAL CONSIDERATIONS

- Evaluation for elongated soft palate performed under general anesthesia when patient is stable.
- Temporary tracheostomy can be placed to facilitate exposure or to treat airway obstruction.
- Stenotic nares are corrected by resection of a wedge of the dorsolateral nasal cartilage and planum. Hemorrhage is controlled with pressure followed by closure of the surgical wound with 3 or 4 sutures of 3–0 or 4–0 absorbable suture material.
- Elongated soft palate is resected using scissors, carbon dioxide laser, or a bipolar sealing device. Remove only enough to allow contact of the center of the soft palate with the tip of the epiglottis.
- Sacculectomy performed by grasping tissue with Allis tissue

forceps and trimming all mucosal tissue with curved scissors.

- Severe laryngeal collapse might require cricoarytenoid and thyroarytenoid caudolateralization or permanent tracheostomy.



MEDICATIONS

DRUG(S)

- Dexamethasone given for 12–24h pre-or postoperatively at 0.1 mg/kg IV q12h to reduce edema and inflammation.
- Broad-spectrum antibiotics indicated if aspiration pneumonia present until culture and sensitivity results are obtained.
- Omeprazole 0.7 mg/kg q24h, cisapride 0.2 mg/kg q8h, and magnesium hydroxide 1 mL/kg after meals or sucrlafate 0.5–1 g q12h for dogs with concurrent esophagitis, gastritis, and/or duodenitis.

CONTRAINDICATIONS

Overuse of steroids can lead to panting, weight gain, and gastrointestinal ulceration, which can all exacerbate signs of brachycephalic airway syndrome.

PRECAUTIONS

Sedation for relief of anxiety, excitement, or fear should be used with caution because of risk of upper airway obstruction with muscle relaxation.



FOLLOW-UP

PATIENT MONITORING

Postoperatively, 24-hour monitoring to observe for airway swelling and obstruction that may require temporary tracheostomy.

PREVENTION/AVOIDANCE

- Selection by breeders for dogs without severe conformational changes—difficult because breed standards encourage these.
- Avoid risk factors, particularly weight gain.

POSSIBLE COMPLICATIONS

- Hyperthermia and heat stroke.
- Aspiration pneumonia.
- Death in about 10% of patients from airway disease.
- The most common postoperative complication is airway swelling and obstruction within the first 24 hours, may necessitate temporary tracheostomy.
- Continued respiratory difficulty after corrective surgery.
- Excessive resection of palate resulting in nasal aspiration of food contents due to inability to close pharynx during swallowing.

EXPECTED COURSE AND PROGNOSIS

- Prognosis is good for improvement in breathing (80% have good to excellent results) but airway is still far from normal.
- Prognosis better for dogs other than English bulldogs and for dogs that have correction of

both stenotic nares and elongated soft palate.

- Without surgery, prognosis is poor due to continued progression of acquired components of brachycephalic airway syndrome.
- Life-long avoidance of risk factors recommended.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Aspiration pneumonia
- Heat stroke
- Hiatal hernia
- Hypoplastic trachea

AGE-RELATED FACTORS

Older dogs may have a worse outcome postoperatively but most have some improvement.

PREGNANCY/FERTILITY/BREEDING

Enlarged abdomen and pressure on the diaphragm in the pregnant bitch can further compromise respiratory function by decreasing tidal volume.

INTERNET RESOURCES

<http://www.acvs.org/AnimalOwners/HealthConditions/SmallAnimalTopics/BrachycephalicSyndrome/>

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Client Education Handout
available online



BASICS

DEFINITION

- Traumatic—caused by external forces.
- Non-traumatic—caused by non-violent forces (e.g., hypoxia, metabolic disorders, vascular disruption, infection, toxicity, neoplasia).
- Primary—direct initial insult when tissue and vessels are stretched, compressed or torn.
- Secondary—alterations of brain vasculature and tissue following primary injury.

PATHOPHYSIOLOGY

- Acceleration, deceleration, and rotational forces traumatize brain tissue.
- High oxygen and glucose requirements put the brain at risk for hypoxia.
- Oxygen delivery dependent on CBF and CPP (= MAP – ICP).
- Intracranial bleeding, edema (vasogenic and cytotoxic), vasodilation, and/or vasospasms increase ICP, causing low CBF, ischemia, brain swelling, and herniation; slow, progressive increase in ICP better tolerated than small, acute rise.
- Hypotension, hypoxia—major contributors to secondary injury.

SYSTEMS AFFECTED

- Nervous—altered mentation, cranial nerve deficits, seizures, twitching, postural changes.
- Cardiovascular—arrhythmias.
- Endocrine/Metabolic—alterations in ADH release and sodium concentration; central temperature dysregulation; insulin resistance; depletion of cortisol.
- Ophthalmic—changes in eye position, eye movements, pupillary light reflexes, papilledema.
- Respiratory—hyper- and hypocapnea; abnormal breathing patterns; neurogenic pulmonary edema.

GENETICS

None

INCIDENCE/PREVALENCE

- Head and neck injuries found in up to 34% of dogs and cats suffering blunt force trauma.
- Parenchymal and extradural hematomas found in 10% of dogs and cats with signs of mild head injury and in up to 80% with severe head injury.

GEOGRAPHIC DISTRIBUTION

Widespread

SIGNALMENT

Species

Dog and cat

SIGNS

Historical Findings

- Determine cause—trauma; cardiac arrest; heart failure; hypertension; toxins; coagulopathies; severe respiratory compromise; prolonged seizures; hypoglycemia.
- Decline in neurologic condition—implies progression from intracranial bleeding, cerebral edema,

ischemia.

- Seizure activity—cerebral or diencephalon involvement.

Physical Examination Findings

- Evidence of head trauma—open wounds, epistaxis, blood in the ear canals.
- Cardiac or respiratory insufficiency—hypoxia, cyanosis, hypoventilation.
- Poor perfusion—weak pulse, pale mucous membranes.
- Skull palpation—fractures, open fontanelles.
- Sustained bradycardia—midbrain, pontine, or medullary lesion.
- Cushing's reflex—bradycardia and hypertension.
- Ecchymosis, petechiae, retinal hemorrhages or distended vessels—hypertension, coagulopathy.
- Papilledema—cerebral edema.
- Retinal detachment—infectious, neoplastic, or hypertensive causes.

Neurologic Examination Findings

Mental Status

- Level of consciousness and cranial nerve deficits—localize lesion to cerebral cortex (better prognosis), midbrain/brainstem, or multifocal.
- Postural changes—decerebrate rigidity with midbrain lesion; decerebellate rigidity with cerebellar lesion.
- Peracute focal deficits suggest vascular or neoplastic causes.

Pupillary Light Reflexes

- Miotic responsive pupils—cerebral or diencephalic lesion (rule out traumatic uveitis, Horner's syndrome).
- Pinpointed unresponsive pupils—diencephalic, pontine or medullary lesion.
- Dilated unresponsive pupil(s) or midpoint fixed unresponsive pupils—midbrain lesion.

Cranial Nerves

- Normal with altered mentation—cerebrum-diencephalon lesion.
- CN II—Loss of menace and dazzle response with dilated unresponsive pupils—cranial forebrain.
- Loss of physiologic nystagmus—brainstem lesion
- CN III—midbrain lesion.
- CN V–XII—pontine or medullary lesion.

Respiratory Patterns

- Cheyne-Stokes—severe diffuse cerebral or diencephalon lesion.
- Hyperventilation—midbrain lesion.
- Ataxic or apneustic—pontine or medullary lesion.

CAUSES

- Trauma
- Prolonged hypoxia or ischemia
- Prolonged shock
- Severe hypoglycemia
- Prolonged seizures
- Severe hyperthermia or hypothermia
- Alterations in serum osmolality
- Toxins
- Neoplasia
- Hypertension
- Hemorrhage
- Inflammatory, infectious, immune-mediated diseases
- Thiamin deficiency
- Hydrocephalus
- Parasitic migration

RISK FACTORS

- Free-roaming—trauma, toxins
- Coexisting cardiac, respiratory, hemostatic, hepatic disease
- Diabetes mellitus—insulin therapy



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Systemic causes of altered states of consciousness or central vestibular signs—metabolic disease; toxins; drugs; infection.

CBC/BIOCHEMISTRY/URINALYSIS

- Reflect systemic effects of neurologic signs
- Alterations in serum sodium suggest central ADH abnormalities

OTHER LABORATORY TESTS

- Arterial blood gas
- Coagulation profile
- Infectious disease titers

IMAGING

- Skull radiographs—detect fractures.
- CT—detects acute hemorrhage, infarcts, fractures, penetrating foreign bodies, hydrocephalus, herniation.
- MRI—detects cerebral edema, hemorrhage, mass, hydrocephalus, infiltrative diseases, inflammation, herniation, fractures.
- Ultrasound optic disk—if > 3 mm diameter, may be associated with brain edema.

DIAGNOSTIC PROCEDURES

- ECG—detects arrhythmias
- BP—determine perfusion
- CSF analysis—if cause unknown and no contraindications

PATHOLOGIC FINDINGS

- Brain edema or inflammation
- Herniation
- Hemorrhage
- Hydrocephalus
- Infarct
- Laceration, contusion
- Hematomas
- Skull fracture
- Necrosis
- Apoptosis



TREATMENT

APPROPRIATE HEALTH CARE

- Goals of therapy—maximize oxygenation and ventilation; support BP and CPP; decrease ICP; decrease cerebral metabolic rate.
- Maintain systolic BP > 90 mmHg and PCO₂ at 35–40 mm Hg; with suspected elevated ICP, hyperventilation to 32–35 mmHg.
- Maintain PaO₂ > 60 mmHg, SaO₂ > 90%, SpO₂ > 94%.
- Avoid cough or sneeze reflex during intubation or nasal oxygen supplementation; lidocaine (dogs: 1–2 mg/kg IV) before.
- Do not compress jugular veins.
- Orotracheal intubation if gag reflex lost.

NURSING CARE

- Aggressive therapy for midbrain/brainstem lesion or declining neurologic signs.
- Overzealous fluid resuscitation can contribute to brain edema.
- Small-volume fluid resuscitation techniques to maintain systolic BP > 90 mmHg with normal heart rate.
- Combination of isotonic crystalloids (10–20 mL/kg increments) with hydroxyethyl starch (5 mL/kg increments) over 5–8 minutes.
- Avoid hypertension.
- Level

BRAIN INJURY

B

head with body or elevate head and neck to a 20° angle. • Keep airway unobstructed; use suction and humidify if intubated; hyperoxygenate and consider IV lidocaine prior to suctioning. • Lubricate eye. • Reposition every 2–4 hours to avoid hypostatic pulmonary congestion. • Prevent fecal/urine soiling. • Maintain normal core body temperature. • Maintain hydration with a balanced electrolyte crystalloid solution. • Rehabilitation exercises.

ACTIVITY

- Restricted. • Consult rehabilitation specialist for appropriate exercises to maintain muscle tone.

DIET

Initiate trickle flow feeding to meet elevated metabolic demands.

CLIENT EDUCATION

- Neurologic signs may worsen before improving. • Neurologic recovery may not be evident for several days; possibly > 6 months for residual neurologic deficits. • Serious systemic abnormalities contribute to CNS instability.

SURGICAL CONSIDERATIONS

Depressed skull fracture, penetrating foreign body, uncontrollable ICP elevation (insufficient CSF drainage, hematoma/mass evacuation, herniation).



MEDICATIONS

DRUG(S) OF CHOICE

Elevated ICP

- Ensure systolic BP > 90 mmHg. Lower ICP by hyperventilation, drug therapy, drainage of CSF from the ventricles, or surgical decompression. • 7% hypertonic saline—2–4 mL/kg IV; can reduce fluid volume needed to reach resuscitation endpoints; combine with colloid. • Furosemide—0.75 mg/kg IV; may decrease CSF production; used in patients with congestive heart failure, volume overload, hyperosmolar diseases, or anuric renal failure; use before mannitol. • Mannitol—0.1–0.5 g/kg IV bolus repeated at 2-hour intervals 3–4 times in dogs, and 2–3 three times in cats; repeated doses must be given on time; improves brain blood flow and lowers ICP; may exacerbate hemorrhage. • Glucocorticosteroids—no benefit in acute management and long-term outcome in humans; higher morbidity. Anti-inflammatory doses (prednisone 1 mg/kg/day) may be of benefit with brain edema related to intracranial neoplasia and infectious meningitis. Immunosuppressive doses (2 mg/kg/day) in combination with additional immunosuppressive drugs in immune-mediated meningitis. • Provide analgesia/sedatives (e.g., fentanyl 3–5 µg/kg IV then 3–5 µg/kg/h CRI ± lidocaine 3–5 mg/kg/h) as indicated. Avoid agents that

can reduce CPP. • Thrashing, seizures, or uncontrolled motor activity—diazepam CRI (0.5–1 mg/kg/h), midazolam CRI (0.2–0.4 mg/kg IV), or propofol (3–6 mg/kg IV titrated to effect; 0.1–0.6 mg/kg/min CRI) monitor for hypotension; intubate if unable to protect airway. • Levetiracetam 20 mg/kg IV/IM/rectal q8h if seizure activity.

Other

- Reducing cerebral metabolic rate with heavy sedation using dexmedetomidine or medically induced coma using pentobarbital (up to 10 mg/kg IV over 30 minutes then 1 mg/kg/h) or propofol (2–4 mg/kg IV then 0.1–0.4 mg/kg/min); must intubate and support blood pressure, oxygenation, and ventilation. • Cooling the patient to 32–33 °C (89–91°F) for 48h may provide cerebral protection when administered within 6 hours of global ischemia or severe brain injury. • Glucose regulation. • Careful nasogastric tube feeding for early trickle flow feeding; cisapride (0.5 mg/kg PO q8–12h) and metoclopramide (1–2mg/kg/day) may promote GI motility. • Desmopressin for refractory hypernatremia. Emergency dosage not established for animals (dogs: 4 µg topical conjunctival q12h; cat: 5 µg SC q12h).

CONTRAINDICATIONS

- Drugs that cause hypertension, hypotension
- Drugs that cause hyperexcitability or increase in metabolic rate

PRECAUTIONS

- Avoid hypotension, hypoxemia, hypertension, hyperglycemia, hypoglycemia, hypernatremia, hypovolemia, hypervolemia.
- Keep head and neck above plane of body.
- Do not compress jugular veins.
- Furosemide, mannitol and hypertonic saline—can cause hypovolemia and hypotension. • Maintain PCO₂ > 32 mmHg; avoid hyperventilation in the first 24–8h and do not perform therapeutic hyperventilation (32–35 mmHg) for extended periods (> 48h).



FOLLOW-UP

PATIENT MONITORING

- Repeated neurologic examinations—deterioration warrants aggressive therapeutic intervention. • BP; maintain systolic BP > 90 mmHg. • Blood gases, pulse oximetry, end-tidal CO₂—to assess need for oxygen supplementation or ventilation. • Blood glucose—avoid severe persistent hyperglycemia and hypoglycemia.
- ECG—arrhythmias may affect perfusion, oxygenation, and CBF. • ICP—to detect elevations and monitor response to therapy.

PREVENTION/AVOIDANCE

Keep pets in a confined area or leashed.

POSSIBLE COMPLICATIONS

- Seizures • Brain herniation • Intracranial hemorrhage • Progression from cerebral

cortical to midbrain signs • Malnutrition

- Aspiration pneumonia • Hypostatic pulmonary congestion • Corneal desiccation
- Urine scalding • Airway obstruction from mucus • Arrhythmias • Hypotension
- Hypernatremia • Hypokalemia
- Respiratory failure • Residual neurologic deficits • Death

EXPECTED COURSE AND PROGNOSIS

- Young animals, minimal primary brain injury, and secondary injury consisting of cerebral edema—best prognosis. • No deterioration of neurologic status for 48 hours—better prognosis. • Rapid resuscitation of systolic BP to > 90 mmHg and avoiding hypoxemia—better neurologic outcome. • Glasgow Coma Score may offer prognostic insight.



MISCELLANEOUS

SYNOMYMS

- Head trauma • Traumatic brain injury

SEE ALSO

Stupor and Coma

ABBREVIATIONS

- ADH = antidiuretic hormone • BP = blood pressure • CBF = cerebral blood flow • CN = cranial nerve • CNS = central nervous system
- CPP = cerebral perfusion pressure • CSF = cerebrospinal fluid • CT = computed tomography • ECG = electrocardiogram
- GI = gastrointestinal • ICP = intracranial pressure • MAP = mean arterial pressure
- MRI = magnetic resonance imaging

INTERNET RESOURCES

www.traumaticbraininjury.com

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Authors Rebecca Kirby and Elke Rudloff

Consulting Editor Joane M. Parent



Client Education Handout
available online



BASICS

DEFINITION

- Brain tumors of cats and dogs may be classified as either primary or secondary, depending on the cell type of origin.
- Primary brain tumors originate from cells normally found within the brain and meninges, including the neuroepithelium, lymphoid tissues, germ cells, endothelial cells, and malformed tissues.
- Secondary tumors are either neoplasms that have reached the brain by hematogenous metastasis from a primary tumor outside the nervous system, or neoplasms that affect the brain by local invasion, or extension, from adjacent non-neural tissues such as bone.
- Pituitary gland neoplasms (adenomas or carcinomas) and tumors arising from cranial nerves (e.g., nerve sheath tumor of the trigeminal, oculomotor, or vestibulocochlear nerves) are considered secondary brain tumors.

PATHOPHYSIOLOGY

- Brain tumors result in cerebral dysfunction by causing both primary effects, such as infiltration of nervous tissue or compression of adjacent anatomic structures, and secondary effects, such as hydrocephalus.
- Additional primary effects include disruption of cerebral circulation, or local necrosis, which may result in further damage to neural tissue.
- The most important secondary effects of a primary brain tumor include disturbance of cerebrospinal fluid (CSF) flow dynamics, elevated intracranial pressure (ICP), cerebral edema, or brain herniation.
- Secondary effects usually are more diffuse or generalized in their clinical manifestations and may mask the precise location of a focal intracranial lesion.

SYSTEMS AFFECTED

Nervous (brain)

GENETICS

- An unusually high incidence of meningiomas has been reported in cats with mucopolysaccharidosis type I.
- Specific genetic factors associated with breed predisposition have not been identified.
- Brachycephaly provisionally has been associated with the *SMOC-2* and *thrombospondin-2* genes on canine chromosome 1, and a component of glioma susceptibility provisionally has been mapped to a region on canine chromosome 2.
- Molecular and genetic classification of brain tumors may permit targeted therapies in the future.

INCIDENCE/PREVALENCE

- Brain tumors appear to be more common in dogs than in other domestic species.
- Reported incidence in dogs 14.5/100000.

- The most common sites for neoplasia to occur in immature dogs (< 6 months), in decreasing order, are the hematopoietic system, brain, and skin.
- Reported incidence in cats 3.5/100000.

SIGNALMENT

Breed Predilections

- Meningiomas occur most frequently in dolichocephalic breeds of dog.
- Glial cell tumors and pituitary tumors occur commonly in brachycephalic breeds of dog.
- Canine breeds overrepresented include the boxer, golden retriever, Doberman pinscher, Scottish terrier, and Old English sheepdog.
- There does not appear to be a breed predisposition for the development of brain tumors in cats.

Mean Age and Range

- Brain tumors occur in dogs and cats of any age.
- Most frequent in older dogs, with the greatest incidence in dogs > 5 years of age.
- Median age for diagnosis of meningiomas, gliomas, and choroid plexus tumors in dogs has been reported as 10–11 years, 8 years, and 5–6 years, respectively.

Predominant Sex

Older male cats appear to be most susceptible to meningiomas.

SIGNS

- Vary with tumor location.
- The most frequently recognized clinical sign associated with a brain tumor of a dog or cat is seizures, particularly should the first seizure occur after 5 years of age.
- Other clinical signs frequently associated with a brain tumor are abnormal behavior and mentation, visual deficits, circling, ataxia, head tilt, and cervical spinal hyperesthesia.
- Signs that result from a disease in a given location in the nervous system are similar, regardless of the precise cause.
- On the basis of signalment, history, and results of complete physical and neurologic examinations, it is possible to localize a problem to the brain and, in some cases, to determine the approximate location.

CAUSES

- Uncertain.
- Dietary, environmental, genetic, chemical, viral, traumatic, and immunologic factors may be considered.

RISK FACTORS

Uncertain



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Categories of disease that may result in clinical signs similar to those of a brain tumor include congenital disorders, infections, immunologic and metabolic disorders, toxicities, nutritional disorders, trauma, vascular disorders, degeneration, and idiopathic disorders.

CBC/BIOCHEMISTRY/URINALYSIS

The major objective in the completion of these tests is to eliminate extracranial causes for signs of cerebral dysfunction.

OTHER LABORATORY TESTS

N/A

IMAGING

- Survey radiographs of the thorax and abdominal ultrasound—to rule out a primary malignancy elsewhere in the body.
- Skull radiographs—of limited value; may detect neoplasms of the skull or nasal cavity that involve the brain by local extension.
- Occasionally, lysis or hyperostosis of the skull may accompany a primary brain tumor (e.g., meningioma of cats), or there may be radiographically visible mineralization within a neoplasm.
- CT—provides accurate determination of the presence, location, size, and anatomic relationships of many intracranial neoplasms.
- MRI—considered superior to CT in the localization and characterization of most brain tumors.

DIAGNOSTIC PROCEDURES

CSF Analysis

- CSF—may help to rule out inflammatory causes of cerebral dysfunction; in some cases may support a diagnosis of a brain tumor.
- Care should be used in the collection of CSF, because an increased ICP may be present in association with a brain tumor, and pressure alterations associated with CSF collection may lead to brain herniation.
- CSF collection usually is delayed until advanced imaging has been completed to evaluate factors such as the presence of cerebral edema or hemorrhage.
- In general, increased CSF protein content and a normal to increased CSF white blood cell count have been considered “typical” of a brain neoplasm.

Biopsy

- Cytologic evaluation of smear preparations from biopsy tissue, rapidly fixed in 95% alcohol and stained with hematoxylin and eosin, may be done within minutes of biopsy collection.
- Tissue biopsy remains the sole method available for the definitive diagnosis of brain tumor type in cats or dogs, and is an essential consideration prior to any type of therapy.
- Biopsy is not always attempted because of practical considerations, such as cost and morbidity.
- CT-guided stereotactic biopsy systems provide a relatively rapid and extremely accurate means of tumor biopsy, with a low rate of complications.

PATHOLOGIC FINDINGS

- The classification of CNS tumors in dogs and cats primarily is based on the characteristics of their constituent cell type, pathologic behavior, topographic pattern, and secondary changes present within and surrounding the tumor.
- Meningioma is the most common intracranial neoplasm of dogs.

BRAIN TUMORS

(CONTINUED)

B

and cats. • Classification of the glial subset of neuroepithelial tumors is based on the predominant cell type (e.g., astrocyte or oligodendrocyte).

Dogs

- Embryonal tumors have been consolidated under the single term “primitive neuroectodermal tumors” (or PNETs) to accommodate their anaplastic nature.
- Brain tumors arising from lymphoreticular cells traditionally have been grouped under a heading of reticulosarcoma or histiocytic lymphoma.
- Skull tumors that affect the brain by local extension include osteosarcoma, chondrosarcoma, and multilobular osteochondrosarcoma.
- The most frequently seen secondary tumors of dogs include local extension of nasal adenocarcinoma; metastases from mammary, prostatic, or pulmonary adenocarcinoma; metastases from hemangiosarcoma; and extension of pituitary adenoma or carcinoma.
- Nerve sheath tumors arising from cranial nerves (particularly oculomotor nerve and trigeminal nerve) may occur in dogs.

Cats

- Meningiomas involving multiple intracranial sites (including the third ventricle) are relatively common in cats.
- Primary brain tumors other than meningiomas occur infrequently in cats.
- Tumors that have been reported include astrocytoma, ependymoma, oligodendroglioma, choroid plexus papilloma, medulloblastoma, lymphoma, olfactory neuroblastoma, and gangliocytoma.
- Lymphoma of the brain may be primary or secondary, or may be an aspect of multicentric lymphoma of cats.
- Secondary tumors that have been reported to occur in the brain of cats include pituitary macroadenomas and macrocarcinomas, and metastatic carcinoma.
- Local extension may occur either from tumors of the middle ear cavity (e.g., squamous cell carcinoma), the nasal cavity (e.g., nasal adenocarcinoma), or the skull (e.g., osteosarcoma).



TREATMENT

APPROPRIATE HEALTH CARE

- Beyond general efforts to maintain homeostasis, the major goals of therapy for a brain tumor are to control secondary effects, such as increased ICP or cerebral edema, and to eradicate the tumor or reduce its size.
- Beyond palliative care, three methods of therapy for a brain tumor currently are available for use in dogs and cats: surgery, irradiation, and chemotherapy.

Surgery

- Neurosurgical intervention is an essential consideration in the management of brain tumors in cats or dogs, whether for complete excision, partial removal, or biopsy.
- Meningiomas, particularly those located over the cerebral convexitities or in the frontal lobes of the cerebrum, may be completely (or almost completely) removed by surgery, especially in cats.
- Primary calvarial tumors also may be removed surgically prior to other types of therapy.

Radiation Therapy

- Irradiation may be used either alone or in combination with other treatments for either primary or secondary brain tumors.
- Careful treatment planning by a qualified and experienced radiation therapist is essential to the success of radiation therapy.
- A major development in radiation therapy is the emergence of more precise protocols that spare tissues surrounding the brain tumor (e.g., stereotactic radiotherapy).

Chemotherapy

Alkylating agents (e.g., carmustine (BCNU), lomustine (CCNU) and temozolamide), antimetabolic agents (e.g., cytosine arabinoside), and ribonucleotide reductase inhibitors (e.g., hydroxyurea) may result in reduction of tumor size and in improvement of clinical signs in dogs with glial cell tumors; however, evidence of efficacy in animals is lacking.



MEDICATIONS

DRUG(S)

- Glucocorticoids may be used for edema reduction and, in some cases (e.g., lymphoma), for retardation of tumor growth.
- Some animals with a brain tumor demonstrate dramatic improvement in clinical signs for weeks or months with sustained glucocorticoid therapy.
- Antiepileptic drugs (e.g., phenobarbital, bromide, levetiracetam) may be utilized for the control of generalized seizures.
- Mannitol or hypertonic saline are the agents best suited for effective reduction of increased ICP.



FOLLOW-UP

PATIENT MONITORING

- Serial neurologic examinations • Serial CT or MRI examinations

POSSIBLE COMPLICATIONS

- Aspiration pneumonia due to depressed swallowing reflexes associated with increased ICP • Seizures

EXPECTED COURSE AND PROGNOSIS

- Little information is available concerning the survival times of dogs or cats with a brain tumor that have received only palliative therapy (i.e., therapy to control the secondary effects of a tumor without an attempt to eradicate the tumor).
- The results of one study indicate a mean and median survival of 81 days and 56 days, respectively, following CT diagnosis of a primary brain tumor in each of 8 dogs.
- The results from several studies confirm that the prognosis for a dog or cat with a primary brain tumor may be significantly improved by surgical removal and irradiation, either alone or in combination.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Dogs that have been treated for a brain tumor may develop a second type of tumor elsewhere in the body.

ABBREVIATIONS

- CSF = cerebrospinal fluid • CT = computed tomography • ICP = intracranial pressure • MRI = magnetic resonance imaging

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Client Education Handout
available online



BASICS

DEFINITION

Timing of insemination(s) to maximize pregnancy risk and litter size.

PATHOPHYSIOLOGY

Dogs

- Must determine ovulation day so that breeding(s) occur(s) at the proper time.
- Fresh, chilled, or frozen semen—usually limited to one or two inseminations; insemination must be timed relative to ovulation for maximum fertility.
- Ovulation may vary relative to onset of standing heat (estrus), vaginal cytology.
- Luteinizing hormone—controls ovulation; peaks on same day or after full cornification is observed; ovulation occurs approximately 2 days after the peak; 2–3 days (54–72 hours) more required for oocyte maturation; mature oocytes viable for a minimum 2–3 days; thus fertile period is 4–8 days after the LH peak, and maximum fertility is 5–6 days after the LH peak.
- Physical signs alone—unreliable for precise determination of fertile period.
- Onset of estrus—usually associated with a change in the vaginal discharge from sanguineous to barely red and decreased vulvar edema; sanguineous discharge may continue during estrus and cease only at the onset of diestrus (fertile period has passed; bitch no longer receptive; cervix closed).
- Receptivity—may be detected by touching the perineum near the vulva; if receptive, female will “flag” by elevating the tail to one side.
- Vaginal cytologic examination—better but imprecise indicator of fertile period; cornification of the vaginal epithelium controlled by estrogen; full cornification with a clear background usually coincides with sexual receptivity.
- Serum progesterone—increase closely associated with the LH peak; useful for estimating ovulation, and thus the fertile period; concentration < 1 ng/mL (3.18 nmol/L) before the LH peak, 1.5–4 ng/mL (4.8–12.7 nmol/L) at LH peak, 4–10 ng/mL (12.7–31.8 nmol/L) at ovulation; continues to rise during diestrus/pregnancy. Commercial laboratories use various methods of progesterone concentration measurement so values indicative of LH and ovulation vary among labs. Documenting a rapid rise in progesterone subsequent to the initial rise is a more reliable indicator of ovulation than is the single measurement of the LH peak or the initial rise in progesterone.

Cats

- Ovulation—usually induced; timing of breeding is not as critical as with dogs; depends on adequate GnRH and then LH release triggered by vaginal stimulation.

- Adequate stimulation—characterized by a copulatory cry and a post-coital reaction; frequency of coital stimuli important in determining adequacy of coital contact.
- LH—peak concentration and duration of the elevation determine ovulation; higher concentration with multiple copulations; response to copulation depends on the day of estrus (greater release on estrus day 3 than on estrus day 1); release partially depends on duration of exposure to estrogen.

SYSTEMS AFFECTED

Reproductive

GENETICS

N/A

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Dog and cat

SIGNS

General Comments

Dogs

- Average bitch—sanguineous vulvar discharge becomes lighter in amount and color during estrus; vulvar edema of proestrus decreases during estrus; receptive to male during estrus.
- If limited number of breedings—must know ovulation day.

Cats

- LH response to a single mating—may vary substantially.

Historical Findings

Dogs

- Refusal to accept male at the expected time.
- Sanguineous vulvar discharge during estrus.

Cats

- Return to estrus in < 30 days may indicate failure to ovulate; interestrus usually 8–10 days, but highly variable even within queen; also some queens will breed while pregnant.

Physical Examination Findings

Dogs

- Interest shown by male
- Vulva less turgid
- Vaginal discharge—less color and amount
- Flagging
- Fully cornified and crenulated pale vaginal epithelium

Cats

- Fully cornified vaginal epithelium
- Interest shown by male
- No changes in external genitalia
- Vocalizes, rubs objects,
- Lordosis

CAUSES

Dogs

- Limited number of breedings
- Female unreceptive to male
- Artificial insemination (fresh, chilled, or frozen semen)

Cats

- Coitus—too early or too late in estrus; too few times
- Artificial insemination

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Vaginal discharge—proestrus or estrus; vaginitis; neoplasia, pyometra, urinary tract infection.
- Refusal to allow intromission—anatomic issue of abnormalities of Müllerian duct development, vulvovestibular or vestibulovaginal junction, acquired abnormality from dystocia or breeding trauma, vaginal hyperplasia, behavioral problem.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

Dogs

- In-house semiquantitative progesterone ELISA—as adjunct to vaginal cytologic examination
- Quantitative progesterone testing preferred when breeding with frozen semen; especially useful in bitch or male with reduced fertility.
- LH testing—must sample daily to observe the LH peak, can use serum progesterone to signal when to start testing or as a surrogate for the LH peak.

Cats

Progesterone testing to verify ovulation.

IMAGING

Ultrasonographic imaging of the ovaries—may help determine ovulation; perform daily, best if using color flow Doppler.

DIAGNOSTIC PROCEDURES

Dogs

- Behavior—flagging, male very interested, females mounting one another.
- Vaginal discharge much less hemorrhagic, vulva softer, less swollen.
- Palpation of vagina *per digitum* may be resented by bitch in proestrus improving throughout proestrus until estrus.
- May feel edematous mass on floor of caudal vagina, just cranial to urethral os that should shrink as optimal breeding period approaches.
- Vaginal cytologic examination—proestrus (in breeder terms, “day 1” at first sign of hemorrhagic vaginal discharge), most epithelial cells are non-cornified; percentage of cornified cells (cells with angular cytoplasm and pyknotic nuclei or nuclei that fail to take up stain) increases during proestrus, often reaching 90% or more by estrus (individuals vary). (Breeders refer to this stage by day, rather than using the term “estrus”; this is usually about day 10–18 in breeder terms.)
- Background of slide is free of debris during estrus.
- Diestrus, an abrupt decline in the percentage of cornified cells (20–50%) occurs in a single day—day 1 of diestrus (D1);

BREEDING, TIMING

(CONTINUED)

B

normal to see neutrophils on days 1–4 of diestrus. • Vaginoscopy—edematous vaginal folds until the LH peak, then vagina pale with slight wrinkling (crenulation) as edema decreases with estradiol decline, by optimum breeding period obvious wrinkles until diestrus when folds are very flat and edema disappears. • Serologic test for *B. canis* (dogs)—rapid slide agglutination test used as a screen (D-TEC® CB; Zoetis, (888)963-8471) sensitive but not specific, looks at antibodies so need 4 to 8 weeks post-exposure for a positive test; confirm by agar gel immunodiffusion test (Cornell University Diagnostic Laboratory, (607)253-3900) or bacterial culture of whole blood or lymph node aspirate.



TREATMENT

APPROPRIATE HEALTH CARE

Dogs

- Fresh semen: multiple breedings; inseminate q48h after the initial rise in progesterone is observed until D1.
- Two vaginal breedings fresh semen: inseminate either on days 3 and 5 or on days 4 and 6 after the LH peak or initial rise in progesterone; use standard AI pipettes or modified Foley catheters (several sizes available); vaginal insemination on or after day 5 may be associated with reduced pregnancy rates and litter sizes due to beginning of cervical closure.
- Frozen or chilled semen: frozen semen is less viable than chilled, thus timing is more critical; one or two intrauterine inseminations most common: inseminate on day 5 or 6 after the LH peak or initial rise in progesterone (day 0) or 3 days after progesterone $\geq 5 \text{ ng/mL}$ (16 nmol/L); intrauterine insemination (via transcervical endoscopy (TCI) or “Norwegian” catheter or surgical insemination).
- Progesterone on day of insemination should be $\geq 12 \text{ ng/mL}$ (38 nmol/L).
- Timing of insemination based on progesterone improves chance of conception and increased litter size.
- Blood collection and vaginal examination q48h are adequate in most cases.

Cats

- Increase the likelihood of ovulation and litter size by maximizing the number of matings; breed on successive days.
- Breed at least four times daily at least 2–3 hours apart on days 2 and 3 of estrus to maximize LH release.
- May induce ovulation by administration of exogenous hormones—GnRH or hCG after mating.

ACTIVITY

- No alteration in activity necessary.
- Must keep strictly away from unintended sexually intact males.

CLIENT EDUCATION

Client education on the physical, behavioral and endocrinologic changes that occur during the estrous cycle, and how variable the timing of these changes can be from animal to animal, can improve owner compliance and satisfaction.

SURGICAL CONSIDERATIONS

Surgical artificial insemination requires standard postoperative care.



MEDICATIONS

DRUG(S) OF CHOICE

Cats—hCG (100–500 IU IM); GnRH (25–50 μg IM)



FOLLOW-UP

PATIENT MONITORING

- Dogs—continue vaginal cytology to determine D1; ovulation is 6 days before D1.
- Dogs—whelping is 65 days from the LH peak, 63 days from ovulation, or 57 days from D1. For fresh, chilled or frozen semen: repeat quantitative progesterone after initial progesterone rise or LH peak to verify $> 10 \text{ ng/mL}$ (32 nmol/L).
- Cats—use progesterone assay one week post insemination to verify ovulation.
- Cats—queening is 62–71 days from first breeding.

PREVENTION /AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Dogs

- Vaginal cytologic examinations—compare D1 with the prospective estimation based on progesterone; if the estimates differ, pregnancy rates are reduced.
- Semiquantitative progesterone kits—must come to room temperature before use; false high values common when using a cold kit.
- Serum progesterone—allow blood to clot at room temperature; separate cells from serum 20 minutes after collection; false low values occur when using serum mixed with RBCs (progesterone binds to RBCs).
- A hemolyzed or lipemic specimen—may give a false low progesterone value.
- Quantitative (chemiluminescence, fluorescence, enzyme immunoassay) progesterone assay—more accurate when performed by a commercial laboratory than semiquantitative kits; in-house analyzers are available; turn-around times should be less than 24h.
- Do not use serum separator tubes—false elevation if progesterone measured by chemiluminescent assay; type of anticoagulant may affect

reported value (serum $>$ heparin plasma $>$ EDTA plasma).



MISCELLANEOUS

ASSOCIATED CONDITIONS

Müllerian duct developmental abnormalities and vulvovestibular, vestibulovaginal strictures

AGE-RELATED FACTORS

Split heats in young bitches—period of proestrus (may be prolonged to 6 weeks or more), followed by cessation of signs, and subsequent resumption of the estrus cycle (1–3 weeks later); no initial rise in progesterone or LH occurs with the first proestrus/estrus; subsequent estrus is usually normal.

ZOONOTIC POTENTIAL

Brucella canis—see chapter, Brucellosis.

PREGNANCY/FERTILITY/BREEDING

Ultrasound—conceptuses can first be detected 19–20 days after LH peak (requires high resolution, high frequency) or a few days earlier in cats; commonly done 4 weeks post breeding; recommend earlier exam in bitches with history of pregnancy loss or infertility.

SEE ALSO

- Brucellosis
- Infertility, Female—Dogs
- Ovulatory Failure
- Vaginal Discharge
- Vaginal Malformations and Acquired Lesions

ABBREVIATIONS

- D1 = first day of diestrus
- ELISA = enzyme-linked immunosorbent assay
- GnRH = gonadotropin-releasing hormone
- hCG = human chorionic gonadotropin
- LH = luteinizing hormone
- RBC = red blood cell

INTERNET RESOURCES

- http://www.ivis.org/advances/Concannon/root2/chapter_frm.asp?LA=1
- http://www.ivis.org/journals/vtfocus/16_2/en/toc.asp

Suggested Reading

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B BRONCHIECTASIS



BASICS

OVERVIEW

- Clinical condition seen primarily in dogs; irreversible dilatation of the bronchi; caused by chronic infectious or inflammatory airway disease or associated with primary ciliary dyskinesia.
- Occurs occasionally in cats as a sequela to long-standing inflammatory lung disease or neoplasia.
- Airways are pulled open by surrounding lung tissue; pooling of secretions can occur, which perpetuates lung damage and allows colonization by bacteria.
- Can be cylindrical or saccular, focal or diffuse.

SIGNALMENT

- Primarily dogs and rarely cats.
- Cocker spaniels and perhaps West Highland white terriers predisposed.
- Young animals (<1 year) with primary ciliary dyskinesia.
- Middle-aged to old dogs with chronic pulmonary disease.

SIGNS

- Chronic cough—usually moist and productive; hemoptysis.
- Recurrent fever.
- Exercise intolerance.
- Tachypnea or respiratory distress.
- Chronic nasal discharge or sinusitis, particularly with primary ciliary dyskinesia.
- Moist, harsh inspiratory crackles; loud expiratory lung sounds or wheezes on physical exam.
- Tracheal hypersensitivity.

CAUSES & RISK FACTORS

- Primary ciliary dyskinesia.
- Inadequately treated infectious or inflammatory lung conditions (pneumonia, bronchitis, or eosinophilic lung disease).
- Smoke inhalation, aspiration pneumonia, radiation injury, and inhalation of environmental toxins—predispose animal to airway injury and colonization by bacteria.
- Chronic bronchial obstruction or foreign body pneumonia—development of bronchiectasis distal to the obstructed region common.
- Signs related to bronchiectasis may not be recognized until long after the primary injury.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Recurrent bacterial bronchopneumonia
- Fungal pneumonia
- Chronic bronchitis
- Infectious or parasitic bronchitis
- Foreign body pneumonia
- Neoplasia

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilia and monocytosis
- Hyperglobulinemia
- Proteinuria—may be seen with secondary amyloidosis, glomerulonephritis, or sepsis.

OTHER LABORATORY TESTS

Arterial blood gas analysis—hypoxemia; widened alveolar-arterial oxygen gradient.

IMAGING

- Radiography—insensitive for the diagnosis. Abnormalities visible late in the course of disease include dilatation of the lobar bronchi with lack of normal tapering in the periphery; diffuse thickening of bronchial walls; mixed bronchial, interstitial, and alveolar pattern.
- Changes can be focal or diffuse.
- CT—bronchus > two times the width of the adjacent pulmonary artery in dogs, abnormally dilated bronchi near the lung periphery; thickened airways; cystic dilatations of the bronchi with or without fluid accumulation.

DIAGNOSTIC PROCEDURES

- Bronchoscopy—saccular or tubular dilatation of the airways.
- Airway sampling—cytologic examination of bronchoalveolar lavage fluid or tracheal wash specimens; culture for aerobic and anaerobic bacteria and *Mycoplasma*; typically find suppurative inflammation with high numbers of neutrophils, or increased eosinophils may be observed indicating eosinophilic bronchopneuropathy; may culture a mixed population of bacteria; some cases appear to have sterile inflammation.

PATHOLOGIC FINDINGS

- Dilated bronchi
- Diffuse peribronchial and alveolar inflammation and fibrosis
- Squamous metaplasia of bronchial epithelium



TREATMENT

- Inpatient—severe condition: intravenous fluids and antibiotics; oxygen administration.
- Airway nebulization and coupage to facilitate removal of viscid pulmonary secretions.
- Gentle activity enhances clearance of secretions.
- Long-term antibiotic administration.
- Stress to owner the importance of appropriate follow-up care.
- Single affected lung lobe or bronchial obstruction—lung lobectomy can be curative.



MEDICATIONS

DRUG(S)

- Intravenous antibiotics—may be required initially; good choices: ampicillin (10–20 mg/kg IV q6–8h) and enrofloxacin (5–10 mg/kg q24h). Broad-spectrum agents with efficacy against both aerobes and anaerobes and that offer good penetration of pulmonary tissue—preferred; combination of

enrofloxacin (5–20 mg/kg PO q24h) and clindamycin (5–11 mg/kg PO q12h) or amoxicillin-clavulanate often effective.

- Azithromycin can be a good alternative antibiotic.
- Long-term use of antibiotics (2 months to life-long)—based on bacterial culture and sensitivity testing; may be required even if culture of airway specimens yields no growth.
- Bronchodilators—may be beneficial, although animals usually have irreversible airflow limitation; extended-release theophylline advised.
- Eosinophilic lung disease requires treatment with glucocorticoids.
- Nebulization and coupage highly beneficial in removing secretions.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Theophylline derivatives and fluoroquinolones—concurrent use causes high and possibly toxic plasma theophylline concentration.
- Furosemide—avoid; dries airway secretions.
- Cough suppressants—avoid; will trap secretions and bacteria in lower airway and perpetuate damage.



FOLLOW-UP

PATIENT MONITORING

- Clinical response—outpatient
- Serial CBC, blood gas analysis, and thoracic radiographs

PREVENTION/AVOIDANCE

- Antibiotics—complete a full course of therapy in patients that appear to have parenchymal infection.
- Early recognition and resolution of foreign body pneumonia.
- Appropriate treatment of eosinophilic pneumonia.

POSSIBLE COMPLICATIONS

Chronic recurrent pulmonary infection likely.

EXPECTED COURSE AND PROGNOSIS

- Chronic and recurrent clinical signs expected; some degree of coughing will always be present.
- Animals can live for years with bronchiectasis if treated properly.
- Patient may succumb to respiratory failure.
- Other organs may fail if bacteremia or glomerulonephritis develops.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Primary ciliary dyskinesia
- Chronic sinusitis
- Chronic bronchitis
- Pneumonia—bacterial, eosinophilic aspiration, foreign body
- Smoke inhalation

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BRONCHITIS, CHRONIC

B



BASICS

DEFINITION

- Chronic coughing for longer than 2 months that is not attributable to another cause (e.g., neoplasia, congestive heart failure, eosinophilic pneumonia, or infectious bronchitis).
- Partly non-reversible and often slowly progressive condition owing to accompanying pathologic airway changes.

PATOPHYSIOLOGY

- Recurrent airway inflammation suspected, but a specific cause is rarely determined.
- Persistent tracheobronchial irritation—causes chronic coughing; leads to changes in the tracheobronchial epithelium and submucosa.
- Airway inflammation, epithelial edema, and thickening—prominent.
- Excess production of a thickened mucus is a hallmark.
- In severe, very chronic cases—probable increased lung resistance; decreased expiratory airflow, especially in cats. In dogs, possible sequelae such as broncholamacia and bronchiectasis.

SYSTEMS AFFECTED

- Respiratory • Cardiovascular—pulmonary hypertension, cor pulmonale • Nervous—syncope (infrequent)

INCIDENCE/PREVALENCE

Common in dogs and cats

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Dogs—small and large breeds.
- Cocker spaniels—bronchiectasis common after a long history of chronic bronchitis.
- Siamese cats and domestic shorthairs affected.

Mean Age and Range

Commonly middle-aged and old animals

Predominant Sex

N/A

SIGNS

Historical Findings

- Coughing—hallmark of tracheobronchial irritation; usually harsh and dry; post-tussive gagging common (owners often misinterpret this as vomiting).
- Exercise intolerance, difficult breathing, wheezing (in cats).
- Cyanosis and syncope can be noted in severe cases.

Physical Examination Findings

- Patients usually bright, alert, and afebrile.
- Tracheal palpation—typically results in coughing because of increased tracheal sensitivity.
- Small airway disease—assumed when an expiratory abdominal push (during

quiet breathing) or end-expiratory wheezing is detected.

- Increased bronchovesicular lung sounds, end-inspiratory crackles, and wheezing can be heard.
- Loud end-expiratory snap is suggestive of concurrent airway collapse.
- Cardiac auscultation—murmurs secondary to valvular insufficiency common in dogs but not always associated with congestive heart failure; chronic bronchitis usually results in a normal or slower than normal resting heart rate and pronounced sinus arrhythmia. In cats, tachycardia is possible.
- Obesity—common; important complicating factor.
- Severe dental disease may predispose to lower airway colonization and possible infection (dogs).

CAUSES

Chronic airway inflammation initiated by multiple causes although specific cause rarely identified.

RISK FACTORS

- Long-term exposure to inhaled irritants.
- Obesity.
- Recurrent bacterial infection.
- Dental disease and laryngeal disease—result in bacterial showering of the lower airways.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Bronchiectasis.
- Eosinophilic bronchopneumopathy.
- Foreign bodies.
- Heartworm disease.
- Bacterial, pneumonia.
- Neoplasia—metastatic more common than primary.
- Pulmonary parasites or parasitic larval migration.
- Pulmonary fibrosis—cats and dogs.
- Congestive heart failure—typically associated with a high resting heart rate, left atrial enlargement, pulmonary venous engorgement, and hilar pulmonary edema (dogs).

CBC/BIOCHEMISTRY/URINALYSIS

- Rarely diagnostic.
- Neutrophilic leukocytosis common.
- Absolute eosinophilia—suggests but not diagnostic for parasitic or allergic bronchitis.
- Polycythemia secondary to chronic hypoxia—can be seen.
- Liver enzymes and bile acids may be elevated due to passive congestion.

OTHER LABORATORY TESTS

- Fecal and heartworm tests—rule out pulmonary parasites.
- Pulse oximetry—useful for detecting hemoglobin desaturation.
- Arterial blood gas analysis—collect, ice, and have analyzed at a local hospital; mild-moderately low PaO₂ seen with severe condition; aids in prognosis and monitoring treatment.

IMAGING

Thoracic Radiography

Common features (in descending order of frequency)—bronchial thickening; interstitial

pattern; middle lung lobe consolidation (cats); atelectasis; hyperinflation and diaphragmatic flattening (primarily cats).

Echocardiography

- Helps rule out cardiac disease as a cause of coughing.
- Can reveal right heart enlargement with pulmonary hypertension. Doppler echocardiography to evaluate.

DIAGNOSTIC PROCEDURES

Electrocardiography (Dog)

Wandering atrial pacemaker, marked sinus arrhythmia, P pulmonale, occasionally evidence of right ventricular enlargement.

Evaluation of Airway Secretions

- Must collect from lower airways—helps to establish underlying cause if present or to determine the severity of inflammation.
- Throat swab cultures are not representative of lower airway flora.
- Tracheal aspiration or bronchoalveolar lavage—collect specimens for cytologic examination and bacterial/mycoplasmal culture.
- Quantitated aerobic BAL cultures help differentiate infection versus airway colonization; reported cutoff is $> 1.7 \times 10^3$ CFU for infection in dogs.
- Anaerobic and *Mycoplasma* cultures recommended as well.
- Cytology—
- inflammation primary finding; most cells are neutrophils, eosinophils, or macrophages; evaluate for bacteria, parasites, neoplastic cells, and contamination with foreign material.

Bronchoscopy

- Preferred test for assessing the lower airways.
- Allows direct visualization of structural as well as functional (dynamic) changes; allows selected airway sampling (e.g., biopsy and lavage).
- Gross changes—excess mucoid to mucopurulent secretions; epithelial edema or thickening with blunting of bronchial bifurcations; irregular or granular mucosa; mucosal polypoid proliferations can indicate chronic bronchitis or chronic eosinophilic pneumonia.
- Large airway caliber changes (e.g., static or dynamic airway collapse and bronchiectasis)—can be detected as complicating problems.

PATHOLOGIC FINDINGS

Histopathology of bronchial nodules reveals neutrophilic inflammation and fibrotic changes; markers of irreversible damage.



TREATMENT

APPROPRIATE HEALTH CARE

- Usually outpatient—oxygen can be given at home in chronic cases.
- Inpatient—if requires oxygen therapy, parenteral medication, or aerosol therapy; patients that owners cannot keep calm at home during initial stages of therapy.

(CONTINUED)

NURSING CARE

Consider saline nebulization followed by coughing and/or gentle exercise to encourage removal of airway secretions.

ACTIVITY

- Exercise—moderate (not forced) useful in clearing secretions; assists with weight loss.
- Limit if exertion causes excessive coughing.
- Use a harness instead of a collar.

DIET

Weight loss critical—improves PaO_2 , attitude, and exercise tolerance in obese patients; reduces cough frequency.

CLIENT EDUCATION

- Warn client that chronic bronchitis is an incurable disease and complete suppression of all coughing is an unattainable goal.
- Stress that aggressive treatment—including weight control, avoiding risk factors, and medical treatment—minimizes the severity of the coughing and slows disease progression in most patients.

SURGICAL CONSIDERATIONS

Treat severe dental disease to minimize secondary bacterial complications.

**MEDICATIONS****DRUG(S) OF CHOICE****Corticosteroids**

- Diminish airway inflammation and coughing regardless of the underlying cause.
- Indicated for non-infectious conditions.
- Require long-term administration; attempt to wean off steroids or determine lowest effective dosage.
- Prednisolone preferred in cats.
- Prednisone or prednisolone usually initiated at 0.5–1 mg/kg PO q12h for a variable time, with tapering of the dosage based on clinical signs.
- Inhaled agents (e.g., budenoside or fluticasone 1–3 puffs a day; variable concentrations exist) are often effective and can be used to reduce systemic side effects of corticosteroids. These drugs are delivered via spacer chamber and face mask (e.g., AeroDawg); however, the most appropriate dose is not clearly established.

Bronchodilators

- Commonly prescribed, although limited evidence of efficacy.
- Beneficial effects: (Theophylline—bronchodilation; increased mucociliary clearance; improvement in diaphragmatic contractility; lowered pulmonary artery pressure).
- Sustained-release theophylline—oral administration; only generic sustained release products currently available. Consider dosing dog, 10 mg/kg PO q12h; cat, 15–20 mg/kg/day in the evening.
- Aminophylline—immediate-release tablets or injectable formulations are not recommended.
- β -agonists—terbutaline (1.25–5 mg/dog PO q8–12h; 0.625 mg/cat

PO q12h) and albuterol (0.02–0.05 mg/kg PO q8–12h in dogs). Can also be administered by inhalation via a spacer and face mask (salbutamol), immediate but transient effect, dose is unclear, can be used for acute relief but not for prolonged treatment.

Antibiotics

- Select on the basis of quantitated culture and sensitivity test results.
- Bacterial culture results unavailable—choose an agent with a good Gram-negative spectrum, with good tissue and secretion penetration that is bactericidal with minimal toxicity (e.g., potentiated sulfa/trimethoprim, amoxicillin/clavulanic acid, or enrofloxacin). Consider drugs suitable for management of *Mycoplasma*, e.g., doxycycline or chloramphenicol.
- Associated chronic aspiration or dental disease—prefer antibiotic with anaerobic and Gram-positive spectrum.

Antitussives

- Indicated for non-productive, paroxysmal, continuous, or debilitating cough associated with airway collapse. Use when inflammation is controlled.
- Dogs—butorphanol (0.55 mg/kg PO q6–12h; 0.055–0.11 mg/kg SC); hydrocodone (2.5–5 mg/dog q6–24h PO); codeine (0.1–0.3 mg/kg q6–8h PO). Over-the-counter cough suppressants are rarely effective.

CONTRAINDICATIONS

Lasix and atropine—do not use because of drying effects on tracheobronchial secretions.

PRECAUTIONS

- β -agonists (e.g., terbutaline and albuterol)—can cause tachycardia, nervousness, and muscle tremors; typically transient.
- Theophylline—can cause tachycardia, restlessness, excitability, vomiting, and diarrhea; evaluate EDTA plasma sample for peak plasma concentration (ideally 5–20 $\mu\text{g}/\text{mL}$). Toxicity may be more common with generic formulations (unpredictable metabolism).

POSSIBLE INTERACTIONS

Fluoroquinolones decrease theophylline clearance in dogs and can result in theophylline toxicity.

ALTERNATIVE DRUG(S)

- Metered dose inhalers (poorly metabolized steroids—fluticasone or budesonide) can be used. These should be administered via face mask and spacing chamber.
- Cyclosporine-induced immune suppression—insufficient evidence to advise this medication in practice.

**FOLLOW-UP****PATIENT MONITORING**

- Follow abnormalities revealed by physical examination and selected diagnostic

BRONCHITIS, CHRONIC

B

tests—determine response to treatment.

- Monitor weight; arterial blood gases usually improve after significant weight loss.

PREVENTION/AVOIDANCE

Avoid and address risk factors (see “Risk Factors”).

POSSIBLE COMPLICATIONS

- Syncope—frequent complication of chronic coughing, particularly in toy-breed dogs.
- Pulmonary hypertension and cor pulmonale—most serious complications.
- Bronchectasis and airway remodeling.

EXPECTED COURSE AND PROGNOSIS

- Progressive airway changes—syncopal episodes, chronic hypoxia, right ventricular hypertrophy, and pulmonary hypertension.
- Acute exacerbations—common with seasonal changes, air quality changes, worsened inflammation, and potentially the development of secondary infection.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Syncope—secondary to chronic coughing or development of pulmonary hypertension.
- Increased susceptibility to airway infection, chronic hypoxia, pulmonary hypertension, and cor pulmonale.

PREGNANCY/FERTILITY/BREEDING

Safety in pregnant animals not established for most of the recommended drugs.

SYNOMYS

- Chronic bronchitis
- Chronic obstructive lung disease (COLD)
- Chronic obstructive pulmonary disease (COPD)

SEE ALSO

- Asthma, Bronchitis—Cats
- Canine Infectious Respiratory Disease
- Cough
- Hypoxemia
- Tracheal and Airway Collapse—Dogs

ABBREVIATIONS

- BAL = bronchoalveolar lavage
- CNS = central nervous system
- EDTA = ethylene diamine tetra-acetate
- SRT = sustained-release theophylline

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Client Education Handout
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BRUCELLOSIS

B



BASICS

DEFINITION

- Contagious disease of dogs caused by *Brucella canis*, a small, intracellular, Gram-negative organism.
- Characterized by abortion and infertility in females and epididymitis and testicular atrophy in males.

PATHOPHYSIOLOGY

B. canis—an intracellular parasite; has a propensity for growth in lymphatic, placental, and male genital (epididymis and prostate) tissues.

SYSTEMS AFFECTED

- Hemic/Lymph/Immune—lymph nodes and spleen; bone marrow; mononuclear leukocytes.
- Reproductive—target tissues of gonadal steroids (gravid uterus, fetus, testes [epididymides], prostate gland).
- Other tissues—intervertebral discs, anterior uvea, meninges (uncommon).

GENETICS

- No known genetic predisposition.
- Occurs most commonly in beagles.

INCIDENCE/PREVALENCE

- Incidence unknown.
- Seroprevalence rates—not accurately defined; false-positive results common with agglutination tests.
- Prevalence—relatively low (1–18%) in the United States and Japan; in the United States, higher in rural areas of the south; in Mexico and Peru, 25–30% in stray dogs.

GEOGRAPHIC DISTRIBUTION

Stray dogs, pets, and kennels—United States (mostly beagles), Mexico, Japan, and several South American countries; seen in Spain, Tunisia, China, and Bulgaria; individual outbreaks in Germany and the former Czechoslovakia (some traced to the importation of dogs).

SIGNALMENT

Species

Dogs and, infrequently, humans

Breed Predilections

- No evidence of breed susceptibility, but exceptionally high prevalence in beagles.
- Infected Labrador retrievers and several other breeds found in commercial kennels (“puppy mills”).

Mean Age and Range

- No age preference.
- Most common in sexually mature dogs.

Predominant Sex

- Both sexes are affected.
- More common in females.

SIGNS

General Comments

Suspect whenever female dogs experience abortions or reproductive failures or males have genital disease.

Historical Findings

- Affected animals, especially females, may appear healthy or have vague signs of illness.
- Lethargy.
- Loss of libido.
- Swollen lymph nodes.
- Back pain.
- Abortion—commonly at 6–8 weeks after conception, although pregnancy may terminate at any stage.

Physical Examination Findings

- Males—swollen scrotal sacs, often with scrotal dermatitis; enlarged and firm epididymides.
- Chronic infection—unilateral or bilateral testicular atrophy; spinal pain; posterior weakness; ataxia.
- Chronic and recurrent unilateral anterior uveitis without other systemic signs of disease; also includes iris hyperpigmentation, vitreal infiltrates, and multifocal chorioretinitis.
- Fever rare.
- Enlarged superficial lymph nodes (e.g., retropharyngeal, external inguinal) common.
- Vaginal discharge may last for several weeks after an abortion.

CAUSES

B. canis—Gram-negative coccobacillus; morphologically indistinguishable from other members of the genus; unlike other *Brucella* spp. (e.g., *B. abortus*, *B. suis*, and *B. melitensis*) can result in a high rate (50%) of false-positive reactions with commonly used tests.

RISK FACTORS

- Breeding kennels and pack hounds.
- Risk increases when popular breeding animals become infected.
- Contact with strays in endemic areas.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Abortions—maternal, fetal, or placental abnormalities.
- Systemic infections—canine distemper, canine herpesvirus infection, *B. abortus* infection, hemolytic streptococci, *E. coli*, leptospirosis, and toxoplasmosis.
- Inguinal hernias—may be provoked by epididymitis and scrotal edema; also caused by blastomycosis and other granulomatous infections, and Rocky Mountain spotted fever.
- Discospondylitis—fungal infections, actinomycosis, staphylococcal infections, nocardiosis, streptococci, or *Corynebacterium diphtheroides*.

CBC/BIOCHEMISTRY/URINALYSIS

- Generally normal in uncomplicated cases.
- Chronically infected dogs may show hyperglobulinemia (with concurrent hypoalbuminemia).
- CSF—pleocytosis mainly consisting of neutrophils, and elevated protein in meningoencephalitis but normal in discospondylitis.
- Urinalysis usually normal even if bacteria can be cultured from urine.

OTHER LABORATORY TESTS

Serologic testing—most commonly used diagnostic method; subject to error;

false-positive reactions to lipopolysaccharide antigens of several species of bacteria common with the RSAT and mercaptoethanol tube agglutination tests.

RSAT

- Commercially available; simple and rapid.
- Detects infected dogs 3–4 weeks after infection; accurate in identifying non-infected (“negative”) dogs.
- Suffers a high rate (50%) of false-positive reactions.
- Results must be confirmed by other tests.

Mercaptoethanol Tube Agglutination Test

- Semiquantitative.
- Generally performed by commercial diagnostic laboratories.
- Provides information similar to the RSAT.
- Suffers from lack of specificity; good screening test.

AGID Tests

- Cell wall antigen test—employs a lipopolysaccharide antigen derived from the cell walls of *B. canis*; highly sensitive; test conditions not standardized; frequent false positives; not recommended.
- Soluble antigen test—employs soluble antigens that consist of proteins extracted from the bacterial cytoplasm; antigens highly specific for antibodies against *Brucella* spp. (including *B. canis*, *B. abortus*, and *B. suis*); reactive antibodies appear 4–12 weeks after infection and persist for a long time; may give precipitin lines after other tests become equivocal or negative; highly recommended.
- ELISA—using purified cytoplasmic antigens but not yet commercially available.
- PCR—shown to be more sensitive than blood culture and serology in detecting infection in human patients. Sensitive in identifying early infections but not yet commercially available.

IMAGING

- Radiographic evidence of discospondylitis—test for brucellosis.
- Radiographic changes are slow to develop and may not be present even when spinal pain is present.

DIAGNOSTIC PROCEDURES

Isolation of Organism

- Blood cultures—when clinical and serologic findings suggest the diagnosis; *Brucella* are readily isolated from the blood of infected dogs if they have not received antibiotics; onset of bacteremia occurs 2–4 weeks after oral-nasal exposure and may persist for 8 months to 5.5 years.
- Cultures of vaginal fluids—after an abortion; usually give positive results.
- Cultures of semen or urine—not practical for routine diagnosis, because overgrowth of contaminants is common.
- Contaminated samples—media that contain antibiotics (e.g., Thayer-Martin medium) have proven useful.

Semen Quality

- Sperm motility, immature sperm, inflammatory cells (neutrophils)—with epididymitis.
- Abnormalities—usually

(CONTINUED)

BRUCELLOSIS**B**

evident by 5–8 weeks post-infection; conspicuous by 20 weeks. • Aspermia without inflammatory cells—common with bilateral testicular atrophy.

Lymph Node Biopsy

- Reveal lymphoid hyperplasia with large numbers of plasma cells. • If done in a sterile manner, tissues should be cultured on appropriate media. • Intracellular bacteria—may be observed in macrophages with special stains (e.g., Brown-Brenn stain).
- Histopathologic examination of the testes—often reveals necrotizing vasculitis, infiltration of inflammatory cells, and granulomatous lesions.

PATHOLOGIC FINDINGS

- Gross findings—lymph node enlargement; splenomegaly; males: enlarged and firm epididymides, scrotal edema, or atrophy of one or both testes; chronic infection: anterior uveitis and discospondylitis. • Microscopic changes—relatively consistent; diffuse lymphoreticular hyperplasia; chronic infection: lymph node sinusoids with abundant plasma cells and macrophages that contain bacteria—diffuse lymphocytic infiltration and granulomatous lesions in all genitourinary organs (especially prostate, epididymis, uterus, and scrotum); may be extensive inflammatory cell infiltration and necrosis of the prostate parenchyma and seminiferous tubules. • Ocular changes—granulomatous iridocyclitis; exudative retinitis; leukocytic exudates in the anterior chamber.

**TREATMENT****APPROPRIATE HEALTH CARE**

Outpatient

ACTIVITY

Restrict working dogs

CLIENT EDUCATION

- Client should be aware that the goal of treatment is the eradication of *B. canis* from the animal (seronegative status and no bacteremia for at least 3 months), but sometimes the result is persistent low antibody titers with no systemic infection.
- Inform client that antibiotic treatment, especially minocycline and doxycycline, is expensive, time-consuming, and controversial (because outcomes are uncertain).
- Treatment is not recommended for breeding or commercial kennels; it is recommended only for non-breeding dogs or those that have been spayed or castrated. • Before treatment is attempted for an intact household pet or breeding dog, the client must clearly agree that the animal must be neutered or destroyed if treatment fails.

SURGICAL CONSIDERATIONS

Neutering/spaying plus treatment—when euthanasia is unacceptable to an owner.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Several therapeutic regimens have been evaluated, but results have been equivocal.
- Most successful—combination of a tetracycline (tetracycline hydrochloride, chlortetracycline, or minocycline at 25 mg/kg PO q8h for 4 weeks) or doxycycline (10 mg/kg PO q12h for 4 weeks) and dihydrostreptomycin (10 mg/kg IM q8h during weeks 1 and 4).
- Enrofloxacin (5 mg/kg PO q24h for 4 weeks) alone shows poor efficacy.

CONTRAINdications

- Tetracyclines—do not use in immature pups. • Gentamicin—contraindicated with kidney disease.

PRECAUTIONS

Gentamicin—monitor renal function closely.

ALTERNATIVE DRUG(S)

Gentamicin—3 mg/kg q12h; limited success; insufficient data on the efficacy combined with tetracycline.

**FOLLOW-UP****PATIENT MONITORING**

- Serologic tests—monthly for at least 3 months after completion of treatment; continuous, persistent decline in antibodies to negative status indicates successful treatment.
- Recrudescent infections (rise in antibody levels and recurrence of bacteremia after therapy)—retreat, neuter and re-treat, or euthanize. • Blood cultures—negative for at least 3 months after completion of treatment.

PREVENTION/AVOIDANCE

- Vaccine—none; would complicate serologic testing. • Testing—all brood bitches, before they come into estrus if a breeding is planned; males used for breeding, at frequent intervals.
- Quarantine and test all new dogs twice at monthly intervals before allowing them to enter a breeding kennel.

POSSIBLE COMPLICATIONS

- Owners may be reluctant to neuter or destroy valuable dogs, regardless of treatment failure. • Remind owners of ethical considerations and their obligation not to sell or distribute infected dogs.

EXPECTED COURSE AND PROGNOSIS

- Prognosis guarded. • Infected for <3–4 months—likely to respond to treatment. • Chronic infections—males may fail to respond to therapy. • Discospondylitis

cases—may need repeated drug treatment but surgical intervention is rarely needed.

- Multiple drug combination therapy with gentamicin or streptomycin, doxycycline, enrofloxacin, and rifampin has been successful in treating ocular disease in dogs.
- Successfully treated (seronegative) dogs—fully susceptible to reinfection.

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

- Human infections—reported; usually mild; respond readily to tetracyclines. • However, an outbreak in six members of a family living in close contact with an infected bitch has been reported.

PREGNANCY/FERTILITY/BREEDING

- Abortions at 45–60 days of gestation typical. • Pups from infected bitches may be infected or normal.

SYNONYMS

Contagious canine abortion

ABBREVIATIONS

- AGID = agar gel immunodiffusion
- CSF = cerebrospinal fluid • ELISA = enzyme-linked immunosorbent assay
- PCR = polymerase chain reaction
- RSAT = rapid 2-mercaptoethanol slide agglutination test

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Client Education Handout
available online

CALCIUM CHANNEL BLOCKER TOXICOSIS



BASICS

OVERVIEW

- Calcium channel blockers (CCBs) are class IV antidysrhythmics used commonly to treat systemic hypertension, cardiac disease, tachydysrhythmias, and potentially oliguric/anuric renal failure in dogs and cats.
- CCBs inhibit movement of calcium (Ca) through L-type voltage-gated slow Ca channels located on cardiac muscle, AV and SA nodes, vasculature smooth muscle, and pancreatic beta cells.
- Three classes of CCBs: phenylalkylamine, benzothiazepine, dihydropyridine. CCB class determines the effect on the body.

SIGNS

- Systems affected include:
- Cardiovascular—bradycardia, AV dissociation and AV block (1st, 2nd, or 3rd degree block), hypotension
 - Gastrointestinal—vomiting, diarrhea, ileus
 - Respiratory—pulmonary edema
 - Nervous—decreased mentation, weakness, collapse, seizures
 - Endocrine/metabolic—hyperglycemia, metabolic acidosis secondary to hypoperfusion



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Beta blocker antagonist toxicosis
- Cardiac disease with secondary bradyarrhythmias
- Cardiovascular drug overdose (e.g., clonidine, digoxin toxicosis)
- Sedative overdose (e.g., opioid or baclofen toxicosis)
- Sick sinus syndrome
- Hyperkalemia
- Decompensated shock/sepsis

CBC/CHEMISTRY/URINALYSIS

- Hyperglycemia
- Azotemia and elevated liver enzymes with prolonged hypoperfusion

OTHER LABORATORY TESTS

Blood gas—metabolic acidosis secondary to hypoperfusion

IMAGING

Chest radiographs to evaluate for intravascular (IV) volume status and pulmonary edema

DIAGNOSTIC PROCEDURES

- ECG—1st, 2nd, and 3rd degree AV block, prolonged PR, QRS and QT intervals
- Echocardiogram—negative inotropy, decreased cardiac output



TREATMENT

- Emesis if asymptomatic and < 2 hours after exposure.
- Gastric lavage if decreased mental status or large number of pills ingested.
- Whole bowel irrigation for extended (XR) or sustained release (SR) medications.

- Central line placement for CVP monitoring, frequent glucose monitoring, and dextrose administration during HDI therapy.
- Temporary pacing considered when medical therapy fails.
- IV fluid administration for hypotension: cats, 10–20 mL/kg over 15–30 minutes; dogs, 20–30 mL/kg over 15–30 minutes.



MEDICATIONS

DRUGS

- Activated charcoal (1–2 g/kg) orally.
- Atropine (0.02–0.04 mg/kg IV) for sinus bradycardia.
- Calcium infusion is the first line therapy despite normocalcemia to increase Ca availability for muscle function and improve contractility.
 - Ca gluconate 10% bolus 0.5–1.5 mL/kg IV over 5–10 minutes followed by a CRI of 0.5–1.5 mL/kg/h, titrated to effect. Monitor continuous ECG and infusion should be slowed or stopped if bradycardia or conduction blockade worsens.
 - Ca chloride 10% bolus 0.15–0.5 mL/kg IV. Central line recommended due to risk of tissue injury secondary to drug extravasation.
 - Serum ionized Ca levels should be maintained at 1.5–2 × the normal range.
- Intravenous fat emulsion (IFE). Used to treat lipid-soluble drug intoxication.
 - Three possible mechanisms: (1) Provide a lipid sink for fat soluble drugs; (2) Supply fatty acid source for cardiac performance; (3) Increase intracellular Ca via activation of voltage gated Ca channels to improve myocyte function.
 - IFE dose: 1.5 mL/kg IV bolus of a 20% solution over 1 minute. Follow with a CRI of 0.25 mL/kg/min for 30–60 minutes. Can repeat bolus every 3–5 minutes as needed up to 3 mL/kg, not to exceed a total dose of 8 mL/kg.

- High dose insulin (HDI)/dextrose administration

◦ Exact mechanism of HDI is unknown but appears to improve uptake and utilization of carbohydrates as an energy source and increase myocardial cell cytosolic Ca levels to increase cardiac contractility and cardiac output. May not improve blood pressure even though clinical signs and perfusion improve.

◦ Recommended treatment: (1) Check blood glucose (BG) concentration and administer dextrose if BG is < 100 mg/dL for dogs and < 200 mg/dL in cats. (2) Administer regular insulin at 1 unit/kg IV. Follow with a CRI IV of regular insulin at 2 units/kg/h. May increase every 10 minutes up to a maximum dose of 10 units/kg/h. When signs resolved, decrease insulin by

- 1–2 units/kg/h. (3) Monitor BG every 10 minutes while titrating insulin dose. Once stabilized, check BG every 30–60 minutes. Dextrose supplementation will be needed to maintain BG concentrations and continued up to 24 hours after discontinuation of the insulin therapy.
- (4) Monitor potassium concentration every hour. Administer potassium chloride to keep potassium concentrations in the low therapeutic range.
- Glucagon—increases inotropy by increasing myocardial cAMP levels. May not be as effective as HDI or ILE. Dose is 0.05–0.2 mg/kg slowly IV bolus followed by a CRI of 0.05–0.1 mg/kg/h.

CONTRAINDICATION/POSSIBLE INTERACTIONS

Vasopressors—may not be as effective as other therapies (Ca infusion, ILE, and HDI) and may make patients less responsive to other therapy.



FOLLOW-UP

PATIENT MONITORING

Monitor heart rate/ECG, blood pressure, ionized Ca, and BG for 12 hours with immediate release preparations and 24 hours for XR/SR preparations.

EXPECTED COURSE AND PROGNOSIS

- Ingestion of immediate release preparations typically result in clinical signs in 8–12 hours.
- SR or XR preparations may take 12–24 hours for clinical signs to develop.
- Prognosis depends on the dose ingested and response to therapy.
- Toxicosis normally results in bradycardia, hypotension, and in severe cases decreased mental status, coma, and apnea.



MISCELLANEOUS

ABBREVIATIONS

- BG = blood glucose
- Ca = calcium
- CCB = calcium channel blocker
- CRI = continuous rate infusion
- CVP = central venous pressure
- ECG = electrocardiogram
- HDI = high dose insulin
- ILE = Intravenous fat emulsion
- IV = intravenous
- SR = sustained release
- XR = extended release

Suggested Reading

Costello M, Syring RS. Calcium channel blocker toxicity. J Vet Emerg Crit Care 2008, 18(1):54–60.

Author Katherine L. Peterson

Consulting Editor Lynn R. Hovda



Client Education Handout
available online

CAMPYLOBACTERIOSIS

C



BASICS

OVERVIEW

- *Campylobacter jejuni*—fastidious, microaerophilic, Gram-negative curved bacteria; often isolated from the intestine of healthy dogs, cats, and other mammals; may cause superficial erosive enterocolitis.
- Infection—fecal-oral route from contamination of food, water, fresh meat (poultry, beef), and the environment; localized in crypts of intestine; darting motility essential for colonization; produces enterotoxin, cytotoxin, cytolethal-distending toxin, invasin. • Invasion gut mucosa—hematochezia; leukocytes in feces; ulceration; edema; congestion of intestine; bacteremia; occasionally septicemia; bacteria shed in feces for weeks to months. • Up to 49% of dogs without diarrhea and 45% of normal cats carry *C. jejuni* and shed it in feces. • In younger dogs (but not cats), more animals with diarrhea shed *Campylobacter* than in diarrheic controls. • *Campylobacter* spp. (and *Salmonella* spp.) often found in raw meat diets (especially chicken).

SIGNALMENT

- Dogs; less commonly cats. • Prevalence—higher in puppies and kittens from birth to 6 months. • Can result in chronic disease.

SIGNS

- Diarrhea—ranges from mucous-like and watery to bloody or bile-streaked; common; may be chronic. • Tenesmus common.
- Fever (mild or absent), anorexia, and intermittent vomiting (3–15 days in duration) may accompany diarrhea. • Young animals (up to 6 months of age)—clinical signs most severe; from enterocolitis/diarrhea.
- Adults—usually asymptomatic carriers.

CAUSES & RISK FACTORS

- *C. jejuni*, *C. coli*, *C. upsaliensis*. • Kennels with poor sanitation/hygiene and fecal buildup in the environment. • Young animals—debilitated, immunosuppressed, or parasitized (e.g., *Giardia*, *Toxocara*, *Isospora*). • Nosocomial infection may develop in hospitalized patients. • Adults—concurrent intestinal infections (e.g., *Salmonella*, parvovirus, hookworms).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Bacterial enterocolitis—*Salmonella*, *Yersinia enterocolitica*, *Clostridium difficile*, and *Clostridium perfringens*. • Parasitic: helminths (particularly whipworms) and protozoa (*Giardia* and *Isospora*). • Viral: parvovirus; signs often more severe than with *Campylobacter*. • Dietary indiscretion or

intolerance. • Drugs and toxins. • Acute pancreatitis. • Severely affected patients—also consider viral gastroenteritis, intussusception, and other causes of abdominal pain. • Distinguish from other causes of chronic diarrhea. • Primary intestinal disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis—if the strain is invasive and bacteremia develops • Biochemistry abnormalities—effects of diarrhea and dehydration (e.g., azotemia, electrolyte disturbances).

DIAGNOSTIC PROCEDURES

- Fecal leukocytes—in gastrointestinal tract and stool. • Fecal culture—submit feces in Amies Transport Medium with charcoal or Cary-Blair Medium kept refrigerated at 4°C in transit. • Species-specific quantitative PCR (qPCR).

Direct Examination of Feces

- Gram stain—make a smear of watery stool. • Wet mount—drop a small amount of stool on glass slide; cover slip; see large numbers of highly motile bacteria (characteristic darting motility).

PATHOLOGIC FINDINGS

- Gross—diffuse colon thickening, congestion/edema; hyperemia of small intestine; enlarged mesenteric lymph nodes. • Thickening of intestinal smooth muscle has been described in infected cats.



TREATMENT

MILD ENTEROCOLITIS

- Outpatient • Usually self-limiting

SEVERE ENTEROCOLITIS

- Inpatient, especially neonatal and immature patients. • Severe neonatal disease—isolate; confine to cage; monitor; encourage rest. • NPO for 24 hours; then bland diet. • Mild dehydration—oral fluid therapy with an enteric fluid replacement solution. • Severe dehydration—intravenous fluid therapy with balanced polyionic isotonic solution. • Plasma transfusion may be required if serum albumin < 2 g/dL. • Locally acting intestinal adsorbents/protectants.



MEDICATIONS

DRUG(S)

- Antibiotics—recommended for signs of systemic illness (e.g., high fever or dehydration) when diarrhea or abnormal clinical signs persist > 7 days and in immune-suppressed patients. • Erythromycin 10–20 mg/kg PO q8h for 5 days; drug of choice. • Enrofloxacin: dog, 5–20 mg/kg q24h PO, IV, IM. Adverse effect of arthropathy in dogs

4–28 weeks of age. Cat, 5 mg/kg q24h PO, IM.

- Tylosin 11 mg/kg PO q8h for 7 days; may be effective.
- Neomycin 10–20 mg/kg PO q6–12h for 5 days; may be ineffective.
- Penicillins and ampicillin—potentially ineffective.
- Septicemia—parenteral antibiotics with aminoglycoside (e.g., amikacin) and cephalosporin may be initiated.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Antidiarrheal drugs that reduce intestinal motility are contraindicated.
- Enrofloxacin—may induce arthropathy in dogs < 28 weeks of age. Do not administer to cats at doses > 5 mg/kg, or give IV.



FOLLOW-UP

PATIENT MONITORING

Repeat fecal culture after treatment.

PREVENTION/AVOIDANCE

- Good hygiene (hand washing). • Routinely clean and disinfect runs, food, and water bowls. • Do not feed raw meat diets to companion animals.

EXPECTED COURSE AND PROGNOSIS

- Adults—usually self-limiting. • Juveniles with severe or persistent enterocolitis—treat with antibiotics.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Concurrent infection with other pathogenic bacteria, enteric parasites, or viruses.

ZOONOTIC POTENTIAL

High potential (*C. jejuni*, *C. coli*, *C. upsaliensis*)

PREGNANCY/FERTILITY/BREEDING

- Erythromycin—safe to use in early pregnancy. • Chloramphenicol and gentamicin—do not use in pregnant animals.

ABBREVIATION

- PCR = polymerase chain reaction

INTERNET RESOURCES

<http://www.cfsph.iastate.edu/DiseaseInfo/disease.php?name=campylobacteriosis&lang=en>

Suggested Reading

Marks SL, Rankin SC, Byrne BA, Weese JS. Enteropathogenic bacteria in dogs and cats: diagnosis, epidemiology, treatment, and control. J Vet Intern Med 2011; 25:1195–1208.

Author Patrick L. McDonough

Consulting Editor Stephen C. Barr

CANDIDIASIS



BASICS

OVERVIEW

- *Candida*—dimorphic fungus with the yeast phase (*Candida* spp.) being part of the normal flora of the mouth, nose, ears, and gastrointestinal and genital tracts of dogs and cats. • *C. albicans* and *C. parapsilosis* most commonly cultured from clinically healthy dogs.
- Recovery from mucosal surfaces does not imply disease; opportunistic infection, colonizing damaged tissues or invading normal tissues of immunosuppressed animals.
- Pathogenic role is determined by identifying a fungemia, infiltration of organisms into the tissues, or signs of organisms in presumed sterile sites (e.g. urinary bladder).
- Conditions that suppress the immune system increase the likelihood of isolation in asymptomatic animals; isolated from throat cultures five times more often in FIV-infected cats than in asymptomatic, non-FIV-infected cats of a similar age and sex.

SIGNALMENT

Cats and dogs of any age and breed.

SIGNS

- Non-healing ulcers in the oral, upper respiratory, GI, or urogenital mucosa—signs frequently reflect the location/extent of disease.
- Urinary bladder involvement—cystitis.
- Ear infection—head shaking and scratching.
- Oral cavity involvement—drooling.
- Inflammation around IV catheters or gastrostomy tubes.
- Ulcerative, red skin lesions.
- Systemic disease with fever, cardiac and/or neurologic signs can be seen.

CAUSES & RISK FACTORS

- Infection—rare; associated with neutropenia, parvovirus infection, diabetes mellitus, hyperadrenocorticism, retrovirus-induced immunosuppression, glucocorticoid therapy, gastrostomy tubes, indwelling urinary catheters/urethrostomy, IV catheters, and incomplete emptying of the bladder.
- Bacterial bladder infection and cystic calculi may predispose to fungal infection.
- Occasionally local or systemic *Candida* infection is seen in animals without predisposing conditions.
- Skin damaged by burns, trauma, or necrotizing dermatitis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Considered whenever the primary condition does not respond as expected.

CBC/BIOCHEMISTRY/URINALYSIS

- Reflect the underlying condition.
- Urinalysis—may show yeast form or clumps of mycelial elements (pseudohyphae)

accompanied by an increase in inflammatory cells; a bacterial urinary tract infection often occurs with the fungal infection.

- Neutropenic patients—Inflammatory response may be absent.

OTHER LABORATORY TESTS

- Cytology—spherical to oval yeast cells 5–7 µm in diameter; pseudohyphae and septate hyphae are 3–5 µm wide.
- Culture—grows well on blood agar and often is isolated from specimens submitted for bacterial culture; more easily isolated from urine than blood.
- PCR and antigen tests are available.

DIAGNOSTIC PROCEDURES

- Lesions—biopsy for histopathologic study to determine if *Candida* is truly a pathogen (samples obtained from mucosal or cutaneous surfaces may not represent true infection); requires demonstration of organisms penetrating the tissues.
- Urine sample—obtain by cystocentesis; culture of a number of colonies of *Candida* strongly supports the diagnosis.
- Otitis (dogs)—culture of *Candida* spp. or identification of yeast or mycelial elements on ear cytology suggests the diagnosis.
- In febrile patients culture tips of catheters for both bacteria and fungi.

PATHOLOGIC FINDINGS

- White cheesy foci in the infected tissue may be noted.
- Usually large numbers of both yeast and pseudohyphae in the tissues surrounded by necrosis and a suppurative inflammatory reaction.
- May be pyogranulomatous in more chronic sites of infection.



TREATMENT

- Regulate diabetes mellitus and control hyperadrenocorticism.
- Remove indwelling catheters.
- Improve immune suppression, if possible.



MEDICATIONS

DRUG(S)

- Topical therapy for mucosal lesions—nystatin or amphotericin B.
- Fluconazole—5 mg/kg PO q12h (dogs and cats); very effective; excreted unchanged in the urine, achieving a high concentration in commonly infected sites.
- Itraconazole—effective; use if the organism becomes resistant to fluconazole; not recommended for urinary tract infection because it is not excreted in the urine.
- In lower urinary tract *Candida* infections resistant to fluconazole; infuse 10–30 mL of 1% clotrimazole into the bladder every other day for three treatments.

- *Candida* may develop drug resistance; consider drug sensitivity testing if suspected.



FOLLOW-UP

PATIENT MONITORING

- Fluconazole and itraconazole—hepatotoxicity; monitor serum ALT monthly and check if patient becomes anorexic.
- After signs have resolved—re-culture sites of infection; continue treatment for 2 weeks more; repeat cultures 2 weeks after completion of treatment and again if signs recur.

EXPECTED COURSE AND PROGNOSIS

- Should resolve within 2–4 weeks of treatment with correction of immunosuppression.
- Control of the underlying disease is necessary to prevent recurrence.
- May resolve spontaneously if the underlying condition is corrected.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Genetic similarities between human and animal isolates suggest a potential for transfer of *C. albicans* between species.

ABBREVIATIONS

- ALT = alanine transaminase
- GI = gastrointestinal
- PCR = polymerase chain reaction
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus

Suggested Reading

- Bradford K, Meinkoth J, McKeirnen K, et al. *Candida* peritonitis in dogs: report of 5 cases. *Vet Clin Pathol* 2013; 42:227–233.
Forward ZA, Legendre AM, Khalsa HDS. Use of intermittent bladder infusion with clotrimazole for treatment of candiduria in a dog. *J Am Vet Med Assoc* 2002; 220: 1496–1498.

Jin Y, Lin D. Fungal urinary tract infections in the dog and cat: A retrospective study (2001–2004). *J Am Anim Hosp Assoc* 2005; 41:373–381.

Pressler BM. Candidiasis and rhodotorulosis. In: Greene CE, ed., *Infectious Diseases of the Dog and Cat*, 4th ed. St. Louis, MO: Saunders Elsevier, 2012, pp. 666–672.

Pressler BM, Vaden SL, Lane IF, et al. *Candida* spp. urinary tract infections in 13 dogs and seven cats: Predisposing factors, treatment, and outcome. *J Am Anim Hosp Assoc* 2003; 39:263–270.

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CANINE CORONAVIRUS INFECTIONS



BASICS

OVERVIEW

- CCoV—sporadic outbreaks of vomiting and diarrhea in dogs; worldwide distribution.
- CRCoV—associated with canine infectious respiratory disease complex (“kennel cough”); worldwide distribution. • Infection with CCoV—usually inapparent; mild to severe enteritis may occur, from which most dogs recover; death reported in young pups; restricted to the upper two-thirds of the small intestine and associated lymph nodes; unlike CPV-2 infection, crypt cells spared.
- Simultaneous infection with CPV-2 may occur; more severe; often fatal.
- Coronaviruses undergo rapid evolution, are highly variable, and differences in virulence between individual isolates are likely.

SIGNALMENT

- Only dogs susceptible to disease. • CCoV may cause inapparent infections in cats.
- CRCoV infections more common in the winter. • All ages and breeds. • Disease more severe in young animals.

SIGNS

- Vary greatly. Rarely virulent isolates that cause systemic disease can occur. • Adults—most infections inapparent. • Puppies—may develop mild to severe, occasionally fatal enteritis. • Incubation period 1–3 days.
- Sudden onset of vomiting, usually only once. • Diarrhea—may be explosive; yellow-green or orange; loose or liquid; typically malodorous (characteristic); may persist for a few days up to > 3 weeks; may recur later. • Coughing; CRCoV associated with canine kennel cough complex. • Young pups—may suffer severe, protracted diarrhea and dehydration. • Anorexia and depression common. • Fever rare. • Mild respiratory effects. • Signs included pyrexia, anorexia, depression, vomiting, hemorrhagic enteritis, respiratory distress, and leukopenia that persisted > 1 week. Ataxia and seizures also occurred in pups, with deaths in 2 days after onset of symptoms.

CAUSES & RISK FACTORS

- CCoV—closely related to FIP virus, feline enteric coronavirus, and transmissible gastroenteritis virus of swine; pig and cat viruses not known to cause natural illness in dogs; readily inactivated by common disinfectants. • CRCoV—genetically and serologically distinct from CCoV; more closely related to bovine coronavirus and human coronavirus OC43. • Stress (e.g., intensive training, crowding)—greatest risk; sporadic outbreaks have occurred in dogs attending shows and in kennels where introductions of new dogs are frequent; crowding and unsanitary conditions promote

clinical illness. • For CCoV, feces primary source of infection; virus shed for about 2 weeks. • For CRCoV, respiratory secretions and fomites are likely sources of infection.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infections caused by enteric bacteria, protozoa, or other viruses and other agents associated with kennel cough complex.
- Other causes of mild to moderate upper respiratory disease. • Food intoxication or intolerance.

CBC/BIOCHEMISTRY/URINALYSIS

Normal; lymphopenia with more virulent CCoV isolates.

OTHER LABORATORY TESTS

- Serologic tests—available; not standardized.
- Antibody titers—generally low; may not indicate recent infection because of high rate of asymptomatic infection.

DIAGNOSTIC PROCEDURES

- Viral isolation for CCoV—from feces in feline cell cultures at onset of diarrhea. Viral isolation for CRCoV is difficult and not recommended. • PCR—using type-/strain-specific probes. • Immunofluorescence of the small intestine—fatal cases; may reveal viral antigen in cells lining the villous epithelium.

PATHOLOGIC FINDINGS

- Gross—may be dilated loops of small intestine filled with gas and watery green-yellow material. • Bowel loops may be congested or hemorrhagic; mesenteric lymph nodes usually enlarged and edematous.
- Typical microscopic changes—atrophy and fusion of intestinal villi; deepening of the crypts; increased cellularity of the lamina propria; flattening of epithelial cells with increased goblet cells. • Lesions—commonly obscured by post-mortem autolysis. • The “Pantrropic” strains described in Europe caused hemorrhagic lesions in the lungs, small intestines, kidneys and lymph nodes, and serosanguineous abdominal fluid.



TREATMENT

- Most affected dogs recover without treatment. • For CCoV, supportive fluid and electrolyte treatment if dehydration is severe.
- For CRCoV, treatment as for canine kennel cough complex.



MEDICATIONS

DRUG(S)

Antibiotics—not usually indicated, except with enteritis, sepsis, or respiratory illness.



FOLLOW-UP

PREVENTION/AVOIDANCE

- Vaccines—controversial; inactivated and live viral vaccines available; appear to be safe; efficacy unknown, except for brief periods (2–4 weeks) after vaccination. Not recommended. Vaccines for CCoV do not cross-protect against CRCoV. • Strict isolation and sanitation are essential in kennels. • CCoV and CRCoV—highly contagious; spread rapidly.

POSSIBLE COMPLICATIONS

Diarrhea with CCoV—may persist 10–12 days; may recur.

EXPECTED COURSE AND PROGNOSIS

- Prognosis—normally good, except severe infections of young pups. • Majority recover after a few days of illness.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Infection with canine parvovirus or other agent may occur concurrently. • Infections with other respiratory pathogens are commonly associated with CRCoV.

ABBREVIATIONS

- CCoV = canine enteric coronavirus
- CPV = canine parvovirus • CRCoV = canine respiratory coronavirus • FIP = feline infectious peritonitis • PCR = polymerase chain reaction

Suggested Reading

Decaro N, Cordonnier N, Demeter Z, et al. European surveillance for pantrropic canine coronavirus. J Clin Microbiol 2013, 51:83–88.

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C CANINE DISTEMPER



BASICS

DEFINITION

- An acute to subacute, contagious, febrile, and often fatal disease with respiratory, urogenital, gastrointestinal, ocular, and CNS manifestations.
- Caused by CDV, a Morbillivirus in the Paramyxoviridae family.
- Affects many different species of the order Carnivora; mortality rate varies greatly among species.

PATOPHYSIOLOGY

- Natural route of infection—airborne and droplet exposure; from the nasal cavity, pharynx, and lungs, macrophages carry the virus to local lymph nodes, where virus replication occurs; within 1 week, viral shedding occurs (mainly in respiratory exudates but also urine) and virtually all lymphatic tissues become infected; spreads via viremia to the surface epithelium of respiratory, gastrointestinal, and urogenital tracts and to the CNS.
- Fever for 1–2 days and lymphopenia may be the only findings during initial period; further disease progression depends on the virus strain and the host's immune response.
- Strong cellular and humoral immune response—host may remain subclinical.
- Weak immune response—subacute infection; host may survive longer.
- Failure of immune response—acute death of host within 2–4 weeks after infection; convulsions and other CNS disturbances frequent causes of death.
- Viral excretion can occur up to 2–3 months but usually shorter.

SYSTEMS AFFECTED

- Multisystemic—all lymphatic tissues; surface epithelium in the respiratory, alimentary, and urogenital tracts; endocrine and exocrine glands.
- Nervous—skin; gray and/or white matter of brain and/or spinal cord in the CNS.

INCIDENCE/PREVALENCE

- Dogs—restricted to sporadic outbreaks.
- Wildlife (raccoons, skunks, fox, tigers)—fairly common.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

- Most species of the order Carnivora—Canidae, Hyaenidae, Mustelidae, Procyonidae, Viverridae.
- Felidae families—large cats in California zoos and in Tanzania.

Mean Age and Range

Young, especially unvaccinated animals are more susceptible than are adults.

SIGNS

- Fever—first peak 3–6 days after infection, may pass unnoticed; second peak several days later (and intermittent thereafter), usually associated with nasal and ocular discharge, depression, and anorexia.
- Gastrointestinal and/or respiratory signs—follow, often exacerbated by secondary bacterial infection.

- CNS—many infected dogs; often, but not always, after systemic disease; depends on the virus strain; either acute gray or white matter disease.
- Gray matter disease: affects cerebral cortex, brainstem, and spinal cord and may cause a non-suppurative meningitis, seizures, stupor, hysteria, and ataxia. Dogs may die in 2–3 weeks; some dogs recover (associated with prompt humoral and cell-mediated immunity), others progress to develop white matter disease.
- White matter disease: variable signs of multifocal disease, commonly cerebellovestibular signs, spinal cord paresis and ataxia, occasionally myoclonus; some dogs die 4–5 weeks after initial infection with non-inflammatory, demyelinating disease; some dogs may recover with minimal CNS injury.
- Optic neuritis and retinal lesions may occur; sometimes infected scleral blood vessels from anterior uveitis.
- Hardening of the footpads (hyperkeratosis) and nose—some virus strains; but relatively uncommon.
- Enamel hypoplasia of the teeth after neonatal infection common.

CAUSES

- CDV, a Morbillivirus within the Paramyxoviridae family; closely related to measles virus, rinderpest virus of cattle, and phocine (seal) and dolphin distemper viruses.
- Incompletely attenuated vaccines (rare).
- Secondary bacterial infections frequently involve the respiratory and gastrointestinal systems.

RISK FACTORS

Contact of non-immunized animals with CDV-infected animals (dogs or wild carnivores).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Diagnosis usually based on clinical suspicion (typical history in a 3- to 6-month-old unvaccinated puppy showing multifocal signs).
- Kennel cough—can mimic the respiratory disease.
- Enteric signs—differentiate from canine parvovirus and coronavirus infections, parasitism (giardiasis), bacterial infections, gastroenteritis from toxin ingestion, inflammatory bowel disease.
- CNS form—differentiate from autoimmune meningoencephalitis (granulomatous meningoencephalomyelitis, necrotizing encephalitis), protozoal (e.g., toxoplasmosis, neosporosis), fungal (e.g., cryptococcosis), and rickettsial (e.g., ehrlichiosis, Rocky Mountain spotted fever) meningoencephalitis.

CBC/BIOCHEMISTRY/URINALYSIS

Lymphopenia during early infection; intracytoplasmic inclusions in WBCs and RBCs.

OTHER LABORATORY TESTS

- Serology—limited value; positive antibody tests do *not* differentiate between vaccination and exposure to virulent virus; patient may die from acute disease before neutralizing antibody is produced; IgM responses may occur up to 3 months after exposure to virulent virus and for up to 3 weeks after vaccination.
- CDV antibody in CSF—indicative, but not always diagnostic, of distemper encephalitis.

IMAGING

- Radiographs—may determine the extent of pneumonia.
- CT and MRI—may or may not disclose lesions. MRI sensitive for visualization of demyelination.

DIAGNOSTIC PROCEDURES

- Immunohistochemical detection in haired skin, nasal mucosa, and footpad epithelium.
- Viral antigen or viral inclusions—in buffy coat cells, urine sediment, conjunctival or vaginal imprints (negative results do not rule out the diagnosis).
- RT-PCR—on buffy coat, urine sediment cells, conjunctival swabs and CSF.
- CSF—moderate pleocytosis of mononuclear cells (lymphocytes and macrophages), CDV-specific antibody, interferon, and viral antigen early in disease course.
- Post-mortem diagnosis—histopathology, immunofluorescence and/or immunocytochemistry, virus isolation, and/or RT PCR; preferred tissues from lungs, stomach, urinary bladder, lymph nodes, and brain.

PATHOLOGIC FINDINGS

Gross

- Thymus—in young animals greatly reduced in size; sometimes gelatinous.
- Lungs—patchy consolidation as a result of interstitial pneumonia.
- Footpads and nose—rarely hyperkeratosis.
- Mucopurulent discharges—from eyes and nose, bronchopneumonia, catarrhal enteritis, and skin pustules; probably caused by secondary bacterial infections; commonly seen.

Histologic

- Intracytoplasmic eosinophilic inclusion bodies—frequently found in epithelium of the bronchi, stomach, and urinary bladder; also seen in reticulum cells and leukocytes in lymphatic tissues.
- Inclusion bodies in the CNS—glial cells and neurons; frequently intranuclear; can also be found in cytoplasm.
- Staining by fluorescent antibody or immunoperoxidase may detect viral antigen where inclusion bodies are not seen.

(CONTINUED)

CANINE DISTEMPER**TREATMENT****APPROPRIATE HEALTH CARE**

Inpatients and in isolation, to prevent infection of other dogs. Unlike systemic signs, presenting neurologic signs are usually not reversible.

NURSING CARE

- Symptomatic.
- Intravenous fluids—with anorexia and diarrhea.
- Once fever and secondary bacterial infections are controlled, patients usually begin to eat again.
- Clean away ocular discharges.

ACTIVITY

Limited

DIET

Depends on the extent of gastrointestinal involvement

CLIENT EDUCATION

- Inform client that mortality rate is about 50%.
- Inform client that dogs that appear to recover from early catarrhal signs may later develop fatal CNS signs.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Antiviral drugs—none known to be effective.
- Broad-spectrum antibiotics—to reduce secondary bacterial infection, because CDV is highly immunosuppressive. Ampicillin, tetracycline, and chloramphenicol are good choices.
- Anticonvulsant therapy—phenobarbital, potassium bromide; to control seizures.

CONTRAINDICATIONS

Corticosteroids—use anti-inflammatory doses with caution; may provide short-term control; immunosuppressive doses may enhance viral dissemination.

PRECAUTIONS

Tetracycline and fluorinated quinolones—best avoided in young and growing animals.

**FOLLOW-UP****PATIENT MONITORING**

- Monitor for CNS signs, because seizures often follow.
- Monitor for signs of pneumonia or dehydration from diarrhea in the acute phase of the disease.

PREVENTION/AVOIDANCE

- Vaccination is key.
- Isolate puppies to prevent infection from wildlife (e.g., raccoons, foxes, skunks) or from CDV-infected dogs.
- Recovered dogs are not carriers.

Vaccines

- MLV-CD—prevents infection and disease; two types available:
 - Canine tissue culture-adapted vaccines (e.g., Rockborn strain)—induce complete immunity in virtually 100% of susceptible dogs; rarely, a post-vaccinal fatal encephalitis develops 7–14 days after vaccination, especially in immunosuppressed animals.
 - Chick embryo-adapted vaccines (e.g., Lederle strain)—safer; post-vaccinal encephalitis does not occur; only about 80% of susceptible dogs seroconvert.
- Other species—chick embryo can safely be used in a variety of wildlife species (e.g., gray fox); Rockborn type fatal in these animals.
- Killed vaccines—useful for species in which either type of MLV-CD is fatal (e.g., red panda, black-footed ferret).
- Canarypox recombinant CDV vaccine.
- Duration of immunity from most vaccines is over 3 years.

Maternal Antibody

- Important.
- Most puppies lose protection from maternal antibody at 6–12 weeks of age; 2–3 vaccinations should be given during this period.
- Heterotypic (measles virus) vaccination—recommended for puppies that have maternal antibody; induces protection from disease but not from infection.

POSSIBLE COMPLICATIONS

Possibility of occurrence of CNS signs for 2–3 months after catarrhal signs have subsided.

EXPECTED COURSE AND PROGNOSIS

- Depends on the strain and the individual host response—subclinical, acute, subacute, fatal, or nonfatal infection.
- Mild CNS signs—patient may recover; myoclonus may continue for several months or indefinitely.
- Death—2 weeks to 3 months after infection; mortality rate approximately 50%.
- Euthanasia—owner may elect if or when neurologic signs develop; indicated when uncontrollable seizures occur.
- Fully recovered dogs do not shed CDV.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Persistent or latent *Toxoplasma gondii* infections—reactivated because of the immunosuppressive state.
- Respiratory infections with *Bordetella bronchiseptica* (a major cause of kennel cough).

AGE-RELATED FACTORS

- Young puppies—more susceptible; mortality rate is higher.
- Non-immunized old dogs—highly susceptible to infection and disease.

ZOONOTIC POTENTIAL

- Possible that humans may become subclinically infected with CDV;

immunization against measles virus also protects against CDV infection.

- Once speculated that CDV triggers MS but several studies have refuted this proposition.

PREGNANCY/FERTILITY/BREEDING

In utero infection of fetuses—occurs in antibody-negative bitches; rare; may lead to abortion or to persistent infection; infected neonates may develop fatal disease by 4–6 weeks of age.

SYNONYMS

- Canine distemper
- Hard pad disease
- Hundestaupe
- Maladie de Carré

SEE ALSO

Myoclonus (although not unique to CDV)

ABBREVIATIONS

- CDV = canine distemper virus
- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- MLV-CD = modified live virus of canine distemper
- MRI = magnetic resonance imaging
- MS = multiple sclerosis
- RT-PCR = reverse transcriptase polymerase chain reaction

INTERNET RESOURCES

http://www.ivis.org/advances/Vite/braund27/chapter_frm.asp?LA=1#Distemper_Encephalomyelitis

Suggested Reading

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**Client Education Handout
available online**

C CANINE INFECTIOUS RESPIRATORY DISEASE



BASICS

DEFINITION

A multifaceted disease whereby infectious disease and environment contribute to the genesis of cough and other respiratory signs in dogs.

PATHOPHYSIOLOGY

Initiated by injury to the respiratory epithelium by viral infection followed by invasion of damaged tissue by bacterial, mycoplasmal, or other virulent organisms, resulting in further damage and clinical signs.

SYSTEMS AFFECTED

Respiratory—upper and lower airways can be involved. Multisystemic—cases that develop sepsis.

GENETICS

None

INCIDENCE/PREVALENCE

Most common in areas of high density with immunologically naïve or immunosuppressed patients (i.e., training homes, shelters, veterinary hospitals).

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog

Breed Predilections

None

Mean Age and Range

- Most severe in puppies 6 weeks–6 months old.
- Can develop in dogs of all ages, particularly with preexisting airway disease.

Predominant Sex

None

SIGNS

General Comments

- Related to the degree of respiratory tract damage and age of the affected dog and virulence of infectious organism.
- Can be subclinical, mild, or severe with pneumonia.
- Most viral, bacterial, and mycoplasmal agents spread rapidly from seemingly healthy dogs to others in the same environment; signs usually begin about 3–7 days after exposure to the infecting agent(s).

Historical Findings

- Uncomplicated—acute-onset cough in an otherwise healthy animal; dry and hacking, soft and dry, moist and hacking, or paroxysmal, followed by gagging, retching, and expectoration of mucus; excitement, exercise, and pressure on the trachea induce coughing spells.
- Complicated (severe)—inappetance to anorexia; cough is moist and productive; lethargy, difficulty breathing, hemoptysis, and exercise intolerance can occur.

Physical Examination Findings

- Uncomplicated—cough readily induced with minimal tracheal pressure; lung sounds

often normal; systemically healthy.

- Complicated—low-grade, or intermittent fever (39.4–40.0°C, 103–104°F); increased intensity of normal lung sounds, crackles or wheezes possible.

CAUSES

- Viral—canine distemper virus; CAV-2; CPIV; canine respiratory coronavirus, canine reovirus; canine herpesvirus-1; canine influenza virus (H3N8 or H3N2); canine bovacivirus, canine hepacivirus; canine pneumovirus.
- Most viral pathogens (except CHV and CDV) primarily infect epithelial and lymphoid tissue of the upper and lower respiratory tract; in severe cases, cause desquamation of the epithelium and aggregation of inflammatory cells in the lungs leading to secondary bacterial colonization and infection; canine respiratory coronavirus infection leads to loss of cilia associated with the respiratory epithelium, increasing the severity and duration of secondary infections.
- Bacterial—*Bordetella bronchiseptica*, with no other respiratory pathogens, produces clinical signs indistinguishable from those of other bacterial causes; *Streptococcus equi* subsp *zooepidemicus* is associated with a particularly virulent course that can progress to death; *Pseudomonas*, *Escherichia coli*, *Klebsiella*, *Pasteurella*, *Streptococcus*, *Mycoplasma*, and other species equally likely.

RISK FACTORS

- Substandard hygienic conditions and overcrowding—encountered in some pet shops, shelters, research facilities, and boarding and training kennels.
- Coexisting subclinical airway disease—congenital anomalies; chronic bronchitis; bronchiectasis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- In systemically well dogs—parasitic bronchitis, irritant tracheobronchitis, tracheal foreign body, airway collapse.
- In a dog with systemic signs—fungal pneumonia, primary or metastatic neoplasia, congestive heart failure, migrating foreign body.
- Provisional diagnosis of infectious tracheobronchitis is made in a dog with compelling clinical signs and a history of exposure to the implicated organisms.
- See chapter, Cough.

CBC/BIOCHEMISTRY/URINALYSIS

- Early, mild leukopenia (5,000–6,000 cells/dL)—can be detected; suggests viral cause.
- Neutrophilic leukocytosis with a toxic left shift—frequently found with severe pneumonia.

OTHER LABORATORY TESTS

Pulse oximetry and arterial blood gas analysis—can reveal hypoxemia in pneumonia.

IMAGING

- Uncomplicated disease: radiographs—unremarkable; most useful for ruling out other differential diagnoses.
- Complicated disease: radiographs—interstitial and alveolar lung pattern with a cranoventral distribution typical of bacterial pneumonia; can see diffuse interstitial lung pattern typical of viral pneumonia; mixed lung pattern can be present.

DIAGNOSTIC PROCEDURES

- In cases with severe disease—ideally perform bronchoalveolar lavage via bronchoscopy for cytology and microbial culture; tracheal wash sample acceptable but increased likelihood for upper airway contamination.
- Antimicrobial sensitivity pattern of cultured bacteria—identification aids markedly in providing an effective treatment plan.
- PCR can be used to detect virus in BAL fluid, though there are limited reports of sensitivity and specificity.

PATHOLOGIC FINDINGS

- CPI—causes few to no clinical signs; lungs of infected dogs 6–10 days after exposure may contain pertracheal hemorrhages that are evenly distributed over the surfaces; detected by immunofluorescence in columnar epithelial cells of the bronchi and bronchioles 6–10 days after aerosol exposure.
- CAV-2—lesions confined to the respiratory system; large intranuclear inclusion bodies found in bronchial epithelial cells and alveolar septal cells; clinical signs tend to be mild and short-lasting; lesions persist for at least a month after infection.
- Canine influenza virus (H3N8)—fulminant disease characterized by secondary *Mycoplasma* infection and pulmonary hemorrhage.
- Canine respiratory coronavirus—characterized by marked inflammation of the trachea and nares with cilia loss in the former; detected by immunohistochemistry of the trachea or bronchioles.
- *Streptococcus equi* subsp *zooepidemicus* infection—acute, fibrinosuppurative pneumonia with large numbers of cocci found within the pulmonary parenchyma and, often, septic thromboemboli.
- Bordetellosis and severe bacterial infection—evidence of purulent bronchitis, tracheitis, and rhinitis with hyperemia and enlargement of the bronchial, mediastinal, and retropharyngeal lymph nodes; may see large numbers of Gram-positive or -negative organisms in the mucus of the tracheal and bronchial epithelium.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—strongly recommended for uncomplicated disease.
- Inpatient—strongly recommended for complicated disease and/or pneumonia.

(CONTINUED)

CANINE INFECTIOUS RESPIRATORY DISEASE

NURSING CARE

Fluid administration—indicated for complicated disease and/or pneumonia.

ACTIVITY

Enforced rest—14–21 days with uncomplicated disease; for at least the duration of radiographic evidence of pneumonia in severely affected dogs.

DIET

Good-quality commercial food

CLIENT EDUCATION

- Isolate patient from other animals; infected dogs can transmit the agent(s) before onset of clinical signs and afterward until immunity develops.
- Dogs with uncomplicated disease should respond to treatment in 10–14 days.
- Once infection spreads in a kennel, it can be controlled by evacuation for 1–2 weeks and disinfection with commonly used chemicals, such as sodium hypochlorite (1:30 dilution), chlorhexidine, and benzalkonium.



MEDICATIONS

DRUG(S) OF CHOICE

- Amoxicillin/clavulanic acid (12.5–25 mg/kg PO q12h) or doxycycline (5 mg/kg PO q12h)—initial treatment of uncomplicated disease.
- Penicillin (ampicillin 10–20 mg/kg IV q6–8h or ticarcillin 40–50 mg/kg IV q6–8h) with aminoglycoside (gentamicin 2–4 mg/kg IV, IM, SC q6–8h or amikacin 6.5 mg/kg IV, IM, SC q8h) or fluoroquinolone (enrofloxacin 5–10 mg/kg PO, IM, IV q24h)—usually effective for severe disease.
- Antimicrobial therapy—continue for at least 10 days beyond radiographic resolution.
- *B. bronchiseptica* and other resistant species—some antimicrobials may not reach adequate therapeutic concentrations in the lumen of the lower respiratory tract, so oral or parenteral administration may have limited effectiveness; nebulization with gentamicin (3–5 mg/kg) can decrease bacterial numbers when administered daily for 3–5 days. Use in conjunction with systemic antibiotics in dogs with parenchymal disease.
- Butorphanol (0.55 mg/kg PO q8–12h) or hydrocodone bitartrate (0.22 mg/kg PO q6–8h)—effective suppression of dry, non-productive cough not associated with bacterial infection.
- Bronchodilators (e.g., terbutaline 0.625–5 mg/dog q8–12h)—may use to control bronchospasm and wheeze.

CONTRAINDICATIONS

- Do not use cough suppressants in patients with pneumonia.
- Employ glucocorticoids only in cases with significant inflammatory disease refractory to conventional supportive care.

PRECAUTIONS

None

POSSIBLE INTERACTIONS

Fluoroquinolones and theophylline derivatives—concurrent use causes high and possibly toxic plasma theophylline concentration. Dose reduce theophylline while concurrently administering fluoroquinolones.

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

- Uncomplicated disease—should respond to treatment in 10–14 days; if patient continues to cough 14 days or more after establishment of an adequate treatment plan, question the diagnosis of uncomplicated disease.
- Complicated disease—repeat thoracic radiography until at least 7 days beyond resolution of all clinical signs.

PREVENTION/AVOIDANCE

Shedding of the causative agent(s) of infectious respiratory disease in airway secretions of dogs undoubtedly accounts for the persistence of this problem in kennels, animal shelters, boarding facilities, and veterinary hospitals.

Viral and Bacterial Vaccines

- Modified live CDV and CAV-2 vaccines provide reliable protection and are considered core vaccines for all puppies; can be administered at 6 weeks of age, every 2–4 weeks.
- *B. bronchiseptica* and CPiV vaccine—can vaccinate puppies mucosally or intranasally as early as 2–4 weeks of age without interference from maternal antibody and follow with annual revaccination; can vaccinate mature dogs with a one-dose intranasal vaccination (at the same time as their puppies or when they receive their annual vaccinations).
- Inactivated *B. bronchiseptica* parenteral vaccine—administered as two doses, 2–4 weeks apart; initial vaccination of puppies is recommended at or about 6–8 weeks of age; revaccinate at 4 months of age.
- Inactivated canine influenza vaccine available to reduce severity and duration of clinical signs, but considered noncore; can be administered starting at 6 weeks as two doses, 2–4 weeks apart. Results in seroconversion.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

- Natural course of uncomplicated disease, if untreated—10–14 days; simple restriction of exercise and prevention of excitement shortens the course.
- Typical course of severe disease—2–6 weeks; patients that die often

developed severe pneumonia that affected multiple lung lobes and multiple organ dysfunction due to sepsis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

May accompany other respiratory tract anomalies

AGE-RELATED FACTORS

Most severe in puppies 6 weeks–6 months old and in puppies from commercial pet shops and humane society shelters.

ZOONOTIC POTENTIAL

Potential zoonotic risk of *Streptococcus equi* subsp *zooepidemicus* reported in a single case report.

PREGNANCY/FERTILITY/BREEDING

High risk in dogs on extensive medical treatment; especially risky for dogs in overcrowded breeding facilities.

SYNOMYNS

Kennel cough, infectious tracheobronchitis—uncomplicated disease

ABBREVIATIONS

- CAV = canine adenovirus • CDV = canine distemper virus • CHV = canine herpes virus
- CPiV = canine parainfluenza

INTERNET RESOURCES

www.cdc.gov/flu/canine/

Suggested Reading

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Client Education Handout
available online

CANINE INFLUENZA



BASICS

OVERVIEW

- An acute to subacute contagious viral disease with an almost exclusive respiratory manifestation caused by canine influenza viruses (CIV), orthomyxoviruses with a direct genetic link to equine influenza virus H3N8 (US) or to avian H3N2 and H5N2 viruses (East Asia).
- Natural route of infection is airborne particles or oral contact with contaminated surfaces. Replication of the virus appears to be restricted to epithelial cells of the upper and lower airways with possible involvement of alveolar macrophages. Antibody response detectable by 8 days post-infection and titers remain detectable for > 1 year. Protective immune responses have not been defined.
- H3N8 CIV activity was first detected in all areas with greyhound racetracks in the United States in 2004. Virus is currently enzootic in non-racing dogs in the eastern seaboard from Connecticut to Virginia with sporadic incursions into other areas through the movement of infected dogs.
- H3N2 CIV was first detected in Korea in 2007, but existed in China several years earlier. Genetic lineage is of avian origin and probably arose in the live animal markets of East Asia.

SIGNALMENT

- Natural infections of H3N8 CIV currently limited to dogs: H3N2 virus is capable of infecting cats.
- All breeds of dog are susceptible and there is no age restriction on susceptibility.
- Greyhounds sometimes show more severe signs with H3N8 CIV infections, but factors other than breed may contribute to the disease pattern.
- H3N2 CIV infections show more severe clinical signs than H3N8 CIV.

SIGNS

- 60–80% of infected dogs develop clinical signs.
- Incubation period 2–4 days post-infection.
- Modest febrile response 39.4–40°C (103–104°F) 3–6 days post-infection.
- Clear nasal discharge, which can progress to thick, mucoid discharge, most frequently caused by secondary bacterial colonization.
- More severe form of disease shows higher temperatures with development of

pneumonia and increased respiration rate 6–10 days post-infection.

- Many dogs develop a cough that can last for several weeks.

CAUSES & RISK FACTORS

- Respiratory infection caused by canine influenza viruses.
- Most cases have a history of group housing: kennels, day care centers, and rescue shelters, or contact with dogs that have recently been in group housing.
- As CIV is a relatively new viral infection of dogs, virtually all dogs are susceptible.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- On an individual basis, the early signs of canine influenza are indistinguishable from signs of kennel cough.
- Distinction from typical respiratory pathogens of dogs is found in group settings in which 60–80% of dogs can show clinical signs.
- Later in disease course—pneumonia may develop with or without secondary bacterial infections.

CBC/BIOCHEMISTRY/URINALYSIS

- Generally normal.
- CBC may reflect stress initially, then bacterial pneumonia later in disease (leukocytosis, left shift).

OTHER LABORATORY TESTS

Hemagglutination inhibition test on serum can be used to assess exposure to CIV.

DIAGNOSTIC PROCEDURES

- In acute phase of disease (1–3 days post-onset of clinical signs), a nasal swab may be used to detect the agent by a RT-PCR test or viral isolation.
- More than 7 days post-onset of clinical signs—serum collected for hemagglutination inhibition test can determine exposure to CIV.
- Antigen-capture ELISA tests—give unacceptable levels of false negatives.

PATHOLOGIC FINDINGS

Primary lesion caused by the infection is the destruction of the ciliated epithelial cell layer in the upper airways with extension into the lungs. Areas of lung consolidation can be found 6–10 days post-infection.



TREATMENT

- Affected animals should be managed to prevent infection of other dogs.
- Contagious period for CIV extends to approximately 6 days post-onset of clinical signs.
- Continued coughing of affected animal beyond 6 days is not a sign of virus shed.
- Strongly recommend treating uncomplicated cases as outpatients to prevent hospital contamination.
- Only hospitalize those with pneumonia that require IV fluid support.
- Enforced rest—for at least 14–21 days (uncomplicated cases); 2 months in cases of pneumonia.
- If dogs develop *Bordetella bronchiseptica* bacterial pneumonia, they may be infectious for this bacterium even up to months after recovery.



MEDICATIONS

- Antiviral drugs have not been tested for efficacy.
- Treatment with broad-spectrum antibiotics may be necessary to prevent and control secondary bacterial infections—amoxicillin/clavulanic acid, doxycycline, or trimethoprim-sulfadiazine.
- Severe cases, resistant to first-choice antibiotic therapies above—combination therapy of an aminoglycoside (gentamicin or amikacin) with a cephalosporin (cefazolin). May use enrofloxacin as alternative to gentamicin.
- In severe cases (bronchopneumonia)—continue antibiotic therapy at least 2 weeks past radiographic resolution of signs.
- Resistant bacteria (*B. bronchiseptica* and others)—important to culture and establish the bacterial sensitivity; may need to deliver antibiotics by nebulization (kanamycin 250 mg; gentamicin 50 mg; polymixin B 333,000 IU) for 3–5 days.
- Cough suppressants (butorphanol or hydrocodone bitartrate)—often effective in suppressing a dry non-productive cough.
- Bronchodilators (theophylline or aminophylline)—offer little help but may relieve wheezing.

(CONTINUED)



FOLLOW-UP

- If infection is established in a kennel situation, evacuate the kennel for 1–2 weeks and disinfect with sodium hypochlorite (1:30 dilution), chlorhexidine, or benzalkonium.
- Uncomplicated cases should resolve within 10–14 days; if patient continues to cough beyond 14 days, question the diagnosis of uncomplicated disease.
- Dogs recovering from *B. bronchiseptica* infection are immune for at least 6 months.
- Mortality rate is highly variable and is most likely linked to the degree of secondary bacterial infection, strain of virus, and intensity of veterinary care.

- Currently there are two licensed vaccine for H3N8 CIV for use in dogs.



MISCELLANEOUS

ZOONOTIC POTENTIAL

There is no evidence to indicate that CIV can infect humans.

RISK TO OTHER ANIMALS

Given the close genetic link to equine H3N8, there is the potential for H3N8 CIV to infect horses. Cats can be experimentally infected with H3N8 CIV; H3N2 virus was isolated from cats in an animal shelter.

CANINE INFLUENZA

ABBREVIATIONS

- CIV = canine influenza virus
- ELISA = enzyme-linked immunosorbent assay
- HI = hemagglutination inhibition assay
- RT-PCR = reverse transcriptase polymerase chain reaction

INTERNET RESOURCES

<http://www.diaglab.vet.cornell.edu/issues/civ.asp>

Suggested Reading

Dubovi EJ, Njaa BL. Canine influenza. *Vet Clin Small Anim* 2008, 38:827–836.

Author Edward J. Dubovi

Consulting Editor Stephen C. Barr

C

C CANINE PARVOVIRUS INFECTION



BASICS

DEFINITION

- CPV-2 infection is an acute systemic illness characterized by vomiting and hemorrhagic enteritis.
- Often fatal in pups, that may collapse in a “shock-like” state and die suddenly without enteric signs, after only a brief period of illness.
- The myocardial form was observed in pups during the early outbreaks in the late 1970s when the dog population was fully susceptible, and is now rare.
- Most pups are now protected against neonatal infection by maternal antibodies.
- Monoclonal antibodies have revealed antigenic changes in CPV-2 since its emergence in 1978 and CPV2a, b, and c strains have been identified.
- The original virus is now virtually extinct in the domestic dog population.
- CPV2c viruses are more virulent than the original isolates, and case mortality rates appear to be higher than in the earliest outbreaks.

PATOPHYSIOLOGY

- CPV-2 is very closely related to feline panleukopenia virus (FPV) and several other parvoviruses that infect carnivores.
- Parvoviruses, including CPV-2, require actively dividing cells for growth.
- After ingestion of virus there is a 2- to 4-day period of viremia, with concomitant growth in lymphatic tissues throughout the body.
- Early lymphatic infection is accompanied by lymphopenia and precedes intestinal infection and clinical signs.
- By the third post-infection (PI) day, the rapidly dividing crypt cells of the small intestine are infected.
- Viral shedding in the feces starts ~3–4 days PI, and peaks about the time clinical signs first appear.
- Virus ceases to be shed in detectable amounts by PI days 8–12.
- Absorption of bacterial endotoxins from the damaged intestinal mucosa is believed to play a role in CPV-2 disease.
- Intensity of illness appears to be related to the viral dose and the antigenic type.

SYSTEMS AFFECTED

- Cardiovascular—myocarditis with sudden death (now rare).
- Gastrointestinal—small intestinal crypt cells and adjacent mucosal epithelium; severe hemorrhagic diarrhea, vomiting, dehydration; hypovolemic and septic/endotoxic shock.
- Hemic/Lymphatic/Immune—thymus, lymph nodes, spleen, Peyer's patches.

GENETICS

Unknown

INCIDENCE/PREVALENCE

Most common in breeding kennels, animal shelters, pet stores, or wherever pups are reared. Rates vary.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog

Breed Predilections

Certain breeds have been shown to be at increased risk for severe CPV enteritis, including rottweiler, doberman pinscher, American pit bull terrier, Labrador retriever, German shepherd, and Yorkshire terrier. A recent Australian study demonstrated higher case fatality rates in hounds, gundogs and non-sporting pedigree groups than in mixed breed dogs.

Mean Age and Range

- Illness may occur at any age.
- Most severe illness occurs in pups 6–24 weeks of age.

Predominant Sex

None

SIGNS

General Comments

Suspect CPV-2 infection whenever pups have an enteric illness, especially with sudden onset lethargy, vomiting, and/or diarrhea.

Historical Findings

- Sudden onset of bloody diarrhea, anorexia, and repeated episodes of vomiting.
- Rapid weight loss.
- Some pups may collapse in a shock-like state and die without enteric signs.
- In breeding kennels, several littermate pups may become ill simultaneously or within a short period of time.
- Occasionally, one or two pups in a litter have minimal or no signs, followed by the death of littermates that presumably encounter greater amounts of virus.

Physical Examination Findings

- Dehydration, weight loss and abdominal discomfort are consistent features.
- Often there is severe hemorrhagic diarrhea.
- Fluid-filled intestinal loops may be palpated.
- Occasionally enlarged mesenteric lymph nodes are palpable.
- May have fever or hypothermia.

CAUSES

Canine parvovirus

RISK FACTORS

- Unvaccinated dogs from kennels, animal shelters, pet shops, or elsewhere where dogs have congregated.
- Pups < 4 months of age are at higher risk of severe infection.
- Co-pathogens such as parasites, viruses, and certain bacterial species (e.g., *Campylobacter* spp., *Clostridium* spp.) are hypothesized to exacerbate illness.
- Severe, often fatal, parvoviral infections have been demonstrated in pups exposed simultaneously to CPV-2 and canine coronavirus.
- Crowding and poor sanitation increases the risk of infection.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Canine coronavirus infection
- Salmonellosis; colibacillosis; other enteric bacterial infections
- Gastrointestinal foreign bodies
- Gastrointestinal parasites
- Hemorrhagic gastroenteritis
- Intussusception
- Toxin ingestion

CBC/BIOCHEMISTRY/URINALYSIS

- Lymphopenia—characteristic of CPV-2 infection; commonly occurs between PI days 4–6.
- Severely affected dogs often exhibit severe neutropenia concurrently with the onset of intestinal damage.
- Hemograms are an important part of the diagnostic regimen.
- Leukocytosis is common during recovery.
- Serum chemistry profiles help assess electrolyte disturbances (especially hypokalemia), the presence of azotemia associated with dehydration, panhypoproteinemia, and hypoglycemia.

OTHER LABORATORY TESTS

Serologic tests are not diagnostic because dogs often have high titers from vaccination and/or maternal antibodies.

IMAGING

- Abdominal radiographs often reveal generalized small intestinal ileus; exercise caution to prevent misdiagnosis of an intestinal obstruction.
- Typical ultrasonographic changes include fluid-filled, atonic small and large intestines; duodenal and jejunal mucosal layer thinning with or without indistinct wall layers and irregular luminal-mucosal surfaces; extensive duodenal and/or jejunal hyperechoic mucosal speckling; and duodenal and/or jejunal corrugations.
- Intussusceptions can also occur.

DIAGNOSTIC PROCEDURES

- May detect virus antigen in stool or intestinal contents at the onset of disease and for 2–4 days afterward by use of commercial solid phase ELISA assays in which sensitivity and specificity appear high.
- Electron microscopy is another method of detecting fecal virus during the early stages of infection.
- Samples for virus detection should be submitted during the acute phase of infection; ship specimens refrigerated, not frozen.

PATHOLOGIC FINDINGS

- Gross changes include subserosal congestion and hemorrhage or frank hemorrhage into the small intestinal lumen.
- Some dogs exhibit intestines that are empty or contain yellow or blood-tinged fluid.
- Mesenteric lymph nodes are often enlarged and edematous, with hemorrhages in the cortex.
- Thymic atrophy is common in young dogs.
- Pulmonary edema and hydropericardium may be the only gross change in pups with myocarditis and acute heart failure.
- Histopathology reveals

(CONTINUED)

CANINE PARVOVIRUS INFECTION

C

intestinal inflammation and necrosis, with severe villus atrophy.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Symptomatic and supportive (refer to sections on treatment of acute vomiting, acute diarrhea, and hemorrhagic gastroenteritis). Therapies include intravenous fluids, antibiotics, antiemetics and analgesics.
- Intensity depends on the severity of signs on examination. • Goals are to provide intestinal nutrients, restore and maintain fluid and electrolyte balance, and resolve shock, sepsis and endotoxemia. • Prompt, intensive in-patient care leads to treatment success.
- Proper, strict isolation procedures are essential. • Exercise care to prevent the spread of CPV-2, a very stable virus.

NURSING CARE

- Hospitalize patients and monitor for dehydration and electrolyte imbalance.
- Fluids are usually supplemented with potassium chloride, 5% dextrose, and possibly sodium bicarbonate (if severe metabolic acidosis).

ACTIVITY

Restrict until symptoms abate.

DIET

Puppies receiving early enteral nutrition via a nasoesophageal tube, compared to puppies that received nil PO until vomiting cease, show earlier clinical improvement, significant weight gain, as well as improved gut barrier function, which could limit bacterial or endotoxin translocation.

CLIENT EDUCATION

- Inform about the need for thorough disinfection, especially if other dogs are on the premises. Strict sanitation is essential. • A 1:30 dilution of bleach (5% sodium hypochlorite) destroys CPV-2 in a few minutes. • If possible, isolate pups until they reach 3 months of age and vaccinate repeatedly; typical protocol involve vaccination at 6, 9, and 12 weeks of age.
- Pups can be infected with virulent virus before any vaccine will engender immunity.
- CPV-2 is shed for less than 2 weeks after infection; no carrier state has been substantiated.

SURGICAL CONSIDERATIONS

- Exercise caution to prevent misdiagnosis of an intestinal obstruction, especially if vomiting is the only clinical sign. • Although uncommon, intussusceptions can occur.

**MEDICATIONS**

Refer to sections on treatment and management of acute vomiting, acute diarrhea, and hemorrhagic gastroenteritis.

DRUGS OF CHOICE

Additional recommended drugs include parenteral antibiotics (ampicillin and gentamicin) and antiemetics (e.g., ondansetron, maropitant).

PRECAUTIONS

Gentamicin can cause renal toxicity in dehydrated puppies.

**FOLLOW-UP****PATIENT MONITORING**

There seems to be an increased incidence of discospondylitis in pups that had parvovirus infection.

PREVENTION/AVOIDANCE

- Inactivated and live vaccines are available for prophylaxis and vaccines differ in their capacity to immunize pups with maternal antibodies. • Results of a recent study indicated that vaccination with a modified live vaccine at 4 weeks of age in pups with high maternally-derived antibody concentrations resulted in seroconversion rates of up to 80% that may lead to a reduction in the window of susceptibility with respect to CPV infection and might be used as an adjunct control method in contaminated environments. • Control of CPV-2 requires efficacious vaccines, isolation of puppies, and stringent hygiene.

POSSIBLE COMPLICATIONS

- Septicemia/endotoxemia • Secondary bacterial pneumonia • Intussusception • Discospondylitis

EXPECTED COURSE AND PROGNOSIS

• Prognosis is guarded in severely affected puppies. • Prognosis is good for dogs that receive prompt initial treatment and survive the initial crisis of illness—approximately 80% survival rate. • A patient is likely to have a poor prognosis if it is purebred, has a low bodyweight, and, after 24 hours of intensive therapy, the following biomarker levels are present: severe persistent leuko- and lymphopenia, a persistently elevated or rising serum cortisol concentration ($> 8.1 \text{ ug/dL}$), severe hypothyroxinemia ($< 0.2 \text{ ug/dL}$), hypocholesterolemia ($< 100 \text{ mg/dL}$), and persistently elevated serum CRP ($> 97.3 \text{ mg/L}$) and/or TNF concentrations.

• Conversely, the literature would suggest that puppies with a good prognosis are those that are of mixed breed, > 6 months old, and show the following biomarker values: total leukocyte count $> 4.5 \times 10^3/\mu\text{L}$, lymphocyte

count $> 1 \times 10^3/\mu\text{L}$, and mature neutrophil count $> 3 \times 10^3/\mu\text{L}$, all associated with a 100% survival when measured at 24 hours post-admission; a serum cortisol $< 8.1 \text{ ug/dL}$ is associated with a 96% survival when measured at 48 hours after admission and a serum thyroxine concentration $> 0.2 \text{ ug/dL}$ associated with 100% survival when measured at 24 hours after admission as well as a HDL-cholesterol of $> 50.2 \text{ mg/dL}$ is associated with a 100% survival when measured at admission.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Coinfection with intestinal helminths and *Giardia* are indicative of unhygienic housing conditions and can worsen the clinical picture and contribute to morbidity if not treated.

AGE-RELATED FACTORS

Infection is less likely in dogs older than 1 year of age, but can still occur, especially if the dogs are unvaccinated.

ZOONOTIC POTENTIAL

Parvovirus per se is not zoonotic, but these puppies may harbour coinfections with *Giardia* parasites which can be zoonotic.

PREGNANCY/FERTILITY/BREEDING

Pregnant animals are likely to abort due to the septicemia.

SEE ALSO

- Canine Coronavirus Infections • Diarrhea, Acute • Gastroenteritis, Hemorrhagic • Sepsis and Bacteremia • Shock, Septic • Vomiting, Acute

ABBREVIATION

ELISA = enzyme-linked immunosorbent assay

Suggested Reading

Mohr AJ, Leisewitz AL, Jacobson LS, Steiner JM, Ruaux CG, Williams DA. Effect of early enteral nutrition on intestinal permeability, intestinal protein loss, and outcome in dogs with severe parvoviral enteritis. J Vet Intern Med 2003; 17: 791–798.

Schoeman JP, Goddard A, Hertrage ME. Serum cortisol and thyroxine concentrations as predictors of death in critically ill puppies with parvoviral diarrhea. J Am Vet Med Assoc 2007; 231:1534–9.

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**Client Education Handout
available online**

C CANINE SCHISTOSOMIASIS (HETEROBILHARZIASIS)



BASICS

OVERVIEW

- *Heterobilharzia americanum* schistosomatid parasite of raccoons.
- Eggs passed in the feces of raccoons hatch to release miracidia that penetrate freshwater snail hosts. After a period of development and asexual multiplication, the snails release cercariae that infect the next host (can be dogs) by skin penetration. After penetrating the skin, the larvae undergo a migration to the lung and then make their way to the mesenteric veins, where separate males and females form pairs. Eggs laid by female worms are carried to the intestinal wall, where they erode their way through to the lumen to be passed in the feces. Other eggs are carried to the liver or other organs by the bloodstream, where they lodge and cause granulomatous disease.
- Dogs infected when in contact with freshwater containing cercariae.
- Restricted to raccoons in southeastern United States; canine cases reported from Kansas, North Carolina, Florida, Louisiana, and Texas.

SIGNALMENT

Dogs, typically adult, that have access to swampy areas or bayous.

SIGNS

- Lethargy (most common sign), weight loss, and decreased appetite are the most common sign at presentation.
- Other signs include vomiting, diarrhea, anorexia, and polyuria/polydipsia; more rarely melena and borborygmus.

CAUSES & RISK FACTORS

Swimming in freshwater in areas contaminated with cercariae from miracidia.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Coccidiosis
- Bacterial diarrhea
- Viral enteritis

CBC/BIOCHEMISTRY/URINALYSIS

- Mild anemia and eosinophilia
- Proteinuria
- Hypercalcemia

OTHER LABORATORY TESTS

ELISA—performed by private laboratory, College of Veterinary Medicine, North Carolina State University.

IMAGING

Contrast radiographs and ultrasound may reveal thickened bowel walls; calcified eggs disseminated into tissues may give the false impression of soft-tissue mineralization.

DIAGNOSTIC PROCEDURES

- Eggs with miracidia can be identified in feces, but feces must be kept in saline—not water—or miracidia will spontaneously hatch, making diagnosis impossible.
- Fecal sedimentation methods are preferred to fecal flotation. Routine fecal flotation will not detect these heavy eggs; if used, requires flotation with sugar solution of specific gravity 1.3.
- Several cases have been diagnosed after laparotomy.
- PCR on feces for DNA detection (Texas A&M Gastrointestinal Laboratory).



TREATMENT

Inpatient care for the first few days of treatment is probably warranted, as the response to worm kill may require supportive care.



MEDICATIONS

DRUG(S)

- Praziquantel (50 mg/kg, PO, once)
- Fenbendazole (50 mg/kg PO q24h for 10 days)



FOLLOW-UP

Check feces after 12 months to ensure that it does not contain eggs.



MISCELLANEOUS

In Japan and other countries with endemic *Schistosoma japonicum*, dogs can be infected with this human and zoonotic species.

ZOONOTIC POTENTIAL

Stages in the dog pose no threat to staff or owners. People entering the same waterways could develop lesions.

SYNONYM

Schistosomiasis

ABBREVIATION

ELISA = enzyme-linked immunosorbent assay

Suggested Reading

Fabrick C, Bugbee A, Fosgate G. Clinical features and outcome of *Heterobilharzia americana* infection in dogs. J Vet Intern Med 2010, 24:140–144.

Flowers JR, Hammerberg B, Wood SL, et al. *Heterobilharzia americana* infection in a dog. J Am Vet Med Assoc 2002, 220:193–196.

Author Dwight D. Bowman

Consulting Editor Stephen C. Barr

CAPILLARIASIS (PEARSONEMA)



BASICS

OVERVIEW

- *Pearsonema* and *Capillaria* are used interchangeably and appear to be identical in taxonomy and biologic behavior.
- *Pearsonema (Capillaria) plica* are small, thread-like, yellowish parasites that invade the mucosa or submucosa of the bladder and rarely the renal pelvis and ureter causing a mild inflammatory response.
- *P. plica* in dogs and cats and *P. feliscati* in cats have been uncommonly associated with signs of lower urinary tract disease.
- *P. plica* passes ova with bipolar plugs in urine. After earthworms ingest embryonated ova, the parasite develops into the infective stage. Ingestion of an infective earthworm results in a patent infection in dogs in 58–88 days. Some investigators have provided evidence of a direct life cycle.
- The life cycle of *P. feliscati* is poorly understood.

SIGNALMENT

- Dogs—no predilection reported. Reported in dogs, foxes, coyotes, raccoons, martens, mink, badgers, otters, bobcats, weasels, and wolves.
- Cats—affected cats almost always > 8 months old.

SIGNS

- Usually none.
- Pollakiuria, hematuria, stranguria, and dysuria in heavily infected animals.

CAUSES & RISK FACTORS

Dogs

- High prevalence of infection (up to 50%) in the natural hosts (e.g., foxes, raccoons) in the southeastern United States may predispose animals in this geographic region.
- In kennels, high infection rates are associated with contaminated soil surfaces.

Cats

Rare in United States; infection prevalence of 18–34% is reported in Australia.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Consider other, more common causes of lower urinary tract disease, such as urolithiasis, urinary tract infection, trauma, and neoplasia.

CBC/BIOCHEMISTRY/URINALYSIS

- Colorless, slightly pitted ova with bipolar plugs in urine sediment are diagnostic.
- Consider the possibility of fecal contamination of urine with *Trichuris vulpis* or other morphologically similar ova if free-catch urine specimens are used, or if inadvertent rectal puncture and aspiration of feces with *T. vulpis* occurs during cystocentesis.
- Alternatively, in an affected animal, urine contamination of feces can produce false fecal examination findings.
- Symptomatic infections are usually associated with evidence of inflammation (red blood cells, white cells, and proteinuria). Bacterial urine cultures are typically sterile.

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Infection is usually self-limiting in both cats and dogs.
- If infected dogs are isolated, after 10–12 weeks ova are no longer detectable in the urine sediment.
- Replacing soil surfaces with sand, gravel, or concrete may reduce prevalence of infection in kennels contaminated with *P. plica* and *P. feliscati*.



MEDICATIONS

DRUG(S)

- Consider anthelmintic therapy if clinical signs are present and persist; monitor therapeutic success by examining urine sediment for ova and observing status of clinical signs.
- Multiple courses of treatment may be necessary to eliminate the infection.

- Fenbendazole (50 mg/kg PO q24h for 3 days) has been reported to result in disappearance of ova from urine sediment in dogs and cats.

- Ivermectin (0.2 mg/kg SC once) has been suggested as an alternative therapy, but objective information on its efficacy in this disease is limited.
- Oral treatment with albendazole (50 mg/kg PO q12h for 30 days) was reported to be effective in dogs.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- Monitor treatment success by examining urine sediment for ova and observing status of clinical signs.
- In the absence of reinfection, urinary capillariasis may be self-limiting. Therefore, isolation of dogs and cats from earthworms should be sufficient to eliminate a *Capillaria* bladder infection in 90 days.



MISCELLANEOUS

PUBLIC HEALTH RISK

Capillaria spp. pose no known public health risks.

SYNONYMS

Pearsonema

INTERNET RESOURCES

Companion Animal Parasite Council:
<http://www.capcvet.org>

Suggested Reading

Brown SA, Prestwood KA. Parasites of the urinary tract. In: Kirk RW, ed., Current Veterinary Therapy IX. Philadelphia: Saunders, 1986, pp. 1153–1155.

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CAR RIDE ANXIETY—DOGS AND CATS



BASICS

DEFINITION

Car ride anxiety is excessive or disruptive distress, fear or panic associated with vehicle travel. Anxiety exhibited during travel can be mistaken for excitement or enthusiasm.

PATHOPHYSIOLOGY

The pathophysiology of car ride anxiety is often unknown or cannot be definitively determined. Lack of car ride experiences, generalized anxiety disorder or lessons learned from previous experiences; underlying nausea, a traumatic event during travel (e.g., accident or storms) or experiences with poor drivers during a car ride can result in acute or chronic car ride anxiety.

SYSTEMS AFFECTED

- Behavioral
- Gastrointestinal
- Neuromuscular

GENETICS

May be a genetic basis but early experience is probably the more significant contributor.

INCIDENCE/PREVALENCE

The incidence/prevalence of car ride anxiety is unknown and may be underreported. Owners may desire to take pets to destinations (e.g., veterinary visits, grooming, boarding, or training) but anxiety may prevent travel, even for important medical care.

SIGNALMENT

Dog and cat

Breed Predilections

None

Mean Age and Range

Any. Young or ill animals may be predisposed to motion sickness.

Predominant Sex

None

SIGNS

Historical Findings

- Signs of fear and anxiety vary between individuals.
- Frequent owner complaints include: pacing, restlessness, inappetance, vigilance, excitability and vocalization.
- Distress vocalization by dogs may include whining or high-pitched barking.
- Cats may growl, hiss, meow or yowl.
- Locomotion signs of fear and anxiety vary between individuals: some animals may pace while another may remain immobile. Immobility should not be mistaken for calmness.
- Owner reports may not identify all symptoms of anxiety and those that interfere with the driver may be reported more than those symptoms that result in freezing.
- Owners may report their cat's troublesome behaviors such as vocalization, vomiting, or

elimination in the carrier while overlooking the association with car ride anxiety.

- Owners often transport cats in carriers, so severe anxiety that manifests as freezing may be under recognized. Similarly, a large dog pacing or panicking in a car might draw more attention while even severe anxiety displayed by a small dog may be under recognized.

Physiologic and physical signs

Physiologic signs include panting, rapid heart rate, drooling, urination, vomiting, and defecation.

Physical Examination

No abnormal findings unless underlying medical problems

CAUSES AND RISK FACTORS

- Behavioral causes for car ride anxiety include: unruliness, limited prior experience outside the home; inadequate prior experience traveling; insufficient adaptation to carriers, leashes or restraint devices; fear and reactivity to visual stimulus such as people, animals, bikes or cars; and generalized anxiety.
- Prior stressful car rides or fearful consequences such as veterinary visits or shelter relinquishment may contribute to learning and exacerbate car ride anxiety.
- Traumatic events such as sudden stops or car accidents.
- Medical conditions may influence progression or manifest as car ride anxiety. Motion sickness, musculoskeletal pain or discomfort, osteoarthritis, dental disease or pain, gastrointestinal upset, and sensory hypersensitivity may all exacerbate travel anxiety.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Fear and anxiety-related behaviors.
- Manifestation of pain, nausea or physical discomfort.
- Acute onset or abrupt change in car ride anxiety warrants a complete physical examination to consider possible contributory medical conditions.

CBC/BIOCHEMISTRY/URINALYSIS

Only if indicated by clinical signs

IMAGING

Only if indicated by clinical signs

OTHER LABORATORY TESTS

Only if indicated by clinical signs



TREATMENT

ACTIVITY

Normal. Recommend adequate exercise and play before car ride.

DIET

- Normal.
- Provision of highly palatable foods during car travel may distract, reduce stress, and promote a positive association with car travel.
- If the pet has experienced nausea or vomiting in association with car travel then fasting is recommended.

CLIENT EDUCATION

A complete behavior program includes environmental management, anxiety reduction and behavior modification.

Compassion

Give thoughtful preparation and consideration for the pet's perspective before traveling. Avoid reprimands or scolding for fear-related behaviors. Allow enough time for travel and be patient. Anticipate and avoid evoking the pet's fears to prevent exacerbating established fears. For example: when carrying a pet inside a carrier, consider their view point and the unsettling motion which may be experienced. Avoid forcing a crated animal to be adjacent to an animal which may show aggression.

Management and safety

Provide stable footing and secure resting locations. Consider crating if pet is already acclimated to crate confinement. Seat belts, barriers and seat slings can also be beneficial. Unruly, hypervigilant or excitable dogs may benefit from a head halter or front attaching body harness. Animals should never receive corrections from shock, prong, or choke collars while traveling.

Anxiety reduction

Multimodal comforting and anxiolytic support provides the best outcome. Restricting views using window shades, covered crates or solid wall carriers may alleviate visual reactivity. The effect of visual stimuli may be reduced by use of a ThunderCap, a sheer panel of fabric which is worn over the cat's or dog's eyes to filter visual stimuli. Some dogs may wear Doggles to reduce the impact of visual stimuli. Psychoacoustically designed music (e.g., Through a Dog's Ear; Through a Cat's Ear) utilizes principle of simple sound intentionally selected, arranged and recorded to provide useful auditory assimilation. Classical music may also be calming. Music therapy may also obscure perception of fear-evoking sounds. Comforting pressure wraps apply a gentle, constant pressure on a dog's torso (e.g., Anxiety Wrap, ThunderShirt) which may alleviate anxiety. Synthetic pheromone analogues (Adaptil, Feliway) may also reduce anxiety. Anxiety-reducing supplements or medications should be considered, especially for severe or persistent anxiety.

Behavior modification

Rehearse settle and relax positions when not traveling. Teach the dog to get in and out of the car by positive reinforcement (e.g., food

(CONTINUED)

CAR RIDE ANXIETY—DOGS AND CATS

Table 1

	<i>Canine</i>	<i>Feline</i>
Alprazolam	0.02–0.1 mg/kg PO q6–12h	0.025–0.1 mg/kg PO q8–24h
Diazepam	0.5–2 mg/kg PO PRN (e.g., q 6h)	0.2–0.5 mg /kg PO q8–12h
Clonazepam	0.1–1.0 mg/kg PO q8–12h	0.02–0.2 mg/kg PO q12–24h
Clorazepate	0.55–2.2 mg/kg PO q8–24h	0.2–0.5 mg/kg PO 12–24h
Lorazepam	0.025–0.2 mg/kg PO q24h to PRN	0.025–0.05 mg/kg PO 12–24h
Midazolam	up to 0.2 mg/kg IV, IM, SC	up to 0.2 mg/kg IV, IM, SC
Oxazepam	0.2–1 mg/kg PO q12–24h	0.2–0.5 mg/kg PO 12–24h

or toy reward). Teach cats and small dogs to go in and out of carriers willingly. Practice training sessions when travel is not imminent. Use positive reinforcement training methods and avoid reprimand or intimidation training. Cats and small dogs should be acclimated to the motion of being in a carrier that is being carried. During travel, provide comforting activities: chew toys, food chews or feeding puzzles. These activities may distract the pet, reduce anxiety or even countercondition the pet to enjoy car rides.



MEDICATIONS

DRUG(S) OF CHOICE

General Comments

- Psychotropic medications, supplements or pheromones may be a beneficial or even a necessary adjunct to the behavior program. Short-acting anxiolytics are appropriate for pets travelling occasionally. Administer anxiolytics such that optimal effect precedes the onset of mild to moderate anxiety and distress. The effect of all anxiolytics may be overcome by severe anxiety or distress. Extreme distress may not be completely manageable by medication. Low doses for mild anxiety may be very safe, but high or repeated doses, extreme anxiety, and other medical conditions increase the risk for profound sedation and drug interactions.
- Correction based training or management strategies such as verbal reprimands, shock collars and other forms of punishment should not be utilized in conjunction with anxiolytic medications.
- Address concurrent behavioral conditions (e.g. Separation Distress Syndrome; Fears, Phobias, and Anxieties) that may warrant longer-acting anxiolytics (e.g. TCAs or SSRIs) to treat pets with multiple manifestations of anxieties in addition to travel-related anxiety. See Table 1.

Benzodiazepines

- Potentiate the effects of GABA an inhibitory neurotransmitter.

- Give 30–60 minutes prior to travel and titrate to effect with future travel based on therapeutic response as time to onset, dose, and duration of effect will vary.
- Side effects might include sedation, hyperphagia, muscle relaxation, and an amnesia effect.
- An amnesia effect may be desirable for traumatic car rides but may interfere with learning during purposeful behavior modification sessions.
- Hyperphagia may be advantageous for pets with stress anorexia especially if food is offered as part of the behavior modification program.
- Clonazepam, oxazepam, and lorazepam have no active intermediate metabolites and may be safer when hepatic function is compromised. Midazolam is available as injectable medication that may be useful if administered when the pet is leaving the veterinary hospital and rapid onset is desired.

Maropitant

- NK-1 neurokinin receptor antagonist.
- Canine dose for motion sickness: 8 mg/kg PO 2 hours before travel every 24 hours for up to 2 days in a row. The dose for motion sickness is higher than the antiemetics dose. Fast 1 hour prior to administration. Avoid high fat foods.
- Feline dose for emesis: 1 mg/kg SC daily for up to 5 days.

Trazodone

Serotonin receptor antagonist and reuptake inhibitor (SARI). Dog: 2–10 mg/kg PO. Begin at 2–5 mg/kg and titrate upward to 5–10 mg/kg based on effect and tolerance. Even higher doses may be utilized by experienced clinicians. Absorption is more rapid in fasted subjects, with peak blood concentrations occurring approximately 1 hour after administration versus 2 hours with food.

Acepromazine

- Antipsychotic.
- Dog and cat: 0.55–2.2 mg/kg PO. Sedative but not anxiolytic. Consider combination with an anxiolytic (e.g., a benzodiazepine, pheromones).
- Poor choice for monotherapy.

Pheromone

Feliway or Adaptil sprayed onto a blanket or into the pet's carrier.

Natural supplements

- Anxitane, Composure, Harmonease, and Zylkene may exert an anxiolytic effect.
- Lavender essential oils may have a calming effect in dogs but avoid lavender for cats since floral scents may be aversive to cats.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Caution should be used when combining drugs that enhance serotonin transmission (e.g trazodone, SSRIs, TCAs) which may pose an increased risk for serotonin syndrome.

PRECAUTIONS

- All listed medications are considered extra-label or off-label (except Cerenia).
- Benzodiazepines: May cause sedation, paradoxical excitability, incoordination and amnesia that might interfere with learning during behavior modification. Diazepam has been associated with acute liver failure in rare cases in cats.
- Trazodone: Potential adverse effects: sedation; lethargy; incoordination; cardiac conduction disturbances; increased anxiety.
- Clonidine: Use with caution in patients with cardiac disease or compromised liver or kidney function.
- Acepromazine: ataxia, inhibits thermoregulation, peripheral vasodilation, muscle tremor or spasm, decreased social behaviors.

ALTERNATIVE DRUG(S)**Clonidine**

- An alpha-2 agonist, antihypertensive agent, which might be used alone or together with ongoing medications such as an SSRI or a TCA, in the treatment of anxiety.
- Dog: 0.01–0.05 mg/kg PO. Begin at low dose and titrate to the most effective dose if not sufficiently effective. Maximum effect may take one-half to two hours with faster absorption on an empty stomach.
- Cat: Dose not established.

CAR RIDE ANXIETY—DOGS AND CATS

(CONTINUED)

Trazodone

Cats: Although not extensively evaluated, trazodone dosing for cats of 25–100 mg/cat may warrant consideration for car travel.

**FOLLOW-UP****PATIENT MONITORING**

Ask about travel-related distress as part of overall wellness assessment, and recommend early intervention and prevention.

Travel-related difficulties pose a barrier for bringing pets to the veterinary hospital.

PREVENTION/AVOIDANCE

May be necessary to avoid travel for severely affected pets.

EXPECTED COURSE AND PROGNOSIS

May habituate spontaneously but more likely to worsen if untreated.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Generalized anxiety disorder, noise-related fears and phobias, separation anxiety related distress, hyper attachment.

AGE-RELATED FACTORS

Cognitive decline may exacerbate anxiety.

ZOONOTIC POTENTIAL

A distressed pet may cause distraction and put drivers at risk for automobile accidents.

PREGNANCY/FERTILITY/BREEDING

Drug use in breeding, pregnant or lactating animals should be avoided. Distress during pregnancy may adversely affect the neurologic development of the unborn offspring.

SEE ALSO

- Fear and Aggression of Veterinary Visits
- Fears, Phobias, and Anxieties
- Separation Distress Syndrome

ABBREVIATIONS

- GABA = gamma aminobutyric acid
- SSRI = selective serotonin reuptake inhibitors
- TCA = tricyclic antidepressant

INTERNET RESOURCES

Tips for taking your cat to the veterinarian: www.catalystcouncil.org/resources/video

Suggested Reading

Landsberg GM, Hunthausen WL, Ackerman LJ, Behavior Problems of the Dog and Cat. Edinburgh: Saunders/Elsevier, 2013.

Author Theresa L. DePorter

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CARBON MONOXIDE TOXICOSIS



BASICS

OVERVIEW

- Carbon monoxide (CO)—odorless, colorless, non-irritating gas produced by inefficient combustion of carbonaceous fuels.
- Common sources are fires, automotive exhaust, and leaking coal, oil, or natural gas/propane furnaces, gas appliances or fireplaces, and some paint strippers or paint sprays. • Absorbed into the blood, forming carboxyhemoglobin (COHb) and reducing blood oxygen, causing hypoxia of brain and heart. • Lethal concentration is approximately 1,000 ppm (0.1%) for 1 hour. • Affinity of CO for hemoglobin is approximately 240 times that of oxygen. • Carboxyhemoglobin cannot bind oxygen and impairs release of oxygen from remaining hemoglobin. • Major effect is acute cellular hypoxia leading to death. • Survivors may have cardiac necrosis, brain damage, or delayed neurotoxicity.

SIGNALMENT

- Dogs and cats are equally susceptible.
- Exposures from fossil fuel heater malfunction, radiant heaters, gas/wood fireplaces or stoves may affect humans and pets living in the same space. • Other high-risk areas are kennels using unvented gas or kerosene heaters in poorly ventilated buildings, and transport in vehicles with exhaust leaks.

SIGNS

Historical Findings

- Exposure to automobile exhaust indoors or fumes from indoor carbon-based fuel heating devices for 5–10 minutes. • Building fires produce high concentrations of CO that cause death quickly.

Physical Findings

Acute Exposure

- Acute signs progress within minutes to hours and include drowsiness, lethargy, decreased mentation, and weakness.
- Tachycardia and tachypnea commonly occur. • Dyspnea and clonic seizures can precede depression. • Deafness, incoordination, and coma signal fatal outcome. • Hypotension, arrhythmia, premature ventricular contractions, and acidosis develop. • Red skin and mucous membranes are rarely apparent in animals.

Chronic Exposure

- Chronic exposure can cause nausea, vomiting, acidosis, and cough; may mimic “flu” or infectious disease. • Low exercise tolerance. • Disturbance of postural and position reflexes and gait also follow chronic moderate exposure. • Deafness of variable persistence may occur in survivors.

CAUSES & RISK FACTORS

- Incomplete combustion of carbon fuels.
- Poor ventilation or blocked exhaust vents or chimneys. • Automobile exhaust in closed spaces. • Unvented/faulty furnaces, gas appliances, kerosene space heaters.
- Fires—carbon monoxide may reach 10% inside a burning building. • Animals with impaired cardiac or pulmonary function.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Barbiturate, ethanol, ethylene glycol, petroleum hydrocarbons, lead poisoning; cyanide, or hydrogen sulfide gas toxicosis
- Smoke inhalation, cerebral hemorrhage or neoplasia, and metabolic disease.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC, serum biochemistry profile, urinalysis, blood gases, and anion gap.
- Creatine kinase—high due to muscle ischemia. • ECG. • Pulse oximetry may overestimate saturated hemoglobin because carboxyhemoglobin and oxyhemoglobin absorb light at the same wavelength.

OTHER LABORATORY TESTS

- Carboxyhemoglobin percentage in whole blood; may return to normal levels within a few hours after carbon monoxide exposure stops. Know advance location of a carboxyhemoglobin lab, either human or veterinary. • Blood pH is lower than normal due to metabolic acidosis. • Acidemia and increased lactate in blood. • Pa_O₂—normal, but not indicative of oxyhemoglobin saturation.

DIAGNOSTIC PROCEDURES

ECG—ST-T wave changes consistent with myocardial hypoxia/anoxia may be present.



TREATMENT

- Restore adequate oxygen to brain and heart.
- Supplemental 100% oxygen via endotracheal tube—promotes four-fold faster recovery against ability of CO to bind haemoglobin. • Eucapnic hyperoxic hyperpnea has been used to increase CO elimination by two to three fold more than 100% oxygen at normal breathing rate. Hyperbaric oxygen is not generally available for veterinary use. • Rapid therapy is important to avoid permanent damage to the CNS (malacia, demyelination) and cardiac muscle necrosis. • Provide fresh air and provide artificial respiration if necessary.
- Supportive fluids to correct acidosis and maintain blood flow and perfusion of brain.



MEDICATIONS

DRUG(S)

Prompt 100% oxygen therapy.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Avoid respiratory depressants. • Limit 100% oxygen to < 18 hours to avoid oxygen toxicosis. • Monitor for delayed neurotoxicity.



FOLLOW-UP

- Significant response to therapy—expected in 1–4 hours, depending on damage from hypoxia. • Signs persisting for 24 hours or more suggest a poor prognosis. • Monitor cardiac, pulmonary, neurologic function; limit physical activity for 2 weeks. • Eliminate source of carbon monoxide; recommend in-home CO detectors.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Humans in the same CO-contaminated environment are at risk.

PREGNANCY/FERTILITY/BREEDING

- CO—reduces oxygen-carrying ability of maternal blood, producing fetal hypoxia, abortion, or neurologic impairment of the fetus. • Pregnant animals in late gestation abort dead fetuses with only minimal effects in the dam.

ABBREVIATIONS

- CNS = central nervous system • CO = carbon monoxide • ECG = electrocardiogram

Suggested Reading

- Berent AC, Todd J, Sergeeff Jet al. Carbon monoxide toxicity: A case series. *J Vet Emerg Crit Care* 2005, 15(2):128–135.
Fitzgerald KT. Carbon monoxide. In: Peterson ME, Talcott PA, eds. *Small Animal Toxicology*, 3rd ed. St. Louis, MO: Elsevier:Saunders, 2013, pp. 479–487.
Powell LL. Carbon monoxide. In: Osweiler GD, Hovda LR, Brutlag AG, Lee JA, eds. *Blackwells Five Minute Veterinary Consult: Small Animal Toxicology*. Ames, IA: Wiley-Blackwell, 2011, pp. 801–804.
Author Gary D. Osweiler
Consulting Editor Lynn R. Hovda

CARCINOID AND CARCINOID SYNDROME



BASICS

OVERVIEW

• Siegfried Oberndorfer coined the term karzinoide ("carcinoma-like") in 1907 to describe a gastrointestinal tumor in a human with the unique feature of behaving like a benign tumor. Carcinoid tumors are neuroendocrine tumors that arise from amine precursor uptake and decarboxylation (APUD) cells. • The origins of carcinoids are most commonly the enterochromaffin and enterochromaffin-like cells of the gastrointestinal tract, but they can also be found in the liver, tracheobronchial tree, pancreas, and genitourinary system due to embryologic origins. • Carcinoids may secrete a variety of amines such as histamine, serotonin, and peptides such as bradykinins and tachykinins. In humans, these secretory substances can cause a well-recognized "carcinoid syndrome" and/or "carcinoid crisis" in approximately 5–10% of patients with carcinoid tumors once metastasis has occurred in the liver and hepatic degradation is bypassed. The human carcinoid syndrome is most commonly characterized by flushing, abdominal pain, diarrhea, bronchospasm, and cyanosis. Domestic small animals have not been reported to date to show these clinical signs, although a dog has been recently reported to have episodic collapse and melena in association with an ileocecal carcinoid.

Morbidity and mortality are more often a function of tumor size and gastrointestinal blockage in dogs and cats with carcinoid.

- Primary carcinoid tumors have been reported in the stomach, small intestine, colon, lung, gallbladder, and liver in dogs. In cats, carcinoids have been found in the stomach, small intestine, liver, and heart.

SIGNALMENT

- Dog—rare, generally > 8–9 years of age
- Cat—rare, generally > 7–8 years of age

SIGNS

- Clinical signs generally depend on the location of the primary tumor and/or metastases and may include:
 - Anorexia ◦ Vomiting ◦ Dyschezia ◦ Melena
 - Episodic collapse ◦ Ascites ◦ Weight loss
 - Signs of hepatic failure. • Carcinoid heart disease is a syndrome in humans with advanced carcinoid syndrome that occurs due to the development of fibrotic endocardial plaques and secondary valvular dysfunction in response to excess secretion of serotonin.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentials include primary gastrointestinal diseases such as other neoplasia, infection,

inflammation, parasites, foreign body ingestion, dietary indiscretion, or liver/biliary disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Results can appear normal except for a mild anemia that is generally non-regenerative.
- Electrolyte abnormalities and elevated liver enzymes can be present depending on the location and clinical presentation.

OTHER LABORATORY TESTS

• Serum serotonin, serum chromogranin A, and urinary 5-hydroxyindoleacetic acid are measured in humans suspected of carcinoid tumors. These tests appear more diagnostic than direct measurement of serum amine and peptide levels. • Serum serotonin levels were found to be increased ten-fold in a dog with an intestinal carcinoid with multiple metastases. Other serum and urinary testing has not been documented in animals with carcinoid tumors.

IMAGING

• Ultrasound has been used to identify both primary tumors and metastases in the abdomen and the thorax of dogs and cats. • CT scans and MRI have been used with mild to moderate success for localization of carcinoids in humans. • Newer and more sensitive molecular imaging modalities include (1) radiolabeled somatostatin receptor scintigraphy ("OctreoScan"), (2) radioiodinated metaiodobenzylguanidine (MIBG) imaging, and (3) PET scans.

DIAGNOSTIC PROCEDURES

- Biopsy of the affected tissue with histopathologic examination often confirms the diagnosis. • If histopathologic results are equivocal, electron microscopy and/or immunohistochemistry (looking for chromogranin A and/or synaptophysin expression) may be used to determine the amines and peptides actively secreted to aid in the confirmation of a carcinoid diagnosis.

PATHOLOGIC FINDINGS

These tumors typically have a fine fibrovascular stroma with minimal-to-moderate cellular pleomorphism. The cytoplasm is eosinophilic and usually contains secretory granules that often stain argyrophilic and/or argentaffin-positive.



TREATMENT

In many cases, surgical excision can be curative, especially when there is no evidence of metastasis. Debulking can decrease hormone secretion in humans, and it may relieve gastrointestinal signs in animals that are obstructed because of tumor size.



MEDICATIONS

DRUG(S)

- Octreotide, a somatostatin analog, is often used in humans for palliative therapy when surgery is not an option. Octreotide inhibits hormone secretion from the tumor cells. As carcinoid syndrome does not appear to be the primary mechanism of disease in the animals that have been reported with carcinoid tumors, octreotide may be of little benefit in veterinary patients with carcinoids.
- High-dose radioiodinated MIBG is being used with moderate success in humans with non-resectable and/or metastatic carcinoid.
- Interferons have demonstrated limited success in humans with carcinoid tumors. The use of interferons for the treatment of dogs or cats with carcinoids has not been reported to date.
- Chemotherapy and radiotherapy have been reported to have minimal efficacy in humans with carcinoid tumors, as carcinoids are believed to be relatively chemoresistant and radioresistant.
- The use of adjuvant carboplatin has been reported in a dog with a completely excised non-metastatic jejunal carcinoid.



FOLLOW-UP

- Blood work should be serially monitored postoperatively to delineate destructive hepatic metastasis. • Abdominal ultrasound and three-view chest radiographs should be serially performed postoperatively to delineate liver and/or other organ metastasis.



MISCELLANEOUS

ABBREVIATIONS

- CT = computed tomography • MIBG = metaiodobenzylguanidine • MRI = magnetic resonance imaging

INTERNET RESOURCES

- www.carcinoid.com. • www.carcinoid.org.

Suggested Reading

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CARDIAC GLYCOSIDE PLANT TOXICOSIS



BASICS

OVERVIEW

- Cardiotoxic cardenolides are aglycone constituents of cardiac glycosides.
- Present the same toxic profile as digoxin, in particular cardiovascular (CV) and gastrointestinal (GI) signs.
- Over 400 different cardenolides exist with digoxin, digitoxin, and ouabain the most widely known and used.
- All plant parts, fresh or dry, are considered toxic, but the concentration of cardenolides varies depending on specific plant and plant part.
- Plants are best identified by scientific name.
- Common plants include:
 - *Adenium obesum* (desert rose)
 - *Apocynum cannabinum* (dogbane)
 - *Asclepias* spp. (milkweed)
 - *Convallaria majalis* (lily of the valley)
 - *Digitalis lanata* (woolly foxglove)
 - *Digitalis purpurea* (common or purple foxglove)
 - *Kalanchoe* spp. (mother of millions)
 - *Nerium oleander* (oleander)
 - *Ornithogalum umbellatum* (star of Bethlehem).

SIGNALMENT

- Cats are more sensitive to some of the plant toxins than dogs.
- Dogs with the ABCB1-1 Δ gene mutation may be more sensitive to toxins but this has not been well documented.

SIGNS

- CV—bradycardia (rarely tachycardia), AV block, all forms of arrhythmias, death from asystole.
- GI—hypersalivation, vomiting, diarrhea.
- Neuromuscular (NM)—coma, tremors, seizures (rarely); may be related to decreased cardiac output.

CAUSES & RISK FACTORS

- Animals with a prior history of cardiac or renal disease are at a higher risk as are those receiving digoxin or other cardiac glycoside drugs.
- Consumption of cardiac glycoside containing plants results in the release of cardiotoxic cardenolides which interfere with the ATPase sodium/potassium pump. Intracellular sodium is increased and potassium is decreased; the normal resting membrane potential of the heart is decreased and loss of normal myocardial function occurs.
- Increased intracellular (myocyte) calcium results in increased cardiac contractions.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Beta blocker or calcium channel blocker toxicosis.
- Cardiac disease in general.
- Digoxin/digitoxin toxicosis.
- Ingestion of medications with known cardiac effects.
- Ingestion of plants with known cardiac effects such as *Taxus* spp. (yew), *Rhododendron*

spp. (azalea, rhododendron), *Kalmia* spp. (mountain laurel, lambkill), and *Pieris japonica* (Japanese pieris).

CBC/BIOCHEMISTRY/URINALYSIS

Serum chemistry, hyperkalemia early and severe, may switch to hypokalemia.

OTHER LABORATORY TESTS

Serum digoxin levels may be useful in some ingestions.

DIAGNOSTIC PROCEDURES

- Presence of plant pieces in vomit or stool
- ECG monitoring for cardiac arrhythmias

PATHOLOGIC FINDINGS

Sudden death is common. Plant pieces are often found in the stomach and small intestine. Clotted blood may be present in the ventricles with a mottled appearance to the epicardium. Histopathology findings are similar to digoxin toxicosis.



TREATMENT

- Animals consuming any amount of cardiac glycoside-containing plants should be decontaminated with emesis quickly after the ingestion.
- Activated charcoal (1–2 g/kg) with a cathartic should be given as a single dose followed by activated charcoal without a cathartic every 6–8 hours for 2–3 subsequent doses.
- Asymptomatic animals should be hospitalized for 12 hours and monitored for clinical signs.
- Symptomatic animals should be monitored with an ECG for 24 hours and IV fluids administered judiciously to maintain blood pressure but not overload the CV system. Blood pressure should be monitored closely as hypotension may be persistent.
- Hyperkalemia may be severe and appropriate IV fluids chosen.



MEDICATIONS

DRUGS

- Digoxin-specific Fab fragments (Digibind) may be useful in some cases such as oleander toxicosis. The cost is often prohibitive.
- Antiemetics if vomiting is severe or persistent: Maropitant 1 mg/kg SQ q24h in dogs and cats; ondansetron 0.1–0.2 mg/kg IV q8–12h in dogs and cats.
- Bradycardia: Atropine 0.02–0.04 mg/kg IV, IM, SQ in dogs and cats. Repeat every 4–6 hours as needed.
- Antiarrhythmics may be necessary in patients that have ventricular dysrhythmias, evidence of poor perfusion, or who remain tachycardic despite IV fluid therapy. Lidocaine – dogs, 2–8 mg/kg IV to effect while continuous ECG monitoring.
- GI protectants as needed: H2 blockers such as famotidine (0.5–1 mg/kg PO, SQ, IM, IV

q12h); omeprazole (0.5 mg/kg PO daily), or sucralfate (0.25–1 g PO q8h).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Beta-blockers and calcium channel blockers may have an additive effect on AV conduction and cause complete heart block.



FOLLOW-UP

PATIENT MONITORING

- ECG strips for first 24 hours, then prn
- Frequent blood pressure monitoring • Strict attention to serum electrolytes

PREVENTION/AVOIDANCE

- Identify and recognize plants.
- Oleander grows seemingly everywhere in parts of the SW United States and off-leash dogs and cats should be monitored closely.

POSSIBLE COMPLICATIONS

Sudden death

EXPECTED COURSE AND PROGNOSIS

- Good nursing care for 5–7 days.
- Prognosis is good with early and appropriate care.
- Cardiac arrhythmias prolong treatment and hospitalization.



MISCELLANEOUS

ABBREVIATIONS

- AV = atrioventricular
- ECG = electrocardiogram
- Fab = fragment antigen binding

INTERNET RESOURCES

- <http://plants.usda.gov/java/>
- <http://www.petpoisonhelpline.com/poisons>
- <http://www.aspca.org/pet-care/animal-poison-control/toxic-and-non-toxic-plants>

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Client Education Handout
available online

CARDIOMYOPATHY—BOXER (ARRHYTHMOGENIC RIGHT VENTRICULAR)



BASICS

OVERVIEW

A myocardial disease commonly characterized by ventricular tachyarrhythmias that can be accompanied by syncope or sudden death. A small percentage (<5%) develop congestive heart failure with systolic dysfunction, comparable to the dilated cardiomyopathy observed in other breeds.

SIGNALMENT

- Dog. • Specific to the boxer, although a similar presentation is infrequently observed in the English bulldog. • Usually observed in mature dogs between 5 and 8 years of age. Dogs as young as 6 months have been reported and some affected dogs may not develop clinical signs until > 10 years of age.

SIGNS

- Usually 1 of 3 presentations:
 - Asymptomatic dog with ventricular premature complexes (VPCs) detected on routine examination.
 - Syncope with VPCs detected on an ECG or Holter monitor.
 - Signs of left heart failure (e.g., coughing, tachypnea) or biventricular failure (e.g., ascites, tachypnea, coughing) with VPCs. This presentation is the least common.
- Sudden death may occur before development of obvious clinical signs.

CAUSES & RISK FACTORS

- Adult onset, inherited (autosomal dominant). • A genetic mutation (deletion) in a cardiac desmosomal gene (Striatin) is associated with the development of the disease. Dogs that are homozygous for the striatin deletion appear to be more likely to be more severely affected with a higher number of VPCs and are more likely to have cardiac dilation and myocardial dysfunction. It is not yet known if this is the only genetic cause or if additional genetic mutations will be identified.
- At least one family of boxers with VPCs, ventricular dilation, and systolic dysfunction was found to have decreased myocardial l-carnitine levels and demonstrated some clinical improvement when supplemented with l-carnitine. The cause and effect of this relationship is unclear, and response to this supplementation does not occur in all dogs with myocardial dysfunction.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Aortic stenosis—moderate and severe forms can be associated with VPCs.
- Uncommon forms of acquired cardiac disease (neoplasia, endocarditis).
- Abdominal disease (especially splenic disease) can be associated with VPCs.
- Echocardiography and abdominal

ultrasonography can be used to differentiate other causes of cardiac and abdominal disease.

OTHER LABORATORY TESTS

- Genetic testing can now be performed to screen for the genetic mutation (<http://www.ncstatevets.org/genetics/>) associated with boxer cardiomyopathy. Submission samples can be either a blood sample in an EDTA tube or a buccal swab of the oral mucosal surface.
- Plasma l-carnitine levels may be evaluated in boxers with ventricular dilation and systolic dysfunction. However, plasma levels are not always reflective of myocardial levels. If plasma levels are not low, it is still possible to have low myocardial levels, and supplementation with l-carnitine might be considered.

IMAGING

Thoracic Radiography

- Normal in most affected dogs.
- Dogs with ventricular dilation and systolic dysfunction may have cardiac enlargement and evidence of heart failure (e.g., pulmonary edema).

Echocardiography

- Normal in most affected dogs.
- A small percentage of dogs have ventricular dilation and systolic dysfunction particularly if they are homozygous of the deletion mutation.

DIAGNOSTIC PROCEDURES

Electrocardiogram

- Many dogs will not have VPCs on an ECG of brief duration since the arrhythmia can be intermittent. However, some dogs will have one or more upright VPCs on a brief lead II ECG.
- In either case, if suspicion of disease is present, Holter monitoring is recommended to determine the severity and complexity of the arrhythmia and to have a baseline for comparison once treatment is started. If Holter monitoring is not available and the dog is symptomatic with upright VPCs on an ECG, therapy should be considered.

PATHOLOGIC FINDINGS

- Gross pathology is non-specific in most cases. In a small percentage of cases, left and right ventricular dilation may be observed.
- Histopathologic abnormalities include a fatty and fibrous infiltrate into the right ventricular (and sometimes interventricular and left ventricular) free wall.



TREATMENT

- The goals of therapy include reduction of the number of VPCs, reduction of clinical signs, and reduction of the risk of sudden cardiac death. Unfortunately, there is no evidence that therapy can reduce the risk of sudden death. The decision to start therapy in the asymptomatic boxer with VPCs is controversial, since all antiarrhythmics have the potential to make the arrhythmia worse.

However, dogs with as few as 300 VPCs/24 hours have been observed to die suddenly. In general, initiate therapy drugs if there are > 1,000 VPCs/24 hours and/or significant runs of ventricular tachycardia or other signs of arrhythmia complexity (e.g., bigeminy, couplets), or clinical signs (syncope, exercise intolerance) related to the VPCs.

- Syncope and sudden cardiac death may be more frequently associated with stress and excitement. Reduce stress and effort when possible. There is no direct relationship between exercise restriction and survivability. Some dogs die while asleep. Thus, strict exercise restriction is not recommended.



MEDICATIONS

DRUG(S)

- The two best choices for treating the ventricular arrhythmia are sotalol (1.5–3.5 mg/kg PO q12h) or mexiletine (5–6 mg/kg PO q8h). Some cases continue to have significant ventricular ectopy after treatment with one of the above; these cases seem to respond well to the combination of sotalol and mexiletine. These drugs have different mechanisms and appear to work in a safe and complimentary fashion.
- In dogs with systolic dysfunction and heart failure, consider treatment with furosemide, enalapril, pimobendan, spironolactone, and l-carnitine.

CONTRAINdications/POSSIBLE INTERACTIONS

Any antiarrhythmic drug has the potential to make an arrhythmia worse.



FOLLOW-UP

- If possible, repeat the Holter monitor 2 weeks after starting therapy to evaluate for a response. Affected dogs can have an 85% day-to-day variability in VPC number before medications; therefore, a good response to therapy would be an 85% reduction in VPC number. However it may not always be possible to achieve this reduction; in those cases an improvement in arrhythmia complexity and clinical signs would be reasonable goals.
- Annual Holter monitoring and echocardiography are suggested since in some cases the disease can be progressive.
- Advise owners that dogs are always at risk of sudden death. However, the majority of affected dogs can be maintained on antiarrhythmics for years with good quality of life. Dogs with systolic dysfunction and dilation have the worst prognosis, although some of these dogs do show improvement and a decreased rate of progression on l-carnitine supplementation.

Author Kathryn M. Meurs

CARDIOMYOPATHY, DILATED—CATS



BASICS

DEFINITION

- Dilated cardiomyopathy is a disease of the heart muscle characterized by systolic myocardial failure and a dilated, volume overloaded heart that leads to signs of congestive heart failure or low cardiac output.
- Before 1987, dilated cardiomyopathy was the second most commonly diagnosed heart disease in cats. Most cats had a secondary dilated cardiomyopathy as a result of taurine deficiency. Primary idiopathic dilated cardiomyopathy is now an uncommon cause of heart disease in cats.

PATOPHYSIOLOGY

Histopathologically, the myocardium of cats with idiopathic DCM has evidence of myocytolysis, fibrosis, myofibril fragmentation, and vacuolization. Gross examination reveals global eccentric enlargement of all four cardiac chambers. These anatomic changes are associated with progressive myocardial systolic failure, decreased contractility, decreased compliance and secondary mitral valve regurgitation due to mitral valve annular dilation. These changes are typically identified by echocardiography. Eventually, the chronic myocardial dysfunction leads to congestive heart failure and clinical signs.

SYSTEMS AFFECTED

- Cardiovascular**—DCM is a primary myocardial disease and primarily affects the heart and its ability to maintain an adequate cardiac output to maintain the body's needs.
- Musculoskeletal**—cats with DCM can present with aortic thromboembolism, which causes acute paraparesis or monoparesis.
- Renal/Urologic**—cats with DCM and congestive heart failure often have poor renal perfusion and commonly have prerenal azotemia.
- Respiratory**—cats usually present with tachypnea or dyspnea due to congestive heart failure with DCM. These cats can develop both pulmonary edema and pleural effusion.

GENETICS

Because of the human experience with DCM, it is likely that feline DCM has a genetic mutation, either inherited or de novo, as the cause of their disease. No definitive mutation has been identified in the cat to date. Additionally, a quantitative genetic evaluation of a large cattery suggested an inherited factor in the development of DCM.

INCIDENCE/PREVALENCE

Idiopathic feline DCM is relatively uncommon now that taurine is adequately supplemented in cat foods. A retrospective survey 106 cats with feline myocardial disease from 1994 to 2001 from Europe revealed that DCM was diagnosed in approximately 10%

of the cases in this series. In the author's experience, the prevalence of feline idiopathic DCM may be less than 10%.

SIGNALMENT

Species

Cat

Breed Predilections

Because the prevalence is low, breed predictions are not clearly defined. That said, the Burmese cat may have an increased incidence.

Mean Age and Range

9 years (5–13 years)

Predominant Sex

None. (One study cites a male predisposition while another states a female overrepresentation.)

SIGNS

General Comments

- Cats with idiopathic DCM usually present for signs of congestive heart failure.
- They are rarely diagnosed prior to onset of clinical signs.

Historical Findings

- Signs related to low cardiac output:
 - Anorexia
 - Weakness
 - Depression
- Signs related to congestive heart failure:
 - Dyspnea
 - Tachypnea
- Signs related to thromboembolism:
 - Sudden-onset pain and paraparesis

Physical Examination Findings

- Heart rate can be fast, normal, or slow
- Soft systolic heart murmur
- Weak left cardiac impulse
- Gallop rhythm
- Possible arrhythmia
- Hypothermia
- Prolonged capillary refill time
- Tachypnea
- Quiet lung sounds (pleural effusion)
- Crackles (pulmonary edema)
- Ascites
- Hypokinetic femoral pulses
- Possibly, posterior paresis and pain as a result of aortic thromboembolism

CAUSES

The underlying etiology of idiopathic dilated cardiomyopathy remains unknown, although a genetic predisposition has been identified in some families of cats. Taurine deficiency was a common cause of secondary myocardial failure before 1987.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Taurine deficiency dilated cardiomyopathy. Because primary idiopathic dilated

cardiomyopathy and taurine deficiency have similar clinical presentations, cats with myocardial failure should be assumed to have taurine deficiency until shown to be unresponsive to taurine.

- Myocardial failure secondary to long-standing congenital or acquired left ventricular volume overload diseases.
- End-staged remodeled hypertrophic cardiomyopathy may manifest with a dilated hypocontractile heart.
- Arrhythmogenic right ventricular cardiomyopathy.

CBC/BIOCHEMISTRY/URINALYSIS

Many cats will have prerenal azotemia related to low cardiac output.

OTHER LABORATORY TESTS

- Ensure that thyroid concentrations are normal.
- Plasma taurine concentrations less than 40 nmol/L or whole blood taurine concentrations less than 250 nmol/L are subnormal and suggestive of taurine-deficiency dilated cardiomyopathy. Taurine assays are performed at a limited number of institutions and require special handling.
- Cardiac biomarkers such as plasma amine terminal B-type natriuretic peptide (NT-proBNP) and cardiac troponin I (cTnI) concentrations would be elevated in a cat with congestive heart failure due to idiopathic dilated cardiomyopathy.

IMAGING

Radiographic Findings

- Radiography often shows pleural effusion or pulmonary edema.
- Generalized cardiomegaly.

Echocardiographic Findings

- Diagnostic modality of choice.
- Characteristic findings include thin ventricular walls, enlarged left ventricular end systolic and end diastolic dimensions, left atrial enlargement, and low fractional shortening.
- Pleural and pericardial effusion may be visualized.
- Spontaneous echocardiographic contrast or a thrombus may be visualized.

DIAGNOSTIC PROCEDURES

Electrocardiography

- Electrocardiography may be normal or may show left atrial or ventricular enlargement patterns.
- Both ventricular and supraventricular arrhythmias can be seen.

Pleural Effusion Analysis

Pleural effusion typically is a modified transudate with total protein < 4 g/dL and nucleated cell counts of less than 2,500/mL. Chylous effusion may also be present. Analysis of the pleural effusion is important to rule out other causes of pleural effusion such as pyothorax, infectious peritonitis, or lymphosarcoma.

CARDIOMYOPATHY, DILATED—CATS

(CONTINUED)

PATHOLOGIC FINDINGS

- Heart:body ratio is increased.
- All four cardiac chambers are dilated. Ventricular walls are thin and left ventricular lumen is enlarged.
- Valve anatomy is normal.
- Histopathology shows myocytolysis and myocardial fibrosis.



TREATMENT

APPROPRIATE HEALTH CARE

These cats usually present in congestive heart failure and should be treated as inpatients, typically in an intensive care setting until more stable.

NURSING CARE

- Thoracocentesis is often utilized for both therapeutic and diagnostic purposes.
- Supplemental oxygen therapy is beneficial for cats in congestive heart failure to decrease the work of breathing.
- If hypothermic, cautious external heat (incubator or heating water pad) is recommended.

ACTIVITY

Indoors only after hospital discharge to reduce stress. Let cat dictate its own activity.

DIET

These cats typically are anorexic, thus tempting their appetite with many types of food may be necessary. Eventually, a low-sodium diet is recommended.

CLIENT EDUCATION

Some cats will need chronic intermittent thoracocentesis to manage large amount pleural effusion despite medical therapy.



MEDICATIONS

DRUG(S) OF CHOICE

- Furosemide is recommended to manage pulmonary edema and pleural effusion. Recommended dose range is 1–4 mg/kg q8–12h. Initially, administer parenterally then switch to oral. Chronically the lowest effective dose of furosemide is recommended.
- Pimobendan, an inodilator, is also recommended to strengthen contractility and provide some vasodilation. Recommended dose range is 0.1–0.3 mg/kg PO q12h. Although pimobendan is not currently licensed for use in cats, several recent publications have demonstrated its safety in cats and possibly a beneficial effect, albeit in retrospective studies. One study in cats with non-taurine responsive dilated cardiomyopathy who were treated with pimobendan had a median survival time that

was four times longer than the cats not treated with pimobendan (49 vs. 12 days).

- Taurine supplementation is recommended initially in all cats with dilated cardiomyopathy at 250 mg PO q12h until it is demonstrated that the patient is unresponsive to taurine or is not taurine deficient based on diagnostic testing.
- Nitroglycerin (2% ointment) one-fourth to one-half inch applied topically can be used in conjunction with diuretics in the acute management of severe congestive heart failure to further reduce preload. Nitroglycerin will lower the dose of furosemide and is particularly useful in patients with hypothermia or dehydration.
- Enalapril or benazepril, at a dose of 0.25–0.5 mg/kg PO q24h is recommended to reduce afterload and preload as soon as the cat is able to take oral medications and is clinically stable. Use with caution and possibly avoid if creatinine > 2.5 mg/dL.
- Digoxin is optionally recommended to strengthen contractility and for its positive neurohumoral effects at a dose of 0.03 mg/cat (one-fourth of a 0.125-mg tablet) or 0.01 mg/kg PO q48h. Digoxin can be given concurrently with pimobendan. However, digoxin is often omitted when pimobendan is given because of the difficulties in giving a cat several pills and digoxin's side-effect profile.
- Dobutamine at extremely low dosages can be given to a patient with severe signs of congestive heart failure and low cardiac output that cannot take oral medications. Dose varies 0.25–5 µg/kg/minute IV CRI. ECG monitoring is recommended.

- Because thromboembolic disease is a concern, an antithrombotic agent is also recommended. Clopidogrel given at a dose of 18.75 mg (one-fourth of a 75-mg tablet) PO q24h is generally the author's preferred antithrombotic agent. Other options include aspirin 81 mg PO q72h (with food) or low molecular weight heparin (e.g., dalteparin 100–150 units/kg SC q8–24h or enoxaparin 1 mg/kg SC q12–24h).
- Antiarrhythmic drugs may also be needed to control supraventricular or ventricular arrhythmias. If hemodynamically significant supraventricular tachycardia or rapid atrial fibrillation is present, diltiazem is recommended. Usually, diltiazem is given orally in either a non-sustained-release formulation (7.5 mg/cat PO q8h) or a sustained-release oral formulation (Cardizem CD at 10 mg/kg PO q24h or Dilacor 30 mg/cat [or 1/2 of an inner 60-mg tablet] PO q12h). Diltiazem is also available in an injectable formulation for urgent control of a supraventricular arrhythmia in a cat that cannot take oral medications (0.05–0.1 mg/kg slow IV, repeated PRN up to 0.25 mg/kg). If rapid and sustained ventricular tachycardia, lidocaine slow IV

0.2–0.5 mg/kg (repeat once or twice max) or sotalol PO 2 mg/kg q12h is recommended.

- Beta-blockers, such as atenolol, may be useful in the chronic management of both supraventricular and ventricular arrhythmias. Beta-blockers are used in the long-term management of dilated cardiomyopathy in humans because of their positive myocardial effects and survival benefit. Clinical experience is limited in feline dilated cardiomyopathy and they must be used cautiously as they acutely decrease contractility and could worsen congestive heart failure. Recommended dose ranges from 3.125 to 6.25 mg PO q12–24h. Start low and titrate up based on heart rate and clinical signs.

PRECAUTIONS

- Unless needed for acute cardiac rhythm control, drugs such as calcium channel blockers (diltiazem) or β -adrenergic blockers may reduce contractility and lower cardiac output. Use cautiously.
- Overzealous diuretic and vasodilation therapy may cause azotemia and electrolyte disturbances.
- Digoxin should not be used if renal insufficiency is documented or suspected.
- Enalapril or benazepril should be used with caution and possibly withheld if serum creatinine is > 2.5 mg/dL.
- Dobutamine may cause seizures and cardiac tachyarrhythmias.



FOLLOW-UP

PATIENT MONITORING

- Repeat examination with ideally a blood pressure, diagnostic imaging (either a thoracic radiograph or focused thoracic ultrasound for fluid assessment) and chemistry panel within 1 week to determine response of therapy.
- Home resting respiratory rate monitoring is helpful to determine need for diuretic dose adjustment or thoracocentesis.
- Periodically monitor electrolyte and renal parameters. Periodically monitoring of congestive heart failure fluid accumulation with diagnostic imaging.
- If using digoxin, serum blood concentrations should be measured approximately 10–14 days after initiating therapy. Therapeutic range is 0.5–1.5 ng/dL 8–12 hours post-pill.
- Repeat diagnostic echocardiogram in 2–3 months after initiating taurine supplementation to determine echocardiographic response to therapy. Although echocardiographic response may take 2–3 months to assess, one should see dramatic clinical response within 2 weeks of initiating taurine therapy if cat has taurine responsive dilated cardiomyopathy.

(CONTINUED)

CARDIOMYOPATHY, DILATED—CATS

C

PREVENTION/AVOIDANCE

Ensure that cats eat a high-protein diet with sufficient dietary taurine. No vegetarian diets.

POSSIBLE COMPLICATIONS

Thromboembolism is the most feared complication of any feline myocardial disease.

EXPECTED COURSE AND PROGNOSIS

- These cats have a poor prognosis despite intensive therapy. If cat is not taurine-responsive, survival is usually weeks to months.
- Congestive heart failure can be medically refractory and recurrent despite appropriate medical therapy.
- Repeated thoracocentesis is not uncommon.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Congestive heart failure, thromboembolism, pleural effusion, cardiac arrhythmias.

SYNOMYS

Cardiomyopathy

SEE ALSO

- Aortic Thromboembolism
- Congestive Heart Failure—Left-Sided
- Congestive Heart Failure—Right-Sided

ABBREVIATIONS

- CHF = congestive heart failure
- DCM = dilated cardiomyopathy

Suggested Reading

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CARDIOMYOPATHY, DILATED—DOGS



BASICS

DEFINITION

Characterized by left- and right-sided dilation, normal coronary arteries, normal (or minimally diseased) atrioventricular valves, significantly decreased inotropic state, and myocardial dysfunction occurring primarily during systole; however, progressive diastolic dysfunction with restrictive physiology may represent an independent negative predictor of survival.

PATOPHYSIOLOGY

- Myocardial failure leads to reduced cardiac output and CHF.
- A-V anulus dilation and altered papillary muscle function promote valvular insufficiency.
- Although left-sided signs commonly predominate, evidence of severe right-sided disease is common late in the clinical course.

SYSTEMS AFFECTED

- Cardiovascular
- Renal/Urologic—prerenal azotemia
- Respiratory—pulmonary edema
- All organ systems are affected by reductions in cardiac output

GENETICS

Genetic cause or heritable susceptibility strongly suspected in most breeds and documented in some (Portuguese water dog, boxer, and Doberman pinscher) with variable forms of inheritance. A genetic test is commercially available for the causative mutation in boxer dogs (striatin) and Doberman pinscher (pyruvate dehydrogenase kinase). These mutations do not appear to be causative in other predisposed breeds. Complete characterization of the correlation between genotype and phenotype in each breed will require further study.

INCIDENCE/PREVALENCE

Estimated at 0.5–1.1% in predisposed breeds and perhaps higher in specific geographic regions.

GEOGRAPHIC DISTRIBUTION

None with the exception of Chagas' cardiomyopathy, which is limited to the southern United States (Gulf Coast).

SIGNALMENT

Species

Dog

Breed Predilections

- Doberman pinscher, boxer
- Giant breeds: Scottish deerhound, Irish wolfhound, Great Dane, Saint Bernard, Afghan hound, Newfoundland
- Cocker spaniel, Portuguese water dog

Mean Age and Range

4–10 years

Predominant Sex

Males > females in most but not all breeds

SIGNS

Historical Findings

- Respiratory—tachypnea, dyspnea, coughing.
- Weight loss.
- Weakness, lethargy, anorexia.
- Abdominal distention.
- Syncope (usually associated with important arrhythmias).
- Some dogs are asymptomatic; having what is termed preclinical dilated cardiomyopathy, the diagnosis of which in specific breeds is well described.
- Breed-specific echocardiographic parameters coupled with cardiac biomarkers (NT-proBNP; cTnI) may help identify dogs in the preclinical stage of the disease.

Physical Examination Findings

- May be completely normal with preclinical disease.
- Weakness, possibly cardiogenic shock.
- Hypokinetic femoral pulse from low cardiac output.
- Pulse deficits with atrial fibrillation, ventricular or supraventricular premature contractions, and paroxysmal ventricular tachycardia.
- Jugular pulses from tricuspid regurgitation, arrhythmias, or right-sided CHF.
- Breath sounds—muffled with pleural effusion; crackles with pulmonary edema.
- S3 or summation gallops.
- Mitral and/or tricuspid regurgitation murmurs are common but usually focal and soft.
- Auscultatory evidence of cardiac arrhythmia is common.
- Slow capillary refill time, infrequent cyanosis.
- Hepatomegaly with or without ascites.

CAUSES

- Most authors believe that the majority of cases represent familial abnormalities of structural, energetic or contractile cardiac proteins many of which have been identified.
- Nutritional deficiencies (taurine and/or carnitine) have been documented in several breeds including golden retriever, boxer, Newfoundland, Doberman pinscher, and cocker spaniel.
- Viral, protozoal, and immune-mediated mechanisms have been proposed.
- Toxic doxorubicin.
- Hypothyroidism and persistent tachyarrhythmias (sometimes associated with congenital tricuspid valve malformation) may cause reversible myocardial failure.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Endocardiosis
- Congenital heart disease
- Heartworm disease
- Bacterial endocarditis
- Cardiac tumors and pericardial effusion
- Airway obstruction—foreign body, neoplasm, laryngeal paralysis
- Primary pulmonary disease—bronchial disease, pneumonia, neoplasia, aspiration, vascular disease (e.g., heartworms)
- Pleural effusions (e.g., pyothorax, hemothorax, chylothorax)
- Trauma resulting in diaphragmatic hernia, pulmonary hemorrhage, hemothorax, pneumothorax

CBC/BIOCHEMISTRY/URINALYSIS

Routine hematologic tests and urinalysis are usually normal unless altered by severe reductions in cardiac output or severe elevations in venous pressures (e.g., prerenal azotemia, high ALT, hyponatremia), therapy for heart failure (e.g., hypokalemia, hypochloremia, and metabolic alkalosis from diuresis), or concurrent disease.

OTHER LABORATORY TESTS

Cardiac biomarkers including NT-proBNP and cTnI are elevated in both the preclinical and clinical stages of the disease. Clinical studies investigating the use of these markers for diagnosis, prognosis, and optimization of therapy are ongoing.

IMAGING

Radiographic Findings

- May be completely normal in the preclinical phase.
- Generalized cardiomegaly and signs of CHF are common.
- Left ventricular enlargement and left atrial enlargement may be most evident in early cases.
- In some cases, the degree of cardiomegaly may be less than might be expected with the severity of clinical signs.
- The degree of cardiomegaly is often substantially less than would be expected in a dog with primary valvular heart disease and comparable clinical signs.
- Pleural effusion, hepatomegaly, ascites.

Echocardiographic Findings

- Left ventricular dilation often precedes overt reductions in indices of systolic function.
- Gold standard for diagnosis.
- Ventricular and atrial dilation.
- Echocardiographic indices of myocardial systolic function (low FS%, ejection fraction, area shortening, and mitral annular motion;

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CARDIOMYOPATHY, DILATED—DOGS

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tissue Doppler imaging [TDI]) may be reduced.

- Spectral Doppler studies may confirm decreased velocity and/or acceleration of tran-saortic flow as well as mitral regurgitation and/or tricuspid regurgitation.
- Doppler evidence of restrictive LV filling is an independent predictor of decreased survival.

DIAGNOSTIC TESTS***Electrocardiography***

- Sinus rhythm or sinus tachycardia with isolated atrial or ventricular premature complexes.
- Atrial fibrillation and ventricular tachycardia (paroxysmal or sustained) are very common in Doberman pinschers.
- Boxers commonly have isolated ventricular arrhythmias without evidence of functional or anatomic heart disease.
- Prolonged QRS (> 0.06 second), possible increased voltages ($R > 3$ mV lead II), suggesting LV enlargement.
- May have "sloppy" R wave descent with ST-T coving, suggesting myocardial disease or LV ischemia.
- May have low voltages (pleural or pericardial effusion, concurrent hypothyroidism).

PATHOLOGIC FINDINGS

- Dilatation of all chambers with thinning of the chamber walls.
- Slightly thickened endocardium with pale areas within the myocardium (necrosis, fibrosis).
- Two histologically distinct forms—(1) fatty infiltration: degenerative type seen in boxers and Doberman pinschers; and (2) an attenuated wavy fiber type: seen in many giant-, large-, and medium-sized breeds, including some boxers and Doberman pinschers.

**TREATMENT****APPROPRIATE HEALTH CARE**

With the exception of severely affected dogs, most therapy can be administered on an outpatient basis.

ACTIVITY

Allow the dog to choose its own level of activity.

DIET

- During initial therapy for clinical signs, simply maintain adequate caloric intake is paramount.
- Goal—reduce dietary sodium intake to $< 12\text{--}15$ mg/kg/day.
- Severe sodium restriction is typically not necessary when using potent cardioactive therapy and may adversely affect appetite.
- Best to use commercially prepared diets.

CLIENT EDUCATION

- Emphasize potential signs associated with progression of disease and adverse side effects of medication.
- Monitoring sleeping respiratory rate often gives insight into impending decompensation.

**MEDICATIONS****DRUG(S) OF CHOICE**

First identify patient problems—CHF (left- or right-sided), arrhythmia, hypothermia, renal failure, shock.

Preclinical Disease

- There is clinical evidence (PROTECT Trial) that early intervention with pimobendan monotherapy substantially changes the course of preclinical disease in Doberman pinschers.
- These results should not be extrapolated to other diseases and other breeds.
- Critical evaluation suggests that early intervention with monotherapy with ACEi is of minimal survival benefit.

Initial Stabilization

- Treat hypoxemia with oxygen administration; prevent heat loss if hypothermic (warm environment); administer IV or SC fluids (D_5W or 0.45% NaCl with 2.5% dextrose) only after pulmonary edema is controlled or pleural effusion has been aspirated.
- If there is pulmonary edema—furosemide (2–4 mg/kg IM or IV, then 1–2 mg/kg q6–12 hours for the first 1–3 days), or a CRI 1–2 mg/kg/h.
- 2% topical nitroglycerin for the first 24–48 hours for severe pulmonary edema—apply 1 inch–2 inches q8h (beware of hypotension).
- If there is significant pleural effusion, drain each hemithorax with an 18- to 20-gauge butterfly catheter.
- If there is severe heart failure and cardiogenic shock, dobutamine may be indicated. This may predispose to malignant arrhythmias, particularly in the hypoxic dog. Oral pimobendan (see dosing below) may have important acute (2–4 hours) hemodynamic benefit as well.
- Digoxin—oral therapy (see below).
- Dobutamine 5–15 μ g/kg/min infused for 24–72 hours with care (start low and gradually up-titrate based on response).
- If paroxysmal ventricular tachycardia is present, administer lidocaine slowly in 2 mg/kg boluses (up to 8 mg/kg total) to convert to sinus rhythm. Follow with lidocaine infusion (50–75 μ g/kg/minute).
- If lidocaine is ineffective, administer procainamide slowly at a dose of 10–25 mg/kg to convert to sinus rhythm. Follow with a 25–50 μ g/kg/minute CRI (beware of proarrhythmia).

Maintenance Therapy

- ACE inhibitors (enalapril, benazepril, lisinopril) are considered a cornerstone of therapy for DCM.
- Enalapril (0.25–0.5 mg/kg PO q12h), benazepril (0.5 mg/kg PO q12–24h), or lisinopril (0.5 mg/kg PO q 12–24h) should be initiated early in the therapeutic regimen.
- A daily maintenance dose of 0.375–0.50 mg of digoxin (divided q12h) is given to some giant-breed dogs. Do not exceed 0.015 mg/kg/day and do not exceed 0.375 mg/day in Doberman pinschers. Therapeutic drug monitoring should be utilized in any dog receiving digoxin. Pimobendan has replaced digoxin as the positive inotropic of choice with digoxin used primarily for control of ventricular response rate in atrial fibrillation (see below).
- Furosemide (0.5–3 mg/kg PO q8–q24h) is used to control pulmonary edema, pleural effusion, or ascites.
- Spironolactone (0.5–1 mg/kg PO q12h) may impart independent survival benefit by blocking aldosterone. Higher doses can be used for refractory heart failure (1–2 mg/kg PO q12h). Hydrochlorothiazide (1–2 mg/kg PO q12h) may be beneficial as a third diuretic.
- Beta-blockers can be used cautiously once heart failure is controlled with other drugs (see "Precautions"). If tolerated, they may improve myocardial function with chronic use. Carvedilol (0.25–1.25 mg/kg PO q12h) is an alpha- and beta-blocker with antioxidant activity. Start at the low end of the dose range and gradually up-titrate over a 6-week period if tolerated. Consult with a cardiologist before using beta-blockers in clinical DCM patients as it can result in rapid and profound clinical deterioration.
- Pimobendan (0.25–0.3 mg/kg PO q12h) is a calcium-sensitizing drug that is a vasodilating positive inotropic that, when added to furosemide, ACE inhibitor, and digoxin, improves functional heart failure class and in Doberman pinschers increases survival time. The author has administered pimobendan 0.25–0.3 mg/kg PO q8h in refractory cases with perceived clinical benefit.
- The role of carnitine and taurine in the therapy of DCM remains controversial. However, American cocker spaniels with dilated cardiomyopathy generally respond favorably to taurine and l-carnitine supplementation but still require additional cardiac medications.

Arrhythmias

- In the case of atrial fibrillation, slowing of the ventricular rate response typically achieved with chronic administration of extended release diltiazem (Dilacor) 2–7 mg/kg PO q12h , or atenolol 0.75–1.5 mg/kg PO q12h (never start in a patient with active CHF), sometimes combined with digitalis.

CARDIOMYOPATHY, DILATED—DOGS

(CONTINUED)

- The therapeutic goal is obtaining a resting ventricular rate of 100–140 bpm.
- The above therapy merely controls the ventricular rate, by depressing AV nodal conduction; it generally does not convert the rhythm from atrial fibrillation to sinus rhythm.
- Amiodarone (10–15 mg/kg PO q24h for 7–10 days followed by 5–10 mg/kg PO q24h) may either control ventricular response rate or in some cases result in conversion to normal sinus rhythm.
- Chronic oral therapy for ventricular tachycardia includes procainamide (8–20 mg/kg PO q6–8h), mexiletine (5–10 mg/kg PO q8h), amiodarone (5–10 mg/kg PO q24h) or sotalol (1–2 mg/kg PO q12h).
- Procainamide and mexiletine can be combined with a beta-blocker if necessary.

CONTRAINDICATIONS

Digoxin should be avoided in severe uncontrolled paroxysmal ventricular tachycardia, in animals with compromised renal function and in animals with important hypokalemia.

PRECAUTIONS

- Beta-blockers and calcium channel blockers are negative inotropes and may have an acute adverse effect on myocardial function. Numerous human studies, however, have suggested that chronic administration of beta-blockers may be of benefit in DCM.
- The combination of diuretics and ACE inhibitors may result in azotemia, especially in patients with severe heart failure or preexisting renal dysfunction.

POSSIBLE INTERACTIONS

- Quinidine, amiodarone, and diltiazem may increase serum digoxin levels and predispose to digitalis intoxication.
- Renal dysfunction, hypothyroidism, and hypokalemia predispose to digitalis intoxication.

ALTERNATIVE DRUG(S)

- Other vasodilators, including hydralazine and amlodipine, may be used instead of or in

- addition to an ACE inhibitor (beware of hypotension).
- The role of co-enzyme Q10 remains to be determined.



FOLLOW-UP

PATIENT MONITORING

- Serial clinical examinations, thoracic radiographs, blood pressure measurements, routine serum biochemical evaluations (including electrolytes), and ECG are most helpful.
- Repeat echocardiography is rarely informative or indicated.
- Serial evaluation of serum digoxin levels (therapeutic range = 0.5–1 ng/mL) taken 6–8 hours post-pill and serum biochemistries may help prevent iatrogenic problems.

POSSIBLE COMPLICATIONS

- Sudden death due to arrhythmias.
- Iatrogenic problems associated with medical management (see above).

EXPECTED COURSE AND PROGNOSIS

- Always fatal.
- Death usually occurs 6–24 months following diagnosis.
- Dobermanns typically have a worse; however, with the addition of pimobendan, survival following identification in the preclinical stage averages over 700 days.
- Atrial fibrillation, paroxysmal ventricular tachycardia, Doppler evidence of restrictive LV filling, and markedly decreased FS% are believed to be markers for short survival and sudden death.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Prevalence increases with age

SYNOMYS

- Congestive cardiomyopathy
- Giant-breed cardiomyopathy

SEE ALSO

- Atrial Fibrillation and Atrial Flutter
- Carnitine Deficiency
- Taurine Deficiency
- Ventricular Tachycardia

ABBREVIATIONS

- ACEI = angiotensin converting enzyme inhibitor
- ALT = alanine aminotransferase
- AV = atrioventricular
- CHF = congestive heart failure
- DCM = dilated cardiomyopathy
- ECG = electrocardiogram
- FS% = percent fractional shortening
- LAE = left atrial enlargement

INTERNET RESOURCES

North Carolina State University Veterinary Cardiac Genetic Laboratory:
<http://www.cvm.ncsu.edu/vhc/csds/vcgl/>

Suggested Reading

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Client Education Handout
available online

CARDIOMYOPATHY, HYPERTROPHIC—CATS



BASICS

DEFINITION

Inappropriate concentric hypertrophy of the ventricular free wall and/or the interventricular septum of the non-dilated left ventricle. The disease occurs independently of other cardiac or systemic disorders.

PATHOPHYSIOLOGY

- Diastolic dysfunction results from a thickened, non-compliant left ventricle.
- High left ventricular filling pressure develops, causing left atrial enlargement.
- Pulmonary venous hypertension causes pulmonary edema. Some cats develop biventricular failure (i.e., pulmonary edema, pleural effusion, small volume pericardial effusion without tamponade, and, rarely, ascites). • Stasis of blood in the large left atrium predisposes the patient to ATE.
- Dynamic aortic outflow obstruction and systolic anterior mitral motion (SAM) with secondary mitral insufficiency may occur.

SYSTEMS AFFECTED

- Cardiovascular—CHF, ATE, and arrhythmias
- Pulmonary—dyspnea if CHF develops
- Renal/urologic—prerenal azotemia

GENETICS

Some families of cats have been identified with a high prevalence of the disease, and the disease appears to be an autosomal dominant trait in Maine coon cats and ragdoll cats, due to a mutation in the MyBPC gene. The genetics have not been definitively determined in other breeds; however, the Maine coon and ragdoll mutations have not been identified in affected Sphynx, Norwegian forest cats, Bengals, Siberians, or British shorthair cats.

INCIDENCE/PREVALENCE

Unknown, but relatively common. May be as high as 15% of the population.

SIGNALMENT

Species: Cat

Breed Predilections

Maine coon cats, ragdolls, Sphynx, British and American shorthairs, and Persians.

Mean Age and Range

5–7 years with reported ages of 3 months–17 years. Some breeds of cats including ragdolls and Sphynx may develop the disease at a younger age (average of 2 years of age). HCM is most often a disease of young to middle-aged cats; unexplained murmurs in geriatric cats are more likely associated with hyperthyroidism or hypertension.

Predominant Sex: Male

SIGNS

Historical Findings

- Dyspnea.
- Anorexia.
- Exercise intolerance.
- Vomiting.
- Collapse.
- Sudden

death. • Coughing is uncommon in cats with cardiomyopathy and usually suggests pulmonary disease.

Physical Examination Findings

- Gallop rhythm (S3 or S4).
- Systolic murmur in many animals.
- Apex heartbeat may be exaggerated.
- Muffled heart sounds, lack of chest compliance, and dyspnea characterized by rapid shallow respirations may be associated with pleural effusion.
- Dyspnea and crackles if pulmonary edema is present.
- Weak femoral pulse.
- Acute pelvic limb paralysis with cyanotic pads and nailbeds, cold limbs, and absence of femoral pulse in animals with ATE. Emboli rarely affect thoracic limbs.
- Arrhythmia in some animals.
- May have no clinical signs.

CAUSES

- Usually unknown—multiple causes exist
- MyBPC mutations in some cats with HCM

Possible Causes

- Abnormalities of the contractile protein myosin or other sarcomeric proteins (e.g., troponin, myosin binding proteins, tropomyosin).
- Abnormality affecting catecholamine-influenced excitation contraction coupling.
- Abnormal myocardial calcium metabolism.
- Collagen or other intercellular matrix abnormality.
- Growth hormone excess.
- Dynamic left ventricular outflow obstruction may contribute to secondary left ventricular hypertrophy.

RISK FACTORS

Offspring of animals with familial mutations of MyBPC



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other forms of cardiomyopathy
- Hyperthyroidism
- Aortic stenosis
- Systemic hypertension
- Acromegaly
- Non-cardiac causes of pleural effusion

CBC/BIOCHEMISTRY/URINALYSIS

- Results usually normal
- Prerenal azotemia in some animals

OTHER LABORATORY TESTS

- MyBPC assay. Mutation differs for Maine coon cats and ragdoll cats.
- In cats > 6 years old, check thyroid hormone concentration. Hyperthyroidism causes myocardial hypertrophy that might be confused with HCM.
- Serum BNP concentrations are higher in cats with HCM than in normal cats, and higher still in cats with symptomatic HCM. The positive predictive value of this test to differentiate normal cats from those with asymptomatic HCM is unknown in the general population, and this test should therefore not be used to screen all asymptomatic cats. Serum BNP testing is useful, in identifying cats with a high

suspicion of HCM from an asymptomatic population of cats with abnormal physical exam findings (e.g., murmur).

IMAGING

Radiography

- Dorsal ventral radiographs often reveal a valentine-appearing heart because of biatrial enlargement and a left ventricle that comes to a point.
- Pulmonary edema, pleural effusion, or both in some animals.
- Radiographs may be normal in asymptomatic cats.
- The different forms of cardiomyopathy cannot be reliably differentiated by radiography.

Echocardiography

- Hypertrophy of the interventricular septum or the left ventricular posterior wall (diastolic wall thickness > 6 mm).
- Hypertrophy may be symmetric (affecting IVS and posterior wall) or asymmetric (affecting IVS or posterior wall, but not both).
- Hypertrophy of the papillary muscles.
- Normal or high fractional shortening.
- Normal or reduced left ventricular lumen.
- Left atrial enlargement.
- Systolic anterior motion of the mitral valve (some animals).
- Left ventricular outflow obstruction (some animals).
- Specialized Doppler studies performed by experienced sonographers often reveal left ventricular relaxation abnormalities (e.g., mitral inflow E:A wave reversal).
- Thrombus in the left atrium (rare).
- Note: There is some overlap between normal cats (especially ketaminized and dehydrated) and cats with mild HCM. Correlate echo findings with physical findings. Presence of left atrial enlargement favors HCM.

DIAGNOSTIC PROCEDURES

Electrocardiography

- Sinus tachycardia (HR > 240) is common with heart failure; however, some cats with severe heart failure and hypothermia are bradycardic.
- Atrial and ventricular premature complexes seen more often in cats with cardiomyopathy, but are also occasionally seen in normal cats.
- Atrial fibrillation is seen in some advanced cases.
- A left axis deviation is often seen.
- Cannot differentiate different forms of cardiomyopathy. May be normal.

Systemic Blood Pressure

- Normotensive or hypotensive.
- Evaluate blood pressure in all patients with myocardial hypertrophy to rule out systemic hypertension as the cause of hypertrophy.

PATHOLOGIC FINDINGS

- Non-dilated left ventricle with hypertrophy of intraventricular septum or left ventricular free wall.
- Hypertrophy of papillary muscles.
- Left atrial enlargement.
- Mitral valve thickening.
- Myocardial hypertrophy with disorganized alignment of myocytes (myofiber disarray).
- Interstitial fibrosis.
- Myocardial scarring.
- Hypertrophy and luminal narrowing of intramural coronary arteries.

CARDIOMYOPATHY, HYPERTROPHIC—CATS

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

Cats with CHF should be hospitalized.

NURSING CARE

- Minimize stress • Oxygen if dyspneic
- Warm environment if hypothermic

ACTIVITY

Restricted with CHF

DIET

Modest to moderate sodium restriction in animals with CHF

CHF CLIENT EDUCATION

- Many cats diagnosed while asymptomatic eventually develop CHF and may develop ATE and die suddenly. • If cat is receiving warfarin, dalteparin, lovenox, or a combination of clopidogrel and any of those medications, minimize potential for trauma and subsequent hemorrhage.



MEDICATIONS

DRUG(S) OF CHOICE

Furosemide

- Dosage—1–2 mg/kg PO, IM, IV q8–24h.
- Critically dyspneic animals often require high dosage (4 mg/kg IV). This dose can be repeated in 1 hour if the cat is still severely dyspneic. Indicated to treat pulmonary edema, pleural effusion, and ascites.
- Cats are sensitive to furosemide and prone to dehydration, prerenal azotemia, and hypokalemia.
- Once pulmonary edema resolves, taper to the lowest effective dose.

Pimobendan

- Dosage—0.25–0.3 mg/kg PO q12h.
- Appears to be useful in the management of congestive heart failure (e.g., pulmonary edema or pleural effusion) in cats with HCM, possibly by enhancing diastolic function.
- Pimobendan is not used in the management of asymptomatic HCM at this time.

ACE Inhibitors

- Dosage—enalapril or benazepril 0.25–0.5 mg/kg PO q24h.
- Indications in cats with HCM not well defined—authors currently use for CHF.

Beta-Blockers

- Dosage—atenolol (6.25–12.5 mg/cat PO q12h).
- Beneficial effects may include slowing of sinus rate, correcting atrial and ventricular arrhythmias, platelet inhibition.
- More effective than diltiazem in controlling dynamic outflow tract obstruction.
- Role in asymptomatic patients unresolved, but authors generally use if dynamic outflow obstruction and hypertrophy present.
- Contraindicated in the presence of CHF.

Diltiazem

- Dosage—7.5–15 mg/cat PO q8h or 10 mg/kg PO q24h (Cardizem CD) or 30 mg/cat q12h (Dilacor XR).
- Beneficial effects may include slower sinus rate, resolution of supraventricular arrhythmias, improved diastolic relaxation, coronary and peripheral vasodilation, platelet inhibition.
- May reduce hypertrophy and left atrial dimensions in some cats.
- Role in asymptomatic patients unresolved.

Aspirin

- Dosage—81 mg/cat q2–3 days if severe atrial enlargement.
- Depresses platelet aggregation, hopefully minimizing the risk of thromboembolism.
- Warn owners that thrombi can still develop despite aspirin administration. Aspirin appears to be not as effective as clopidogrel (1/4 of a 75-mg tablet PO q24h) in the prevention of ATE, at least in cats with a previous embolic episode.

Nitroglycerin Ointment

- Dosage—one-fourth inch/cat topically applied q6–8h or 2.5 mg/24-hour patch.
- Often used in the acute stabilization of cats with severe pulmonary edema or pleural effusion.
- When used intermittently, it may be useful for long-term management of refractory cases.

CONTRAINDICATIONS

Avoid beta-blockers in cats with emboli; these agents cause peripheral vasoconstriction. If beta-blockers must be used in this setting for arrhythmia control, choose a beta-1 selective blocker such as atenolol.

PRECAUTIONS

Use ACE inhibitors cautiously in azotemic animals.

ALTERNATIVE DRUG(S)

Spironolactone

- Dosage—1 mg/kg q12–24h.
- Used in conjunction with furosemide in cats with CHF.
- May cause facial pruritis.

Warfarin and Low Molecular Weight Heparin

- Used sometimes in cats at high risk for thromboembolism.
- See chapter, Aortic Thromboembolism.

Clopidogrel

Dosage—18.75 mg/cat/day. Platelet function inhibitor, superior to aspirin in cats with previous ATE.

Beta-Blocker Plus Diltiazem

- Cats that remain tachycardic on a single agent can be treated cautiously with a combination of a beta-blocker and diltiazem.
- Monitor for bradycardia and hypotension.



FOLLOW-UP

PATIENT MONITORING

- Observe closely for dyspnea, lethargy, weakness, anorexia, and painful posterior

paralysis or paresis.

- If treating with warfarin, monitor prothrombin time.
- If treating with an ACE inhibitor or spironolactone, monitor renal function and electrolytes.
- Repeat echocardiogram in 6 months to assess efficacy of treatment for hypertrophy. If a beta-blocker or diltiazem was prescribed in an asymptomatic animal and there is evidence of progressive hypertrophy/left atrial enlargement, consider switching to another class of medications (or adding ACEI) and recheck 4–6 months later.

Echocardiographic evaluations that reveal LA diameters > 2 cm or loss of LV systolic function should prompt more aggressive prophylaxis against ATE (e.g., clopidogrel with low molecular weight heparin).

PREVENTION/AVOIDANCE

Avoid stressful situations that might precipitate CHF.

POSSIBLE COMPLICATIONS

- Heart failure • ATE and paralysis • Cardiac arrhythmias/sudden death

EXPECTED COURSE AND PROGNOSIS

- Animals homozygous for MyBPC mutations more likely to develop severe HCM and at earlier age than heterozygous animals.
- Prognosis varies considerably, probably because there are multiple causes. In one study of cats with HCM living at least 24 hours following presentation:
- Asymptomatic cats: median survival 563 days (range 2–3,778 days)
- Cats with syncope: median survival 654 days (range 28–1,505 days)
- Cats with CHF: median survival 563 days (range 2–4,418 days).
- Cats with ATE: median survival 184 days (range 2–2,278 days).
- Older age and larger left atria predicted shorter survival.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Aortic thromboembolism

PREGNANCY/FERTILITY/BREEDING

- High risk of complications • Avoid aspirin

SEE ALSO

- Acromegaly—Cats • Aortic Thromboembolism • Congestive Heart Failure, Left-Sided • Hypertension, Systemic • Hyperthyroidism • Murmurs, Heart

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- ATE = aortic thromboembolism • HCM = hypertrophic cardiomyopathy • IVS = interventricular septum • MyBPC = myosin binding protein C

Authors Francis W.K. Smith, Jr., Bruce W. Keene, and Kathryn M. Meurs



Client Education Handout
available online

CARDIOMYOPATHY, HYPERTROPHIC—DOGS



BASICS

OVERVIEW

Hypertrophic cardiomyopathy has been defined as “inappropriate myocardial hypertrophy of a non-dilated left ventricle, occurring in the absence of an identifiable stimulus for the hypertrophy.” HCM is a rare disease in dogs characterized by left ventricular concentric hypertrophy (increased wall thickness). The primary disease process is confined to the heart and only affects other organ systems when congestive heart failure is present. Increased LV wall thickness leads to impaired ventricular filling (due to lack of compliance and abnormal relaxation) with a resultant increase in LV end-diastolic pressure and left atrial pressure. The left atrium usually enlarges in response to increased LV end-diastolic pressure. Mitral insufficiency and/or dynamic LV outflow tract obstruction commonly occur secondary to structural and/or functional changes of the mitral valve apparatus caused by papillary muscle malalignment secondary to the hypertrophy.

SIGNALMENT

- The incidence of HCM in dogs is very low, such that accurate accounts of signalment are lacking.
- Young (<3 years) male dogs.
- Rottweiler, Dalmatian, and German shepherd and pointer breeds are overrepresented.
- HCM is also encountered with some regularity in mature Boston terrier dogs.

SIGNS

Historical Findings

- Most are asymptomatic.
- Signs of left congestive heart failure predominate in symptomatic dogs.
- Syncope, generally during activity or exercise.
- Sudden death is the most commonly reported clinical sign.

Physical Examination Findings

- Systolic heart murmur.
- Cardiac gallop rhythm.
- Signs of left congestive heart failure (e.g., cough, dyspnea, cyanosis, exercise intolerance).

CAUSES & RISK FACTORS

The cause of hypertrophic cardiomyopathy is unknown. Genetic abnormalities in genes coding for myocardial contractile proteins have been documented in humans and in cats, but not in dogs. A genetic basis is suspected in that most affected dogs are young, but none has been proven.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Systemic hypertension
- Infiltrative cardiac disorders
- Other causes of congestive heart

failure

- Thyrotoxicosis
- Congenital mitral dysplasia

IMAGING

Radiography

- May be normal.
- May show LA or LV enlargement.
- Pulmonary edema is present in dogs with left congestive heart failure.

Echocardiography

- Dogs with severe HCM usually have markedly thickened left ventricular walls, papillary muscle hypertrophy, and an enlarged left atrium. The hypertrophy is usually global, affecting all areas of the left ventricular wall, but can be more regional or segmental (asymmetric). Milder forms may have subtle LV hypertrophy.
- Systolic anterior motion of the mitral valve, suggesting dynamic LV outflow tract obstruction, is common in dogs with HCM.

OTHER DIAGNOSTIC PROCEDURES

Electrocardiography

- May be normal.
- ST segment and T wave abnormalities have been reported.
- Atrial or ventricular ectopic arrhythmias may rarely occur.

Blood Pressure

Usually normal. Should be evaluated to rule out systemic hypertension as the cause of LV hypertrophy.

PATHOLOGIC FINDINGS

- Abnormal heart:body weight ratio.
- Left ventricular concentric hypertrophy.
- There may be an impact lesion on the interventricular septum, displaying a range of appearances from a small opaque lesion to a thickened plaque.
- The mitral valve itself is often thickened and elongated.
- Varying degrees of left atrial enlargement may be present



TREATMENT

Outpatient management unless in congestive heart failure. Exercise restriction and sodium restriction are beneficial.



MEDICATIONS

DRUG(S)

- Treatment is generally only pursued if there is evidence of congestive heart failure or severe arrhythmias or in patients with frequent syncope.
- In patients with left congestive heart failure, diuretics and ACE inhibitor therapy are advocated.
- In dogs with high LV-aorta pressure gradients due to dynamic LV outflow obstruction, administration of a β -adrenergic blocker or calcium channel blocker has been

advocated; however, benefit has not been proven.

- Beta-adrenergic blockers or calcium channel blockers may also improve myocardial oxygenation, reduce heart rate, improve LV diastolic function, and control arrhythmias and therefore may also be beneficial in dogs with left congestive heart failure.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Positive inotropic drugs should be avoided as they may worsen dynamic LV outflow obstruction.
- The use of a calcium channel blocker in combination with a beta-blocker should be avoided, as clinically significant bradycardia can develop.
- The use of potent arteriolar dilators should be avoided in patients with dynamic LV outflow tract obstruction. However, the use of milder vasodilators such as ACE inhibitors in patients with congestive heart failure is generally well tolerated.



FOLLOW-UP

Reevaluation depends on the severity of the clinical signs. Reevaluation with radiography and echocardiography may be useful to characterize disease progression and make appropriate medication adjustments.

- Due to the rarity of this condition in dogs, information regarding prognosis is lacking. In dogs with severe congestive heart failure or other complications, prognosis is generally guarded.



MISCELLANEOUS

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- HCM = hypertrophic cardiomyopathy

Suggested Reading

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CARDIOMYOPATHY, RESTRICTIVE—CATS



BASICS

DEFINITION

A rare, primary heart muscle disease characterized *functionally* by severe diastolic dysfunction with restrictive left ventricular filling and normal to near normal systolic function, *morphologically* by a non-dilated non-hypertrophied left ventricle with increased endocardial and/or myocardial fibrosis and severe atrial enlargement, and *clinically* by advanced heart failure, thromboembolic disease, and cardiac death.

PATOPHYSIOLOGY

- Increased cardiomyofilament calcium sensitivity leading to severely impaired relaxation and high myocardial stiffness due to endomyocardial fibrosis (endomyocardial type) and/or interstitial fibrosis (myocardial type), and disorganized myofiber architecture (disarray; both types) are main characteristics of primary RCM. RCM-like myocardial changes and clinical syndromes can result from myocardial remodeling and dysfunction secondary to other causes (e.g., endomyocarditis, immune-mediated disease, or end-stage hypertrophic cardiomyopathy).
- Diastolic heart failure and arterial thromboembolism lead to high mortality.

SYSTEMS AFFECTED

- Cardiovascular • Respiratory

GENETICS

Primary RCM can be a spontaneous or familial disease but is generally considered of genetic cause in humans with an autosomal dominant pattern of inheritance. Several genes encoding α -actin, β -myosin heavy chain, cTnI, and cTnT can be affected. RCM-causing mutations have not been identified in cats.

INCIDENCE/PREVALENCE

Primary feline RCM is rare. Prevalence ranging from present 1–15% of all myocardial diseases in cats has been reported.

SIGNALMENT

- Cats • No breed predilection • Middle-aged to older cats • Male predisposition

SIGNS

Historical Findings

- If cat does not have CHF: ° Lethargy, weakness, weight loss ° Syncope (usually indicates relevant arrhythmia) ° Paresis or paralysis (i.e., signs of arterial thromboembolism)
- If cat has CHF: ° Laboring breathing ° Tachypnea ° Ascites ° Jugular venous distension ° Cyanosis

Physical Examination Findings

- If not in CHF: ° Depression ° Tachycardia ° Arrhythmias ° Prominent gallop sounds
- Heart murmur uncommon • If in CHF: above signs plus the following: ° Tachypnea

- ° Labored breathing ° Panting ° Cyanosis
- ° Hepatomegaly or ascites with jugular venous distention ° Pulmonary crackles ° Muffled cardiac or respiratory sounds if cat has pleural effusion ° Paralysis or paresis with loss of femoral pulses; one or more extremities cold and painful (arterial thromboembolism).

CAUSES

- Primary RCM: Currently unknown; genetic cause documented in humans.
- Secondary RCM: Late or end stage of underlying disease (e.g., hypertrophic cardiomyopathy), link between prior interstitial pneumonia and feline endomyocarditis suspected in one study.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Advanced stages of other feline cardiomyopathies: ° Hypertrophic, dilated, arrhythmogenic right ventricular, unclassified, and tachycardia-induced cardiomyopathy
- Myocardial infarct ° CHF secondary to thyrotoxicosis or hypertensive heart disease.

CBC/BIOCHEMISTRY/URINALYSIS

Routine chemistry panel and urinalysis helpful to document concurrent or complicating conditions (e.g., prerenal azotemia and potassium depletion).

OTHER

LABORATORY TESTS

- Plasma T4 concentration in cats \geq 6 years old
- Plasma cardiac troponin I concentration (more specific if ischemic heart disease or myocarditis suspected).

IMAGING

Thoracic Radiography

- Cardiomegaly with severe bi-atrial enlargement (“valentine” heart on v/d projections).
- Interstitial or alveolar infiltrates or pleural effusion with pulmonary venous distention if in CHF.

Echocardiography

- Note:* Definitive diagnostic criteria are poorly defined and remain controversial. Early (non-congestive) RCM has rarely been documented in cats.
- Anatomical findings:
 - Severe bi-atrial enlargement
 - Non-hypertrophied, non-dilated left ventricle (normal chamber dimension, normal wall thickness)
 - Severe enlargement of the left atrium with spontaneous echocardiographic contrast or thrombi frequently seen
 - Prominent, often diffuse echogenic scar (“moderator bands”, false tendons) leading to a small left ventricular lumen size and narrowing of the mid-ventricle (endomyocardial fibrosis)
 - Focal areas of highly echogenic and often thin myocardium indicative of ischemia or scarring
 - Myocardium can appear normal with pure myocardial form of RCM
 - Pleural effusion

and mild to moderate pericardial effusion may be present.

- Functional findings:
 - Severe left ventricular diastolic dysfunction (restrictive left ventricular filling with an E:A ratio > 2.0 , short isovolumic relaxation time (< 37 msec), shortened deceleration time of E (< 50 msec), and E:E' $\gg 15$)
 - Normal to low normal left ventricular systolic function (in some cases LV systolic dysfunction is present)
 - Regional wall motion abnormalities possible.
 - Severe left atrial appendage enlargement with evidence of blood stasis
 - Midventricular obstruction with flow turbulence in cats with bridging endomyocardial fibrosis
 - In cats with secondary RCM, characteristics of the underlying disease can predominate; however, severe atrial enlargement and restrictive LV filling will be present in nearly all cats.

DIAGNOSTIC PROCEDURES

Electrocardiography

- Note:* ECG findings are neither sensitive nor specific.
- Sinus tachycardia is common, but cats with severe CHF and hypothermia may be bradycardic.
- Ventricular or supraventricular ectopic beats, paroxysmal or sustained supraventricular or ventricular tachycardia, or atrial fibrillation
- Atrial or ventricular enlargement patterns
- ST segment elevation or depression.

Pathology

- Note:* Histopathologic confirmation is needed in the definitive diagnosis of RCM.
- Increased heart weight (> 19 g)
- Severe bi-atrial dilatation
- Locally or diffusely thickened opaque endocardium
- False tendons (“moderator bands”) present in some cats
- Normal luminal size of the left and right ventricle (enlargement possible with secondary RCM or CHF)
- Diffuse or focal cardiomyocyte disarray
- Increased interstitial and replacement fibrosis
- Abnormal intramural coronary arterioles with medial hypertrophy and narrowed lumen
- Increased number of inflammatory cells seen only in cats with acute endomyocarditis—this finding is commonly absent in cats with endocardial fibrosis.



TREATMENT

APPROPRIATE HEALTH CARE

- Patients with acute, severe CHF are hospitalized for emergency care.
- Mildly symptomatic animals can be treated with outpatient medical management.

NURSING CARE

- Dyspneic animals should receive oxygen.
- Sedation and preload-reducing drugs are mandatory.
- Thoracocentesis if relevant pleural effusion.
- Low-sodium fluids are only administered if dehydration present and kidney function is compromised.
- Maintain

(CONTINUED)

CARDIOMYOPATHY, RESTRICTIVE—CATS

C

a low-stress environment (e.g., cage rest, minimize handling). • Heating pad for hypothermic patients. • Respiratory rate should be used to monitor the immediate success of treatment.

ACTIVITY

- Cage rest is suggested for CHF patients.

DIET

- In acute heart failure, maintain intake with hand feeding if necessary.

CLIENT EDUCATION

- The owner should be counseled regarding the technique of pill administration in cats, possible adverse effects of medications, the importance of maintaining stable food and water intake, and monitoring their cat's resting respiratory rate at home.

**MEDICATIONS****DRUG(S) OF CHOICE*****Acute Congestive Heart Failure***

- Parenteral administration of furosemide (0.5–2 mg/kg IV, IM, SC q1–6h). CRI may be considered. • Dermal application of nitroglycerin ointment (2%, one eighth—one fourth inch q12h). • Oxygen delivered by cage, mask, nasal tube. • Thoracocentesis as necessary to reduce or eliminate pleural effusion. • Dobutamine only if cats are hypotensive (systolic blood pressure < 90 mmHg); 1–5 µg/kg/minute as continuous rate infusion, start a lower dose and increase over 0.5 to 1 hour). • Severe supraventricular tachyarrhythmias can be treated with regular diltiazem (1.5–2.5 mg/kg PO q8h) or long-acting diltiazem (10 mg/kg PO q24h). • Ventricular tachycardia may resolve with resolution of CHF. • Acute therapy of ventricular tachycardia may include lidocaine (0.25–0.5 mg/kg IV SLOWLY); monitor closely for neurologic signs of toxicity. • Pimobendan (1.25 mg/cat PO q12h) may be helpful to increase cardiac performance in acute heart failure but is only used in animals that cannot be stabilized and systemic hypotension cannot be corrected.
- Note:* Pimobendan is not approved for clinical use in cats and clinical safety and efficacy data are limited. Antiplatelet medication (Clopidogrel bisulfate, 18.75 mg PO q24h) or anticoagulants (e.g., unfractionated heparin, 150–250 IU/kg SC q6h) may be administered, in particular in cats with severe left atrial enlargement and spontaneous echocardiographic contrast.

Chronic Therapy

- Furosemide is gradually decreased to lowest effective dose. • Angiotensin-converting enzyme inhibitors (ACEIs) may reduce fluid retention, decrease the need for diuretics, and counterbalance adverse effects of diuretics

(e.g., enalapril 0.25–0.5 mg/kg PO q12–25h). • Diltiazem decreases heart rate and improves supraventricular arrhythmias in affected cats. The addition of digoxin (0.007 mg/kg PO q48h) may allow better control of ventricular response rate in cats with atrial fibrillation. Cats with hemodynamically important ventricular and supraventricular ectopy can also benefit from sotalol (0.5–2.0 mg/kg PO q12h). • Pimobendan (0.625–1.25 mg/cat PO q12h) may be helpful in the management of chronic heart failure. *Note:* Pimobendan is not approved for clinical use in cats. • Treat associated conditions (e.g., dehydration, hypothermia, hypokalemia). • Clopidogrel (one fourth of a 75-mg tablet PO q24h) to inhibit platelet chronically. Aspirin (25 mg/kg PO q72h) may also be considered but efficacy is questionable. In cases of echogenic smoke or prior thromboembolism, both drugs (clopidogrel and aspirin) may be used concurrently. • Treatment of cats with preclinical RCM has rarely been reported but includes ACEIs and antiplatelet drugs. There is currently no specific treatment for left ventricular diastolic dysfunction available.

CONTRAINdications

- For beta-blocking drugs—should not be administered in cats with RCM. • For diltiazem—bradycardia, atrioventricular block, myocardial failure, and hypotension.
- For furosemide—severe dehydration, severe hypokalemia, and moderate to severe azotemia. • For ACEIs—moderate to severe azotemia, hypotension, and hyperkalemia.

POSSIBLE INTERACTIONS

- Use of ACEIs in cats on high doses of furosemide may result in hypotension, azotemia, and hyperkalemia. • Chronic aspirin therapy may increase risk of renal side effects of ACEIs and may lead to inappetence and gastrointestinal upset.

**FOLLOW-UP****PATIENT MONITORING**

- Frequent physical re-examinations to assess response to treatment and resolution of CHF.
- Frequent re-evaluation of hydration status and renal function is important in the first few days of therapy to avoid dehydration, hypokalemia, and azotemia. • Repeated thoracocentesis if necessary. • “Hands-off” hourly assessment of respiratory rate in first 12–24 hours can be used to monitor efficacy of CHF therapy. • Radiographs may be repeated in 12–24 hours to monitor pulmonary infiltrate resolution. • Repeat physical examination and analysis of blood biochemistries after 3 to 7 days of treatment of acute CHF. • ECG and radiographs repeated at clinician’s discretion. • Stable patients are reevaluated every 2–4 months or

more frequently if problems occur. Repeat echocardiograms are indicated every 6 to 9 months.

PREVENTION/AVOIDANCE

- No known preventative measures for RCM.

POSSIBLE COMPLICATIONS

Tissue necrosis or loss of function in limbs affected by thromboembolic complications, adverse effects of medications, sudden death, and euthanasia due to refractory heart failure.

EXPECTED COURSE AND PROGNOSIS

- Somehow variable, but most cats have a grave prognosis.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Aortic thromboembolism

AGE-RELATED FACTORS

Hyperthyroidism should be ruled out with appropriate testing in feline cardiovascular patients ≥ 6 years of age.

SYNONYMS

- Intermediate cardiomyopathy • Unclassified cardiomyopathy

SEE ALSO

- Aortic Thromboembolism • Congestive Heart Failure, Left-Sided • Congestive Heart Failure, Right-Sided

ABBREVIATIONS

- A = peak velocity of late transmitral flow
- ACEI = angiotensin converting enzyme inhibitor • CHF = congestive heart failure
- cTnI = cardiac troponin I • cTnT = cardiac troponin T • E = peak velocity of early transmural flow • E' = peak velocity of mitral annular motion • RCM = restrictive cardiomyopathy

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**Client Education Handout
available online**

CARDIOPULMONARY ARREST



BASICS

DEFINITION

- Cessation of effective perfusion and ventilation because of the loss of coordinated cardiac and respiratory function.
- Cardiac arrest invariably follows respiratory arrest if not recognized and corrected.

PATHOPHYSIOLOGY

- Generalized or cellular hypoxia may be the cause or effect of sudden death.
- After 1–4 minutes of airway obstruction, breathing efforts stop while circulation remains intact.
- If obstruction continues for 6–9 minutes, severe hypotension and bradycardia lead to dilated pupils, absence of heart sounds, and lack of palpable peripheral pulse.
- After 6–9 minutes, myocardial contractions cease even though the ECG may look normal—pulseless electrical activity (formerly electrical mechanical dissociation).
- Ventricular fibrillation, ventricular asystole, and pulseless electrical activity are rhythms indicating cessation of myocardial contractility.

SYSTEMS AFFECTED

- All systems are affected, but those requiring the greatest supply of oxygen and nutrients are affected first.
- Cardiovascular.
- Renal/Urologic.
- Neurologic.

SIGNALMENT

- Dog and cat
- Any age, breed, or sex

SIGNS

- Lack of response to stimulation
- Loss of consciousness
- Dilated pupils
- Cyanosis
- Agonal gasping or absence of ventilation
- Absence of peripheral pulses
- Hypothermia
- Absence of audible heart sounds

CAUSES

- Hypoxemia caused by ventilation perfusion mismatch, diffusion barrier impairment, hypoventilation, or shunting.
- Poor oxygen delivery due to anemia or vasoconstriction.
- Myocardial disease—infectious, inflammatory, infiltrative, traumatic, neoplastic, or embolic.
- Acid-base abnormalities.
- Electrolyte derangements—hyperkalemia, hypocalcemia, and hypomagnesemia.
- Hypovolemia.
- Shock.
- Anesthetic agents.
- Sepsis/septic shock.
- CNS trauma.
- Electrical shock.

RISK FACTORS

- Cardiovascular disease
- Respiratory disease
- Trauma
- Anesthesia
- Septicemia
- Endotoxemia
- Ventricular arrhythmias—ventricular tachycardia, R on T phenomenon, multifocal ventricular complexes
- Increased parasympathetic tone—gastrointestinal disease, respiratory disease, manipulation of eyes, larynx, or abdominal viscera
- Prolonged seizing
- Invasive cardiovascular

manipulation—pericardiocentesis, surgery, angiography



DIAGNOSIS

- Sudden cardiovascular collapse associated with inadequate cardiac output can lead to severe consequences.
- Quick assessment and diagnosis are critical.
- Assess the ABCs—airway, breathing, circulation.

DIFFERENTIAL DIAGNOSIS

- Severe hypovolemia and absence of palpable pulses.
- Pericardial effusion with cardiac tamponade, decreased cardiac output, and muffled heart sounds.
- Pleural effusion with respiratory arrest.
- Respiratory arrest can be confused with CPA.
- Upper airway obstruction can rapidly progress to CPA.

CBC/BIOCHEMISTRY/URINALYSIS

May help identify an underlying cause for CPA but should not be part of initial triage.

OTHER LABORATORY TESTS

- Arterial blood gas evaluation may be useful during or after resuscitative procedures, but is not part of initial emergency management.
- Venous blood gas evaluation may be more useful during resuscitation than arterial blood gas and provides electrolyte and lactate concentrations.

IMAGING

- Thoracic FAST (TFAST) focused assessment with sonography for trauma may be useful in identifying underlying disease.
- Abdominal FAST (AFAST) focused assessment with sonography for trauma may be useful in identifying underlying disease.
- Thoracic radiographs may help identify underlying disease processes but only consider after the patient has been stabilized.
- Echocardiography may confirm pericardial effusion or underlying myocardial disease but should not interfere with resuscitative procedures.
- Abdominal radiographs or ultrasound may be useful once patient is stabilized to identify underlying disease.

DIAGNOSTIC PROCEDURES

Once CPA has developed, continuous ECG monitoring, blood pressure monitoring, pulse oximetry, and capnography may be useful in monitoring effectiveness of resuscitative procedures.



TREATMENT

- Institute cardiopulmonary resuscitation (CPR) immediately upon diagnosing CPA; CPR can be divided into Basic Life Support and Advanced Life Support.
- Current (2010) American Heart Association recommendations are published and electrical defibrillation was

introduced into Basic Life Support in the 2000 recommendations.

- The Reassessment Campaign on Veterinary Resuscitation (RECOVER) published evidence based guidelines in 2012.

BASIC LIFE SUPPORT

Immediate recognition of CPA

A—Airway

- Assessment—visualize the airway by extending the patient's head and neck and pulling the tongue forward; clear any debris (e.g., secretions, blood, or vomitus), manually or with suction.
- Establish an airway by either oral endotracheal intubation or, if complete obstruction exists, emergency tracheostomy.
- Correct endotracheal placement should be confirmed visually, by auscultation and/or capnography.

B—Breathing

- Assessment—make sure animal is not breathing.
- Institute artificial ventilation—administer two short breaths of ~2 seconds in duration each and reassess; if no spontaneous respiration occurs, continue ventilations at a rate of approximately 10 breaths per minute with a tidal volume of 10 mL/kg and an inspiratory time of 1 second. Peak airway pressures should not exceed 20 cm H₂O.
- Techniques for ventilation include mouth to mouth, mouth to nose, or mouth to endotracheal tube; these techniques provide ~16% oxygen; use of a mechanical resuscitator (Ambu bag) and room air provides 21% oxygen.
- The preferred technique is endotracheal intubation and ventilation with 100% oxygen using an Ambu bag or an anesthesia machine.
- The suggested rate of oxygen administration is 150 mL/kg/minute.

C—Circulation

- Assessment—palpate peripheral pulses and auscultate heart to confirm CPA.
- External thoracic compression provides at best ~30% of normal cardiac output; internal cardiac compression is two to three times more effective in improving cerebral and coronary perfusion.
- Hemodynamic studies in animal models suggest that several different mechanisms exist for generation of blood flow during chest compressions (artificial systole); during external cardiac massage the cardiac pump theory takes advantage of direct compression of the heart in patients weighing <7 kg; in patients >7 kg the thoracic pump theory is used; this technique uses increases in intrathoracic pressures to increase cardiac output via indirect effects on the major

COMPRESSION/VENTILATION TECHNIQUES

- Perform CPR in continuous, uninterrupted, 2-minute cycles when possible.
- Perform chest compressions rapidly, at a rate of between 100 and 120 compressions/minute;

(CONTINUED)

CARDIOPULMONARY ARREST

C

the chest should be displaced ~30%. • Use the cardiac pump in patients weighing < 10 kg body weight; with the patient in right lateral recumbency, perform compressions directly over the heart (intercostal spaces 3–5); this can be performed using one or two hands. • Use the thoracic pump for patients weighing > 10 kg body; with the patient in right lateral recumbency, apply thoracic compressions at the widest portion of the thorax. • Different compression and ventilation regimes have been reported. • Providing appropriate compressions (100–120 per minute) and appropriate ventilations (10 per minute) without stopping compressions for ventilations and without trying to synchronize ventilations with compressions is the goal. • Try to minimize discontinuing compressions to interpret ECG. • Avoid leaning on patient during chest compressions and allow full chest wall recoil. • Interposing abdominal compressions between chest compressions enhances cerebral and coronary blood flow by increasing aortic diastolic pressure. This technique has not been shown to improve survival but should be considered if adequate personnel are available.

OPEN-CHEST CPR

- Indicated if closed-chest CPR is ineffective or pre-existing conditions such as flail chest, obesity, diaphragmatic hernia, pericardial effusion or other significant intrathoracic disease preclude closed-chest techniques.
- Perform through a left thoracotomy at the fifth or sixth intercostal space. • Perform a pericardectomy. • The palmar surface of the fingers and thumb are used to push the ventricular blood toward the great vessel; digital compression of the descending aorta may help improve coronary and cerebral perfusion.

ADVANCED LIFE SUPPORT**D—Drugs**

- Base drug selection on the arrhythmia present. • Atropine and epinephrine are most often correct selections. • Atropine—0.04 mg/kg IV (0.54 mg/mL) ~1 mL/10 kg patient. • Epinephrine low dose—0.01 mg/kg IV (1:10,000) 1 mL/10 kg patient. • Other agents such as vasopressin (0.8 U/kg IV) may be considered if initial therapy fails. • Drugs can be administered every other CPR cycle (approximately every 4 minutes).

E—ECG

- Accurate ECG interpretation is imperative.
- Check ECG leads. • Minimize discontinuation of chest compressions while reading ECG

F—Fibrillation Control and Fluids

- Defibrillation is time-dependent; perform immediately. • Administer fluids cautiously unless known hypovolemia has led to CPA. Crystalloids, colloids, or blood products may be considered, including Oxyglobin.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Base drug selection on the arrhythmia present.
- Administer drugs via central vein, intratracheal, intraosseous, or peripheral vein, in descending order of preference. Volumes should be doubled if administering via the intratracheal route and diluted in saline.
- Use intracardiac drug administration only as a last resort unless open-chest CPR is being performed. Administration of agent into the left ventricle with concurrent digital or mechanical compression of descending aorta is optimal.

PRECAUTIONS

Only use high rates of fluid administration if there is a known history of hypovolemia; excessive fluid administration may lead to decreased coronary perfusion.

**FOLLOW-UP****PATIENT MONITORING**

- Maintain normal heart rate and blood pressure with fluids and inotropic agents.
- Arterial blood pressure. • Central venous pressure. • Blood gas analysis. • Support respiration with artificial ventilation and supplemental oxygen. • Neurologic status—if signs of increased intracranial pressure develop, consider mannitol, corticosteroids, and furosemide. • ECG—continuously.
- Urine output. • Body temperature.
- Radiograph thorax to assess resuscitative injury. • Diagnose and correct factors that led to initial CPA.

PREVENTION/AVOIDANCE

Careful monitoring of all critically ill patients

POSSIBLE COMPLICATIONS

- Vomiting • Aspiration pneumonia
- Fractured ribs or sternebrae • Pulmonary contusions and edema • Pneumothorax
- Acute renal failure • Neurologic deficits
- Cardiac arrhythmias

EXPECTED COURSE AND PROGNOSIS

- Prognosis depends on underlying disease process. • Rapid return to spontaneous cardiac and respiratory function improves the prognosis. • Overall prognosis is poor; < 10% of patients are discharged.

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

None

SYNONYMS FOR CPA

- Cardiac arrest • Heart attack

SYNONYMS FOR CPR

CPCR = cardiopulmonary cerebral resuscitation

SEE ALSO

- Ventricular Fibrillation • Ventricular Standstill (Asystole)

ABBREVIATIONS

- CNS = central nervous system • CPA = cardiopulmonary arrest • CPR = cardiopulmonary resuscitation • ECG = electrocardiogram • FAST = focused assessment with sonography for trauma

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CARNITINE DEFICIENCY



BASICS

OVERVIEW

L-carnitine is a quaternary amine that is an important part of the enzyme systems that transport fatty acids into mitochondria so that they can be oxidized to make energy available to the cell. It also has other important metabolic and scavenging functions within the cell. In the heart and other organs that depend on the oxidation of fatty acids to supply their high energy requirements for contraction or other work, L-carnitine deficiency results in inadequate production of energy to meet those needs. Carnitine deficiency complicates some cases of dilated cardiomyopathy in dogs. The presence of L-carnitine deficiency in association with cardiomyopathy does not mean that the deficiency is the sole cause of the myopathy, although correcting the deficiency (if possible) makes medical and physiologic sense.

L-carnitine is not synthesized in heart or skeletal muscle and must therefore be transported into those cells from plasma. In the dog, dietary carnitine intake influences plasma concentrations significantly, and oral carnitine supplementation is usually an effective means of raising plasma and subsequently muscle carnitine levels. The FDA has approved the addition of physiologic amounts of carnitine to commercial dog foods for the prevention of plasma (and subsequently muscle) carnitine deficiency. This action is prudent based on current knowledge regarding the lack of L-carnitine in most commercial dog food and the effect of those diets on canine carnitine plasma levels. It is not known whether this action will affect the prevalence of dilated cardiomyopathy or other manifestations of carnitine deficiency.

SIGNALMENT

Dogs

- Boxer, Doberman pinscher, Great Dane, Irish wolfhound, and other large- and giant-breed dogs appear to be most commonly affected with dilated cardiomyopathy.
- At least some American cocker spaniels with DCM are carnitine-deficient, and a blinded, placebo-controlled trial suggests that L-carnitine supplementation combined with taurine supplementation is beneficial in the medical management of these patients.

SIGNS

- Clinical signs of carnitine deficiency can be diverse; mitochondria in all tissues use L-carnitine to produce energy from fatty acids.
- Signs range from heart muscle failure and dilated cardiomyopathy (most frequently

recognized) to skeletal muscle pain, weakness, exercise intolerance, and/or lethargy.

- See Cardiomyopathy, Dilated—Dogs.

CAUSES & RISK FACTORS

• Some dogs with cardiomyopathy have been documented to have carnitine transport defects, in which muscle carnitine is low even in the face of adequate plasma carnitine concentrations. In order to transport fatty acids or other compounds (such as acetyl Co-A) into or out of the mitochondria, free L-carnitine is esterified to the substance, forming a carnitine ester. With some mitochondrial enzyme defects (e.g., multiple Co-A dehydrogenase defects), free L-carnitine is used to "scavenge" potentially toxic metabolites, which appear harmlessly in the urine as carnitine esters. In these cases, the total amount of carnitine (free carnitine plus esterified) in the plasma or muscle may be normal or even high, but the ratio of free carnitine to esterified carnitine is decreased. This situation is known as carnitine insufficiency (because even though the concentration of free carnitine may be within the normal range, it is insufficient to meet the body's pathologically increased need for free carnitine).

- Certain families of boxers appear to be at especially high risk of developing symptomatic dilated cardiomyopathy in association with and probably caused by carnitine deficiency.



DIAGNOSIS

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

Plasma carnitine concentrations appear to be a specific but insensitive indicator of myocardial or skeletal muscle carnitine deficiency. Plasma free carnitine concentrations of less than 8 micromoles/L are considered diagnostic of systemic carnitine deficiency. Plasma concentrations in the normal or supernormal range do not rule out myocardial carnitine deficiency or insufficiency.

DIAGNOSTIC TEST

Endomyocardial biopsy specimens must be blotted dry and snap frozen in liquid nitrogen. Measurement of free and esterified L-carnitine concentrations normalized to the amount of non-collagenous protein in the biopsy remains the only definitive diagnostic test. Myocardial free carnitine concentrations of less than 3.5 nanomoles/mg of non-collagenous protein are considered diagnostic of myocardial carnitine deficiency. Ratios of esterified to free carnitine > 0.4 are

considered diagnostic of carnitine insufficiency.



TREATMENT

Treatment with L-carnitine does not replace conventional treatment for DCM, even in most dogs with carnitine deficiency. Some dogs, including some families of carnitine-deficient boxers, fail to respond clinically to supplementation. While supplementation dramatically improves a small percentage (about 5%, in the author's experience) of dogs with dilated cardiomyopathy, the overall efficacy of L-carnitine supplementation for the treatment of dilated cardiomyopathy is untested. If a trial of metabolic supplementation is desired in the absence of known L-carnitine deficiency, the combination of L-carnitine with taurine (500 mg q8–12h), and Co-Q10 (100 mg q8–12h) seems prudent.



MEDICATIONS

DRUG(S)

Carnitine Supplementation

- Large-breed dogs—2 g (approximately 1 tsp L-carnitine powder) q8–12h.
- American cocker spaniels—(in combination with taurine) 1 g (approximately one-half tsp L-carnitine powder) q8–12h.



FOLLOW-UP

Repeat echocardiogram 3–6 months after initiating L-carnitine supplementation to assess the efficacy of treatment.



MISCELLANEOUS

Suggested Reading

- Keene BW, Panciera DP, Atkins CE, et al. Myocardial L-carnitine deficiency in a family of dogs with dilated cardiomyopathy. JAVMA 1991, 201:647–650.
Sanderson SL, Gross KL, Ogburn PN, et al. The effect of dietary fat and L-carnitine on plasma and whole blood taurine concentrations and cardiac function in healthy dogs consuming protein-restricted diets. Am J Vet Res 2001, 62:1616–1623.
Author Bruce W. Keene
Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

CATARACTS



BASICS

DEFINITION

Opacification of the lens (focal or diffuse).

PATHOPHYSIOLOGY

- The normal lens is composed of perfectly aligned lens fibers that create a transparent structure. A clear capsule surrounds the cortex and nucleus. New lens fibers are continually produced at the equatorial region of the lens cortex throughout life. The aqueous humor provides nutrition to the lens.
- A cataract occurs when there is derangement of lens fibers due to alterations in lens nutrition, energy metabolism, protein synthesis or metabolism, or osmotic balance.
- Anterior uveitis is a common cause of alteration of lens nutrition. Genetics can result in altered protein and energy metabolism, or protein synthesis, in the lens.
- Diabetes mellitus will affect the osmotic balance within the lens of the dog. Hyperglycemia increases glucose in the aqueous and lens overwhelming the normal glycolysis pathway; glucose is then shunted to the sorbitol pathway; when sorbitol is produced it creates an osmotic gradient that draws water into the lens, resulting in the rapid formation of a cataract from lens fiber swelling and derangement. Because the sorbitol pathway requires aldose reductase enzyme, the more aldose reductase in the lens, the more readily diabetic cataracts will form. Dogs have more aldose reductase than cats, making cats more resistant to developing diabetic cataracts. There is some variability between individual dogs, which may explain why some diabetic dogs are more resistant to cataract development.

SYSTEMS AFFECTED

Ophthalmic

GENETICS

- Inheritance has been established for many dog breeds (see "Suggested Reading"); the most common mode of inheritance is autosomal recessive.
- Inheritance has been established in the Himalayan cat (autosomal recessive).

INCIDENCE/PREVALENCE

- Cataract is one of the leading causes of blindness in dogs.
- The prevalence of genetic cataracts varies significantly between breeds; it has been reported as high as 10% in some breeds.
- Most diabetic dogs will develop cataracts regardless of their diabetic control.
- Cataracts are rare in cats.

SIGNALMENT

Species

Dog and cat

Breed Predilections

Over 135 dog breeds are suspected as being predisposed to hereditary cataracts.

Mean Age and Range

Cataracts can develop at any age; genetic cataracts can develop as early as 6 months of age.

SIGNS

Historical Findings

- The owner may notice the cloudy/white appearance of the lens.
- Vision loss may be noted by the owner when the cataracts are bilateral, especially diabetic cataracts that have a rapid, bilateral onset.
- Polyuria/polydipsia is usually noticed by the owner prior to cataract development in diabetic dogs.

Physical Examination Findings

- General physical examination findings: unremarkable unless the dog is an undiagnosed diabetic.
- Ophthalmic examination findings: opacification in one or both lenses.
 - Incipient stage: small, focal opacity/opacities in the lens that does not interfere with the view of the fundus; no vision deficits.
 - Immature stage: diffusely cloudy appearance to the lens with the tapetal reflection still visible and some portions of the fundus visible through a dilated pupil; the menace reflex is positive but tracking may be negative.
 - Mature stage: completely opaque lens with no tapetal reflection visible; blind.
 - Hypermature stage: wrinkled lens capsule, areas of dense white mineralization, may have portions of liquefied cortex (white, sparkly to clear); deep anterior chamber; blind unless there is a large area of clear liquefied cortex.
 - Intumescent mature cataract: opaque, swollen lens usually due to the hyperosmotic effect of diabetes; shallow anterior chamber.

CAUSES

- Hereditary—most common cause in dogs.
- Diabetes mellitus.
- Anterior uveitis—either by altered nutrition of the lens from the abnormal aqueous, or by posterior synechia and inflammatory debris causing opacification of the anterior lens capsule.
- Trauma—perforating injury that disrupts the anterior lens capsule, most commonly a cat claw injury, especially in puppies and kittens.
- Senile—slowly progressive cataract in geriatric animals usually beginning as dense nuclear sclerosis followed by gradual spoke-like opacities extending into the cortex.
- Congenital—due to heredity, *in utero* insult, or associated with other congenital ocular anomalies such as persistent pupillary membranes, persistent hyperplastic primary vitreous/persistent tunica vasculosa lentis, or a hyaloid artery attachment.

- Surgery—transpupillary laser energy, intraocular instrument trauma.

- Toxic—from long-term ketoconazole therapy; suspected secondary to toxic by-products of degenerating photoreceptors in dogs with progressive retinal atrophy.
- Radiation—when the eye is in the radiation treatment field for head neoplasia.
- Hypocalcemia—can cause bilateral, diffuse punctate or incipient cataracts.
- Nutritional—use of unbalanced milk replacers in bottle-fed puppies and kittens.
- Electrical shock—chewing electrical cords or lightning strike.

RISK FACTORS

- Diabetes mellitus is a great risk factor in dogs.
- Chronic anterior uveitis.
- Progressive retinal atrophy.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Lenticular nuclear sclerosis—normal aging change in the lens of dogs and cats starting at 6 years of age due to compression of older lens fibers in the center of the lens; gradually becomes more visible with age and can be mistaken for a cataract in geriatric patients; definitive diagnosis can be made using mydriasis (1% tropicamide) and the observation of a perfectly round, bilaterally symmetrical, homogeneous nucleus in the center of each lens, and the ability to view the fundus through the lens; vision is rarely affected and treatment is not indicated.

CBC/BIOCHEMISTRY/URINALYSIS

Dogs with diabetic cataracts may have hyperglycemia and glucosuria.

IMAGING

Ocular ultrasound can be used to evaluate the posterior lens capsule for any sign of rupture and can evaluate for retinal detachment prior to cataract surgery.

DIAGNOSTIC PROCEDURES

Electroretinogram is performed prior to cataract surgery to evaluate for retinal degeneration when the fundus is not visible due to the cataract.



TREATMENT

ACTIVITY

For safety, blind animals should not be allowed access to an in-ground swimming pool or elevated decks with open railings; use caution near stairs; restrict outside activity to fenced yards or leash walks.

CATARACTS

(CONTINUED)

CLIENT EDUCATION

- Cataract surgery is routinely performed with an overall 80–90% success rate.
- Once the cataracts are removed they cannot return.
- Artificial lens implants will restore essentially normal vision.
- Evaluation for surgery should be done early in the course of cataract development to avoid complications that may result in the cataract becoming inoperable, to allow time to plan for the surgery, and in some cases to eliminate the need and extra cost for an ocular ultrasound and electroretinogram.

SURGICAL CONSIDERATIONS

- Phacoemulsification (removal of the cataract through a 3 mm corneal incision using ultrasonic waves to emulsify and then aspirate the lens cortex and nucleus) is the most common technique for cataract removal.
- The ideal time for cataract surgery is the immature/early mature stage.
- Inherited, diabetic, and senile cataracts are potentially good candidates for surgery; cataracts secondary to anterior uveitis are normally poor surgical candidates.
- Artificial intraocular lenses are routinely placed inside the patient's lens capsule; lens implants restore normal focus and help minimize posterior capsular fibrosis; if a lens cannot be implanted (e.g., due to an unstable lens capsule or luxated lens), the dog or cat will still have very functional vision.
- Traumatic lens perforation with release of lens cortex into the anterior chamber requires immediate removal of the lens to avoid a severe granulomatous anterior uveitis and vision loss.



MEDICATIONS

DRUG(S) OF CHOICE

- Topical anti-inflammatory medication is recommended q6–24h to help prevent or treat lens-induced uveitis with immature, mature, and hypermature cataracts; this can be a topical NSAID such as flurbiprofen, diclofenac, or ketorolac, or a topical steroid such as prednisolone acetate 1% or dexamethasone 0.1%; topical NSAIDs may be preferable in diabetic patients unless the uveitis is severe.
- Topical atropine q8–24h is indicated for lens-induced uveitis; *atropine is contraindicated with glaucoma.*

- Oral NSAIDs (carprofen, meloxicam, deracoxib) are also used to treat lens-induced uveitis.
- Topical antioxidants are advertised as able to reverse cataract changes; to date there has been no published data conclusively showing a significant reversal, or delay in progression, of a cataract with antioxidant therapy; unfortunately time spent trying medical therapy will delay evaluation for surgery, resulting in surgery being performed at a suboptimal stage, or complications from the cataract making it inoperable.
- Topical aldose reductase inhibitors are currently under investigation and may prove helpful in delaying the onset of diabetic cataracts in dogs in the future.



FOLLOW-UP

PATIENT MONITORING

- Incipient or early immature cataracts should be monitored regularly for progression in order to select the ideal time for surgery and to avoid complications associated with cataracts.
- Postoperative monitoring by the surgeon is critical for the success of surgery and should be clearly discussed with the owner prior to surgery.

PREVENTION/AVOIDANCE

Do not breed animals with cataracts.

POSSIBLE COMPLICATIONS

- Lens-induced uveitis—associated with hypermature cataracts and cataracts that progress very rapidly; caused by antigenic lens proteins leaking through the lens capsule. Clinical signs can be very subtle (e.g., low intraocular pressure) to extreme (granulomatous uveitis with dense aqueous flare, miosis, synechia, keratic precipitates); preoperative lens-induced uveitis increases the risk of postoperative complications.
- Secondary glaucoma—impaired aqueous outflow from intraocular changes associated with lens-induced uveitis, or from an intumescent cataract causing a forward displacement of the iris narrowing the iridocorneal angle.
- Retinal detachment—associated with hypermature cataracts and cataracts in young dogs with a rapid onset and cortical liquefaction.

- Lens luxation—associated with hypermature cataracts in which the lens and capsule shrink, causing the zonules to stretch and break, resulting in a lens subluxation or luxation.

EXPECTED COURSE AND PROGNOSIS

- Most cataracts are progressive, although the rate of progression can vary widely depending on age, breed, and location of the cataract.
- Long-term prognosis following cataract surgery is very good; however, some patients have increased risk for postoperative complications; preexisting anterior uveitis (even when medically controlled), genetic predisposition for glaucoma, and unstable peripheral retina or undetected peripheral retinal tears increase the risk for postoperative chronic uveitis, glaucoma, and retinal detachment, respectively.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Retinal detachment
- Lens-induced uveitis
- Congenital ocular anomalies

AGE-RELATED FACTORS

- Immediate referral for cataracts in young dogs (< 2 years of age) is recommended because the cataract can progress very rapidly with partial cortical liquefaction followed by retinal detachment.
- Nuclear sclerosis is prominent in geriatric animals; a dilated exam may be necessary to definitively distinguish nuclear sclerosis from cataract.

SEE ALSO

- Anterior Uveitis—Cats
- Anterior Uveitis—Dogs
- Diabetes chapters

ABBREVIATION

- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

Maggs DJ, Miller PE, Ofri R. Fundamentals of Veterinary Ophthalmology, 5th ed., St Louis, MO:Elsevier, 2013.

Author Margi A. Gilmour

Consulting Editor Paul E. Miller



Client Education Handout
available online

CEREBELLAR DEGENERATION



BASICS

OVERVIEW

- Progressive, breed-specific, genetically induced premature aging and death of cerebellar cortical neurons due to failure in neuronal energy supply, excitotoxicity, and inflammation; neonatal, postnatal, and (rare) adult onset.
- Non-progressive disorder due to *in utero* or neonatal viral infection in cats (feline panleukopenia) and dogs (canine herpesvirus).

SIGNALMENT

Progressive

- Dog and cat. • Autosomal recessive mode of inheritance—Finnish hound (signs at 9 weeks), Kerry blue terrier and Chinese crested (signs at 12–16 weeks), rough-coated collie (signs at 1–2 months), Old English sheepdog and Gordon setter (signs at 6–36 months), American Staffordshire terrier (signs at 1.5–9 years), and domestic shorthair cats (signs at 7–9 weeks). • Suspected autosomal recessive mode of inheritance—beagle and samoyed (signs at 3 weeks), English bulldog (signs at 5–8 months), Bern running dog, and Irish setter, Brittany spaniel (signs at 7–13 years). • X-linked mode of inheritance—probable in English pointer because only males affected. • Rhodesian ridgeback—cerebellar degeneration and coat color dilution reported in one family.
- Adult-onset cerebellar cortical abiotrophy with retinal degeneration reported in a domestic shorthair cat. • Cerebellar cortical abiotrophy described in two Havana brown kittens—signs observed at 4 and 5 weeks, inherited disorder suspected.

Non-progressive

- Dog and cat. • Coton de Tulear—autosomal recessive mode of inheritance.
- Signs appear when patient is 2–5 weeks old.

SIGNS

- Hypermetria. • Broad-based stance.
- Swaying of body. • Intention tremors.
- Lack of menace responses with normal vision and pupillary light reflexes. • Head tilt and episodes of vestibular ataxia with resting or positional nystagmus. • Diffuse tapetal hyperreflectivity on funduscopic exam.
- Decerebrate posture—opisthotonus with extensor rigidity of the forelimbs and flexed hind limbs. • Altered mentation, proprioceptive deficits, and paresis are not features of this condition. • Progression of signs varies. • Use caution in interpreting progression of signs. As a puppy or kitten with cerebellar degeneration due to *in utero* or neonatal infection grows and becomes more

active, cerebellar ataxia may appear to worsen, but the disease itself is non-progressive.

CAUSES & RISK FACTORS

- Feline panleukopenia or canine herpesvirus infection *in utero* or neonatally. • Poor vaccination history or exposure to modified live virus during gestation.
- Breeding affected animals or animals with familial history of cerebellar degeneration.
- A syndrome of hepatocerebellar degeneration was described in a litter of Bernese mountain dogs.
- Paraneoplastic cerebellar degeneration has been reported in humans.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Lysosomal storage diseases—diffuse diseases of the CNS; differentiate by signs related to other parts of the CNS besides the cerebellum.
- Toxicity (e.g., hexachlorophene)—differentiate by history of exposure.
- Inflammatory diseases—*infectious* (e.g., canine distemper and FIP); frequently accompanied or preceded by systemic signs of illness. Immune diseases (dogs); in both cases, differentiate by MRI and CSF analysis.
- Cerebellar cyst—differentiate by imaging (MRI or CT). • Medulloblastoma (cerebellar tumor)—reported in dogs and cats < 1 year old; differentiate by imaging (MRI or CT) and CSF analysis.
- Other primary and metastatic tumors in adult dogs—differentiate by imaging (MRI or CT) and CSF analysis.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

N/A

IMAGING

MRI—cerebellum may be smaller than normal.

DIAGNOSTIC PROCEDURES

- CSF analysis—normal with non-progressive disease; normal or high protein concentration and normal cell counts with progressive disease. • Cerebellar biopsy—may be only definitive means of antemortem diagnosis.



TREATMENT

- Amantadine has potentiating effects on dopaminergic neurotransmission in the CNS and anticholinergic activity; buspirone is a serotonin agonist; research models demonstrate some promise for progressive cerebellar degeneration. • Neuroprotective agents that may have promising effects such as coenzyme Q10 and acetyl-L-carnitine.

- Outpatient—unless severe deficits preclude nursing care at home. • Restrict activity to safe areas; avoid stairs, proximity to swimming pools, etc. • Diet—normal; restrict intake if vestibular episodes are accompanied by emesis (to avoid aspiration pneumonia).
- Non-progressive disease—patient may show some improvement as animal learns to compensate for disabilities.



MEDICATIONS

DRUG(S)

N/A

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- Neurologic status—examine at weekly to monthly intervals if progression of signs is uncertain; consider videotaping patient to determine progression objectively.
- Progression of signs—rate varies; depends on signalment; ranges from days to years.
- Do not vaccinate pregnant animals with modified live virus. • Do not breed animals with a familial history of cerebellar disease.



MISCELLANEOUS

ABBREVIATIONS

- CNS = central nervous system • CSF = cerebrospinal fluid • CT = computed tomography • FIP = feline infectious peritonitis • MRI = magnetic resonance imaging

Suggested Reading

de Lahunta A, Glass E, Kent M. Cerebellum. In: de Lahunta A, Glass E, eds. Veterinary Neuroanatomy and Clinical Neurology, 4th ed. Saint Louis, MO: W.B. Saunders, 2015, pp. 368–408.

Henke D, Bottcher P, Doherr MG, Oechtering G, Flegel T. Computer-assisted magnetic resonance imaging brain morphometry in American staffordshire terriers with cerebellar cortical degeneration. J Vet Intern Med 2008, 22:969–975.

Summers BA, Cummings JF, de Lahunta A. Veterinary Neuropathology. St. Louis, MO: Mosby, 1995, pp. 301–305.

Authors Richard J. Joseph and Anne E. Buglione

Consulting Editor Joane M. Parent

CEREBELLAR HYPOPLASIA



BASICS

OVERVIEW

Caused by incomplete development of parts of the cerebellum owing to intrinsic (inherited) or extrinsic (infectious, toxic, or nutritional) factors.

SIGNALMENT

- Symptoms may not be visible until puppies and kittens begin to stand/walk (usually by 6 weeks old).

• Hereditary in Airedale, chow chow, Boston terrier, Labrador retriever, weimaraner, shih-tzu, miniature schnauzer, and bull terrier.

SIGNS

- Symmetrical, non-progressive cerebellar disorder—head bobbing; limb tremors; aggravated by movement or eating and disappear during sleep (intention tremors).
- Cerebellar ataxia, wide-base stance.
- Dysmetria and disequilibrium—falling, flipping over.

CAUSES & RISK FACTORS

- Cats—usually transplacental or perinatal infection with panleukopenia virus (wild or from modified live virus used in some vaccines), which selectively attacks rapidly dividing cells, e.g., external germinal layer of the cerebellum at birth and for 2 weeks post-natal.
- Dogs—hereditary in some breeds (autosomal recessive).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Age, breed, history, typical symmetrical and non-progressive symptoms—usually sufficient for tentative diagnosis.
- Early cerebellar abiotrophy—postnatal degeneration after normal development; slow progression of signs over weeks to months; neonatal onset (beagle, Samoyed, Rhodesian ridgeback, Irish setter, Jack Russell terrier, miniature poodle) or postnatal onset

(Australian kelpie at 5–6 weeks; Kerry blue terrier at 8–16 weeks; rough-coated collie at 4–8 weeks; bullmastiff at 4–9 weeks).

- Neuroaxonal dystrophy—slowly progressive cerebellar signs starting around 5 weeks of age in cats and 7 weeks in Chihuahuas.
- Cerebellar sequels of systemic canine herpesvirus infection—follow systemic illness.
- Concomitant seizures or other cerebral signs—suggest other malformations, such as lissencephaly (wirehaired fox terrier and Irish setter) or hydrocephalus.
- Final diagnosis possible only at necropsy.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

N/A

IMAGING

Magnetic resonance imaging—cerebellar atrophy or malformation (incomplete or asymmetrical filling of the caudal cranial fossa by the cerebellum); rule out other malformations.

PATHOLOGIC FINDINGS

- Cerebellum—normally very small in newborn kitten or puppy (cerebellar development continues for up to 10 weeks post-natal); subtle to marked atrophy; as necropsy is performed weeks to months after birth, there is no sign of active inflammation.
- Transverse fibers of the pons—decreased size associated with marked cortical cerebellar atrophy.
- Hydrocephalus—may be concomitant, resulting from multifocal inflammation or multiple malformations (e.g., Dandy-Walker syndrome).
- Microscopic—depletion of cerebellar cortex cellular layers.



TREATMENT

None

PREVENTION

Avoid using modified live panleukopenia vaccines in reproducing female cats and keep cats vaccinated against panleukopenia.



MEDICATIONS

DRUG(S)

N/A

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

Helps confirm the diagnosis (as necessary)

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

- Slight improvement may occur as patient compensates for deficits.
- Deficits—permanent; do not progress; compatible with a normal lifespan.
- Some patients may be acceptable indoor pets.

CARE

- Restrict environment to prevent injuries and road accidents—no climbing, falling, or escaping.
- Nutritional support as needed.
- Euthanasia—severely affected animals that are unable to feed, groom, or be house-trained.



MISCELLANEOUS

Suggested Reading

de Lahunta A, Glass E, Kent M. Veterinary Neuroanatomy and Clinical Neurology, 4th ed. Saint Louis, MO: W.B. Saunders, 2015, pp. 389–390.

Author Christine F. Berthelin-Baker

Consulting Editor Joane M. Parent

CEREBROVASCULAR ACCIDENTS

C



BASICS

DEFINITION

- Sudden onset of non-progressive focal brain signs.
- Signs must remain for > 24 hours for a diagnosis of CVA.
- Permanent brain damage usually ensues.
- Called transient ischemic attack or "TIA" if clinical signs resolve within 24 hours.

PATOPHYSIOLOGY

- Cerebrovascular diseases are the underlying cause of CVA.
- Brain abnormality resulting from a pathologic process that compromises the blood supply to the brain.
- Lesions affecting the cerebral blood vessels are divided into two broad categories:
 - Hemorrhagic stroke—ruptured blood vessel with hemorrhage into or around the brain
 - Ischemic stroke—abrupt disruption of blood flow from blockage of an artery depriving the brain tissue of oxygen and glucose.

SYSTEMS AFFECTED

- Nervous
- Multisystemic—if underlying cause present

INCIDENCE/PREVALENCE

Unknown; supposed low compared to human

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Ischemic stroke—Cavalier King Charles spaniel and greyhound seem predisposed; small breed (≤ 15 kg) more likely to have cerebellar infarct; large breed (> 15 kg) more likely to have midbrain or thalamic infarct.
- Hemorrhagic stroke—unknown.

Mean Age and Range

Unknown

Predominant Sex

Unknown

SIGNS

Historical Findings

- Ischemic stroke—peracute to acute non-progressive focal brain signs.
- Hemorrhagic stroke—acute to subacute focal or multifocal brain signs that can progress over a short period of time.

Physical Examination Findings

- Fundus examination—may reveal tortuous vessels (systemic hypertension), hemorrhage (coagulopathy or systemic hypertension), or papilledema (elevated ICP).
- Coagulation defects—may underlie hemorrhagic stroke and cause hemorrhage in any tissue or organ and anemia.

Neurologic Examination Findings

- Ischemic stroke—signs depend on the localization of the vascular insult

(prosencephalon, midbrain, pons, medulla, cerebellum). • Hemorrhagic stroke—signs relate to increased ICP with nonspecific forebrain and/or brainstem disturbance.

CAUSES

Ischemic Stroke

Dogs

- Unknown in 50% of cases.
- Endocrine diseases—hyperadrenocorticism, hypothyroidism, diabetes.
- Embolism, thromboembolism—neoplastic (hemangiosarcoma, lymphoma), infectious (associated with bacterial endocarditis or other sources of infection), and aortic or cardiac.
- Systemic hypertension—chronic kidney disease, protein losing enteropathy.
- Fibrocartilaginous embolism.
- Intravascular lymphoma.
- Parasite migration (*Cuterebra*) or embolism (*Dirofilaria immitis*).

Cats

- Parasite migration (*Cuterebra* or heartworms)
- Systemic hypertension—hyperthyroidism, chronic kidney disease, heart disease
- Neoplastic embolism

Hemorrhagic Stroke

Dogs

- Ruptured congenital vascular anomalies
- Primary and secondary brain tumors
- Inflammatory disease of arteries and veins (vasculitis)
- Intravascular lymphoma
- Brain hemorrhagic infarction
- Impaired coagulation

Cats

- Primary and secondary brain tumors
- Inflammatory disease of arteries and veins (vasculitis)
- Brain hemorrhagic infarction
- Impaired coagulation—cerebral amyloid angiopathy
- Systemic hypertension

RISK FACTORS

- Ischemic stroke—systemic hypertension, systemic condition associated with hypercoagulability syndrome.
- Hemorrhagic stroke—systemic hypertension, coagulopathy.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Head trauma—history and physical findings suggestive of trauma.
- Decompensation from primary or metastatic brain tumor—signs are progressive.
- Infectious and non-infectious encephalitis—acute to subacute clinical signs that gradually worsen.
- Neurotoxicity—bilateral, symmetrical neurologic deficits.

CBC/BIOCHEMISTRY/URINALYSIS

Most often normal; may show changes reflecting underlying cause.

OTHER LABORATORY TESTS

- Cerebrospinal fluid—unlikely to confirm CVA, may help rule out inflammatory CNS disease. Variable findings; either normal, or

mild mononuclear or neutrophilic pleocytosis; protein concentration occasionally elevated.

- Prothrombin time—screening test for extrinsic mechanism defects.
- Activated partial thromboplastin time—screening test for intrinsic mechanism defects.
- Bleeding time—prolonged in patients with von Willebrand's disease; normal with most other coagulation defects, except disseminated intravascular coagulation.
- Thromboelastography, D-dimer assay and antithrombin III—screening tests for hypercoagulability syndrome as possible cause of ischemic stroke.
- Endocrine testing—hyperadrenocorticism, thyroid disease, and pheochromocytoma.
- Renal disease—urine protein/creatinine ratio.

IMAGING

Ischemic Stroke

- CT—often normal during acute phase.
- MRI—within 12–24 hours of onset to distinguish hemorrhage from infarction. T2-weighted and fluid-attenuated inversion recovery (FLAIR) images particularly useful. T2*-weighted (gradient echo) images to show presence of or exclude intracranial hemorrhage. DWI sequence: ideal for identification of hyperacute stroke, excluding stroke mimics. Perfusion-weighted MRI can be used to depict brain regions of hypoperfusion and derive the tissue at risk by comparing the results with the findings on DWI. Time of flight magnetic resonance angiography and contrast-enhanced MRA can be used to assess intracranial vascular status of stroke patients.

Hemorrhagic Stroke

- CT—very sensitive for detection of acute hemorrhage; hyperdensity due to hyperattenuation of X-ray beam by the globin portion of blood. Attenuation decreases until the hematoma is isodense at about 1 month from onset. Periphery of hematoma contrast-enhances from 6 days to 6 weeks after onset due to revascularization.
- MRI—signal intensity of intracranial hemorrhage is influenced by several intrinsic (time from ictus, source, size and location of hemorrhage) and extrinsic (pulse sequence and field strength) factors. As hematoma ages, oxyhemoglobin in blood breaks down sequentially into several paramagnetic products (deoxyhemoglobin, methemoglobin, hemosiderin) with each different MRI signal intensities. Compared to other conventional sequences, T2*-weighted (gradient echo) images demonstrate readily detectable hypointensity regardless of the time from ictus, the source and location of hemorrhage, or the field strength.
- Multiple hemorrhagic lesions— < 5 mm most often associated with hyperadrenocorticism, hypertension, chronic kidney disease or hypothyroidism. Single hemorrhagic lesion—most often associated

CEREBROVASCULAR ACCIDENTS

(CONTINUED)

with *Angiostrongylus vasorum*. Multiple hemorrhagic lesions— ≥ 5 mm most often associated with *Angiostrongylus vasorum*, primary extracranial neoplasia with metastases (haemangiosarcoma).

DIAGNOSTIC PROCEDURES

Diagnosis of potential underlying causes.

Ischemic Stroke

Evaluate for hypertension (and potential underlying causes), endocrine disease (hyperadrenocorticism, hypothyroidism, hyperthyroidism, diabetes mellitus), chronic kidney disease (especially protein-losing nephropathy), protein-losing enteropathy, heart disease and metastatic diseases (particularly hemangiosarcoma).

Hemorrhagic Stroke

- Evaluate for coagulopathy (and potential underlying causes), hypertension (and potential underlying causes) and metastatic diseases (particularly hemangiosarcoma).

PATHOLOGIC FINDINGS

Ischemic Stroke

• Ischemic necrosis centered on grey matter due to selective vulnerability. • Lesions limited to brain area vascularized by the affected vessel with sharply demarcated borders; normal surrounding brain tissue; minimal to no mass effect. • Global brain ischemia usually affects a dense area of selectively vulnerable neurons. Specific anatomical areas including cerebral cortex, hippocampus, certain basal nuclei (e.g., caudate nuclei), thalamus and cerebellar Purkinje cell layers are more susceptible to hypoxic injury. • Early ischemic cell changes occur rapidly and are a result of energy deprivation with swelling of the mitochondria and endoplasmic reticulum, which causes cytoplasmic microvacuolation. More chronic lesions are characterized by post-necrotic atrophy of the brain parenchyma, endothelial proliferation in viable capillaries and accumulation of Gitter cells.

Hemorrhagic Stroke

• Parenchymal bleeding results from rupture of the small penetrating brain arteries. Most acute cases reveal fresh hemorrhage and acute neuronal necrosis that is slowly removed by macrophages, leaving over time a cystic cavity lined by fibrillary astrocytes. • Histology is characterized by presence of edema, neuronal damage, macrophages and neutrophils in the region surrounding the hematoma. • While some cerebral hemorrhages stop quickly as a result of clotting and tamponade by the surrounding regions, others tend to expand over time. The latter is a result of continued bleeding from the primary source and to the mechanical disruption of surrounding vessels. The hemorrhage spreads between planes of white-matter cleavage with minimal destruction, leaving nests of intact neural

tissue within and surrounding the hematoma.



TREATMENT

APPROPRIATE HEALTH CARE

- Any identified underlying disease should be treated. • Provide supportive care, maintain adequate tissue oxygenation, and manage neurologic and non-neurologic complications.
- More specific therapies aim at preventing further neurologic deterioration.

NURSING CARE

Ischemic Stroke

- Monitoring and correction of basic physiologic variables (e.g., oxygen level, fluid balance, blood pressure, body temperature).
- Maintenance of systemic arterial blood pressure within physiologic range; aggressive lowering of blood pressure should be avoided during the acute stages unless the patient is at high risk of end-stage organ damage (systolic blood pressures > 180 mmHg). • No evidence that glucocorticoid provides beneficial neuroprotection; most neuroprotective agents tested have either failed to prove their efficacy in clinical trials or are awaiting further investigation.

Hemorrhagic Stroke

- Patient stabilization (airway protection, monitoring and correction of vital signs).
- Assessment and monitoring of neurologic status. • Determination and treatment of potential underlying causes of hemorrhage.
- Assessment for the need of specific treatment measures including management of raised ICP, which revolves around reducing cerebral edema, optimizing cerebral blood volume and eliminating space-occupying mass. • Risk of neurologic deterioration and cardiovascular instability highest during the first 24 hours after onset of intracranial hemorrhage as the space-occupying lesion slowly expands and cerebral vasogenic edema develops.



MEDICATIONS

DRUG(S) OF CHOICE

Ischemic Stroke

- Antihypertensive—consider if systemic BP > 180 mmHg on serial evaluation and/or severe ocular manifestations of hypertension.
- ACE inhibitor—enalapril (0.25–0.5 mg/kg q12h) or benazepril (0.25–0.5 mg/kg q12h) and/or calcium channel blockers such as amlodipine (0.1–0.25 mg/kg q24h).
- Prevention of clot formation—consider in proven cardiac sources of embolism; antiplatelet therapy with low-dose aspirin

(0.5 mg/kg PO q24h) or clopidogrel (2–4 mg/kg PO q24h) and low molecular weight heparin can be used prophylactically. Low molecular weight heparin 80–150 IU/kg SC can be used in suspected or confirmed case of hypercoagulable state. Anti-factor Xa activity should be monitored although this may not be practical.

Hemorrhagic Stroke

Mannitol—if suspected elevated ICP unresponsive to extracranial stabilization measures (0.25–1 g/kg IV over 10–20 minutes).



FOLLOW-UP

PATIENT MONITORING

Frequent neurologic evaluations in the first 48–72 hours to monitor progress.

POSSIBLE COMPLICATIONS

Relapse of ischemic stroke.

EXPECTED COURSE AND PROGNOSIS

- Maximum severity of signs usually reached within 24h for ischemic stroke. • Resolution of signs—gradual within 2–10 weeks. Some dogs/cats may be left with permanent neurologic signs due to irreversible brain damage. • Dogs with causal medical condition significantly more likely to relapse and have significant shorter survival time than dogs with no identifiable medical condition.
- Prognosis for global brain ischemia difficult to predict as there are no controlled studies.



MISCELLANEOUS

SYNOMYS

Stroke

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- CNS = central nervous system • CT = computed tomography • CVA = cerebrovascular accident • DWI = diffusion weighted imaging • ICP = intracranial pressure • MRI = magnetic resonance imaging

Suggested Reading

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Consulting Editor Joane M. Parent

CERUMINOUS GLAND ADENOCARCINOMA, EAR



BASICS

OVERVIEW

- Most common primary malignant tumor of the external auditory meatus arising from modified apocrine sweat glands (ceruminous glands).
- Often locally invasive but associated with a low metastatic rate.

SIGNALMENT

- Uncommon overall but the most common malignant tumor of the ear canal in both dogs and cats, followed by squamous cell carcinoma.
- Cocker spaniels are overrepresented.
- Mean age—dogs, 10 years; cats, 11 years.
- No known sex predisposition.

SIGNS

- Similar to chronic, recurrent otitis externa: discharge, odor, pruritus, inflammation.
- Early appearance—pale pink, friable, ulcerative, bleeding nodular mass(es) within the external ear canal.
- Late appearance—large mass(es) filling the canal and invading through canal wall into surrounding structures.
- Regional lymph node enlargement.
- Neurologic signs (vestibular signs, Horner's syndrome) may be present secondary to middle ear involvement.
- Signs of pain and discomfort; pain upon opening the mouth.

CAUSES & RISK FACTORS

Chronic inflammation and ceruminous gland hyperplasia/dysplasia appear to play a role in tumor development.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Proliferative chronic otitis externa.
- Nodular hyperplasia.
- Inflammatory polyps (cats).
- Other tumors including squamous cell carcinoma, basal cell tumor, mast cell tumor, papilloma, sebaceous gland tumor, ceruminous gland adenoma.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

- Ear swab cytology for bacteria and yeast.
- Bacterial culture and sensitivity as needed.

IMAGING

- Skull radiography to assess potential involvement of the tympanic bulla.
- Thoracic radiography to evaluate for pulmonary metastasis.
- CT or MRI is most useful for loco-regional staging and before surgery and radiation therapy; providing greater detail than with radiographs.

DIAGNOSTIC PROCEDURES

- Cytologic examination of aspirate from regional lymph nodes
- Biopsy and histopathology

PATHOLOGIC FINDINGS

- Histopathologic characteristics—apocrine type differentiation from ceruminous glands and local invasion into stroma.
- Tumor cells—show moderate to marked nuclear atypia with frequent mitotic figures.



TREATMENT

- Total ear canal ablation and lateral bulla osteotomy (TECABO) is the preferred surgical approach over lateral ear resection.
- Radiation therapy may be considered for either large (palliative intent) or incompletely excised masses (curative intent).



MEDICATIONS

DRUG(S)

- Chemotherapy not evaluated but occasionally considered based on histologic information and clinical staging results.
- Multimodal therapy incorporating NSAIDs and other analgesics.
- Antibiotic therapy based on culture and sensitivity results.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Physical examination and thoracic radiography at regular intervals following therapy (every 3–4 months) is recommended for the first year postoperatively.
- Serial CT or MRI to monitor for local tumor regrowth may be recommended.

POSSIBLE COMPLICATIONS

- Permanent or transient Horner's syndrome secondary to surgery.
- Permanent or transient facial paralysis following surgery (more frequent in cats).

EXPECTED COURSE AND PROGNOSIS

- Median survival after lateral ear resection is around 10 months for both dogs and cats.
- Median survival after TECABO is greater than 3 years in both dogs and cats.
- Median survival after radiation therapy is > 3 years, but published information is on small numbers only.
- Poor prognosis associated with extensive tumor involvement (advanced stage), preoperative neurologic signs, and conservative therapy (e.g., lateral ear canal ablation alone).



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Otitis externa
- Peripheral vestibular disease, Horner's syndrome
- Chronic pain

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug
- TECABO = total ear canal ablation and bulla osteotomy

Suggested Reading

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Consulting Editor Timothy M. Fan

CERVICAL SPONDYLOMYELOPATHY (WOUBLER SYNDROME)



BASICS

DEFINITION

- Cervical spondylomyelopathy or wobbler syndrome is a disease of the cervical spine of large- and giant-breed dogs.
- CSM is characterized by compression of the spinal cord and/or nerve roots, which leads to neurologic deficits and/or neck pain.

PATHOPHYSIOLOGY

- Compressive lesion caused by intervertebral disc herniation, osseous malformation, or both, in a stenotic vertebral canal.
- Disc-associated compression—dogs > 3 years. The intervertebral disc degeneration and subsequent protrusion might be secondary to abnormal articular facet articulation in Doberman pinschers, which predisposes to increased rotational strain in the intervertebral discs.
- Vertebral malformation (bony associated compression)—most commonly seen in giant breeds of dogs, usually in young adult dogs (< 3 years). The osseous malformation can compress the spinal cord dorsoventrally (vertebral arch malformation), dorsolaterally (articular process malformation), or laterally (pedicular malformation).
- Dynamic spinal cord compression (one that changes with movements of the cervical spine) is always a component of the pathophysiology with any type of compression.
- Current evidence does not suggest that instability has a primary role in the pathogenesis of CSM.

SYSTEMS AFFECTED

Nervous

GENETICS

- Inheritable basis proposed for Borzoi and Basset hound.
- Recent evidence suggests that the disease is inherited as an autosomal dominant trait (with incomplete penetrance) in Doberman pinscher.

INCIDENCE/PREVALENCE

CSM is probably the most common neurologic disorder of the cervical spine of large- and giant-breed dogs.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Breed Predilections

- Doberman pinscher dogs are the most commonly affected, with approximately 50% of the cases seen in this breed.
- Other breeds with a high incidence include Great Dane, Rottweiler, Weimaraner, and Dalmatian. CSM can be seen in any breed, including small-breed dogs.

Mean Age and Range

- Doberman pinschers and other large-breed dogs are usually presented > 3 years of age, with a mean age of 6 years.
- Giant-breed

dogs are usually presented < 3 years of age, although late presentations can be seen.

Predominant Sex

Males slightly overrepresented, primarily in giant-breed dogs.

SIGNS

General Comments

The classic clinical presentation is a slowly progressive pelvic limb ataxia with less severe thoracic limb involvement.

Historical Findings

- Chronic, slowly progressive gait dysfunction is characteristic. Acute presentations are usually associated with neck pain.
- Occasionally, acute worsening of a dog with chronic history is observed.
- Neck pain or cervical hyperesthesia is a common historical finding. It occurs in approximately 65–70% of Dobermanns, and 40–50% of other breeds.

Neurologic Examination Findings

- Neck pain is the primary complaint in only approximately 5% of patients.
- Gait changes are characterized by proprioceptive ataxia and paresis (weakness). The ataxia and paresis are more obvious in the pelvic limbs with lesions in the caudal cervical spine (C5–6, C6–7).
- Compressive lesions in the mid-cervical spine tend to cause ataxia in all four limbs.
- The thoracic limb gait can appear short-strided, spastic with a floating appearance, or very weak.
- Proprioceptive positioning deficits are usually present, but dogs with chronic ataxia may not display them.
- The gait exam (presence of ataxia) provides a more sensitive indication of myelopathy than proprioceptive positioning deficits.
- Dogs can present non-ambulatory.
- Supraspinatus muscle atrophy and worn toenails can be seen in some cases.
- Extensor muscle tone is commonly increased in all four limbs.
- Patellar reflexes are normal or increased.
- Flexor reflex may be difficult to elicit in the thoracic limbs due to increased extensor tone.

CAUSES

- Inpatient if surgical treatment is elected.
- Nutrition—excess protein, calcium, and caloric intake were proposed in Great Danes. Nutrition does not appear to play a role in the development of CSM in large breed dogs.
- The cause of CSM is likely multifactorial.

RISK FACTORS

- Body conformation—large head and long neck have been proposed, but later studies found no correlation between body dimensions and incidence of CSM.
- Fast growth rate has been proposed but not confirmed by other studies.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Orthopedic conditions such as hip dysplasia and cruciate ligament rupture. Differentiated

by the neurologic examination (absence of ataxia).

- Spinal neoplasia, spinal subarachnoid diverticulum, spinal synovial cysts, discospondylitis, osteomyelitis, meningomyelitis, trauma. Differentiated by results of survey radiographs, CSF, myelography, CT, CT-myelography or MRI findings.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

IMAGING

Survey Cervical Radiographs

- Survey radiographs serve as a screening tool to rule out bony disorders. Although intervertebral disc narrowing or vertebral tipping can be seen, these findings are not specific for CSM since they can be observed in clinically normal large-breed dogs.
- Osteoarthritic changes of the articular processes can be seen in giant breeds.

Myelography

Myelography can define the location(s) and direction (ventral, dorsal, lateral) of the spinal cord compression. Stressed views (flexion or extension) may cause significant risk of neurologic deterioration. Linear traction myelography is a safer procedure and can distinguish a static from dynamic lesion.

Advanced Imaging

- CT myelography—cross-sectional visualization of the spinal cord compression and determination of sites with spinal cord atrophy.
- MRI—visualization of the spinal cord parenchyma, intervertebral disc, soft tissues, and nerve roots; images can be obtained in sagittal, transverse and dorsal planes. Spinal cord signal changes allow more precise identification of the main site of compression than CT and myelography.

DIAGNOSTIC PROCEDURES

CSF analysis—usually normal; mild mixed or neutrophilic pleocytosis can be seen in dogs with acute presentations; elevated protein concentrations can be observed with chronic presentations.

PATHOLOGIC FINDINGS

- Spinal cord white matter tract demyelination at the site of spinal cord compression. Axonal damage can lead to Wallerian degeneration in the ascending and descending white matter tracts.
- Neuronal loss, gliosis, and necrosis can be observed in the gray matter.
- Chronic severe focal spinal cord compression can lead to focal myelomalacia.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient if surgical treatment is elected.
- Outpatient if medical management is chosen.

(CONTINUED) CERVICAL SPONDYLOMYELOPATHY (WOBBLER SYNDROME)

C

NURSING CARE

- Non-ambulatory dogs—keep patients on soft bedding and alternate recumbence side every 4 hours to avoid bed sores.
- Bladder catheterization.
- Physical therapy is essential to avoid muscle atrophy and ankylosis, and to hasten recovery.

ACTIVITY

- Medically treated dogs should have restricted activity for at least 2 months.
- Restriction of activity is also important for the first 2 or 3 months postoperatively to allow bone fusion and prevent implant displacement.

DIET

Avoid excess of protein, calcium, or caloric intake in giant-breed dogs with osseous compression.

CLIENT EDUCATION

Inform that surgery offers the best chance of improvement (approximately 80%) but there is a 1–5% risk of significant complications associated with cervical surgical procedures.

SURGICAL CONSIDERATIONS

- Ventral slot—commonly used and recommended for single ventral compressions; could also be used for two ventral compressions.
- Dorsal laminectomy—primary indication for dorsal or dorsolateral compressions; can also be used for multiple ventral compressions.
- Distraction/stabilization/fusion techniques are recommended primarily for single dynamic ventral compressions, but could be used for multiple compressions.
- Cervical disc arthroplasty—novel technique that appears safe and as effective as the traditional procedures. It can be used for multiple compressions.
- Recurrence rate is approximately 20% with any surgical technique.
- Fenestration provides a very low success rate and is not recommended.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Corticosteroids—Prednisone 1 mg/kg q24h or 0.5 mg/kg q12h progressively decreasing the dosage and frequency. Most dogs can have prednisone discontinued after 4–8 weeks of treatment. Dexamethasone 0.1–0.25 mg/kg q24h can be used as an alternative to prednisone in dogs severely affected.

- Gabapentin—10 mg/kg q8–12h can be used for analgesia in cases of severe pain.

CONTRAINDICATIONS

N/A

PRECAUTIONS

Monitor for signs of gastroenteritis, gastric hemorrhage, and cystitis. A proton pump inhibitor may be used to minimize the risk of gastrointestinal bleeding.

POSSIBLE INTERACTIONS

Do not use corticosteroids in combination with NSAIDs.

ALTERNATIVE DRUG(S)

NSAIDs such as meloxicam 0.1 mg/kg q24h can be used in dogs with only cervical hyperesthesia or mild ataxia.

**FOLLOW-UP****PATIENT MONITORING**

Repeat the neurologic evaluation as often as needed to monitor response to treatment.

PREVENTION/AVOIDANCE

- Excessive activity, jumping, and running should be avoided.
- Avoid use of neck collars; use a body harness instead.

POSSIBLE COMPLICATIONS

Recurrence of clinical signs can occur in dogs treated medically or surgically.

EXPECTED COURSE AND PROGNOSIS

- About 80% of patients improve with surgery.
- Approximately 50% patients improve with medical treatment (restricted activity ± corticosteroids) and 25% remain stable.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Dilated cardiomyopathy, hypothyroidism, and von Willebrand's disease are common in Doberman pinscher dogs. These diseases can affect diagnostic and treatment options.

Doberman pinschers suspected of having CSM should be routinely evaluated for these conditions.

AGE-RELATED FACTORS

- Young giant- or large-breed dogs—vertebral malformation and compression.
- Older dogs—disc-associated compression.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYS

- Cervical malformation-malarticulation
- Cervical spondylopathy • Cervical vertebral instability

SEE ALSO

Intervertebral Disc Disease—Cats

ABBREVIATIONS

- CSF = cerebrospinal fluid
- CSM = cervical spondylopathy
- CT = computed tomography
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug

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Author Ronaldo Casimiro da Costa
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Client Education Handout
available online

CHAGAS DISEASE (AMERICAN TRYPARASITIASIS)



BASICS

OVERVIEW

- Caused by the zoonotic hemoflagellate protozoan parasite *Trypanosoma cruzi*.
- Infection—transmission occurs after infected feces of a vector (Triatominae) are deposited in a wound (bite site of vector) or mucous membrane; dog eats an infected vector, or by contaminated blood transfusion.
- After local multiplication at entry site (5 days post-infection), hematogenous spread occurs to most organs but mainly the heart and brain. • Organisms become intracellular, multiply, then rupture out into circulation to produce maximal parasitemias, associated particularly with acute myocarditis and less commonly with diffuse encephalitis (14 days post-infection). • Parasitemias wane (subpatent 30 days post-infection).
- Antibody titers rise (detectable by 16 days post-infection). • Dog enters a protracted asymptomatic period (can last for months to years); progressive and insidious development of myocardial degeneration; eventual dilative cardiomyopathy. • South and Central America—endemic (in both humans and pets). • United States—mostly in Texas but other southern states also, where infected vectors and reservoir hosts live, with raccoons, opossums, and armadillos the main reservoirs in the southeast and mice, rats, and squirrel species in the southwest.

SIGNALMENT

- Young dogs—most common • Acute—dogs usually < 2 years • Chronic—old dogs
- Hunting breeds—likely to contact vectors or reservoir hosts • More often males
- Cats—no cases reported in North America.

SIGNS

General Comments

Two syndromes—acute (myocarditis or encephalitis in young dogs) and chronic (dilated cardiomyopathy in old dogs).

Historical Findings

Acute

- Sudden death • Lethargy • Depression
- Anorexia • Diarrhea • Weakness • Exercise intolerance • Mild to severe CNS dysfunction (such as distemper) • Ataxia, seizures

Chronic

- Weakness • Exercise intolerance • Syncope
- Sudden death

Physical Examination Findings

Acute

- Generalized lymphadenopathy • Heart failure • Tachycardia and arrhythmias
- Neurologic—weakness; ataxia; chorea; seizures (indistinguishable from distemper)

Chronic

- Tachycardia—sustained or paroxysmal

CAUSES & RISK FACTORS

T. cruzi



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cardiomyopathy • Congenital cardiac defects • Traumatic myocarditis • Distemper
- Toxoplasmosis • Neosporosis

CBC/BIOCHEMISTRY/URINALYSIS

Generally normal

OTHER LABORATORY TESTS

- Serology—positive titer confirms diagnosis available from the CDC's parasitology unit.
- On-site immunochromatographic antibody tests have high sensitivity and specificity when used in dogs—excellent tool for survey work not only in dogs but also wildlife. • Antibody titers very sensitive and specific but most cross-react with *Leishmania*. • Organism isolation—LIT culture; collect 50 mL heparinized blood. • Examination above the buffy coat in a microhematocrit tube (spun down to read PCV) using 40× microscope objective—organisms during period of high parasitemia. • PCR—very useful during indeterminate and chronic stages when blood trypomastigotes are very difficult to demonstrate. Has high specificity but low sensitivity unless samples from multiple tissues are examined. Not yet commercially available. • Elevated troponin I—acute disease.

IMAGING

- Radiography—acute: cardiomegaly, pulmonary edema, and (rarely) mild pleural effusion; chronic: cardiomegaly.
- Echocardiography—acute: rarely shows chamber or wall abnormalities; chronic: reduced ejection fraction, fractional shortening, and thinning of right and left ventricular free wall.

DIAGNOSTIC PROCEDURES

Electrocardiography

- Acute—atrioventricular block; depression of QRS amplitude; right bundle branch block.
- Chronic—low QRS amplitude; right bundle branch block; ventricular arrhythmias (initially unifocal VPC, becomes multifocal, then degenerates into various forms of ventricular tachycardia).



TREATMENT

- Medical therapy does not produce clinical cure. • With poor prognosis and zoonotic potential, euthanasia is an option. • The bradyarrhythmias which some dogs develop may respond to pacemaker therapy.

CLIENT EDUCATION

- Alert owner to possible zoonotic risk and potential for sudden death. • Acute—usually develops into the chronic form, which is often fatal. • Infected intact female—can transfer infection to offspring.



MEDICATIONS

DRUG(S)

- Several drugs have limited efficacy during the acute stage; none produces a clinical cure; even treated animals may progress to chronic disease.
- Benzimidazole (Ragonil) 5 mg/kg PO q12h for 60 days; preferred drug for use in dogs; markedly improves acute disease in humans and probably dogs also. Available from CDC.
- Cythioate (Proban)—3.3 mg/kg PO q48h; effective in reducing vector populations; Fipronil Spot-on (Frontline Top Spot, Merial) has been shown to be ineffective in preventing reduviidae from feeding on dogs.
- Supportive treatment of dilated cardiomyopathy (right and left cardiac failure) and ventricular arrhythmias.



FOLLOW-UP

- Cardiac disease—prognosis always guarded
- Chronic—prognosis guarded to hopeless



MISCELLANEOUS

ZOONOTIC POTENTIAL

Exists; essentially incurable in humans, thus euthanasia of infected dogs is an option.

ABBREVIATIONS

- CNS = central nervous system • LIT = liver infusion tryptose • PCR = polymerase chain reaction • PCV = packed cell volume • VPC = ventricular premature complex

Suggested Reading

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CHEDIAK-HIGASHI SYNDROME



BASICS

OVERVIEW

- Autosomal recessive inherited disorder of Persian cats characterized by abnormalities in cellular morphology and pigment formation.
- Large intracytoplasmic granules in circulating leukocytes and melanocytes formed by fusion of preexisting granules.
- Storage pool deficiency of ADP, ATP, magnesium, and serotonin results from lack of platelet-dense granules.
- Prolonged bleeding from trauma, venipuncture, or minor surgery occurs because of impaired platelet aggregation and release reaction.
- Normal coagulation times.
- Depressed chemotaxis.
- No change in rates of infection.
- Mildly depressed neutrophil count but within reference range.

SIGNALMENT

- Persian cats with dilute smoke-blue coat color and yellow-green irises (and white tigers).
- Not reported in dogs.
- Some Arctic foxes with blue or pearl hair coat color.

SIGNS

Historical Findings

Prolonged bleeding from trauma, venipuncture, or minor surgery.

Physical Examination Findings

- Red fundic reflex (lack of choroidal pigment).
- Dilute smoke-blue coat color and yellow-green irises.
- Photophobia (blepharospasm and epiphora) in bright light.

CAUSES & RISK FACTORS

Genetic disease



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Dilute hair coat color

CBC/BIOCHEMISTRY/URINALYSIS

Romanowsky-stained blood smear—leukocytes, especially neutrophils, contain

pink to magenta cytoplasmic inclusions 2 μm in diameter.

OTHER LABORATORY TESTS

None

IMAGING

N/A

DIAGNOSTIC PROCEDURES

None



TREATMENT

- Provide ascorbic acid (vitamin C) to increase cGMP concentration and to improve cell and platelet function (no controlled studies in cats).
- Transfusion of platelet-rich plasma from healthy cats will temporarily normalize bleeding time in affected individuals.
- Experimentally, bone marrow transplantation has restored neutrophil and platelet function in cats, but is impractical for general clinical use.



MEDICATIONS

DRUG(S)

Ascorbic acid (100 mg PO q8h)

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

None



FOLLOW-UP

PATIENT MONITORING

None

PREVENTION/AVOIDANCE

- Advise owner of potential for prolonged bleeding after trauma, venipuncture, or minor surgery.
- Provide genetic counseling to eliminate Chediak-Higashi syndrome from animals used for breeding.

- Neuter affected and carrier animals or advise owner not to breed.

POSSIBLE COMPLICATIONS

Prolonged bleeding time

EXPECTED COURSE AND PROGNOSIS

Normal lifespan



MISCELLANEOUS

ABBREVIATIONS

- ADP = adenosine diphosphate
- ATP = adenosine triphosphate

Suggested Reading

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Author Kenneth S. Latimer

Consulting Editor Alan H. Rebar

CHEMOLECTOMA



BASICS

OVERVIEW

- Chemodectomas are tumors arising from the chemoreceptor cells (such as in the aortic body and the carotid body).
- Other names—*aortic body tumors, cardiac paraganglioma, APUDoma (amine precursor uptake decarboxylase), and glomus body tumor.*
- Aortic body tumors more common (80–90%) in dogs than carotid body tumors (10–20%).

SIGNALMENT

- Rare in cats.
- Dogs age 6–15 years.
- Any breeds—but brachycephalic breeds predisposed—especially boxers, Boston terriers, English bulldogs, and German shepherd dogs.
- Males predisposed for aortic body tumors, no sex predilection for carotid body tumors.

SIGNS

- Nonspecific and dependent upon tumor size and anatomic localization, and can include lethargy, anorexia, weakness, collapse, coughing, respiratory distress, exercise intolerance, distended abdomen, vomiting, sudden death.
- Carotid body tumor—may notice neck mass, regurgitation, dyspnea, Horner's syndrome, laryngeal paralysis.
- May be associated with pericardial effusion and cardiac tamponade—muffled heart sounds, poor pulses, tachycardia, tachypnea, weak pulses, slow capillary refill time, ascites.
- May be associated with cranial vena cava syndrome (edema of head, neck and forelimbs), and in long-standing cases peritoneal effusion might develop consequent to right-sided heart deficits.
- May be associated with pleural effusion—decreased lung sounds ventrally, cyanosis.
- Cardiac arrhythmias with pulse deficits.

CAUSES & RISK FACTORS

Chronic hypoxia may play a role in the development of this disease in brachycephalic breeds.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other masses located at the heart base (i.e., hemangiosarcoma, thymoma, ectopic thyroid carcinoma, mesothelioma, abscess, and granuloma).
- Idiopathic pericardial effusion.
- Pericarditis.
- Cardiomyopathy.
- Valvular insufficiency.

CBC/BIOCHEMISTRY/URINALYSIS

Typically normal, but 36% of patients can have nucleated red blood cells without anemia.

OTHER LABORATORY TESTS

N/A

IMAGING

- Thoracic radiography—to evaluate for mass in the region of the heart base, pericardial effusion, metastatic lesions in the lungs.
- Cervical ultrasound, CT or MRI—to evaluate for masses arising in the neck.
- Echocardiography—to image mass and aorta/pulmonary arteries/veins.

DIAGNOSTIC PROCEDURES

- Biopsy of mass.
- ECG—if evidence of arrhythmia, may see low-amplitude QRS complexes with pericardial or pleural effusion, or electrical alternans with pericardial effusion.



TREATMENT

AORTIC BODY TUMORS

- Surgical removal of mass—if possible.
- Subphrenic pericardectomy has been shown to prolong survival.
- Symptomatic pericardiocentesis or thoracocentesis.
- Conformal radiation therapy.
- Palliative thoracoscopic-guided pericardial window.

CAROTID BODY TUMORS

Surgical removal if possible—discuss with owners possibility of postoperative Horner's syndrome and laryngeal paralysis.

BOTH

Possible role of chemotherapy (doxorubicin) and radiation therapy; however, definitive studies are lacking.



MEDICATIONS

DRUG(S)

- The role of chemotherapy in this disease has not been published.
- Pharmacologic intervention for cardiac insufficiency.



FOLLOW-UP

PATIENT MONITORING

Serial thoracic radiography or advanced imaging for monitoring tumor progression and metastasis.

EXPECTED COURSE AND PROGNOSIS

- Carotid body tumors treated with surgery—median survival time 25.5 months.
- Aortic body tumors—animals treated with pericardectomy MST 730 days versus animals that did not have pericardectomy MST 42 days. Larger tumors (as determined by tumor weight to body weight ratio) more likely associated with metastasis.
- Conformal radiation therapy in 1 dog—survival > 42 months.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

It is not recommended to breed animals with cancer. Chemotherapy is teratogenic—do not give to pregnant animals.

SEE ALSO

Pericardial Effusion

ABBREVIATIONS

- ECG = electrocardiogram
- MST = median survival time

Suggested Reading

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Author Rebecca G. Newman

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CHEYLETIELLOSIS

C



BASICS

OVERVIEW

- A contagious parasitic skin disease of dogs and cats, caused by surface-living *Cheyletiella* spp. mites (*C. yasguri*, *C. blakei*, *C. parsitovorax*). • Signs of mild pruritus and scaling resemble other more common dermatoses. • Potential for lesions in human beings (zoonotic).

SYSTEMS AFFECTED

- Skin/Exocrine

SIGNALMENT

- Dogs and cats. • More severe in young animals. • Cocker spaniels, poodles, and longhaired cats may be inapparent carriers.

SIGNS

Historical Findings

- Cats may exhibit bizarre behavior, head shaking, or excessive grooming. • Pruritus—usually absent to mild, but can be severe depending on individual immune status and response to infestation. • Infestation often suspected only after lesions in human beings develop (pseudo-scabies).

Physical Examination Findings

- Scaling—most important clinical sign; diffuse or plaque-like; more severe in chronically infested or debilitated animals.
- Often referred to as “walking dandruff,” because of the large mite size and excessive scaling. • Prevalence varies by geographic region owing to mite susceptibility to common flea-control insecticides and differences in climate. • Some locations may have low or no incidence of the mite.
- Lesions—dorsal orientation is commonly noted; head can be affected in cats.
- Underlying skin irritation may be minimal.
- Cats may exhibit bilaterally symmetrical alopecia.

CAUSES & RISK FACTORS

- *Cheyletiella* mites are considered partially host-specific for the following species:
 - Dogs—*C. yasguri*. ◦ Cats—*C. blakei*.
 - Rabbits—*C. parsitovorax* (mites are not highly host-specific). • Cheyletiellosis should be considered in every animal that shows scaling, with or without pruritus, especially in young animals or animals living in communities. • Contagion is by direct contact or by fomites. • Common sources of infestation—animal shelters, breeders, and grooming facilities. • Adult female mites may transiently survive in the environment up to 10 days. • Eggs can be found on shed hair.
 - In specific individuals, hypersensitivity to mite allergens may develop, producing clinical signs of pruritus (similar to infestations with *Sarcoptes* or *Notoedres* mites).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Keratinization disorders • Flea allergic dermatitis • *Sarcoptes* and *Notoedres* spp. mite infestation; other fur mites • Atopy • Food hypersensitivity • Endocrinopathy
- Dermatophytosis • Lice infestation

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

DIAGNOSTIC PROCEDURES

- Examination of epidermal debris with a lens or microscope (10X objective)—effective in diagnosing infestation. • Mite numbers may be low; concentration of debris for examination increases the likelihood of diagnosis. • Collection of debris—flea combing (most effective), skin scraping, hair plucking, acetate tape preparation, scale collection, and fecal flotation. • *Cheyletiella* mites are large and can be visualized with a simple handheld magnifying lens; scales and hair may be examined under low magnification; staining is not necessary; finding mite eggs is diagnostic. • Response to insecticide treatment may be required to definitively diagnose suspicious cases in which mites cannot be identified.



TREATMENT

- All animals in the same household must be treated at the same time. • Clip long coats to facilitate treatment if topical treatment is chosen. • Mainstay—six to eight weekly baths to remove scale, followed by rinses with an insecticide. • Lime-sulfur rinses—cats, kittens, dogs, and puppies. • Routine flea sprays and powders—not always effective. Treat all animals in the home before introducing a new pet. • Environmental treatment with frequent cleanings and insecticide sprays—reduces possibility of reinfestation. • Treatment—continue for at least 6–8 weeks to prevent reinfestation from shed eggs. • Combs, brushes, and grooming tools—discard or thoroughly disinfect before reuse.



MEDICATIONS

DRUG(S)

- Amitraz rinses—dogs only; 2-week intervals for four applications.
- Fipronil spray or spot-on—2-week intervals for one to four applications.
- Ivermectin—highly effective (300 µg/kg PO or SC three times at 2-week intervals);

dogs and cats > 3 months old; pour-on forms have shown efficacy in cats (500 µg/kg two times at 2-week intervals) (non-FDA-approved usage).

- Selamectin (Revolution)—apply every 2–4 weeks for three applications (non-FDA-approved usage).
- Imidacloprid/Moxidectin (Advantage-Multi) spot-on at 2-week intervals for three applications (non-FDA-approved usage).
- Milbemycin oxime (Interceptor)—2 mg/kg PO once weekly for 4 weeks.
- Moxidectin (Cydectin)—subcutaneous injection every 2 weeks for three treatments (non-FDA-approved usage—dogs).
- Doramectin (Dectomax)—subcutaneous injection every week for three treatments (non-FDA-approved usage—dogs).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Ivermectin—several dog breeds (e.g., collie, sheltie, Australian shepherd) have shown increased sensitivity and should not be treated with ivermectin. • Selamectin can be safely used in the above-mentioned dog breeds.
- Prevent ingestion of avermectins in sensitive dogs (*MDR1/ABCB1* gene mutation).



FOLLOW-UP

- Treatment failure requires a thorough reevaluation for other causes of pruritus and scaling. • Reinfestation may indicate contact with an asymptomatic carrier or the presence of an unidentified source of mites (e.g., untreated bedding, boarding, wild animals).



MISCELLANEOUS

ZOONOTIC POTENTIAL

A pruritic papular rash may develop in human beings, in areas of contact with the pet.

Suggested Reading

Elsheikha H, Patterson JS. Veterinary Parasitology: Self-Assessment Color Review. Hoboken, NJ: Taylor & Francis Group, 2013.

Hnilica KA, Small Animal Dermatology: A Color Atlas and Therapeutic Guide. St Louis, MO: Saunders, 2011.

Authors Guillermrina Manigot and Alexander H. Werner

Consulting Editor Alexander H. Werner

CHLAMYDIOSIS—CATS



BASICS

DEFINITION

A chronic respiratory infection of cats caused by an intracellular bacterium, characterized by mild to severe conjunctivitis, mild upper respiratory signs, and mild pneumonitis.

PATHOPHYSIOLOGY

- Chlamydophila felis* (previously *Chlamydia psittaci* var. *felis*)—an obligate intracellular bacterium; replicates on the mucosa of the upper and lower respiratory epithelium; produces a persistent commensal flora that causes a local irritation with resulting mild upper and lower respiratory signs; can also colonize the mucosa of the gastrointestinal and reproductive tracts.
- Incubation period—7–10 days; longer than that for other common respiratory pathogens of the cat.

SYSTEMS AFFECTED

- Gastrointestinal—cat: infection without clinical disease; other species: may have clinical gastroenteritis.
- Ophthalmic—chronic conjunctivitis, often unilateral but may be bilateral.
- Reproductive—infection without clinical disease.
- Respiratory—mild rhinitis, bronchitis, and bronchiolitis.

INCIDENCE/PREVALENCE

- Incidence of clinical disease—sporadic; outbreaks of respiratory disease may occur, especially in multi-cat facilities.
- Prevalence of *C. felis* in the feline population—not uncommon, 5–10% chronically infected.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

- Cat
- Human

Mean Age and Range

Usually cats < 1 year of age; any age cat possible.

SIGNS

General Comments

- Infection often subclinical.
- Clinical disease—commonly as a co-infection with other organisms.

Historical Findings

- Upper respiratory infection, with some sneezing, watery eyes, and coughing.
- Sometimes difficult breathing.
- Varying degrees of anorexia.

Physical Examination Findings

- Conjunctivitis—often granular; initially unilateral, usually progresses to become bilateral.

- Lacrimation, photophobia, and blepharospasm.
- Rhinitis with nasal discharge—usually mild.
- Pneumonitis—with the inflammatory process in the alveoli; bronchiolar tubes and airways give audible rales.

CAUSES & RISK FACTORS

- Concurrent infections with other respiratory pathogens.
- Lack of vaccination.
- Multi-cat facilities, especially adoption shelters and breeding catteries.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Feline viral rhinotracheitis—short incubation period (4–5 days), rapid bilateral conjunctivitis, severe sneezing, and ulcerative keratitis.
- Feline calicivirus infection—short incubation period (3–5 days), ulcerative stomatitis, and severe pneumonia.
- Feline reovirus infection—very mild upper respiratory infection; short incubation and duration.
- Bronchial pneumonia caused by bacteria such as *Bordetella bronchiseptica*—localized areas of density within the lungs on radiographs.

CBC/BIOCHEMISTRY/URINALYSIS

Leukocytosis

IMAGING

Radiographs of lungs—helpful with pneumonitis.

DIAGNOSTIC PROCEDURES

- PCR assay for *C. felis*—preferred; conjunctival swab sample.
- Serum antibody assay—unvaccinated cats; indicates infection.
- Conjunctival scrapings stained with Giemsa stain—characteristic intracytoplasmic inclusions.
- Swab samples taken from conjunctiva—isolation of the causative organism in cell cultures.

PATHOLOGIC FINDINGS

- Gross—evidence of chronic conjunctivitis with mucopurulent ocular discharge; minor rhinitis with nasal discharge; sometimes lung changes indicative of pneumonitis.
- Histopathologic (conjunctiva)—an early intense infiltration of neutrophils; inflammatory response changes to lymphocytes and plasma cells; inclusions detected with special stains; inclusions invisible with routine H&E stains.



TREATMENT

APPROPRIATE HEALTH CARE

Generally as outpatient

NURSING CARE

- Keep nostrils and eyes clean of discharge.
- Generally does not require other supportive therapy (e.g., fluids), unless complicated by concurrent infections.

ACTIVITY

- Quarantine affected cats from contact with other cats.
- Do not allow affected cats to go outside.

DIET

Normal

CLIENT EDUCATION

Inform clients of the causative organism, the anticipated chronic course of disease, and the need to vaccinate other cats before exposure.



MEDICATIONS

DRUG(S) OF CHOICE

- Systemic—tetracycline antibiotic of choice (22 mg/kg PO q8h for 3–4 weeks); doxycycline (10 mg/kg q24h PO daily for 4 weeks to prevent recrudescence).
- Ocular—ophthalmic ointments containing tetracycline (q8h).

CONTRAINdicATIONS

Tetracycline—may affect growing teeth of young kittens.

PRECAUTIONS

Colonies/shelters/breeding catteries—all cats may have to be treated; treatment may have to be continued for as long as 4 weeks.



FOLLOW-UP

PATIENT MONITORING

Monitor for improved health as treatment proceeds.

PREVENTION/AVOIDANCE

Vaccines

- Both inactivated and modified live vaccines are available to reduce the severity of infection.
- Vaccines do not prevent infection; rather, they reduce severity and duration of clinical disease.
- American Association of Feline Practitioners—classifies as non-core; for at-risk cats, give a single vaccination at initial visit as early as 9 weeks of age, repeat in 3–4 weeks; revaccinate annually where *C. felis* is endemic.

(CONTINUED)

POSSIBLE COMPLICATIONS

Adverse vaccine reactions—mild clinical disease with modified live vaccines; small percentage of vaccinated cats.

EXPECTED COURSE AND PROGNOSIS

- Tends to be chronic, lasting for several weeks or months, unless successful antibiotic treatment is given.
- Prognosis good.

**MISCELLANEOUS****AGE-RELATED FACTORS**

Primarily a disease of young cats

ZOONOTIC POTENTIAL

C. felis can infect humans, especially immunocompromised individuals; limited number of reports of mild conjunctivitis in humans transmitted from infected cats.

PREGNANCY/FERTILITY/BREEDING

- Endemic breeding catteries—treat all cats with doxycycline for at least 4 weeks; then vaccinate.

- Role of *C. felis* as a pathogen during pregnancy—unclear; can colonize the reproductive mucosa; severe conjunctivitis neonatorum can occur in neonatal kittens infected at or shortly after birth.

SYNONYM

Feline pneumonitis

ABBREVIATIONS

- H&E = hematoxylin and eosin
- PCR = polymerase chain reaction

Suggested Reading

- Gaskell RM. Upper respiratory disease in the cat (including *Chlamydia*): Control and prevention. *Feline Pract* 1993, 21:29–34.
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CHLAMYDIOSIS—CATS

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Client Education Handout available online

CHOCOLATE (METHYLXANTHINE) TOXICOSIS



BASICS

DEFINITION

Acute gastroenteric, neurologic, and cardiac toxicosis is caused by excessive intake of methylxanthine alkaloids present in chocolate. Theobromine is the largest fraction of methylxanthines in chocolate products and in cacao bean mulch. A lower concentration of caffeine is also present. Other sources include diet pills, over-the-counter stimulants, and herbal medications.

PATOPHYSIOLOGY

- Methylxanthines are variably absorbed (caffeine < 1 hour; theobromine 10 hours), metabolized by liver; excreted in bile and reabsorbed (enterohepatic cycling).
- Estimated theobromine and caffeine half-life in dogs is 17 hours and 4.5 hours respectively.
- They cross placenta and blood-brain barrier; may be resorbed via urinary bladder.
- Inhibition of phosphodiesterase increases cAMP, potentiating catecholamines and increasing cellular calcium.
- Cause vasoconstriction, increased force of cardiac and skeletal muscle contraction, CNS stimulation, seizures, bronchodilation, and tachycardia.
- Toxic dosages:
 - Theobromine LD₅₀ (dog) 250–500 mg/kg; LD₅₀ (cat) 200 mg/kg
 - Caffeine LD₅₀ (dog) 140 mg/kg; LD₅₀ (cat) 80–150 mg/kg.
 - **Caution:** one-tenth of the LD₅₀ may still be a lethal dosage for some animals.

SYSTEMS AFFECTED

- Cardiovascular—increased myocardial contractility and tachyarrhythmias; tachycardia, hypertension, ventricular premature contractions (VPC).
- Gastrointestinal—early vomiting and diarrhea; may result even from parenteral administration of methylxanthine alkaloids.
- Metabolic—hypokalemia, hyperthermia.
- Nervous—stimulation; enhanced alertness and reflex hyperactivity; tremors; tonic-clonic seizures.
- Renal/Urologic—polyuria, polydipsia.
- Respiratory—tachypnea, hypoxia, cyanosis, respiratory failure.

INCIDENCE/PREVALENCE

- Dogs—among 20 most common poisonings in recent literature, reported by small animal practices, and animal and human poison control centers.
- More common at holiday times—chocolate products and candies readily available.
- Caffeine-containing stimulant tablets, as much as 200 mg/tablet—occasional source.
- Cacao bean hull mulch for landscaping—increasing risk for dogs.

GEOGRAPHIC DISTRIBUTION

Urban and indoor dogs—may be more at risk owing to close proximity to chocolate products or cacao landscape mulch.

SIGNALMENT

Species

- Dogs frequently poisoned based on proximity to methylxanthine products, consuming large doses, and longer half-life of theobromine in dogs (theobromine 17.5 hours vs. caffeine 4.5 hours).
- Cats rarely affected.
- Other species likely have more limited access to chocolate; cacao bean hulls are an increasing source in dogs, horses, and poultry.

Breed Predilections

Small dogs—may be more at risk (amount of chocolate relative to body weight).

Mean Age and Range

- Puppies and young dogs—likely to ingest large amounts of unusual foods.
- Young animals are typically more compromised in metabolism and excretion.

SIGNS

Historical Findings

- Recent confirmed chocolate or cacao hull ingestion.
- Evidence of chewed containers or remnants of packaging from chocolate products.
- Vomiting and diarrhea—often first reported sign, 2–4 hours after ingestion.
- Early restlessness and increased activity or nervousness.
- Polyuria—may result from diuretic action.
- Hematuria occasionally.
- Advanced signs—stiffness; excitement; seizures; hyperreflexia.

Physical Examination Findings

- Vomiting and diarrhea followed by combination of CNS excitation and tachycardia (often extreme) is characteristic.
- Hyperthermia.
- Hyperactivity
- Hyperreflexia.
- Muscle rigidity.
- Tonic-clonic seizures.
- Mydriasis.
- Tachypnea.
- Tachycardia (> 200/min).
- Hypertension.
- Premature ventricular contractions.
- Advanced signs—cardiac failure, weakness, cyanosis, coma, and death.
- Polyuria/polydipsia.
- Death—12–48 hours after ingestion.

CAUSES

- Usually processed chocolate (used for candies and baking).
- Minimum lethal dosage for caffeine and theobromine (dogs)—100–200 mg/kg.
- Potentially lethal exposure (dogs):
 - 5 g baking chocolate provides 20 mg caffeine and 80 mg theobromine (total 100 mg).

◦ A 20 kg dog could be poisoned at 100 g/kg by consuming 5 g chocolate/kg × 20 kg = 100 g chocolate (3.5 oz).

◦ Milk chocolate provides only 2 mg of alkaloids per gram (50 g chocolate/kg bw) or nearly 2 oz/kg, which would be 40 oz (2.5 lb) for a 20 kg dog (unlikely amount).

• Dogs are poisoned by cacao bean hulls (contains both alkaloids) used as landscaping mulch. Several aids to canine risk from chocolate can be found online. See “Internet Resources.”

RISK FACTORS

Chocolate—palatable and attractive; often readily available and unprotected in homes and kitchens.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Convulsant or excitatory alkaloids—strychnine; amphetamine; nicotine; 4-aminopyridine; cocaine; tricyclic antidepressants; serotonin syndrome.
- Metaldehyde snail and slug bait.
- Acute bromethalin poisoning.
- Zinc phosphide poisoning.
- Convulsant pesticides—organochlorines (e.g., chlordane, lindane) and pyrethrins.
- Tremorgenic mycotoxins—penitrem A; aflatrem; roquefortine.
- Acute psychogenic drugs—LSD; cocaine; morning glory.
- Medications (phenylpropanolamine, phenylephrine, pseudoephedrine).
- Cardioactive glycosides—*Digitalis* spp.; *Nerium oleander*.
- Hypomagnesemia and hypocalcemia.

CBC/BIOCHEMISTRY/URINALYSIS

- Hyperglycemia or hypoglycemia—both have been noted and hence not a reliable indicator.
- Hypokalemia.
- Low urine specific gravity and proteinuria.

OTHER LABORATORY TESTS

Methylxanthine Assay

- Stomach contents, plasma, urine.
- Detectable plasma or serum concentration should persist 3–4 days.
- Stable in serum samples for 7 days (room temperature), 2 weeks refrigerated.
- Theobromine in serum of poisoned dogs may range from 100 to 300 mg/L.

DIAGNOSTIC PROCEDURES

ECG—sinus tachycardia, premature ventricular contractions, and ventricular tachyarrhythmia.

PATHOLOGIC FINDINGS

- Small or large amounts of chocolate in stomach or intestine.
- Gastroenteritis—non-specific.
- No distinctive microscopic lesions.

(CONTINUED)

CHOCOLATE (METHYLXANTHINE) TOXICOSIS

C

Table 1

Comparative concentrations of caffeine and theobromine.		
Caffeine Source	Amount (mg/g)	Amount (mg/oz)*
Coffee beans	10–20	284–570
Drip coffee	90–100 mg/6 oz. cup	Ca. 15
Cola drinks	60–90 mg/12 oz. can	5–8
Baking chocolate	Up to 4	Up to 112
Dark chocolate	4–5	135
Milk chocolate	0.2	6
Cocoa	Up to 1.5	46
Cacao bean hulls	5–8.5	142–240
Guarana	30–50	850–1,400
Stimulant tablets	200 mg/tablet	
OTC pain control	60 mg/tablet	
Theobromine Source	Amount (mg/g)	Amount (mg/oz)
Cacao beans	10–50	280–1,400
Baking chocolate	14–16	398–454
Milk chocolate	1.5–2	46–57
Cacao bean hulls	5–9	142–256
Cacao bean mulch	2–30	57–852
Cacao powder	14–29	398–832

* To convert mg/g to mg/oz, multiply by 28.4 g/oz.

- Microscopic renal lesions not consistent; characterized by hyaline droplet degeneration, pyknosis, and karyorrhexis, potentially from impaired renal perfusion.



TREATMENT

APPROPRIATE HEALTH CARE

- By phone—attempt to determine type and amount of exposure; if not possible, refer to hospital as a potential toxicologic emergency.
- Control seizures.
- Detoxification (if seizures controlled) using emesis early, or gastric lavage, and activated charcoal; most effective within 2–4 h post exposure, longer if chocolate remaining in stomach.
- Give activated charcoal daily up to 3 days to reduce enterohepatic recycling of the alkaloids. Only the first dose of charcoal should contain a cathartic.
- Control hyperthermia.
- Treat tachycardia (see “Medications”).
- Urinary catheterization or frequent urine voiding may reduce urinary bladder resorption.
- Provide IV fluid therapy to prevent dehydration, promote diuresis, and avoid hypernatremia.
- Control tremors with methocarbamol or diazepam (see “Medications”). Seizure control may require treatment with diazepam; if not controlled, use either pentobarbital or other general anesthetics (see “Medications”).

NURSING CARE

Fluid therapy—correct electrolyte disturbances caused by vomiting.

ACTIVITY

Avoid stress and excitement—could precipitate hyperreflexia or seizures.

DIET

- Acutely affected patient—no food.
- Convalescence—bland diet for several days to allow recovery from gastroenteritis.

CLIENT EDUCATION

Warn client of the hazards of chocolate ingestion.

SURGICAL CONSIDERATIONS

Rarely, a mass or concretion of chocolate could form that must be removed surgically.



MEDICATIONS

DRUG(S) OF CHOICE

- Induce emesis**—only if patient is not seizing; apomorphine (0.03 mg/kg IV); hydrogen peroxide 3% (1–3 mL/kg PO).
- Gastric lavage—only before onset of vomiting and other clinical signs, if emetics are not effective, seizures controlled, and endotracheal tube in place.
- Once vomiting is controlled—activated charcoal (0.5–1 g/kg PO) adsorbs remaining alkaloids in the gastrointestinal tract—repeated at 4- to 8-hour intervals for 1–2 days to prevent enterohepatic recycling.

- Osmotic cathartic—sodium sulfate (0.25 g/kg PO) or sorbitol 70% at 1–3 mL/kg PO; promotes gastrointestinal elimination of chocolate.

- Hyperactivity and seizures**—control with diazepam (0.5–1 mg/kg IV q10–20min up to 2 times or diazepam CRI at 0.5–1 mg/kg/h).

- Ventricular tachycardia** (dogs)—lidocaine (without epinephrine), 2–4 mg/kg IV followed by 0.03–0.05 mg/kg/min IV drip. Lidocaine NOT RECOMMENDED in cats.
- Serious refractory arrhythmias—metoprolol or propranolol (0.02–0.06 mg/kg IV; rate not > 1 mg/minute); metoprolol preferred but may be difficult to obtain; use oral therapy once patient is stable (metoprolol at 0.2–0.4 mg/kg PO q12h; propranolol at 0.1–0.2 mg/kg PO q8h); monitor the ECG and watch for hypotension as a sequel to this treatment.

- In the rare instance of bradycardia, use atropine at 0.02–0.04 mg/kg IV, IM or SC.

CONTRAINdicATIONS

- Do not use epinephrine concurrent with lidocaine.
- Avoid erythromycin and corticosteroids—these reduce the excretion of methylxanthines.
- Do not use lidocaine in affected cats.

PRECAUTIONS

- Effects may persist longer than the effective life of therapeutic drugs.
- Keep patient under observation until drug administration is no longer needed.
- Methylxanthines—cross the placenta; excreted in milk.

CHOCOLATE (METHYLXANTHINE) TOXICOSIS

(CONTINUED)

ALTERNATIVE DRUG(S)

- Control of hyperreflexia and muscle rigidity may be obtained with methocarbamol (50–220 mg/kg slowly IV).
- If response to diazepam inadequate—consider phenobarbital (5–8 mg/kg IV administered over 5–10 minutes q4–6h) or propofol titrated to effect.
- Refractory seizures—pentobarbital coma or mask down with general anesthetic.



FOLLOW-UP

PATIENT MONITORING

- ECG—arrhythmias.
- Watch for mild to moderate nephrosis in convalescent patients.

PREVENTION/AVOIDANCE

Warn owners about toxicologic hazards of chocolate.

POSSIBLE COMPLICATIONS

Pregnant or nursing animals—risk for teratogenesis of newborns or stimulation of nursing neonates.

EXPECTED COURSE AND PROGNOSIS

- Expected course—12–36 hours, depending on dosage and effectiveness of decontamination and treatment.
- Successfully treated patients—usually recover completely.
- Prognosis—good if oral decontamination occurs within 2–4 hours of ingestion; guarded with advanced signs of seizures and arrhythmias.



MISCELLANEOUS

AGE-RELATED FACTORS

Young animals are typically more compromised in metabolism and excretion.

ZOONOTIC POTENTIAL

Not transmissible, but humans and dogs may access similar sources.

PREGNANCY/FERTILITY/BREEDING

Methylxanthines are teratogens in laboratory animals.

SEE ALSO

- Antidepressant Toxicosis—SSRIs and SNRIs.
- Antidepressant Toxicosis—Tricyclic
- Metaldehyde Toxicosis
- Poisoning (Intoxication) Therapy

ABBREVIATIONS

- CNS = central nervous system
- CRI = continuous rate infusion
- ECG = electrocardiogram.

INTERNET RESOURCES

- ASPCA: Dog and Chocolate Risk Wheel: Order at 888.426.4435 or email VLPP@aspca.org
- Various cell phone apps for chocolate poisoning in dogs
- Chocolate Toxicity Table: http://www.vspn.org/library/misc/vspn_m01325.htm

Suggested Reading

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Client Education Handout
available online

CHOLANGITIS/CHOLANGIOHEPATITIS SYNDROME



BASICS

DEFINITION

- Cholangitis—bile duct inflammation.
- Cholangiohepatitis—inflammation of bile ducts and surrounding liver parenchyma.
- CCHS—more common in cats; histologically classified as suppurative, nonsuppurative (lymphoplasmacytic, lymphocytic), lymphoproliferative (transition to lymphosarcoma); or granulomatous.

PATOPHYSIOLOGY

- Antecedent or coexisting conditions— inflammation or obstruction involving the extrahepatic bile duct (EHBDO) or pancreatic duct (cat), pancreatitis or IBD (dog, cat); CIN (cat).
- Bacterial infection may be primary or secondary; cholestasis is permissive to bacterial infection.
- Acute or chronic cholangitis—associates with bile duct hyperplasia, biliary epithelial hyperplasia, and a ductular reaction.
- Chronic inflammation—may cause bile duct dystrophic mineralization or choleliths.
- Suppurative disease—usually associated with positive bacterial culture or bacteria are observed cytologically (tissue or bile).
- Nonsuppurative disease—immune mediated.
- Sclerosing or destructive cholangitis— inflammation causing bile duct involution/destruction, immune-mediated or infectious—leads to ductopenia of small- and medium-sized bile ducts; a severe lesion.
- Pyogranulomatous CCHS—infectious or immune mechanisms (dog or cat).
- Lymphoproliferative disease—speculated transition stage of inflammation to neoplasia.

SYSTEMS AFFECTED

- Hepatobiliary—liver and biliary system
- Gastrointestinal—pancreas and intestines

INCIDENCE/PREVALENCE

Nonsuppurative CCHS—most common chronic liver disorder of the cat

SIGNALMENT

Species

Cat (common) and dog (uncommon)

Breed Predilections

Possibly Himalayan, Persian, Siamese cats

Mean Age and Range

- Suppurative CCHS—range 0.4–16 years; but mostly young to middle-aged cats.
- Nonsuppurative CCHS—range, 2–17 years; mostly middle-aged cats.

Predominant Sex

- Suppurative CCHS—male cats predisposed
- Nonsuppurative CCHS—none

SIGNS

General Comments

- Suppurative CCHS—most severe clinical illness, acute onset often < 5 days; abdominal pain, pyrexia; associated with EHBDO.
- Nonsuppurative—ill > 3 week (mo to yrs).

Historical Findings

CCHS—cyclic illness; chronic vague signs: lethargy, vomiting, anorexia, and weight loss; ductopenia (cats) if destructive cholangitis—polyphagic (reduced bile flow compromises nutrient assimilation, causing acholic stool, steatorrhea, and reduced uptake of fat-soluble substances, e.g. vitamin K₁, essential fatty acids, vitamin E).

Physical Examination Findings

- Suppurative CCHS—fever; painful abdomen; anicteric to jaundiced; dehydrated; shock.
- Nonsuppurative CCHS—few physical abnormalities other than hepatomegaly; thickened intestines with IBD; variable jaundice, rare abdominal effusion.
- Ductopenia (cats)—unkempt coat, variable lateral thoracoabdominal alopecia; acholic feces may vacillate with cyclic disease.

CAUSES

Suppurative CCHS

- Bacterial infection—more common in cats: *E coli*, *Enterobacter*, *Enterococcus*, β-hemolytic *Streptococcus*, *Klebsiella*, *Actinomyces*, *Clostridia*, *Bacteroides*; rare toxoplasmosis; dogs: usually enteric opportunists; rare *Campylobacter*, *Salmonella*, *Leptospirosis*, others.
- May represent sequela to EHBDO or other cause of mechanical cholestasis.

Nonsuppurative CCHS

Concurrent disorders—cholecystitis, cholelithiasis, pancreatitis, EHBDO, and IBD (dogs, cats); and CIN (cats).

RISK FACTORS

- Suppurative CCHS—EHBDO; cholelithiasis; cholestasis; infections elsewhere.
- Feline nonsuppurative CCHS—IBD, pancreatitis, EHBDO, cholelithiasis, CIN.



DIAGNOSIS

DIFFERENTIAL DIAGNOSES

- Feline hepatic lipidosis (FHL)—may coexist; similar enzyme abnormalities and jaundice but low GGT unless concurrent biliary or pancreatic inflammation.
- EHBDO and obstructive cholelithiasis; variable jaundice, increased ALP, GGT, and transaminase activities; increased cholesterol; US evidence of EHBDO.

- Pancreatitis—may reflect cholelithiasis initiated CCHS in cats; lipemia, high cholesterol, and hyperbilirubinemia; inconsistent high fPLI, lipase, and amylase, and ultrasound features; high fPLI implicates pancreatic inflammation but also may reflect IBD and duct inflammation.

- Lymphoproliferative disease and lymphosarcoma—may involve any enteric segment (thick wall), mesenteric lymphadenopathy; dense portal infiltrates spilling across the limiting plate; shares clinical features with CCHS; multisystemic lymphoma or lymphocytic leukemia may cause circulating “blast” cells; hepatic infiltrates may require immunohistochemical characterization.

- Jaundice of septicemia—hyperbilirubinemia dominates clinical biochemical features, usually disproportionate to magnitude of liver enzyme activity.
- Ductal plate malformations (DPM)—polycystic disease, (dogs, cats), especially Persian and Himalayan cats—normal or modestly increased liver enzymes; progressive peribiliary fibrosis in some DPM phenotypes (see Ductal Plate Malformations); variable mild suppurative or nonsuppurative portal aggregates, cholangitis, or CCHS.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Poikilocytes: common in cats with severe liver disease; non-regenerative anemia: anemia of chronic disease; Heinz body hemolysis: severely ill cats with low RBC GSH.
- Suppurative CCHS—neutrophilic leukocytosis, left shift, toxic neutrophils. Nonsuppurative CCHS—may be normal, lymphoproliferative disorder or lymphoma may have lymphocytosis ± abnormal cell morphology.

Serum Biochemistry

- Consistent findings—high ALT, AST, ALP, variable GGT; in cats higher enzymes in non-suppurative disease.
- Variable findings—high total serum bile acids, bilirubin, and cholesterol: depends on severity and extent of cholestasis, coexistent illness, liver dysfunction.

OTHER LABORATORY TESTS

- Species-specific PLI—may be high with pancreatitis and enteritis.
- Vitamin B₁₂—in cats low values indicate small bowel malabsorption (infiltrative disorders: IBD, lymphoma), pancreatic dysfunction, chronic oral antimicrobials causing bowel bacterial overgrowth.
- Coagulation tests—variable; PT and PIVKA most sensitive for vitamin K₁-induced coagulopathy.
- T₄—rules out hyperthyroidism as cause of liver enzyme activity in cats.

CHOLANGITIS/CHOLANGIOHEPATITIS SYNDROME

(CONTINUED)

IMAGING

- Thoracic radiography—sternal lymphadenopathy suggests abdominal inflammation, general lymphadenopathy suggests lymphoma. Abdominal radiography—normal to large liver in nonsuppurative CCHS; rare mineralized choleliths or biliary structures in suppurative or nonsuppurative CCHS.
- Abdominal ultrasonography—normal to large liver; thick bile duct or GB wall (inflammation, edema, infiltrates, fibrosis); echogenic intraluminal debris; choleliths; focal parenchymal lesions (abscess, inflammation, neoplasia); lymphadenopathy (peripancreatic, perihilar hepatic, or mesenteric) suggests pancreatic, liver, intestinal inflammation or enteric neoplasia; hepatic parenchymal hyperechogenicity (concurrent FHL, inflammation, fibrosis); cysts (DPM, polycystic disease, cystadenoma); **Note:** no US lesions in some animals with severe CCHS.

OTHER DIAGNOSTIC PROCEDURES

Fine-Needle Aspiration Cytology

- Hepatic aspiration—for culture, identify FHL; cytology may reveal bacteria not visualized by light microscopy evaluation of biopsy. **Note:** cytology rules in FHL but is unreliable for diagnosis of nonsuppurative CCHS. Hepatocellular vacuolation is common in ill cats, may be misdiagnosed as FHL.

- Cholecystocentesis—may reveal suppuration, bacteria, trematode eggs, or neoplasia. Normal bile is devoid of cells, blue amorphous appearance with Wright's Giemsa stain.

Percutaneous Biopsy

- US-guided core-needle biopsy—may misdiagnose CCHS due to small sample size; need a minimum of 15 portal triads for accurate diagnosis; if 18-G core needle used, collect a minimum of 4 samples.
- Inaccuracy with needle biopsy methods and biopsy of only a single liver lobe reflects differential lobe involvement and sample size.
- Post-biopsy complications esp. cats: collapse, vasovagal due to biliary trauma, unintentional sampling of non-hepatic tissues with US needle sampling in cats.

Laparoscopy

- Permits direct visualization of GB, porta hepatis, pancreas, and perihepatic and peripancreatic lymph nodes; permits biopsy of multiple liver lobes, as well as pancreas and bile collection (cholecystocentesis).
- In EHBDO—avoid laparoscopy.

Laparotomy

- Esp. if suspected EHBDO—recommended. Permits inspection of biliary structures; biliary

decompression and biliary enteric anastomosis; biopsy of: liver, biliary structures, pancreas, intestines, lymph nodes, and cholecystocentesis.

TISSUE SAMPLING

If nonsuppurative CCHS suspected, also biopsy bowel and pancreas.

BILE AND TISSUE CULTURES

Aerobic and anaerobic bacterial cultures—of liver tissue and bile.

MOLECULAR GENETICS

Genetic test for feline polycystic disease may be appropriate.

PATHOLOGIC FINDINGS

- Suppurative CCHS—swollen liver, blunt edges, focal discolorations; may note erythematous, necrotic, or thick-walled GB (cholecystitis); peripancreatic steatonecrosis or fat saponification (pancreatitis); perihepatic and peripancreatic lymphadenopathy; EHBDO, may observe choleliths or cystic lesions (DPM).
- Nonsuppurative CCHS—large to normal size firm liver (small in very chronic disease); blunt margins; variable surface irregularity, may observe choleliths or cystic lesions (DPM).
- If concurrent FHL: yellow or pale friable parenchyma, samples float in formalin.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient Management

- *Suppurative CCHS with acute febrile illness*, painful abdomen, left-shifted leukogram—hydration support, “best guess” bactericidal antimicrobials: initially based on cytology and Gram stain; start antibiotics if EHBDO or cholecystitis *before* surgery; continue antibiotics ≥ 4 weeks with choleretic therapy (ursodeoxycholic acid, SAMe) until enzymes normalize or signs resolve.

- *Nonsuppurative symptomatic cats*—fluid therapy as necessary; if jaundiced: give vitamin K₁ (0.5–1.5 mg/kg IM q12h for 3 doses) before invasive diagnostics and liver biopsy. Cats with CCHS—may need blood transfusion consequent to surgery or biopsy.
- Polyionic fluids—supplement with B-soluble vitamins (2 mL/L), KCl, and K phosphate as needed; avoid dextrose supplements (see Hepatic Lipidoses).

Outpatient Management

- Suppurative—after acute crisis managed.
- Nonsuppurative—after resolution of acute crisis, provide life-long immunomodulation (if no bacteria observed or cultured), antioxidants, and hepatoprotectants.

ACTIVITY

Restricted while symptomatic.

DIET

Nutritional support—avoid FHL by feeding a balanced high-protein, high-calorie feline diet; supplement water-soluble vitamins; antigen-restricted diet if concurrent IBD; fat-restricted diet if severe ductopenia causing fat malabsorption, or chronic pancreatitis causing maldigestion; may require feeding tubes (esophagostomy preferred, jejunal feeding if symptomatic pancreatitis); rarely require parenteral nutrition (provoke FHL).

CLIENT EDUCATION

Emphasize chronic nature of nonsuppurative CCHS and requirement for life-long therapy.

SURGICAL CONSIDERATIONS

- Cholecystectomy—if cholecystitis.
- Cholecystoenterostomy—may be necessary in patients with EHBDO which increases life-long risk for septic cholangitis. Cholelith removal.



MEDICATIONS

DRUG(S)

Antibiotics for Suppurative CCHS

- Bactericidal—against enteric opportunists; initially use combination of: ticarcillin or clavamox, enrofloxacin, combined with metronidazole (7.5–15 mg/kg PO q12h; low dose if jaundiced).
- Modify initial or empiric antimicrobials based on culture and sensitivity reports. Resistant enterococcus—vancomycin (10 mg/kg q12h IV slow infusion for 7–10 days).

Immunomodulation: Nonsuppurative CCHS

- Glucocorticoids—prednisolone (dogs: 2 mg/kg/day; cats: 4 mg/kg/day) for 14–21 days, taper to lowest effective alternate-day dose; chronic therapy usually needed; ensure prednisolone used in cats as prednisone is not bioavailable in this species; beware of development of diabetes mellitus in cats.
- Metronidazole—combination with prednisolone, for cell-mediated immunomodulation, antiendotoxin effect, and antibacterial, especially if IBD. Recent work implicates chronic bacterial involvement in nonsuppurative feline CCHS that may be attenuated by metronidazole.
- Cats with confirmed ductopenia—require more aggressive immunomodulation; *do not use azathioprine in cat*; clinical experience suggests combination of prednisolone, metronidazole with pulsed methotrexate (see

(CONTINUED)

CHOLANGITIS/CHOLANGIOHEPATITIS SYNDROME

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below) OR chlorambucil 1–2 mg per cat, load q24h for 3 days then every 3 days.

- *Methotrexate protocol feline nonsuppurative destructive or sclerosing CCHS:* 0.4 mg total dose given in 3 divided doses on 1 day [0.13 mg total at 0, 12, and 24h] and repeated at 7–10 day intervals); may be given PO, IV, IM (parenteral routes require 50% dose reduction); concurrently provide folate (folic acid) at 0.25 mg/kg daily. If lymphoproliferative or neoplastic infiltrates, use chemotherapy protocols developed for enteric lymphoma.

Antioxidants

- Vitamin E (α -tocopherol acetate)—10–30 IU/kg, high dose if chronic EHBDO or ductopenia PO because of fat malabsorption (see EHBDO for alternative form of Vitamin E that is water soluble).
- S-adenosylmethionine (SAMe, use form with proven bioavailability and efficacy as a GSH donor)—20 mg/kg/day enteric-coated tablet PO 2h before feeding; many beneficial effects including anti-inflammatory influence that achieved remission in cats with mild nonsuppurative CCHS (without duct destruction).

Other

- Ursodeoxycholic acid (UDCA)—10–15 mg/kg/day PO divided with food for best bioavailability; can formulate aqueous suspension (refrigerate); provides immunomodulatory, hepatoprotectant, choleretic, antifibrotic, and antioxidant effects. Recent information (humans with destructive cholangitis and knockout mouse models of such) indicate that UDCA may hasten small duct injury in destructive/sclerosing cholangitis. Thus, liver biopsy recommended before prescribing UDCA for cats with “suspected” chronic CCHS. Chronic UDCA in cats should be accompanied by taurine supplementation (250 mg/day) as all bile acids are obligatorily conjugated with taurine in cats.
- B vitamin supplementation with thiamine (B_1) and B_{12} —thiamine 50–100 mg PO q24h for 3 days, then in water-soluble vitamin supplements; B_{12} (0.25–1.0 mg SC) if suspect gut malabsorption (use initial and

sequential plasma B_{12} concentrations to verify need and efficacy of treatment; (some cats require weekly injections, then monthly).

CONTRAINDICATIONS

Adjust drug dosages with regard to liver function and cholestasis. Caution with metronidazole to avoid neurotoxicity: if jaundiced use 7.5 mg/kg PO BID.



FOLLOW-UP

PATIENT MONITORING

Nonsuppurative CCHS—initially monitor enzymes and bilirubin q7–14 days; after remission, assess quarterly; serum bile acid measurements complicated by ursodeoxycholic acid administration (detected by assay).

PREVENTION/AVOIDANCE

Control IBD

POSSIBLE COMPLICATIONS

- Suppurative CCHS may transform to nonsuppurative CCHS or sclerosing CCHS.
- Diabetes mellitus in 30% of cats with sclerosing CCHS treated with prednisolone.
- FHL may develop if inadequate nutritional intake or is induced by glucocorticoids.

EXPECTED COURSE AND PROGNOSIS

- Suppurative CCHS—may be cured.
- Nonsuppurative CCHS—chronic, long-term remission possible (> 8 years documented).



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Pancreatitis
- Hepatic lipidosis
- Polycystic liver disease
- Lymphosarcoma
- Lymphoproliferative disease
- Cholangiocarcinoma—may develop in some cats with chronic nonsuppurative CCHS

SEE ALSO

- Bile Duct Obstruction (Extrahepatic)
- Cholecystitis and Choledochitis
- Cholelithiasis
- Hepatic Lipidosis
- Inflammatory Bowel Disease
- Pancreatitis

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- AST = aspartate amino transferase
- CCHS = cholangitis/cholangiohepatitis syndrome
- CIN = chronic interstitial nephritis
- DPM = ductal plate malformation
- EHBDO = extrahepatic bile duct obstruction
- FHL = hepatic lipidosis
- GB = gallbladder
- GGT = gamma glutamyltransferase
- GSH = glutathione
- IBD = inflammatory bowel disease
- PIVKA = proteins invoked by vitamin K absence
- fPLI = feline pancreatic lipase activity
- PT = prothrombin time
- SAMe = S-adenosylmethionine
- TLI = trypsin-like immunoreactivity
- TPN = total parenteral nutrition
- US = ultrasound

Suggested Reading

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**Client Education Handout
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CHOLECYSTITIS AND CHOLEDOCHITIS



BASICS

OVERVIEW

- Cholecystitis = gallbladder (GB) inflammation.
- Choledochitis = large bile duct inflammation.
- Associate with cholelithiasis; GB mucocele (GBM); extrahepatic bile duct obstruction (EHBDO); or inflammation involving intrahepatic biliary structures.
- Severe GB inflammation can lead to rupture and subsequent bile peritonitis, necessitating combined surgical and medical treatments.
- Bile duct obstruction increases risk for biliary infection: enteric bacteria transmigrating the bowel wall, pass into the portal circulation, enter the liver, GB, and bile, dispersing endotoxins and bacteria initiating sepsis, and in some cases, bile and/or septic peritonitis.

SIGNALMENT

- Dog and cat
- No breed or sex predilection
- Necrotizing cholecystitis (dogs)—usually middle-aged or older animals.
- GBM: predisposition for dogs with hyper-lipidemia (e.g., endocrinopathies [hyperadreno-corticism, hypothyroidism, diabetes mellitus], pancreatitis, glucocorticoid administration, nephrotic syndrome, idiopathic hyperlipidemia (e.g., Shetland sheepdogs, miniature Schnauzer)—leads to cholestasis and cholecystitis; (see Gallbladder Mucocele).

SIGNS

- Choledochitis: vague signs, variable icterus.
- Sudden onset: inappetence, lethargy, vomiting, vague abdominal pain (may be postprandial with cholecystitis or GBM).
- Mild to moderate jaundice and fever common.
- Chronic postprandial discomfort/distress.
- Severe disease—shock due to endotoxemia, bacteremia, and hypovolemia.
- Soft tissue mass in right cranial abdomen palpable in small dogs and cats reflecting inflammation and adhesions of GB and pericholecystic tissues.

CAUSES & RISK FACTORS

- Impaired bile flow at cystic duct or GB, GB dysmotility, or ischemic insult to the GB wall may precede cholecystitis.
- Irritants in sludged bile (e.g., lyssolecithin, prostaglandins, choleliths, liver flukes) or retrograde flow of pancreatic enzymes (cats) may initiate/augment GB or duct inflammation.
- Previous enteric disorders, trauma, abdominal surgery—may be contributing factors.
- Anomalous GB or duct development: choledochal cyst (rare, cats > dogs).

• Bacterial infection—common; retrograde invasion via ducts from intestine or hemato-genous dispersal from splanchnic circulation.

- Toxoplasmosis and biliary coccidioides—rare.
- Necrotizing cholecystitis (dogs)—ruptured GB (common) and complicating cholelithiasis; *E. coli* and *Enterococcus* spp—common isolates.
- Emphysematous cholecystitis/choledochitis—rare, associates with diabetes mellitus, traumatic GB ischemia, acute cholecystitis (with or without cholelithiasis); common gas-forming organisms—*Clostridia* spp. and *E. coli* often cultured.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pancreatitis
- Focal or diffuse peritonitis
- Bile peritonitis
- Gastroenteritis causing biliary involvement
- Cholelithiasis
- Cholangiohepatitis
- Hepatic necrosis or abscessation
- EHBDO
- GBM
- Septicemia

CBC/BIOCHEMISTRY/URINALYSIS

- Variable leukocytosis with toxic neutrophils and inconsistent left shift
- High bilirubin; bilirubinuria
- High ALT, AST, ALP, and GGT activity
- Low albumin with peritonitis
- High cholesterol and bilirubin if EHBDO
- Hypercholesterolemia and/or hyperlipidemia (triglycerides): breed-related, endocrine, pancreatitis, nephrotic syndrome.

OTHER LABORATORY TESTS

- Abdominocentesis—inflammatory effusion; (see Bile Peritonitis)
- Bile culture (dogs)—*E. coli*, *Enterococcus* spp., *Klebsiella* spp., *Pseudomonas* spp., *Clostridium* spp., others
- Coagulation tests—abnormal if chronic EHBDO (vitamin K deficiency) or DIC in severe conditions with sepsis.

IMAGING

- Abdominal radiography—may reveal loss of cranial abdominal detail with focal or diffuse peritonitis or effusion; ileus; radiodense choleliths; gas in biliary structures; radiodense GB (dystrophic mineralization due to chronic inflammation, porcelain GB, rare).
- Ultrasonography—fluid interface surrounding GB enhances wall image; diffusely thick GB wall, segmental hyperechogenicity and /or laminated wall in necrotizing cholecystitis; double-rimmed GB wall: acute cholecystitis, hepatitis, cholangiohepatitis, third-space fluid dispersal (hypoproteinemia, right heart failure, renal

failure, pyelonephritis, abdominal effusion, iatrogenic fluid overload); GB lumen filled with amorphous echogenic stellate or finely striated pattern, resembling sliced kiwi fruit (“kiwi sign”) if GBM; GB rupture implicated by discontinuous GB wall, pericholecystic fluid or generalized effusion, and hyperechogenicity of surrounding tissue; failure to image GB: may implicate rupture or agenesis; mineralized GB wall may indicate dystrophic mineralization (Limey GB, sacculated GB or ducts due to malformation—Caroli's malformation); intrahepatic bile ducts difficult to visualize or prominent: ascending cholangitis (thick walls), or EHBDO (dilated ducts); pericholecystic fluid: necrotizing cholecystitis and surgical emergency.

- Choledochitis involving CBD: thick wall, intraluminal debris, extends into hepatic ducts.

PATHOLOGIC FINDINGS

Gross appearance—erythematous GB; may appear green-black if necrotizing lesion; tenacious “inspissated” biliary material common with GBM; pigmented choleliths if infection; blood with hemobilia; CBD with thick wall, variable intraductal debris (e.g., biliary particulates, suppurative inflammation).



TREATMENT

- Inpatient—required for critical care during diagnostic/presurgical evaluation or if septic.
- Place intravenous catheter in peripheral vein for polyionic fluids, and blood component therapy as needed.
- Restore fluid and electrolyte balance; monitor electrolytes frequently.
- Plasma—preferred colloid; indicated if hypoalbuminemia and coagulopathy.
- Whole blood or fresh frozen plasma—for surgical cases with bleeding tendencies. If septic, artificial colloids may delay recovery.
- Monitor urine output.
- Remain vigilant for vasovagal reflex (abrupt pathologic bradycardia, hypotension, cardiac arrest) when biliary structures manipulated or during cholecystostomy; be prepared with anticholinergics (atropine).
- GB resection advised for cholecystitis, best based on evaluation at surgery.



MEDICATIONS

DRUG(S)

- Antibiotics—before surgery; broad spectrum; surgical manipulations may initiate bacteremia; select antibiotics for enteric Gram-negative and anaerobic flora; refine treatment using culture and sensitivity results; good initial choice: triad combination

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CHOLECYSTITIS AND CHOLEDOCHITIS

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of: metronidazole, ticarcillin (or clavamox) and a fluorinated quinolone. Reduce standard dose for metronidazole by 50% if cholestatic jaundice.

- Ursodeoxycholic acid—10–15 mg/kg PO daily divided BID with food, tablet form provides best bioavailability; requires decompression of EHBDO prior to treatment.
- Antioxidants: *vitamin E* (α -tocopherol acetate)—10 IU/kg (see Bile Duct Obstruction (Extrahepatic)); *S-adenosylmethionine* (SAMe) use enteric-coated bioavailable product; on empty stomach)—GSH donor (20 mg/kg PO q24h), 2h before feeding; non-bile acid dependent (GSH) choleresis (40 mg/kg PO q24h).
- Vitamin K₁—0.5–1.5 mg/kg SC or IM q12h for 3 doses; **caution:** never administer IV (anaphylactoid reaction); treat early to allow response before surgical manipulations.

CONTRAINDICATIONS

Ursodeoxycholic acid—contraindicated in uncorrected EHBDO or bile peritonitis.

**FOLLOW-UP****PATIENT MONITORING**

- Physical examination and pertinent diagnostic testing—repeat every 2–4 weeks until abnormalities resolve.
- If septic—continue antibiotics until enzymes resolve.

POSSIBLE COMPLICATIONS

Anticipate a protracted clinical course with ruptured biliary tract or peritonitis.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Cholelithiasis
- Ductal plate malformation
- EHBDO
- Gallbladder mucocele
- Bile peritonitis

AGE-RELATED FACTORS

Congenital malformations of biliary structures do not predispose patients to cholecystitis but predispose to choledochitis.

ZOONOTIC POTENTIAL

Campylobacter and *Salmonella* may cause cholecystitis in dogs; advise owner if diagnosed

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- DIC = disseminated intravascular coagulation
- EHBDO = extrahepatic bile duct obstruction
- GB = gallbladder
- GBM = gallbladder mucocele
- GGT = γ -glutamyltransferase
- GSH = glutathione

Suggested Reading

Center SA. Diseases of the gallbladder and biliary tree. *Vet Clin North Am Small Anim Pract* 2009, 39(3):543–598.

Author Sharon A. Center

Consulting Editor Sharon A. Center

CHOLELITHIASIS



BASICS

OVERVIEW

- Radiopaque or radiolucent calculi in the bile ducts, gallbladder (GB), or rarely bile ductules within the liver (hepatolithiasis). Gallbladder mucocele (GBM) is considered a form of cholelithiasis (see Gallbladder Mucocele).
- May be asymptomatic.
- Symptomatic—signs reflect sludged bile, EHBDO, cholecystitis, cholangiohepatitis, or bile peritonitis.
- Primary constituents of choleliths—mucin, glycoprotein, calcium carbonate, and bilirubin pigments; while dog bile is less lithogenic than human bile (lower cholesterol saturation); dog bile forms bilirubinate sludge with fasting; and provoked by a low-protein low-methionine diet.
- 50% feline choleliths mineralized; may be radiographically visible (calcium carbonate).
- Surgical/medical treatment—not recommended without clinical signs or clinico-pathologic abnormalities (current or historical).

SIGNALMENT

- Cat and dog
- Small-breed dogs may be predisposed
- Hyperlipidemic dogs—predisposed to GBM (see Gallbladder Mucocele)

SIGNS

- May be asymptomatic.
- When accompanied by infection or causing intermittent or complete EHBDO (with or without peritonitis)—vomiting; meal-related discomfort, abdominal pain; fever; ± jaundice.
- Episodic vague peri- or postprandial abdominal pain.

CAUSES & RISK FACTORS

- Predisposing factors—stasis of bile flow (GB dysmotility, choledochal cysts [cats]; lith nidus formation (inflammatory debris, infection, tumor, epithelial exfoliation, residual suture material); bile supersaturation (heme-bilirubin pigments, hemobilia, calcium, enhanced mucin production [inflammation, prostaglandins], cholesterol); fused feline pancreatic and bile duct (ampulla) predisposes to concurrent biliary /pancreatic cholelithiasis, choledochitis, and bile stasis progressing to EHBDO, and pancreatitis.
- Bile sludge and/or GB distention—enhances mucin production and coalescence of bile particulates.
- Inflammatory mediators and bacterial enzymes associated with cholecystitis—aggravate stone precipitation (mucin production, deconjugation, and dehydroxylation of bilirubin-yielding insoluble bili-pigments).
- Low-protein, low-taurine, and low-methionine diet in dogs—lithogenic.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- EHBDO—inflammatory, infectious, or neoplastic conditions involving liver or extrahepatic tissues adjacent to porta hepatis; suggested by marked increases in: ALP, GGT, bilirubin and cholesterol.
- Cholangiohepatitis.
- Cholecystitis/Choledochitis.
- Pancreatitis.
- Bile peritonitis.
- GBM.

CBC/BIOCHEMISTRY/URINALYSIS

- May have no clinicopathologic abnormalities.
- CBC—may be normal; abnormalities reflect bacterial infection, endotoxemia, biliary obstruction, or underlying causal factors; inflammatory leukogram in some cases.
- Biochemistry—if symptomatic: variable hyperbilirubinemia, increases in serum ALP, GGT, ALT, and AST activities.

OTHER LABORATORY TESTS

- Bacterial culture—bile: aerobic and anaerobic bacteria often confirmed in symptomatic patients.
- Cholelith nidus—culture may identify bacterial infection.
- Coagulation profile—bleeding may develop with chronic EHBDO (see Bile Duct Obstruction (Extrahepatic)) associated with prolonged clotting times (especially PIVKA and PT); responsive to parenteral vitamin K₁.
- Cholelith analysis: submit to laboratory equipped for cholelith analysis; usual composition—calcium carbonate complexed with mucin and bilirubinate pigments.

IMAGING

- Abdominal radiography—limited value in delineating GB structure/content; choleliths often small, may be radiolucent; rarely mistaken for dystrophic biliary mineralization in animals with chronic cholangitis.
- Ultrasonography—can detect: choleliths ≥ 2 mm diameter, thickened GB wall, distended biliary tract, increased hepatic parenchymal echogenicity (inflammation, lipid, glycogen, or fibrosis), and extrahepatic ductal involvement; may facilitate specimen collection for culture, cytology, and histopathology; may detect evidence of EHBDO within 72hr; **caution:** a distended GB with bile “sludge” is common in anorectic or fasted patients: do not mistake for GB obstruction. Hepatolithiasis casts acoustic shadow in parenchyma. Imaging of choleliths in extrahepatic ducts may be difficult owing to enteric gas obstructing imaging “window.”

DIAGNOSTIC PROCEDURES

Histopathologic evaluation of liver is necessary in patients undergoing surgical

cholelith removal to detect comorbid conditions influencing treatment and prognosis.



TREATMENT

- Controversial whether choleresis with ursodeoxycholate are indicated in animals lacking clinical or clinicopathologic signs.
- Supportive fluids—if hospitalized, according to hydration, electrolyte and acid-base status.
- If hyperlipidemia a predisposing factor—prescribe fat-restricted diet, identify endocrinopathies and treat.
- Control predisposing conditions, especially biliary tree infection (with antimicrobials) and GB dysmotility (by GB removal).
- Exploratory surgery, choledochotomy, cholecystotomy, and possibly cholecystectomy or biliary-enteric anastomosis—indicated in symptomatic cases according to circumstances.
- Warn client that cholelithiasis is a chronic problem and that stones may reform even after surgical removal despite chronic medical treatment.



MEDICATIONS

DRUG(S)

- Antibiotics—based on cultures of bile, tissue, and cholelith nidus or directed against enteric microbial opportunists; initial treatment with Timentin, metronidazole, combined with a fluoroquinolone is usually successful.
- Ursodeoxycholic acid—10–15 mg/kg/day PO, divided BID given with food; provides choleretic, hepatoprotectant, anti-endotoxic, antifibrotic effects, and may facilitate stone dissolution; therapy continued life-long if no cause for cholelithiasis identified.
- Vitamin K₁—parenterally; 0.5–1.5 mg/kg to a maximum of 3 doses in 36h in jaundiced patients; do not administer IV (anaphylaxis).

Antioxidants

- Vitamin E (α -tocopherol acetate)—10 IU/kg per day for patients with high liver enzymes or confirmed hepatobiliary inflammation.
- S-Adenosylmethionine (SAMe, use form with proven bioavailability and efficacy)—GSH donor (important hepatobiliary antioxidant, GSH provides a driving force for non-bile acid dependent choleresis) and is a potential choleretic for patients with high liver enzymes or confirmed hepatobiliary inflammation; (20–40 mg/kg enteric-coated tablet PO q24h, administer 2h before feeding; higher dose recommended for choleresis); also

(CONTINUED)

CHOLELITHIASIS

C

provides antifibrotic and antiinflammatory benefits.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Ursodeoxycholic acid—contraindicated with EHBDO before biliary decompression.

**FOLLOW-UP****PATIENT MONITORING**

- Postoperatively: physical examination and pertinent diagnostic testing—every 2–4 weeks postoperatively until clinical signs and clinicopathologic abnormalities resolve.
- Periodic ultrasonography—assess cholelith status, integrity of biliary tract, hepatic parenchymal changes.

POSSIBLE COMPLICATIONS

Sudden onset of fever, abdominal pain, and malaise—may signify bile peritonitis and/or

sepsis from a breakdown in bile containment, or recurrent cholelith lodged in sphincter of Oddi.

EXPECTED COURSE AND PROGNOSIS

- May be asymptomatic
- Symptomatic disease—reflects existing infection, EHBDO, cholecystitis, or bile peritonitis.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Bile Duct Obstruction (Extrahepatic)
- Cholecystitis
- Choledochitis
- Gallbladder Mucocele

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- GBM = gallbladder mucocele
- GGT = γ -glutamyltransferase
- GSH = glutathione
- EHBDO = extrahepatic bile duct obstruction
- PIVKA = proteins invoked by vitamin K absence or antagonism
- PT = prothrombin time

Suggested Reading

Center SA. Diseases of the gallbladder and biliary tree. *Vet Clin North Am Small Anim Pract* 2009, 39(3):543–598.

Author Sharon A. Center

Consulting Editor Sharon A. Center

CHONDROSARCOMA, BONE



BASICS

OVERVIEW

• Chondrosarcoma (CSA) is a malignant mesenchymal tumor that produces chondroid and fibrillar matrix, but not osteoid. • CSA is the second most common primary bone tumor in dogs, accounting for 5–10% of all primary bone tumors. In cats, primary bone tumors are uncommon, and CSA is third in incidence behind osteosarcoma and fibrosarcoma. • The majority of CSAs arise from flat bones (axial skeleton).

Approximately 30% occur in the nasal cavity, accounting for 15% of all nasal tumors; 20% of CSAs arise from the ribs, accounting for 30–40% of all primary rib tumors. • 20% of CSAs arise from the appendicular skeleton, often but not always at the typical sites where osteosarcoma occurs. CSA accounts for only 3–5% of all primary bone tumors in the appendicular skeleton. • Other reported sites include facial bones, skull, vertebrae, pelvis, digits, and os penis. • Rarely, CSA can arise in soft tissue (extraskeletal) sites. In cats, CSA can arise at sites of previous injection (injection-site sarcoma).

SIGNALMENT

• Dogs: medium- to large-breed dogs weighing between 20 and 40 kg are affected most commonly. Mixed-breed dogs, golden retrievers, boxers, and German shepherd dogs are overrepresented. • Median age is 8 years (reported range 1–15 years) for dogs. • Cats are rarely affected with no obvious predilections.

SIGNS

Historical Findings

• Patients often present with a visible mass at the affected site. • Appendicular CSA usually is associated with lameness if involvement of weight-bearing bone. • Rarely, rib tumors can be associated with respiratory signs or visible body wall anomaly. • Additional clinical signs vary with the site of involvement.

Physical Examination Findings

• Findings depend on the anatomic location. • Often, but not always, a firm to hard mass will be palpable. The mass often is painful, but not always. • Rib CSA occurs most commonly at the costochondral junction. Any rib can be affected and dyspnea is rare and associated with space-occupying effect.

CAUSES & RISK FACTORS

- Etiology largely unknown.
- Osteochondromatosis (multiple cartilaginous exostosis) lesions can transform into CSA.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other primary bone tumors (osteosarcoma, fibrosarcoma, hemangiosarcoma).
- Metastatic bone tumors (transitional cell, prostatic, mammary, thyroid, apocrine gland anal sac carcinomas). • Tumors that locally invade adjacent bone (especially oral, nasal, digital, and joint tumors). • Bacterial or fungal osteomyelitis.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

IMAGING

• Radiographs of the primary lesion show features of an aggressive bone lesion (bone lysis, cortical destruction, non-homogenous bone formation, ill-defined zone of transition). • Thoracic radiographs are recommended to screen for pulmonary metastasis. • CT is recommended for axial tumors to more accurately stage local disease and plan for surgery and/or radiation therapy. • If patient is undergoing CT, concurrent imaging of the thorax is recommended as a more sensitive way to screen for pulmonary metastasis.

DIAGNOSTIC PROCEDURES

- Histopathology is needed for definitive diagnosis. • Fine-needle aspirate bone cytology may provide a supportive diagnosis.



TREATMENT

• Amputation is recommended for appendicular tumors. • For axial tumors, wide surgical excision is recommended whenever possible. • Stereotactic radiation therapy provides effective local control for canine osteosarcoma and might be an alternative to surgery for patients with CSA. • Palliative therapy is recommended for patients with nonresectable local disease or gross metastasis, or when definitive therapy is declined. Palliative care focuses on pain control.



MEDICATIONS

DRUG(S)

Pain Management

- Nonsteroidal anti-inflammatory drugs.
- Tramadol.
- Gabapentin.
- Intravenous aminobisphosphonates (e.g. pamidronate, zoledronate) might alleviate bone pain and slow pathologic bone resorption.

Chemotherapy

The role of chemotherapy has not been defined in veterinary oncology, but it does not improve outcome in humans.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Use NSAIDs cautiously in all cats and in dogs with renal insufficiency. • Do not combine NSAIDs with corticosteroids.



FOLLOW-UP

PATIENT MONITORING

Physical examination every 2–3 months and thoracic radiographs every 3–4 months to monitor for local tumor control and distant metastases, respectively.

EXPECTED COURSE AND PROGNOSIS

• Overall, 15–30% will develop metastatic disease, with the lungs being the most commonly affected site. Metastatic rates approach 50% for high-grade tumors. • With aggressive surgery, median survival is > 3 years and many dogs will enjoy long-term local control. However, depending on tumor location and completeness of excision, up to 40% will develop local recurrence. • With palliative care alone, survival times of > 1 year are still possible.



MISCELLANEOUS

SEE ALSO

- Chondrosarcoma, Larynx and Trachea
- Chondrosarcoma, Nasal and Paranasal Sinus • Fibrosarcoma, Bone • Osteosarcoma

ABBREVIATIONS

- CSA = chondrosarcoma • CT = computed tomography • NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

Farese JP, Kirpensteijn J, Kik M, et al. Biologic behavior and clinical outcome of 25 dogs with canine appendicular chondrosarcoma treated by amputation: A Veterinary Society of Surgical Oncology retrospective study. Vet Surg 2009, 38:914–919.

Liptak JM, Kamstock DA, Dernell WS, et al. Oncologic outcome after curative-intent treatment in 39 dogs with primary chest wall tumors (1992–2005). Vet Surg 2008, 37(5):488–496.

Waltman SS, Sequin B, Cooper BJ, et al. Clinical outcome of nonnasal chondrosarcoma in dogs: Thirty-one cases (1986–2003). Vet Surg 2007, 36(3):266–271.

Author Dennis B. Bailey

Consulting Editor Timothy M. Fan

CHONDROSARCOMA, LARYNX AND TRACHEA



BASICS

OVERVIEW

- Chondrosarcoma is a malignant mesenchymal tumor that produces chondroid and fibrillar matrix, but not osteoid.
- Osteochondroma is a benign tumor with an apical margin of hyaline cartilage and a base of cancellous bone.
- Laryngeal and tracheal tumors are rare in dogs and cats.

SIGNALMENT

- CSA arises in both the larynx and trachea in dogs with no obvious breed or gender predilections with an age range of 1–10 years.
- Osteochondroma typically occurs in the trachea of young dogs (< 1 year of age) with no obvious breed or gender predilections.
- CSA and osteochondroma have not been reported in the larynx or trachea of cats.

SIGNS

Historical Findings

- Voice change
- Loud or stertorous breathing
- Coughing or dyspnea
- Exercise intolerance
- Severe respiratory distress, cyanosis, collapse
- Dysphagia

Physical Examination Findings

- Inspiratory stertor.
- Respiratory stridor.
- Dyspnea, cyanosis.
- A laryngeal mass might be visible on unsedated oral examination.
- A laryngeal or tracheal mass rarely is externally palpable; however, widening of the laryngeal box might be digitally detectable.

CAUSES & RISK FACTORS

None known



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Laryngeal paralysis.
- Elongated soft palate (brachycephalic breeds).
- Laryngeal collapse.
- Collapsing trachea.
- Reverse sneezing.
- Pharyngeal or laryngeal foreign body.
- Laryngeal trauma and secondary inflammation.
- Other laryngeal tumors: rhabdomyoma, oncocytoma, squamous cell carcinoma, adenocarcinoma, mast cell tumor, osteosarcoma, fibrosarcoma, plasma cell tumor, lymphoma.

- Other tracheal tumors: squamous cell carcinoma, lymphoma, mast cell tumor, leiomyoma, adenocarcinoma, osteosarcoma.
- Thyroid adenocarcinoma.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

Pulse oximetry and/or arterial blood gas

IMAGING

- Cervical radiographs are of limited benefit. Laryngeal tumors typically are visualized radiographically only when very large.
- Cervical ultrasound can help identify a laryngeal mass and guide percutaneous fine-needle aspiration or needle core biopsy.
- Thoracic radiography recommended for evaluating the trachea and screening for pulmonary metastasis.
- Computed tomography can identify the origin of neoplastic growth, as well as the extent of disease.

DIAGNOSTIC PROCEDURES

- Sedated laryngeal exam—sedation and anesthesia are not without risk, be prepared to intubate the patient and/or perform an emergency tracheostomy.
- Laryngoscopy and tracheoscopy—be prepared to perform an emergency tracheostomy.
- Cytology of samples collected via fine-needle aspiration or ultrasound-guided fine-needle aspiration.
- Tissue biopsy and histopathology are needed to reach a definitive diagnosis.



TREATMENT

- Management of respiratory distress—keep patient calm, provide oxygen support and anti-inflammatory medications. In cases of severe respiratory distress, be prepared to intubate or perform an emergency tracheostomy.
- Small, benign laryngeal tumors can be removed surgically by submucosal resection or partial laryngectomy.
- Large, invasive laryngeal cancers are best treated with total laryngectomy and permanent tracheostomy. Owners must be aware of the extensive long-term postoperative care required and high complication rate which include aspiration pneumonia.
- Small, benign tracheal tumors can be debulked via tracheoscopy and electrocautery; however, local recurrence can occur.
- Larger and malignant tracheal tumors should be treated with resection—full-thickness removal with end-to-end anastomosis can be performed on 20–60% of the trachea, usually up to 4–8 tracheal rings.

- Radiation therapy has rarely been used. Because of the chondroid and mineral matrix produced by CSAs and osteochondromas, radiation therapy likely will stabilize tumor size at best and not cause substantial shrinkage.



MEDICATIONS

DRUG(S)

- Dexamethasone sodium phosphate (0.1–0.2 mg/kg IV) to help alleviate secondary inflammation contributing to acute respiratory distress.
- Chemotherapy has not been systemically evaluated, but is not thought to be effective.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Every effort should be made to rule out lymphoma before administering corticosteroids.



FOLLOW-UP

PATIENT MONITORING

- Monthly physical examinations are recommended.
- For laryngeal tumors, a sedated laryngeal exam should be performed every 2–3 months.
- For tracheal tumors, radiographs of the trachea and/or tracheoscopy should be performed every 2–3 months.
- Thoracic radiographs should be taken every 3–4 months to screen for possible pulmonary metastasis.

EXPECTED COURSE AND PROGNOSIS

- Prognosis for CSA is guarded because most dogs have advanced infiltrative disease at the time of diagnosis. Even when tumors can be removed, excision usually is incomplete and local recurrence is common.
- Long-term prognosis for tracheal osteochondroma is good if the lesion can be completely resected.



MISCELLANEOUS

ABBREVIATION

- CSA = chondrosarcoma

Suggested Reading

Carlisle CH, Biery DN, Thrall DE. Tracheal and laryngeal tumors in the dog and cat: Literature review and 13 additional patients. Vet Radiol Ultrasound 1991, 5:229–235.

Author Dennis B. Bailey

Consulting Editor Timothy M. Fan

CHONDROSARCOMA, NASAL AND PARANASAL SINUS



BASICS

OVERVIEW

- Chondrosarcoma is a malignant mesenchymal tumor that produces chondroid and fibrillar matrix, but not osteoid.
- Nasal CSA arises most commonly from the nasal turbinates.
- In dogs, approximately 30% of all CSA occur in the nasal cavity; this accounts for 15% of all nasal tumors.

SIGNALMENT

- For CSA in general, mixed-breed dogs, golden retrievers, boxers, and German shepherd dogs are overrepresented.
- Median age is 8 years (range, 1–15 years).
- CSA tends to develop at a younger age than other nasal tumors.
- Rare in cats—no obvious breed or sex predilections.

SIGNS

Historical Findings

- Unilateral or bilateral epistaxis and/or mucopurulent discharge.
- Sneezing, stertorous breathing, and/or facial deformity.
- Decreased appetite and/or halitosis secondary to oral cavity invasion.
- Seizures, behavior changes, and/or obtundation secondary to cranial invasion.

Physical Examination Findings

- Epistaxis and/or nasal discharge (unilateral or bilateral).
- Decreased nasal air flow (unilateral or bilateral).
- Pain on nasal or paranasal sinus palpation or percussion.
- Facial deformity, decreased retropulsion of the eyes or exophthalmia, and epiphora.
- Visible mass effect protruding through the palate into the oral cavity.

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other nasal tumors—adenocarcinoma, squamous cell carcinoma, osteosarcoma, fibrosarcoma, lymphoma, transmissible venereal tumor (dogs), nasopharyngeal polyp (cats).

- Fungal rhinitis—aspergillosis and penicilliosis (dogs), cryptococcis (cats), sporotrichosis (both).
- Rhinosporidiosis (dogs).
- Foreign body
- Thrombocytopenia or other coagulopathy.
- Tooth root abscess.
- Oronasal fistula.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal—evaluate for thrombocytopenia if signs of epistaxis.

OTHER LABORATORY TESTS

- Nasal flush for cytology and culture—rarely helpful.
- Coagulation profile.
- Buccal mucosal bleeding time.

IMAGING

- Skull radiographs—soft tissue opacity in the nasal cavity and/or frontal sinuses.
- Thoracic radiographs to screen for pulmonary metastasis.
- CT for detecting soft tissue opacity within the nasal cavity and surrounding sinuses, bony destruction, and extension through the cribriform plate into the brain.

DIAGNOSTIC PROCEDURES

- Mandibular lymph node cytology to screen for possible metastasis.
- Rhinoscopy can sometimes be helpful for visualizing a mass or fungal plaque and guiding a subsequent biopsy.
- Tissue biopsy and histopathology is needed for definitive diagnosis. The biopsy instrument should not pass caudal to the level of the medial canthus of the eye to avoid penetrating the cribriform plate.



TREATMENT

- Radiation therapy is the treatment of choice.
- Conventional linear accelerator is used most commonly. However, if available, stereotactic radiation therapy can reduce the number of radiation treatments and reduce adverse effects.
- Palliative radiation protocols (fewer treatments and lower total radiation dose) might be preferable for dogs with very advanced disease.



MEDICATIONS

DRUG(S)

- Prednisone (0.5–1 mg/kg PO q24h) to help relieve nasal congestion.

- Phenylephrine nasal spray can be used intermittently to help with epistaxis.
- Empiric antibiotic therapy can be considered for secondary bacterial infections.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

None



FOLLOW-UP

PATIENT MONITORING

- Physical examinations every 2–3 months and thoracic radiographs every 3–4 months.
- CT of the skull can be considered when clinical signs recur or progress.

EXPECTED COURSE AND PROGNOSIS

- < 10% develop metastasis (lungs affected most commonly).
- Median survival with palliative care alone is 3 months.
- With definitive radiation therapy, median survival is around 15 months, and 2-year survival rate is around 30%.
- Brain involvement is a poor prognostic sign.
- Unilateral versus bilateral involvement is not a significant prognostic factor.



MISCELLANEOUS

SEE ALSO

- Adenocarcinoma, Nasal
- Chondrosarcoma, Bone
- Chondrosarcoma, Larynx and Trachea
- Epistaxis

ABBREVIATIONS

- CSA = chondrosarcoma
- CT = computed tomography

Suggested Reading

Patnaik AK, Lieberman PH, Erlandson RA, et al. Canine sinonasal skeletal neoplasms: Chondrosarcomas and osteosarcomas. *Vet Pathol* 1984, 21(5):475–482.

Sones E, Smith A, Schleis S, et al. Survival times for canine intranasal sarcomas treated with radiation therapy: 86 cases (1996–2011). *Vet Radiol Ultrasound* 2013, 54(2):194–201.

Author Dennis B. Bailey

Consulting Editor Timothy M. Fan

CHONDROSARCOMA, ORAL

C



BASICS

OVERVIEW

- Chondrosarcoma is a malignant mesenchymal tumor that produces chondroid and fibrillar matrix, but not osteoid.
- CSA accounts for 5–10% of all primary bone tumors. Mandibular and maxillary CSA has been reported in dogs, but these are not common locations for this tumor. (See Chondrosarcoma, Bone, and Chondrosarcoma, Nasal and Paranasal Sinus.)
- In patients with CSA involving the maxilla, thorough evaluation is needed to ensure this is not a primary nasal tumor secondarily invading into the maxilla.

SIGNALMENT

- Most common in medium to large-breed dogs. Mixed-breed dogs, golden retrievers, boxers, and German shepherd dogs are overrepresented.
- Median age is 8 years (reported range 1–15 years).
- Cats are rarely affected; no obvious breed or sex predilections.

SIGNS

Historical Findings

- Visible mass involving the mandible or maxilla.
- Halitosis, dysphagia, and/or hypersalivation.
- Bloody oral discharge and oral pain.
- Weight loss secondary to a prolonged decrease in food intake.

Physical Examination Findings

- A firm to hard mass centered on the maxilla or mandible is seen most commonly.
- The overlying gingival mucosa usually is intact, although trauma and ulceration from the occlusal teeth is common with larger tumors.
- Loose or missing teeth.
- Difficulty or pain when opening the mouth (especially caudal tumors).
- Facial deformity.
- Ipsilateral mandibular lymphadenopathy.
- Nasal discharge, epistaxis, or decreased air flow through the nares (maxillary tumors).

CAUSES & RISK FACTORS

None identified



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other primary oral tumors including melanoma, fibrosarcoma, squamous cell carcinoma, and epulis (ameloblastoma or periodontoma)
- Craniomandibular osteopathy
- Dentigerous cyst, tooth root abscess, or osteomyelitis

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

IMAGING

- Skull or dental radiographs will show features of an aggressive bone lesion (bone lysis, cortical destruction, non-homogenous bone formation, ill-defined zone of transition).
- High detail dental radiographs may be appropriate for imaging smaller lesions.
- CT imaging can more accurately stage local disease and is useful for planning surgery and/or radiation therapy.

DIAGNOSTIC PROCEDURES

- Histopathology is required to reach a definitive diagnosis. All tissue removed should be submitted to the pathologist. This allows for the most accurate diagnosis, and allows for margin evaluation to assess completeness of excision.
- Fine-needle aspiration and cytology of ipsilateral mandibular lymph node recommended, especially if it is enlarged.



TREATMENT

- Surgical excision—removal of the affected segment of bone (maxillectomy or mandibulectomy) with a margin of at least 2–3 cm is recommended whenever possible.
- If excision is incomplete, adjuvant radiation therapy might help improve local control, although there is little information regarding efficacy.
- Radiation therapy can be considered as a sole local treatment modality but, because of the chondroid matrix produced by CSAs, radiation therapy likely will stabilize tumor size and not necessarily cause substantial shrinkage.
- Chemotherapy has not been evaluated but is not thought to be effective.
- Palliative care focuses on pain control.



MEDICATIONS

DRUG(S)

- Nonsteroidal anti-inflammatory drugs.
- Tramadol.
- Gabapentin.
- Intravenous aminobisphosphonates (pamidronate or zoledronate) might alleviate bone pain and attenuate bone resorption.
- Empiric antibiotic therapy can be considered for secondary bacterial infections.



FOLLOW-UP

PATIENT MONITORING

Physical examination every 2–3 months and thoracic radiographs every 3–4 months.

EXPECTED COURSE AND PROGNOSIS

- Most patients die or are euthanized due to local disease progression.
- Overall metastatic rate is 15–30%, with the lungs being affected most commonly.
- Metastatic rates approach 50% for high-grade tumors.
- Prognosis depends on tumor size and location, and surgical resectability.
- With complete excision, long-term control is possible; however, with incomplete excision, local recurrence within 6–12 months is likely.



MISCELLANEOUS

SEE ALSO

- Chondrosarcoma, Bone
- Chondrosarcoma, Nasal and Paranasal Sinus

ABBREVIATIONS

- CSA = chondrosarcoma
- CT = computed tomography

Suggested Reading

- Verstraete FJ. Mandibulectomy and maxillectomy. *Vet Clin North Am Small Anim Pract* 2005, 35(4):1009–1039.
Waltman SS, Seguin B, Cooper BJ, Kent M. Clinical outcome of nonnasal chondrosarcoma in dogs: Thirty-one cases (1986–2003). *Vet Surg* 2007, 36:266–271.

Author Dennis B. Bailey**Consulting Editor** Timothy M. Fan

CHORIORETINITIS



BASICS

DEFINITION

- Inflammation of the choroid and retina.
- Choroid is also called posterior uvea.
- Diffuse inflammation may result in frank retinal detachment (see Retinal Detachment).

PATHOPHYSIOLOGY

• Caused by infectious agents, neoplastic cells, or immune complexes (immune-mediated diseases); hematogenous pathogenic factors inducing choroidal inflammation is most common. • Choroid and retina—closely apposed; physiologically interdependent; inflammation of one usually results in inflammation of the other. • May also occur as a retinochoroiditis—retinal inflammation preceding and inducing choroidal inflammation.

SYSTEMS AFFECTED

- Nervous.
- Ophthalmic.
- Other systems if underlying disease is systemic.

INCIDENCE/PREVALENCE

- Fairly common
- Exact incidence unknown

GEOGRAPHIC DISTRIBUTION

Depends on the prevalence of infectious cause (e.g., systemic mycoses, rickettsial disease).

SIGNALMENT

Species

Dog and cat

Breed Predilections

• Systemic mycoses—more common in large hunting breed dogs. • Uveodermatologic syndrome—Akita, chow, and Siberian husky are predisposed. • Borzoi, border collie, beagle: chorioretinopathy. • Bernese mountain dog, golden retriever: systemic histiocytosis.

Mean Age and Range

Depends on underlying cause

Predominant Sex

Uveodermatologic syndrome—more common in young male dogs.

SIGNS

• Not usually painful, except when anterior uvea is affected. • Vitreous abnormalities—may note exudates, hemorrhage, or syneresis (liquefaction). • Interruption or alteration of the course of retinal blood vessels—due to retinal elevation. • Ophthalmomyiasis (cats)—curvilinear tracts from migrating larvae. • Others—related to underlying systemic disease.

Lesions

- Active—indistinct margins; tapetal hyporeflectivity; white-gray color; alter course of retinal blood vessels. • Few or small lesions—may note no apparent visual deficits.
- Extensive lesions involving larger areas of the retina—blindness or reduced vision.

• Inactive (scars)—discrete margins; hyperreflective in the tapetum, sometimes with hyperpigmented central areas; depigmented in the non-tapetum and may have some surrounding or central hyperpigmentation.

CAUSES

Dogs

- Septicemia or bacteremia—discospondylitis; endocarditis.
- Viral—canine distemper; herpesvirus (rare, usually neonates); rabies.
- Bacterial or rickettsial—septicemia or bacteremia; leptospirosis; brucellosis; pyometra (toxic uveitis); *Borrelia*; ehrlichiosis; Rocky Mountain spotted fever; bartonellosis.
- Fungal—aspergillosis; blastomycosis; coccidioidomycosis; histoplasmosis; cryptococcosis; acremoniosis; Pseudallescheriasis (single case report), Candida (single case report); geotrichosis.
- Algal—protothecosis.
- Protozoal—toxoplasmosis; leishmaniasis; *Neospora*.
- Parasitic—ocular larval migrans (*Strongyles*, *Ascarids*, *Baylisascaris*); *Sarcocystis neurona* (one report in dog) and ophthalmomyiasis interna (Diptera larval migrans) can occur in dogs but is more common in cats

Cats

- Viral—FeLV; FIV; FIP.
- Bacterial—septicemia or bacteremia; bartonellosis.
- Fungal—*cryptococcosis*, histoplasmosis, *blastomycosis*, others.
- Parasitic—toxoplasmosis; ophthalmomyiasis interna (Diptera, Cuterebra); ocular larval migrans; leishmaniasis (one report).
- Protozoal—toxoplasmosis,

Idiopathic

• Common.

- Multifocal chorioretinitis or chorioretinopathy in borzoi, border collie, and beagle—an acquired syndrome in which affected dogs have multifocal retinal edema or chorioretinal atrophy.
- Bernese mountain dog and other breeds—systemic or malignant histiocytosis.

Immune

- Any immune-mediated disease may cause vasculitis or inflammation, resulting in exudative retinal detachment or chorioretinitis; exact cause often undetermined; with thrombocytopenia, may see small multifocal or large retinal and/or vitreal hemorrhages with associated inflammation.
- Septicemia or bacteremia with associated immune complex disease.
- Dogs—Vogt-Koyanagi-Harada-like (uveodermatologic) syndrome; target is melanin pigment granule (abundant in uveal tissue), leading to severe anterior and posterior inflammation (affected dogs may also exhibit depigmentation of the skin, especially at mucocutaneous junctions); target of SLE is nuclear antigen.
- Cats—periarteritis nodosa; SLE.

Metabolic

Early hypertensive retinopathy may have multifocal localized lesions.

Neoplastic

Multiple myeloma, lymphoma, malignant histiocytosis, and neoplasia can metastasize to the eye.

Toxic

- Ethylene glycol; idiosyncratic drug reactions (e.g., trimethoprim-sulfa); ivermectin especially in predisposed breeds with multiple drug resistance gene.
- Photic injury: exposure to bright light can burn the retina; i.e., operating microscope lights, welding light exposure.

Trauma

- Exogenous infection—trauma (perforating wound or migrating foreign body).

RISK FACTORS

- FeLV or FIV infection—may predispose cat to ocular toxoplasmosis and/or other infectious causes of chorioretinitis/uveitis.
- Dogs or cats on immunosuppressive therapy for other problems.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Ophthalmic examination—usually sufficient for diagnosis; may note a slow pupillary light reflex if large areas of the retina are affected.
- Blindness or impaired vision—optic neuritis; CNS disease; diffuse retinal inflammation.
- See “Causes.”
- Retinal dysplasia—bilateral, symmetrical folds or geographic clumps of pigment or altered fundus reflectivity; no associated signs of inflammation in the eye; Labrador retrievers and springer spaniels predisposed but occurs in many breeds.

CBC/BIOCHEMISTRY/URINALYSIS

- Normal—if problem confined to the eye.
- Abnormal—depend on underlying systemic disease.

OTHER LABORATORY TESTS

- Depends on suspected systemic problem.
- ANA for suspected SLE.
- Protein electrophoresis for myeloma.
- Documentation of Bence-Jones protein in urine.
- Skin biopsy—SLE; uveodermatologic syndrome.
- Coagulation profile.
- Bacterial culture of ocular or body fluids.
- Serologic or PCR testing—*infectious disease* (see “Causes”).
- Cytology of lymph node aspirates.
- Histopathology of enucleated eyes.

IMAGING

- Thoracic radiography—lymphadenopathy; metastatic disease; infiltrates consistent with infectious agents.
- Spinal radiography—bony changes consistent with discospondylitis or multiple myeloma.
- Ocular ultrasound—

(CONTINUED)

retinal detachments; intraocular masses; especially helpful if the ocular media are not clear. • Abdominal ultrasound—screen for primary neoplasia, organ disease.

DIAGNOSTIC PROCEDURES

- Indirect ophthalmoscopy—screens a large area of the retina.
- Direct ophthalmoscopy—facilitates examination of suspicious areas.
- CSF tap—indicated for signs of CNS disease or optic neuritis.
- Vitreocentesis or subretinal fluid aspirate—may perform if other diagnostic tests fail to yield a causal agent or for suspected infectious agent or neoplasia; vitreocentesis may aggravate inflammation or induce hemorrhage, or retinal detachment, lessening the chance for restoration of vision.
- Measurement of blood pressure.

PATHOLOGIC FINDINGS

- Masses or retinal or choroidal exudates.
- Fungal organisms—in exudates and inflammatory cells.
- Perivascular inflammation—vasculitis; FIP.
- Inactive lesions—retinal and choroidal atrophy (thinning); may note RPE hyperpigmentation and tapetal destruction.



TREATMENT

APPROPRIATE HEALTH CARE

- Depends on physical condition of patient.
- Usually outpatient.

NURSING CARE

Fluid or other therapy for systemic disease.

CLIENT EDUCATION

- Inform client that chorioretinitis may be a sign of systemic disease, so diagnostic testing is important.
- Warn client that immune-mediated disease requires life-long therapy for controlling inflammation.
- Inform client that dogs with uveodermatologic syndrome may also have anterior uveitis and secondary glaucoma, which require treatment.
- Dermatitis may also require management.



MEDICATIONS

DRUG(S) OF CHOICE

- Identify and treat any underlying systemic disease (e.g., itraconazole or fluconazole for systemic mycosis, doxycycline for *Rickettsia*, azithromycin or doxycycline for *Bartonella*).
- Topical medications—not effective in dogs with intact lenses, treat any associated anterior

uveitis, e.g., topical corticosteroids (1% prednisolone acetate or 0.1% dexamethasone given q6–8h) and parasympatholytics (1% atropine given at a frequency that dilates the pupil and reduces pain). Treat any secondary glaucoma with appropriate antiglaucoma drugs (timolol maleate 0.5%, dorzolamide 2%).

- Systemic therapy—required.
- Feline toxoplasmosis—clindamycin 12.5 mg/kg PO q12h for 14–21 days.
- Systemic prednisone at anti-inflammatory doses—0.5 mg/kg PO, then taper; when systemic mycosis has been ruled out or is being treated with appropriate systemic antifungal therapy; avoid use unless large areas of the retina are affected and vision is severely threatened.
- Prednisone at immunosuppressive doses—2 mg/kg divided q12 for 3–10 days (ideal), then taper very slowly over months; for immune-mediated disease; may facilitate retinal reattachment.

CONTRAINICATION

Systemically administered corticosteroids—do not use unless systemic mycosis is ruled out or is being definitively treated.

PRECAUTIONS

With prednisone treatment consider concurrent oral antacids such as ranitidine or famotidine.

ALTERNATIVE DRUG(S)

- Neoplastic conditions (lymphoma, GME, or multiple myeloma)—chemotherapeutic agents.
- Uveodermatologic syndrome or autoimmune etiology—may require azathioprine, cyclosporine, leflunomide or mycophenylate (see Retinal Detachment) and steroids to control inflammation.



FOLLOW-UP

PATIENT MONITORING

- As appropriate for underlying cause and type of medical treatment.
- CBC platelet count and liver enzymes—monitor for side effects of systemic immunosuppressive drugs.
- IOP—for anterior uveitis.

PREVENTION/AVOIDANCE

Tick and flea control measures

POSSIBLE COMPLICATIONS

- Permanent blindness
- Cataracts
- Glaucoma
- Chronic ocular pain
- Death—secondary to systemic disease

CHORIORETINITIS

C

EXPECTED COURSE AND PROGNOSIS

- Prognosis for vision—guarded to good, depending on amount of retina affected; visual deficits or blindness if large areas of the retina were destroyed; focal and multifocal disease do not markedly impair vision but do leave scars.
- Prognosis for life—guarded to good, depending on underlying cause.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Several systemic diseases

ZOONOTIC POTENTIAL

- Toxoplasmosis—may be transmitted to humans if patient is shedding oocysts in feces.
- Vector-borne diseases—infected animals may act as reservoirs, i.e., *Bartonella*, *Rickettsia*, others.

SYNONYMS

Retinochoroiditis

SEE ALSO

- Retinal Degeneration
- Retinal Detachment
- Uveodermatologic Syndrome

ABBREVIATIONS

- ANA = antinuclear antibody
- CNS = central nervous system
- CSF = cerebrospinal fluid
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- GME = granulomatous meningoencephalitis
- IOP = intraocular pressure
- RPE = retinal pigment epithelium
- SLE = systemic lupus erythematosus

Suggested Reading

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Client Education Handout
available online

CHYLOTHORAX



BASICS

DEFINITION

- Accumulation of chyle in the pleural space.
- Chyle—triglyceride-rich fluid from the intestinal lymphatics that empties into the venous system in the thorax.
- Pseudochylous effusion—effusion that contains less triglycerides and more cholesterol compared to serum.
- Thoracic lymphangiectasia—tortuous, dilated lymphatics found in many animals with chylothorax.
- Fibrosing pleuritis—condition in which pleural thickening leads to constriction of the lung lobes; when severe, results in marked restriction of ventilation; can be caused by any chronic pleural exudate but is most commonly associated with chylothorax and pyothorax.

PATOPHYSIOLOGY

- Alteration of flow through the thoracic duct leading to leakage of chyle—can be related to increased pressure or permeability in the thoracic duct or venous obstruction downstream.
- Can be caused by any disease or process that increases systemic venous pressure at the entrance of the thoracic duct to the venous system.
- Cardiac causes—pericardial disease, cardiomyopathy, heartworm disease, other causes of right-sided heart failure.
- Non-cardiac causes—neoplasia (especially mediastinal lymphoma in cats), lung lobe torsion, diaphragmatic hernia, venous granuloma, venous thrombus.
- Less commonly thoracic duct rupture/trauma—surgical (thoracotomy), non-surgical (e.g., hit by car).
- Idiopathic most common.

SYSTEMS AFFECTED

- Respiratory—due to reduced lung expansion.
- Systemic signs can be present secondary to the respiratory distress (e.g., decreased appetite, weight loss).

GENETICS

Unknown

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Dogs—Afghan hounds and Shiba Inus
- Cats—Oriental breeds (e.g., Siamese and Himalayan)

Mean Age and Range

- Any age affected.
- Cats—more common in older cats; could indicate an association with neoplasia.
- Afghan hounds—develop when

middle-aged.

- Shiba Inus—develop when young (< 1–2 years of age).

Predominant Sex

None identified

SIGNS

General Comments

- Signs will depend on the rate of fluid accumulation and volume of pleural effusion.
- Usually not exhibited until there is marked impairment of ventilation.
- Many patients appear to have the condition for prolonged periods before diagnosis.

Historical Findings

- Tachypnea and respiratory difficulty.
- Coughing—can be present for months before examination, likely due to lung compression associated with pleural effusion.
- Lethargy.
- Anorexia and weight loss.
- Exercise intolerance.

Physical Examination Findings

- Vary with cause of effusion.
- Muffled heart and lung sounds ventrally.
- Increased bronchovesicular sounds, particularly in the dorsal lung fields.
- Pale mucous membranes or cyanosis.
- Arrhythmia.
- Heart murmur.
- Signs of right-sided heart failure (e.g., jugular pulses, ascites, hepatomegaly).
- Decreased compressibility of the anterior chest—common in cats with a cranial mediastinal mass.

CAUSES

- Cranial mediastinal masses—lymphoma, thymoma.
- Cardiac disease—heartworm, cardiomyopathy, pericardial disease, congenital diseases.
- Lung lobe torsion.
- Venous obstruction—granuloma, thrombi.
- Congenital abnormality of thoracic duct.
- Cardiac or thoracic surgery.
- Idiopathic—most common cause.

RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other causes of pleural effusion—neoplasia, pyothorax, heart failure, FIP.

CBC/BIOCHEMISTRY/URINALYSIS

- Often normal.
- Lymphopenia and hypoalbuminemia—can be found.
- Hyponatremia and hyperkalemia sometimes noted due to fluid shifts with repeat thoracocentesis.

OTHER LABORATORY TESTS

Heartworm testing

Fluid Analysis

- Classified as an exudate.
- Color will depend on fat content from diet and presence of concurrent hemorrhage—usually milky white and opaque but can appear serosanguinous and range from yellow to pink.
- Protein content varies, and high lipid-content will make refractive index inaccurate.

- Total nucleated cell count—usually < 10,000 cells/ μL .
- Fluid triglycerides—higher compared to serum.
- Fluid cholesterol—lower compared to serum.

Cytology

- Place sample in an EDTA tube to allow cell count to be performed.
- Initially, cytology is comprised of primarily small lymphocytes, neutrophils, and macrophages containing lipid.
- Chronic effusions contain less lymphocytes due to continued loss and more non-degenerate neutrophils due to inflammation from multiple thoracocenteses or irritation of pleural lining by chyle.
- Atypical lymphocytes—suggestive of underlying neoplasia.

IMAGING

Thoracic Radiography

- Two to four views if patient is stable—pleural effusion.
- Dorsoventral view associated with less stress than ventrodorsal view in an animal with respiratory difficulty.
- Repeat radiographs after thoracocentesis to assess for underlying causes of effusion or evidence of fibrosing pleuritis; if collapsed lung lobes do not appear to re-expand after pleural fluid is removed or if respiratory distress persists with only minimal fluid present, suspect underlying pulmonary parenchymal or pleural disease (e.g., fibrosing pleuritis).

Ultrasonography/Echocardiography

- Should be performed before thoracocentesis if patient is stable—fluid acts as an acoustic window, enhancing visualization of thoracic structures.
- Assess for underlying causes—detect abnormal cardiac structure and function, pericardial disease, and mediastinal masses.

CT Lymphangiography

- Can quantify TD branches more accurately than standard radiographic lymphangiography.
- In dogs, percutaneously inject 1–2 mL of non-ionic contrast material into mesenteric lymph nodes using ultrasound or CT guidance.
- Acquire helical thoracic CT images before and after injection of contrast media.
- Can document location and character of the thoracic duct and its tributary lymphatics; likely useful for surgical planning.

PATHOLOGIC FINDINGS

- Lymphatics (including the thoracic duct)—difficult to identify at necropsy.
- Fibrosing pleuritis—lungs appear shrunken; pleural layers (visceral and parietal) are diffusely thickened.
- Fibrosing pleuritis—characterized histologically by diffuse, moderate-to-marked thickening of the pleura by fibrous connective tissue with moderate

(CONTINUED)

infiltrates of lymphocytes, macrophages, and plasma cells.



TREATMENT

APPROPRIATE HEALTH CARE

- Dyspneic animal—immediate thoracocentesis; removal of even small amounts of pleural effusion can markedly improve ventilation.
- Identify and treat the underlying cause, if possible.
- Medical management—usually treated on an outpatient basis with intermittent thoracocentesis as needed based on clinical signs (see “Medications”).
- Chest tubes—place *only* in patients with suspected chylothorax secondary to trauma (very rare), in cases with rapid fluid accumulation, or after surgery.
- Surgery if medical management does not resolve the problem in 2–3 months (see “Surgical Considerations”).

NURSING CARE

- Patients undergoing multiple thoracocenteses can rarely develop electrolyte abnormalities (hyponatremia, hyperkalemia) that may need to be corrected with fluid therapy.
- Thoracocentesis—perform under aseptic conditions to reduce the risk of iatrogenic infection; antibiotic prophylaxis generally unnecessary if proper technique is used.

ACTIVITY

Patients will usually restrict their own exercise as pleural fluid volume increases or if they develop fibrosing pleuritis.

DIET

- Low-fat—potentially decreases the amount of fat in the effusion, which would improve the patient’s ability to resorb fluid from the thoracic cavity; not a cure; may help in management by facilitating reabsorption.
- Medium-chain triglycerides are transported via the thoracic duct in dogs and are no longer recommended.

CLIENT EDUCATION

- Inform client that no specific treatment will stop the effusion in all patients with the idiopathic form of the disease.
- Inform client that the condition can spontaneously resolve in some patients after several weeks or months.

SURGICAL CONSIDERATIONS

Thoracic Duct Ligation and Pericardectomy

- Recommended in patients that do not respond to medical management.
- The duct usually has multiple branches in the caudal thorax where ligation is performed; failure to occlude all branches results in continued pleural effusion.
- Always perform in conjunction with lymphangiography; methylene blue injected in the mesenteric

lymph node greatly facilitates visualization and complete occlusion of all branches.

- Thickening of the pericardium can prevent formation of lymphaticovenous communications—perform pericardectomy simultaneously with TD ligation; reports of up to 100% success rate when both techniques are performed; a second surgery can be necessary if all branches are not occluded.
- Video-assisted thorascopic surgery for thoracic duct ligation and pericardectomy is reported to have similar success rates to thoracotomy (86%).

Other

- Success rates of 83–88% reported for cisterna chyli ablation in combination with thoracic duct ligation.
- Salvage procedures for recurrence after thoracic duct ligation include cisterna chyli and thoracic duct glue embolization, pleuroperitoneal or pleurovenous shunts or placement of a PleuralPort.



MEDICATIONS

DRUG(S) OF CHOICE

- Rutin 50–100 mg/kg PO q8h; believed to increase macrophage removal of proteins, which promotes absorption of fluid; complete resolution of effusion appears to occur in some patients; further study is required to determine whether resolution occurs spontaneously or in response to this therapy.
- Somatostatin analog (octreotide)—a naturally occurring substance that inhibits gastric, pancreatic, and biliary secretions and prolongs gastrointestinal transit time, decreases jejunal secretion, and stimulates gastrointestinal water absorption; in traumatic chylothorax, reduction of gastrointestinal secretions may aid healing of the TD by decreasing TD lymphatic flows; resolution of pleural fluid has occurred in dogs and cats with idiopathic chylothorax in which octreotide has been administered but the mechanism is unknown; octreotide (Sandostatin; 10 µg/kg SC q8h for 2–3 weeks) is a synthetic analog of somatostatin that has a prolonged half-life and minimal side effects.

CONTRAINdications

Cardiac disease or neoplasia—treat the underlying disease rather than the effusion (other than heartworm disease in cats where TD ligation may be beneficial while the heartworm infection clears).



FOLLOW-UP

PATIENT MONITORING

- Monitor for signs of recurrence of pleural effusion (tachypnea, labored breathing,

respiratory distress)—perform thoracentesis as needed.

- Periodically reevaluate for several years to detect recurrence.

POSSIBLE COMPLICATIONS

- Fibrosing pleuritis.
- Iatrogenic infection with repeated thoracocentesis—important to use aseptic technique.

EXPECTED COURSE AND PROGNOSIS

- Can resolve spontaneously or after surgery.
- Untreated or chronic disease—can result in severe fibrosing pleuritis and persistent dyspnea.
- Euthanasia—frequently performed in patients that do not respond to surgery or medical management.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Diffuse lymphatic abnormalities (e.g., intestinal lymphangiectasia, hepatic lymphangiectasia, pulmonary lymphangiectasia, and chylous ascites)—may be noted; may worsen the prognosis.

AGE-RELATED FACTORS

Young patients may have a better prognosis than old animals because of the association of neoplasia with advanced age.

ABBREVIATIONS

- CT = computed tomography
- EDTA = ethylene diamine tetra-acetate
- FIP = feline infectious peritonitis
- TD = thoracic duct

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Client Education Handout
available online

CIRRHOSIS AND FIBROSIS OF THE LIVER



BASICS

DEFINITION

• Hepatic fibrosis—replacement/effacement of hepatic parenchyma, intrasinusoidal, variable zonal, deposition of extracellular matrix (ECM). • Cirrhosis—regenerative nodules with dissecting fibrotic partitions and regions of parenchymal extinction, deranging hepatic architecture; usually reflects chronic necro-inflammatory liver injury.

PATOPHYSIOLOGY

• Fibrosis—usually reflects injury associated release of cytokines / mediators stimulating production and accumulation of ECM; exception: ductal plate malformation (DPM)-with congenital hepatic fibrosis [CHF] phenotype (severe portal-to-portal bridging fibrosis without chronic inflammation). • Cirrhosis—consequence of chronic hepatic injury, fibrogenesis, and hepatic regeneration; typified by: regenerative nodules, reduced functional hepatic mass, collagen deposition in sinusoids (space of Disse) or portal tracts, compromising parenchymal perfusion. • Cirrhosis/fibrosis—lead to hepatic dysfunction, capillarization of hepatic sinusoids, collagenization of the space of Disse, development of sinusoidal hypertension, intrahepatic shunting through collagenized sinusoids and recanalized vascular pathways in fibrotic partitions between regenerative nodules. These microcirculatory disturbances impair exchanges between blood and hepatocytes. • Sinusoidal hypertension—leads to (1) hepatofugal portal flow (away from liver), (2) splanchnic hypertension, (3) APSS formation, (4) episodic HE, (5) splanchnic pooling of blood, decreased effective systemic blood volume, stimulation of renal sodium and water retention, with ascites formation, (6) hypertensive splanchnic vasculopathy predisposing to enteric bleeding.

SYSTEMS AFFECTED

• GI—splanchnic portal hypertension leads to ascites and propensity for enteric bleeding. • Neurologic—HE. • Hemic—RBC microcytosis reflect APSS; bleeding tendencies: failed factor synthesis or activation, thrombocytopenia; reduced anticoagulants increase risk for thrombosis. • Renal/urologic—ammonium biurate crystalluria; isosthenuria: PU/PD; hepatorenal syndrome (rare) may follow therapeutic paracentesis of large volume ascites (Postcentesis Hypotension Syndrome [PHS]). • Endocrine/metabolic—hypoglycemia if end-stage liver failure, usually provoked by prolonged inappetence. • Respiratory—tachypnea if tense ascites; biventricular effusion (rare, leakage across diaphragm (rare), pulmonary edema (rare). • Skin—superficial

necrolytic dermatitis (see Diabetic Hepatopathy), unkempt coat.

GENETICS

Familial predisposition for chronic hepatitis—Doberman pinscher, cocker spaniel, Labrador retriever, Maltese, Bedlington terrier (copper related), others.

INCIDENCE/PREVALENCE

High in dogs with chronic necroinflammatory liver disease, animals with chronic EHBDO, dogs with severe hepatic copper accumulation.

SIGNALMENT

Species

• Cirrhosis: dogs with chronic hepatitis; cats with chronic cholangitis/cholangiohepatitis; dogs and cats with chronic EHBDO. • Severe fibrosis: dogs and cats with severe DPM-CHF phenotype.

Breed Predilection

- Many breeds and mixed breed dogs.
- Copper-associated hepatopathy (Cu-AH—genetics proven only in Bedlington terriers; Labrador retrievers, Doberman pinschers and Dalmatians appear predisposed, but all breeds at risk for Cu-AH due to dietary Cu intake.
- DPM-CHF phenotype; boxers may be predisposed, many breeds of dogs and cats; cats with polycystic malformations at risk.

Mean Age and Range

- Cirrhosis (dogs)—any age; more common in middle to older dogs; Cu-AH any age.
- Biliary cirrhosis (cats)—with chronic cholangiohepatitis often > 7 years old.
- Fibrosis—DPM-CHF phenotype (dogs, cats): ECM accumulates with aging (suspected), genetic cause (see Ductal Plate Malformations).

Predominant Gender

- Cocker spaniels—may be higher in males.
- Doberman pinschers and Labrador retrievers—no sex predilection. • DPM: no gender predilections.

SIGNS

General Comments

- Initially—vague and nonspecific. • Later—relate to complications of portal hypertension (e.g., HE, ascites, gastroduodenal bleeding), and impaired hepatic function.

Historical Findings

• Chronic intermittent lethargy, anorexia, reduced body condition • GI signs: vomiting, diarrhea or constipation • Melena: late stage or as develop APSS • PU/PD • Late onset—ascites, bleeding, HE • Jaundice: acquired necroinflammatory disease often jaundiced. DPM usually anicteric • Cats—ascites uncommon with acquired necroinflammatory disease, more common with DPM; ptalism, aggression, seizures with HE.

Physical Examination Findings

- Lethargy • Poor body condition/coat
- ± Variable jaundice • ± Ascites • ± HE

- Obstructive uropathy: ammonium biurates
- Anasarca—rare; may develop with overzealous fluid therapy • Liver size—dogs microhepatia, cats variable • Coagulopathy: variable, uncommon in DPM • Cutaneous lesions: superficial necrolytic dermatitis (severe degenerative vacuolar hepatopathy; see Diabetic Hepatopathy).

CAUSES

- Chronic necroinflammatory, oxidant, or immune-mediated liver injury has many causes. May develop subsequent to chronic inflammatory bowel disease or pancreatitis.
- Cu-AH. • Drug- or toxin-induced liver injury—anticonvulsants; azole antifungals; NSAIDs oxibendazole; trimethoprim-sulfamethoxazole; chronic food-borne toxins (aflatoxins), others. • Infections—leptospirosis, canine adenovirus I. • Chronic cholangiohepatitis (cats). • Chronic EHBDO (> 6 weeks, dogs and cats). • Single episode of massive hepatic necrosis; sago palm (cycad toxicity), xylitol, NSAIDs in dogs with substantial Cu accumulation.

RISK FACTORS

- Breed predisposition: Cu-AH or other causes yet ill-defined (see above) • Dietary Cu intake > patient tolerance • Hepatic iron accumulation: supplementation • Chronic hepatobiliary inflammation • Chronic EHBDO • Chronic phenobarbital administration (dogs) • NSAIDS: (dogs), especially carprofen



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Chronic hepatitis—common in dogs
- Cholangiohepatitis—common in cats
- Noncirrhotic portal hypertension: dogs
- Chronic EHBDO—dogs, cats • Chronic IBD or pancreatitis—dogs, cats • Hepatic neoplasia • Metastatic neoplasia or carcinomatosis • Congenital portosystemic vascular anomaly (PSVA, shunt) • Congenital portal atresia: intrahepatic or extrahepatic
- Right-sided heart failure, pericardial disease
- Cats—hepatic lipidosis; FIP; toxoplasmosis
- Hemolytic anemia (jaundice differential)

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Microcytic RBCs: APSS; mild anemia: small RBCs with normal cell count; anemia of chronic disease; microangiopathic shearing: sinusoidal fibrosis, APSS. • Mild thrombocytopenia, variable. • Leukogram: variable.

Biochemistry

- Bilirubin variable. • Liver enzyme activities—high (ALT > ALP) noted before clinical signs or liver dysfunction; at end-stage enzymes may decline. • Normal to hypoalbuminemia. • Normal to

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CIRRHOSIS AND FIBROSIS OF THE LIVER

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hyperglobulinemia. • Hypocholesterolemia—reflects APSS. • Low BUN—reduced urea cycle activity, APSS, protein-restricted diet, PU/PD. • Hypoglycemia—rare in dogs, rare in cats. • Hypokalemia—may predispose to HE. • Hyponatremia—fluid imbalance with ascites.

Urinalysis

- Isosthenuria—with PU/PD
- Ammonium biurate crystalluria
- Bilirubinuria, bilirubin crystalluria

OTHER LABORATORY TESTS

- Ascitic fluid—pure or modified transudate
- Coagulation tests—inconsistently prolonged PT, APTT, buccal mucosal bleeding time
- Low protein C and antithrombin activity—reflects APSS, synthetic failure, or DIC
- Serum bile acids—high; reflects APSS or cholestasis in cirrhosis
- Hyperammonemia: inferred from ammonium biurate crystalluria

IMAGING***Radiography***

Abdominal—small to normal sized liver; ascites may obscure details; urate calculi radiolucent unless calcium complexed.

Ultrasonography

- Abdominal—hyperechoic or mixed echogenic parenchyma; ± nodularity; abdominal effusion (ascites); APSS (color flow Doppler); or no parenchymal change in some cases.
- Doppler interrogation of portal vasculature—may confirm hepatofugal flow or nests of APSS especially near left kidney or splenic vessels.

DIAGNOSTIC PROCEDURES

- Fine-needle aspiration cytology—helps rule out neoplasia; rule-in bacterial infection; *cannot define fibrosis or nonsuppurative inflammation*.
- Liver biopsy—for definitive diagnosis; 18G needle core too small for accuracy; use 14–16G.
- Laparoscopy—best biopsy method; permits gross visualization, documents APSS, biopsy access to multiple liver lobes and focal lesions.

PATHOLOGIC FINDINGS***Gross***

- Fibrosis—small, firm irregular to finely nodular liver; DPM-CHF may not be small; fibrotic liver may display APSS, ± ascites.
- Cirrhosis—firm irregular liver; prominent micro- or macro-nodules, APSS, ± ascites.

Histopathology

- Immune-mediated hepatitis—periportal, lobular, or centrilobular lymphoplasmacytic infiltrates, hepatic cord disorganization, sinusoidal fibrosis (space of Disse), biliary hyperplasia (ductular reaction).
- Cu-AH—initially centrilobular, may evolve immune-mediated hepatitis; single necrotic hepatocytes.
- DPM—bridging partitions with proliferative nonfunctional embryonic bile ducts embedded in ECM interconnecting

portal regions.

- Post-necrotic fibrosis—fibrosis marks regenerative repair, disorganized wide hepatic cords, engorged lymphatics reflect sinusoidal hypertension.
- Cirrhosis—diffuse lesion; fibrosis, nodular regeneration distorting lobular architecture (double-wide hepatic cord, 1 cell width = normal), periportal or sinusoidal fibrosis depending on zone of chronic injury, engorged lymphatics reflect sinusoidal hypertension; single hepatocyte necrosis if active disease.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Outpatient—minimally symptomatic patients.
- Inpatient—diagnostic tests; treatment for dehydration, severe HE, enteric bleeding (hypertensive vasculopathy), tense ascites.

NURSING CARE

- Fluids—avoid lactate if hepatic failure; avoid sodium loading if ascites.
- B complex vitamins (esp. cats)—2 mL/L fluid advised.
- Vitamin K₁—0.5–1.5 mg/kg SC q12h for 3 doses initially; titrate with PIVKA or PT.
- Glucose—if hypoglycemia; 2.5–5% dextrose in polyionic solution; titrate to response.
- Potassium chloride—in fluids, as needed.
- Avoid alkalosis—worsens HE.
- Therapeutic large volume abdominocentesis if tense ascites is non-responsive to medical treatment; **caution:** PH_S-hypotensive crisis and acute renal failure (IV volume shifts).

ACTIVITY

Limit

DIET

- Withhold oral food in acute severe HE if stupor, coma, or vomiting associated with enteric bleeding or pancreatitis.
- Consider PPN or TPN.
- If HE: restrict protein intake, use soy or dairy protein sources (dogs) combined with medical interventions to increase nitrogen tolerance; individualize protein intake to maintain body condition, muscle mass, albumin (see Hepatic Encephalopathy).
- Sodium restriction if ascites.
- Fat restriction rarely needed.
- Supplement water-soluble vitamins.

CLIENT EDUCATION

- Treatment is palliative and symptomatic.
- Antifibrotics may reduce fibrosis but limited evidence; fibrosis diminished by control of inflammation and provocative diseases.
- Attenuate factors provoking HE—azotemia, dehydration; infection; catabolism; high protein meals, hypokalemia; alkalemia; constipation, endoparasitism; enteric bleeding; certain drugs.

SURGICAL CONSIDERATIONS

- Cirrhosis—high anesthetic risk; gas anesthesia preferred—isoflurane or

sevoflurane.

- Coagulopathy—predisposes to bleeding with minor invasive procedures/surgeries; BMBT may better assess risk for bleeding.
- Postoperative intensive care—avoid HE, maintain hydration, euglycemia, electrolytes, acid-base balance (avoid alkalemia).
- Predisposed to enteric bacterial translocation—judiciously administer antibiotics esp. if surgical procedures involve alimentary canal or biliary structures.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Treatments for specific etiologies: chelate Cu if Cu-AH; withdraw potentially hepatotoxic drugs, herbal or natural remedies.
- No clinical trials prove efficacy of specific regimens in animals.

Immune Modulation—see Hepatitis, Chronic

- Prednisolone/prednisone—1–4 mg/kg q24h PO; taper to lowest effective dose (e.g., 0.25–0.5 mg/kg PO q48h); reduce dose with polypharmacy; survival effect see reference.
- Azathioprine—dogs: 1–2 mg/kg PO q48h; use 3-day loading SID dose; contraindicated in cats (toxic); dogs: combined with prednisone, antioxidants, antifibrotics PPC, or cyclosporine.

Antifibrotics—see Hepatitis, Chronic

- Immunomodulation, SAMe, silybinin, Vit. E: also considered antifibrotics—interfere in signaling processes that promote fibrogenesis.
- Ursodiol—7.5 mg/kg/day PO q12h with food: use indefinitely; provides hepatoprotectant, antiinflammatory, choleric, antioxidant, and other benefits.
- Polyunsaturated phosphatidylcholine with dilinolylphosphatidylcholine (PhosChol)—25 mg/kg/q24h, mix with food. No side effects.
- Colchicine—0.025–0.03 mg/kg q24–48h: no evidence supporting chronic benefit; side effects complicate use: inhibits mitosis-cell replication, may cause GI, bone marrow, neurologic adverse effects, avoid concurrent p450 cytochrome inhibition (e.g., ketoconazole).
- Losartan and telmisartan—losartan: 0.5 mg/kg/q24h or telmisartan: 0.5–1 mg/kg q24h for initial dosing, closely monitor blood pressure, renal function, and potassium, reducing dose if hypotension or hyperkalemia. These are angiotensin receptor blockers (ARB), selectively antagonizing angiotensin-1 receptor, bypassing intermediary activation steps within the RAAS cascade. Angiotensin-2 acting via angiotensin-1 (AT1) receptors on hepatic stellate cells (HSC) is a key mediator of hepatic sinusoidal fibrosis, increasing HSC proliferation and HSC synthesis of growth factors, cytokines, and additional bioactive molecules. Evidence suggests that AT1

CIRRHOSIS AND FIBROSIS OF THE LIVER

(CONTINUED)

C receptor blockade reduces HSC activation, and attenuates liver fibrosis, but may impose a suppressive influence on hepatic regeneration (evidence supports HSC activation is highly connected to hepatocyte proliferation and differentiation). These drugs also increase PPAR γ expression associated with induced HSC quiescence. ARBs are used in humans as antihypertensives with partial PPAR- γ agonist activity; and shown have nephroprotective (diabetes, renal injury models), to protect against some forms of drug-induced hepatotoxicity, and to limit hepatic fibrosis in various chronic models of liver disease (e.g., chronic EHBDO, Schistosomiasis induced fibrosis, CCl₄ induced injury, others).

Antioxidants

- Necroinflammatory disorders.
- S-adenosylmethionine (SAMe, use bioavailable product as proven GSH donor)—20 mg/kg q24h PO, empty stomach. Vitamin E mixed tocopherols—10 U/kg q24h PO with food.

Hepatoprotectants

- Necroinflammatory disorders.
- Ursodeoxycholate, Vitamin E, SAMe also provide hepatoprotectant effects.
- Silibinin—efficacy unclear, use PPC complexed form (bioavailable), 2–5 mg/kg q24h PO.
- Elemental zinc: 1.5–3 mg PO q24h (if low liver zinc confirmed); adjust dose with plasma zinc measurements; avoid $\geq 800 \mu\text{g/dL}$.

Gastroprotectants

Gastric acid inhibitors—if enteric bleeding (see Hepatitis, Chronic).

- Eliminate endoparasitism.

Specific Conditions

Ascites

- Restrict activity and sodium intake combined with diuretic therapy.
- Dietary sodium restriction (0.2% dry matter basis or $< 100 \text{ mg}/100 \text{ kcal}$).
- Diuretics (see Hypertension, Portal; Hepatitis, Chronic); slowly mobilize effusion: furosemide (0.5–2 mg/kg IV, SC, PO q12h) combined with spironolactone (0.5–2 mg/kg PO q12h); adjust dose to response (4–7 day recheck observation); individualize chronic treatment to response; diuretics may be intermittently used to mobilize recurrent ascites.
- Therapeutic large volume abdominocentesis if nonresponsive ascites mobilization after 7–14 days of diuretics and sodium restriction; may require fluid support as a result of intravascular to abdominal fluid shift causing PHS and ARF.

- Consider vasopressin V₂ antagonists with low dose diuretics for treatment resistant ascites (no published data for dogs or cats); tolvaptan at 10 mg/kg used in dogs with experimentally modeled congestive heart failure.

Coagulopathy

See Coagulopathy of Liver Disease

HE

See Hepatic Encephalopathy

CONTRAINDICATIONS

NSAIDs—avoid; potentiate enteric bleeding; may worsen ascites; potentiates centrilobular hepatic necrosis-hepatotoxic metabolites and Cu-AH.

PRECAUTIONS

- Diuretics—dehydration, hypokalemia, alkalemia worsen HE. • Glucocorticoids—increase susceptibility to infection, enteric bleeding, sodium and water retention and ascites, protein catabolism, HE. • Avoid drugs or reduce dose if first-pass hepatic extraction, if require hepatic conjugation or biotransformation (e.g., metronidazole—reduce conventional dose to 7.5 mg/kg PO q12h, as used for HE).

ALTERNATIVE DRUG(S)

- Dexamethasone—if ascites, replace prednisone/prednisolone to avoid mineralocorticoid effect); divide pred. dose by 7–10, administer q3–4 days; taper dose to efficacy.
- Mycophenolate: alternative for azathioprine.



FOLLOW-UP

PATIENT MONITORING

- Liver enzymes, albumin, BUN, cholesterol, bilirubin—monthly to quarterly, as needed.
- Serial monitoring of TSBA—does not add prognostic or diagnostic information. • Body condition score, weight, muscle mass—reflects nutritional adequacy/nitrogen balance.
- Abdominal girth: reflects ascites volume.
- Azathioprine, mycophenolate, colchicine—monitor for possible bone marrow toxicity (serial CBCs) and other side effects.

POSSIBLE COMPLICATIONS

HE, septicemia, bleeding—may be life-threatening; DIC—may be a terminal event.

EXPECTED COURSE AND PROGNOSIS

- Occasional flare-ups of HE and ascites may require hospitalizations for adjustment of nutritional and medical interventions.

- Sodium restriction and diuretics may require titration to achieve optimal control of ascites. • Natural history of fibrotic/cirrhotic hepatic disease in dogs is poorly characterized.
- Presence of ascites indicates severe disease.
- DPM—survival up to 12 years after diagnosis. • Cirrhosis—survival > 5 years with careful interventional management.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Dogs with leptospirosis-associated chronic liver disease (rare) may shed organisms.

SEE ALSO

- Copper Associated Hepatopathy • Diabetic Hepatopathy • Hepatic Encephalopathy
- Hepatitis, Chronic • Hypertension, Portal
- Ductal Plate Malformations

ABBREVIATIONS

- ACT = activated clotting time • APSS = acquired portosystemic shunt(s) • APTT = activated partial thromboplastin time
- ARF = acute renal failure • Cu = copper
- ECM = extracellular matrix • EHBDO = extrahepatic bile duct occlusion • HE = hepatic encephalopathy • IV = intravascular
- PHS = postcentesis hypotension syndrome
- PIVKA = proteins invoked by vitamin K absence or antagonism • PPC = polyenylphosphatidylcholine • PPN = partial parenteral nutrition • PT = prothrombin time • TPN = total parenteral nutrition

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**Client Education Handout
available online**

CLOSTRIDIAL ENTEROTOXICOSIS



BASICS

DEFINITION

- A complex and poorly understood disorder characterized by diarrhea in dogs and cats associated with *Clostridium perfringens* toxins.
- The presence of CP enterotoxin and enterotoxigenic fecal isolates appears to provide the best evidence of CP-associated diarrhea.
- CP is considered to be associated with antibiotic responsive diarrhea.

PATHOPHYSIOLOGY

- *Clostridium perfringens* is a normal commensal found in the intestinal tract of humans and animals. The organism is found in a vegetative form living in a symbiotic relationship with the host.
- Certain strains of CP (generally type A based on PCR analysis) produce an alpha toxin and are capable of producing a more virulent enterotoxin (CPE) that binds to the enteric mucosa, alters cell permeability, and results in cell damage and/or subsequent cell death.
- CPE production is co-regulated with sporulation of the organism. Conditions that precipitate sporulation in animals include a sudden change in diet, dietary indiscretion, injudicious use of antibiotics causing a severe dysbiosis, and underlying intestinal disease.
- There appear to be a number of intrinsic host-related factors that influence CPE production and pathogenicity of CP.

SYSTEMS AFFECTED

Gastrointestinal

INCIDENCE/PREVALENCE

- Incidence is unknown, but it is suspected that up to 34% of cases of diarrhea in dogs are CP-related. The infection is far less common in cats.
- May also be associated as a nosocomial diarrhea.

SIGNALMENT

Species

Dog and cat

Mean Age and Range

- Disease may occur in any age animal.
- Most animals that develop chronic clinical signs tend to be middle-aged or older.

SIGNS

General Comments

- Clinical signs are associated with either an acquired acute self-limiting diarrhea lasting 5–7 days, chronic intermittent diarrhea, or signs associated with other gastrointestinal or non-gastrointestinal disease.
- Chronic signs are often characterized by intermittent episodes recurring every 4–6 weeks that may persist for months to years. The syndrome may result as a

nosocomial (hospital-acquired) disease with signs precipitated during or shortly following hospitalization or boarding at a kennel.

- CP has also been associated with acute hemorrhagic gastroenteritis (HGE), and frequently observed concurrently with cases having parvovirus.

Historical Findings

- Most common sign is large bowel diarrhea having fecal mucus, small amounts of fresh blood, small scant stools, tenesmus with an increased frequency of stools.
- Dogs may also have signs of small bowel diarrhea characterized by a large volume of watery stool.
- Other signs include vomiting, flatulence, hematochezia, abdominal discomfort, or a generalized unthriftiness in chronic cases.

Physical Examination Findings

- Evidence of systemic illness or debilitation is rare.
- Abdominal discomfort may be detected on palpation.
- There may be evidence of blood or mucus in the feces.
- Fever is uncommon.

CAUSES

- It is unknown if enterotoxigenic CP is a true acquired infection or is an opportunistic pathogen. There are only certain biotypes of CP genetically capable of producing CPE, and only certain animals are affected clinically. The disease may be associated with small intestinal bacterial overgrowth.
- Diarrhea may be associated with dietary indiscretions or diet change.

RISK FACTORS

- Stress factors to the gastrointestinal tract, dietary change, antibiotic administration, concurrent disease, or hospitalization may precipitate signs.
- The pathogenicity of CP may depend on the metabolic, mucosal, and immunologic integrity of the gastrointestinal tract.
- Possibly IgA deficiency.
- An alkaline intestinal luminal environment promotes CP sporulation and CPE production.
- Primary intestinal bacterial overgrowth.



DIAGNOSIS

- Cases having acute or chronic intermittent clinical signs should be suspected of having CP.
- Diagnostic testing should always be evaluated during the onset of clinical episodes.
- Late in the course of disease evidence of CP or CPE may be absent.
- CP is usually an antibiotic-responsive diarrhea; however, a response to empiric antibiotic therapy in a dog with nonspecific

diarrhea does not infer a diagnosis of *C. perfringens*.

DIFFERENTIAL DIAGNOSIS

- All causes of diarrhea, including systemic or metabolic disease as well as specific intestinal disorders, should be considered.
- Gastrointestinal parasites, inflammatory bowel disease, chronic idiopathic colitis, and irritable bowel syndrome may resemble CP enterotoxicosis.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC may show evidence of hemoconcentration secondary to dehydration.
- Dogs with HGE commonly show a discordant PCV or Hct relative to the total protein on CBC. It is not uncommon to observe a Hct of 60% or higher in dogs with severe HGE in conjunction with a normal or low-normal total protein of 6.5 mg/dL. This is due to a combination of hemoconcentration secondary to dehydration and splenic contraction together with intestinal protein loss.
- Biochemical alterations may reflect underlying dehydration.

OTHER LABORATORY TESTS

There is no gold standard diagnostic test for confirming *C. perfringens*-associated diarrhea.

Microbiology

- Fecal culture alone should not be used to diagnose *C. perfringens* because the organism is a normal commensal. *C. perfringens* can be isolated from the feces of approximately 90% of healthy dogs.
- Specific fecal spore cultures will detect high concentrations of clostridial spores ($> 10^6$ spores/gram of feces) in affected animals and correlate well with clinical disease, but are rarely performed.

Enterotoxin Assay

- Detection of CPE via ELISA can be helpful for diagnosing *C. perfringens*-associated diarrhea; however, CPE is detected in approximately 10–14% of healthy dogs and up to 34% of diarrheic dogs, decreasing the utility of this test alone.
- There are many other virulence genes and toxins that appear to play a role in *C. perfringens*-associated diarrhea in dogs, including the necrotizing toxin gene, *netF*.
- RT-PCR for detection of CPE gene (*cpe*) and alpha toxin gene is commercially available; however, many healthy dogs have detectable alpha toxin gene, decreasing the diagnostic utility of this assay as a stand-alone test.
- Detection of *cpe* and CPE concurrently in a dog displaying clinical signs consistent with *C. perfringens* is the most accurate means for making a diagnosis.

Fecal Cytology

- Cytology involves making a thin fecal smear on a microscope slide, air-drying or

CLOSTRIDIAL ENTEROTOXICOSIS

(CONTINUED)

heat-fixing, and staining with Diff-Quik, Wright's stain, or New Methylene Blue.

- CP spores have a "safety-pin" appearance with an oval structure and a dense body at one end of the spore wall.
- Identification of high numbers of CP endospores on fecal cytology correlates poorly with clinical disease or fecal CPE activity.
- High numbers of fecal endospores can be found in the feces of healthy dogs, decreasing the diagnostic utility of fecal cytology in these animals.

DIAGNOSTIC PROCEDURES

Colonoscopy will help rule out concurrent intestinal disease.

PATHOLOGIC FINDINGS

- Colon biopsies taken during asymptomatic periods are usually unremarkable.
- Patients with CP enterotoxicosis may have colonoscopic evidence of hyperemic or ulcerated mucosa.
- Histology may show catarrhal or suppurative colitis.
- Occasionally a mild lymphocytic and plasmacytic enteritis is present.



TREATMENT

APPROPRIATE HEALTH CARE

- Most treated as outpatients.
- When diarrhea or vomiting is severe, and resulting in dehydration and electrolyte imbalance, hospitalization may be required.

NURSING CARE

Fluid and electrolyte therapy may be required to replace losses occurring from diarrhea, particularly in dogs with HGE.

ACTIVITY

Restricted during acute disease

DIET

- Dietary manipulation plays a role in the treatment and management of cases with chronic recurring disease. Diets high in fiber, either soluble (fermentable) or insoluble fiber, often result in clinical improvement by reducing enteric clostridial numbers. This may be due to acidification of the distal intestine, potentially limiting CP sporulation and enterotoxin production.
- Commercial high-fiber diets can be supplemented with psyllium (1/2–2 tsp/day) as a source of soluble fiber.
- Diets low in fiber should be supplemented with fiber (coarse bran 1–3 tbs/day) as a source of insoluble fiber or psyllium added as a source of soluble fiber.

- Probiotics may be beneficial for preventing recurrences of *C. perfringens*-associated diarrhea by altering the intestinal microbiota.

CLIENT EDUCATION

Acute disease is often self-limiting. There have been no documented reports of zoonotic transmission of *C. perfringens* from animals to humans.



MEDICATIONS

DRUG(S) OF CHOICE

Antibiotics

- Antibiotics should be avoided in dogs with mild disease because the infection typically has a brief, self-limiting nature.
- In dogs with severe diarrhea or evidence of systemic disease, antibiotics can be administered for 5 days.
- Antibiotics of choice for treatment of *C. perfringens* in dogs include ampicillin (20 mg/kg q8h) or amoxicillin (20 mg/kg q8h), metronidazole (10 mg/kg q12h), or tylosin (5–10 mg/kg q24h). Tetracyclines should be avoided due to the high incidence of induction of resistance genes.

ALTERNATIVE DRUGS(S)

- Probiotics (such as lactobacillus or others) may alter the intestinal microbiota, reducing the likelihood of recurrences.
- Chronic cases may respond well to high-fiber diets (see "Diet"), and dietary manipulation may be attempted as the sole therapy following resolution of signs.



FOLLOW-UP

PATIENT MONITORING

The patient's response to antibiotic therapy does not confirm a diagnosis of *C. perfringens*-associated diarrhea. Monitoring for hydration status and electrolyte imbalances is warranted in dogs with moderate to severe disease.

PREVENTION/AVOIDANCE

Feeding high-fiber diets or probiotics may decrease the incidence of *C. perfringens*-associated diarrhea.

EXPECTED COURSE AND PROGNOSIS

- Most animals respond well to therapy. Chronic cases may require long-term therapy to control clinical signs.
- A lack of response to therapy suggests concurrent disease, and further diagnostic evaluation is warranted.



MISCELLANEOUS

ASSOCIATED CONDITIONS

CP enterotoxicosis is frequently associated with other enteric disease such as parvovirus, acute hemorrhagic gastroenteritis, or inflammatory bowel disease.

ZOONOTIC POTENTIAL

Unknown

PREGNANCY/FERTILITY/BREEDING

Antibiotic therapy may be contraindicated

SEE ALSO

- Colitis and Proctitis
- Small Intestinal Dysbiosis

ABBREVIATIONS

- CP = *Clostridium perfringens*
- CPE = *Clostridium perfringens* enterotoxin
- cpe = *C. perfringens* enterotoxin gene
- ELISA = enzyme-linked immunosorbent assay
- GI = gastrointestinal
- PCR = polymerase chain reaction

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Client Education Handout
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COAGULATION FACTOR DEFICIENCY



BASICS

DEFINITION

Hemostatic defects characterized by a lack of one or more procoagulant proteins (coagulation factors).

PATHOPHYSIOLOGY

- Coagulation involves a complex series of enzymatic reactions that generate a burst of thrombin (factor IIa) at sites of blood vessel injury. Thrombin then cleaves plasma fibrinogen into fibrin monomers that are subsequently polymerized and cross-linked to form an insoluble fibrin clot.
- Functional and/or quantitative coagulation factor deficiencies cause a failure of fibrin clot formation.
- The liver is the sole or primary site of synthesis of most coagulation factors. After synthesis, factors II, VII, IX, and X require a vitamin K-dependent modification to become fully active.

SYSTEMS AFFECTED

- Coagulation factor deficiency can cause spontaneous hemorrhage, prolonged post-traumatic hemorrhage, and ultimately blood loss anemia.
- Spontaneous hemorrhage—often develops in body cavities or potential spaces (i.e., hemothorax, hemoperitoneum, hemarthrosis, subcutaneous or intramuscular hematoma).

SIGNALMENT

- Acquired factor deficiencies—depends on underlying disease process.
- Heredity factor deficiencies—severe defects manifest by 3–6 months of age, milder hemostatic defects manifest after surgery or trauma.
- Hemophilia A and B (factor VIII and IX deficiencies)—X-linked recessive traits (males express the bleeding tendency, female carriers are clinically normal).
- Hemophilia A is a common hereditary factor deficiency and is seen in all breeds and mixed-breed dogs and cats.
- All other factor deficiencies—autosomal traits; males and females express signs with equal frequency. Specific defects are more likely to be propagated within a single breed, but all breeds are at risk for developing new mutations.
- Factor XII deficiency is common in cats but does not cause a clinical bleeding tendency.

SIGNS

- Hematoma formation
- Intracavitary hemorrhage
- Prolonged hemorrhage post-surgery, trauma
- Blood loss anemia

CAUSES

- Acquired—synthetic failure (liver disease); vitamin K deficiency (cholestasis, anticoagulant rodenticide toxicity, malabsorption, long-term antibiotics, coumadin); factor inhibition (heparin

overdose, envenomation); factor consumption and depletion (DIC); factor dilution (high-volume transfusion, plasma expanders); hyperfibrinolysis (secondary fibrinogen depletion).

- Heredity—distinct mutations in coagulation factor genes.

RISK FACTORS

See acquired causes above.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Thrombocytopenia should be the first rule-out for any patient with abnormal hemorrhage.
- Acquired coagulopathies often develop because of liver disease, anticoagulant rodenticide ingestion, and DIC.
- Liver disease is accompanied by changes in CBC and chemistry profiles (see Coagulopathy of Liver Disease).
- Anticoagulant rodenticide toxicity prolongs the APTT and PT screening tests but does not affect TCT or fibrinogen.
- DIC always develops secondary to systemic disease (especially sepsis or neoplasia) and is often accompanied by low or falling platelet count.
- Massive transfusion (>1 blood volume) with stored blood products may dilute functional factors, fibrinogen, and platelets below hemostatic levels.
- Hyperfibrinolysis may develop after hypovolemic shock and traumatic blood loss but generally does not cause prolongation of APTT and PT screening tests.
- Heredity coagulation factor deficiencies cause prolongation of coagulation screening tests, whereas vWD does not.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

Therapeutic dosages of unfractionated heparin, coumadin, and plasma expanders (dextran, hetastarch) prolong coagulation screening tests.

Disorders That May Alter Laboratory Results

- Improper sample collection will invalidate coagulation test results (poor venipuncture technique, partially filled citrate collection tubes, use of heparin or clot activator tubes).
- Extreme lipemia, hemoglobinemia, or icterus may interfere with clot detection by photo-optical coagulation analyzers.
- Because of factor lability, samples should be assayed on site or plasma separated and sent on ice to the laboratory.

Valid if Run in Human Laboratory?

- Interpretation of coagulation assay results requires same-species reference ranges and controls. For example, human APTT values are generally twice those of dogs and cats.
- The laboratory should confirm cross-reactivity

of antigenic assays and optimization of functional tests for animal plasmas.

CBC/BIOCHEMISTRY/URINALYSIS

- Regenerative anemia develops after blood loss.
- Platelet count is normal unless the patient has DIC or massive bleeding.
- Resorption of blood from large hematoma may cause high bilirubin.

OTHER LABORATORY TESTS

- Coagulation screening tests (ACT, APTT, PT, TCT) are functional tests that measure the time for in vitro clot formation.
- Coagulation factor and fibrinogen deficiencies prolong clotting time (see algorithm, Figure 1).
- ACT is a point-of-care screening test that detects severe deficiencies of all factors (except factor VII). The ACT may be influenced by anemia, thrombocytopenia, and changes in blood viscosity.
- APTT is a screening test of the contact pathway (prekallikrein, high molecular weight kininogen, factor XII) intrinsic system (factors XI, IX, VIII), common system (factors X, V, II), and severe fibrinogen deficiency.
- PT is a screening test of factor VII, common system, and severe fibrinogen deficiency.
- The TCT is a screening test of functional fibrinogen and is sensitive to the presence of fibrinogen inhibitors.
- Acquired coagulation factor deficiencies generally cause prolongation of more than one screening test.
- The most common hereditary factor deficiencies (hemophilia and factor XII deficiency) specifically prolong APTT.
- Individual factor assays can be performed for definitive diagnosis of hereditary or complex coagulopathies.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

The buccal mucosa bleeding time is prolonged in patients with severe thrombocytopenia, platelet dysfunction, von Willebrand disease, and fibrinogen deficiency, but BMBT is insensitive to coagulation factor deficiencies.



TREATMENT

- Transfusion of fresh whole blood, fresh plasma, and fresh frozen plasma will supply all coagulation factors.
- Cryoprecipitate is a specific source of factor VIII, fibrinogen, and vWF. Cryo-supernatant plasma supplies all other factors.
- Component therapy is preferred for surgical prophylaxis and non-anemic patients to prevent red cell sensitization and volume overload.
- Patients with severe acquired or hereditary factor deficiencies may require repeated transfusion (q8–12h) to control or prevent hemorrhage.

COAGULATION FACTOR DEFICIENCY

(CONTINUED)



MEDICATIONS

DRUG(S) OF CHOICE

Vitamin K₁ is an effective treatment for patients with anticoagulant rodenticide poisoning and other causes of vitamin K deficiency.

CONTRAINDICATIONS

NSAIDs, anticoagulants, and plasma expanders should be avoided to prevent further compromise of hemostasis.

PRECAUTIONS

- Intramuscular injections and jugular catheter placement should be avoided because of the risk of inducing additional bleeding.
- Intravenous administration of vitamin K is not recommended because of the risk of anaphylaxis.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

Alternatives such as antifibrinolytic drugs (EACA and tranexamic acid) may prove useful to reduce or eliminate transfusion requirements, but have not yet been evaluated in veterinary clinical trials.



FOLLOW-UP

PATIENT MONITORING

- PT or factor VII assays can be used to monitor effectiveness of vitamin K

administration in animals with anticoagulant toxicity. Test results should normalize after 24–48 hours of initiating therapy. • ACT is a less specific but reasonable substitute for monitoring response to vitamin K.

- Hereditary defects can be monitored by clinical arrest of bleeding, stabilization of Hct, resolution of hematoma, and, if needed, specific factor analyses.

POSSIBLE COMPLICATIONS

Transfusion poses a risk of immune reactions (e.g., RBC sensitization, urticaria) and non-immune reactions (disease transmission, volume overload).



MISCELLANEOUS

ASSOCIATED CONDITIONS

None

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Patients with hereditary factor deficiencies should not be bred.

SYNONYMS

- Coagulation defects • Coagulopathies

SEE ALSO

- Coagulopathy of Liver Disease
- Disseminated Intravascular Coagulation
- Von Willebrand Disease

ABBREVIATIONS

- ACT = activated clotting time • APTT = activated partial thromboplastin time
- BMBT = buccal mucosal bleeding time
- DIC = disseminated intravascular coagulation • NSAID = nonsteroidal anti-inflammatory drug • PT = prothrombin time • RBC = red blood cell • TCT = thrombin clotting time • vWD = von Willebrand disease

INTERNET RESOURCES

http://www.labtestsonline.org/understanding/analytes/coagulation_factors/test.html.

Suggested Reading

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Author Marjory Brooks

Consulting Editor Alan H. Rebar

COAGULATION SCREENING TESTS: APTT, PT, TCT

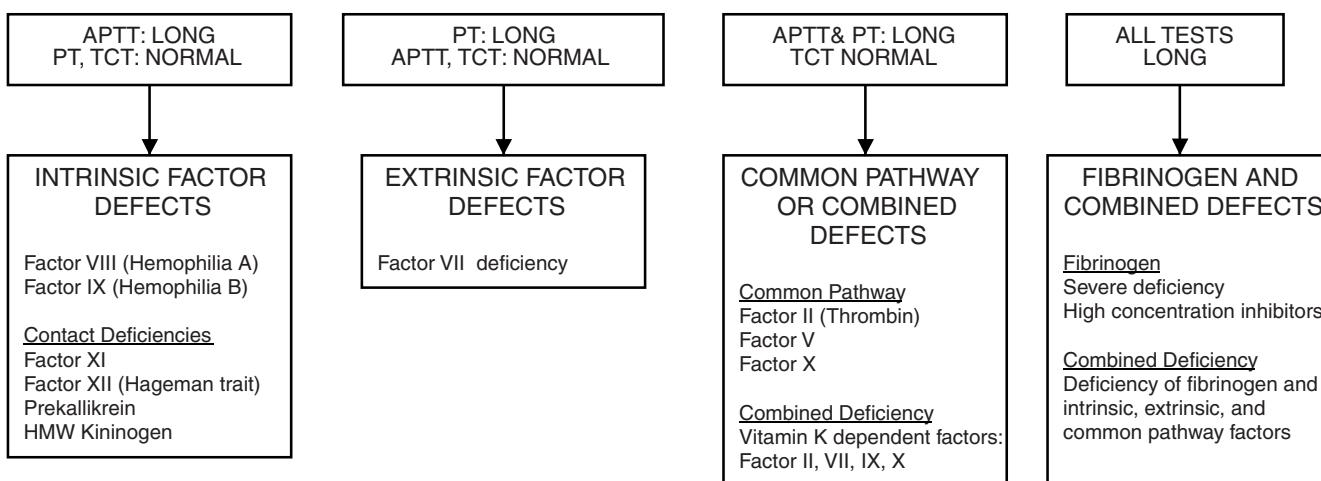


Figure 1.

Diagnostic algorithm for coagulation factor deficiencies.

COAGULOPATHY OF LIVER DISEASE



BASICS

OVERVIEW

- Liver is the sole/primary site of synthesis of coagulation, anticoagulant, and fibrinolytic proteins with few exceptions (e.g. Factors V, VIII, vWF, tPA).
- Despite abnormal clotting time test results, few patients exhibit spontaneous bleeding.
- Causes of hemostatic imbalance:
 - (1) reduced synthesis or activation of procoagulant proteins; vitamin K deficiency,
 - (2) dysfibrinogenemia due to abnormal fibrin polymerization,
 - (3) reduced clearance of FDP,
 - (4) thrombocytopenia or thrombocytopathy,
 - (5) enhanced fibrinolysis.
- Vitamin K deficiency—linked to severe intra- or extrahepatic cholestasis or steatorrhea or prolonged oral antibiotic administration.

SIGNALMENT

Dog and cat of any age, breed, or sex

SIGNS

- Often minor or no bleeding.
- Melena; hematemesis; hematochezia; hematuria.
- Prolonged bleeding if provoked: venipuncture, cystocentesis, biopsy, surgical wounds.
- Spontaneous bruising/hematomas—rare unless severe vitamin K deficiency or fulminant DIC.

CAUSES & RISK FACTORS

- Severe hepatic failure of any etiology
- Acute viral liver disease
- EHBDO
- Chronic liver disease—especially cirrhosis
- Concurrent small bowel disease (e.g., cats with cholangiohepatitis or hepatic lipidosis) predisposing to vitamin K deficiency
- High CVP and portal hypertension
- PSVA: asymptomatic factor deficiency and prolonged APTT common; overt bleeding uncommon.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Toxicities—anticoagulant rodenticides, NSAIDs (GI lesions), causes of acute liver failure (e.g., ingestion of aflatoxin or cycad)
- Hereditary hemostatic defects
- Thrombocytopenia
- DIC—any cause GI infiltrative disorders
- Hepatic amyloidosis (factor deficiency, spontaneous liver lobe fractures)
- Abdominal trauma

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—normal or regenerative anemia; severe bleeding (2–5 days); microcytosis; portosystemic shunting; thrombocytopenia

- Biochemistry—high liver enzymes; bilirubinemia; low albumin; hypoglobulinemia; low cholesterol
- Urinalysis—hematuria; bilirubinuria

OTHER LABORATORY TESTS

Hemostatic tests—thrombocytopenia; prolonged APTT (ACT), PT, TCT, and PIVKA; low fibrinogen and coagulation factors; low anticoagulant factors (AT, protein C); high FDP and D-dimer.

IMAGING

Abdominal Ultrasonography

- Effusion (ascites, hemorrhage)
- Liver changes vary with disorders
- Abnormal enteric motility, thickening in area of bleeding (portal hypertensive vasculopathy)



TREATMENT

- Not necessary unless invasive procedures planned or spontaneous hemorrhage noted.
- Fresh whole blood—provides replacement of red cells, coagulation factors, functional platelets.
- Fresh frozen plasma—provides coagulation factors, other hemostatic proteins and reduces risk of red cell sensitization or volume overload.
- Cryoprecipitate—for severe hypofibrinogenemia or bleeding with coexistent vWD.
- Platelet-rich plasma—rarely indicated.
- Avoid synthetic colloids if bleeding tendencies observed.

BIOPSY

- High risk for bleeding—PIVKA, PT, APTT, or ACT prolonged by > 50%; thrombocytopenia < 50,000/ μ L; prolonged mucosal bleeding time.
- Iatrogenic hemorrhage—grave prognosis if spontaneous bleeding with undetermined cause.
- Hemostasis support—post-procedure bleeding.
- Ultrasound-guided needle core—highest risk; observe biopsy site within 15 minutes, then sequentially over several hours post-procedure.
- Laparoscopy—affords visibility and allows hemostasis (cautery, Gelfoam pack biopsy site).
- Laparotomy—wedge biopsy; ill-advised in patients with overt bleeding.



MEDICATIONS

DRUG(S)

- Based on cause of hepatic abnormality.
- Vitamin K deficiency—parenteral vitamin K₁ (0.5–1.5 mg/kg q12h SC up to 3 doses in

24-hour interval one time); vitamin K₁ PO (Mephyton, 1 mg/kg q24h) if normal enteric bile acid uptake.

• DIC—correct primary disease; consider heparin for overt thrombosis (unfractionated heparin [UFH]: 200 U/kg q6–12h; or low molecular weight heparin [enoxaparin]: 1 mg/kg q12–24h), dose titration based on clinical status and laboratory monitoring (ACT, aPTT [UFH], heparin anti-Xa activity [all heparins]).

- Blood products—fresh whole blood: 12–20 mL/kg q24h; fresh frozen plasma: 10–20 mL/kg q12h; plasma cryosupernatant (albumin, vitamin K-dependent factors): 10–20 mL/kg q12h; cryoprecipitate (fibrinogen, vWF, factor VIII): 1 U/10 kg or dose to effect.
- DDAVP—0.5–1 μ g/kg IV in saline; may increase coagulation factors, shortens bleeding times, reduces bleeding tendencies; empirically used for biopsy-induced bleeding.
- Antifibrinolytics—EACA: 100 mg/kg loading, 30 mg/kg/h; tranexamic acid: 25 mg/kg q8h; if hyperfibrinolysis.

CONTRAINdicATIONS

- Stored whole blood—may provoke HE.
- Vitamin K₁ (cats)—too much causes Heinz body hemolysis and oxidant liver injury.
- Aspirin or other NSAIDs—may predispose to renal failure, worsen ascites, provoke emesis and spontaneous bleeding.
- High-volume transfusion in citrate-based anticoagulants (especially in animals < 5 kg) may induce symptomatic hypocalcemia.
- Avoid provocative procedures—e.g., jugular venipuncture or catheter placement, cystocentesis if recognized bleeding tendencies.



FOLLOW-UP

PATIENT MONITORING

- Optimized PT test, PIVKA, factor VII—most sensitive to vitamin K deficiency; if no improvement after 48 hours of vitamin K₁ injection, unlikely benefit from further dosing.
- Heart rate, blood pressure, mucous membrane color and refill, PCV, and total solids to monitor response if active bleeding.
- Biopsy site—observe immediately and sequentially (ultrasonography) for hemorrhage.
- Sample abdominal effusion to determine if hemorrhage or ascites.

PREVENTION/AVOIDANCE

- Well-balanced diet replete with vitamins.
- Consider impaired vitamin K availability or synthesis from chronic oral antimicrobials.
- Invasive procedures—anticipate bleeding; pretreat with vitamin K₁; give DDAVP within 20 minutes of anticipated biopsy or if

COAGULOPATHY OF LIVER DISEASE

(CONTINUED)

bleeding tendencies persist despite vitamin K₁ therapy (repeated DDAVP of no use); fresh frozen plasma for factor/fibrinogen replacement and active bleeding; avoid volume overload and increased CVP.

- Eliminate enteric parasitism.

POSSIBLE COMPLICATIONS

Hemorrhage, anemia, hypovolemia, HE

EXPECTED COURSE AND PROGNOSIS

Spontaneous hemorrhage, refractory coagulopathy, and DIC—poor prognosis.

**MISCELLANEOUS****ABBREVIATIONS**

- ACT = activated clotting time
- APTT = activated partial thromboplastin time
- AT = antithrombin
- CVP = central venous pressure
- DDAVP = desmopressin acetate
- EACA = epsilon aminocaproic acid
- EHBDO = extrahepatic bile duct obstruction

- FDP = fibrin/fibrinogen degradation product
- HE = hepatic encephalopathy
- NSAID = nonsteroidal anti-inflammatory drug
- PIVKA = proteins induced by vitamin K absence
- PSVA = portosystemic vascular anomaly
- PT = prothrombin time
- TCT = thrombin clotting time
- tPA = tissue plasminogen activator
- vWD = von Willebrand's disease
- vWF = von Willebrand factor

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COBALAMIN DEFICIENCY

C



BASICS

OVERVIEW

- Cobalamin deficiency occurs in patients with cobalamin malabsorption when all body stores of cobalamin have been utilized and cobalamin is deficient on a cellular level.
- Cobalamin is required by virtually all cells in the body and plays a major role in β -oxidation, conversion of certain amino acids, and the formation of tetrahydrofolate, and is thus crucial for energy production, amino acid metabolism, and DNA and RNA synthesis.
- Cobalamin deficiency is associated with gastrointestinal signs and systemic complications, such as immunodeficiencies, central neuropathies, and peripheral neuropathies.
- Cobalamin is absorbed exclusively in the ileum of dogs and cats via a receptor-mediated mechanism.
- The main causes of cobalamin deficiency in dogs and cats include chronic gastrointestinal disease involving the ileum (e.g., inflammatory bowel disease, small intestinal dysbiosis, intestinal lymphoma), exocrine pancreatic insufficiency, short bowel syndrome, and, in rare cases, inherited cobalamin malabsorption or dietary deficiencies.

SIGNALMENT

- In the US, Chinese Shar Pei have a high prevalence of cobalamin deficiency. Isolated families of other breeds, such as the giant schnauzer, beagle, border collie, and Australian shepherd dog, have also been described as having cobalamin deficiency.
- Exocrine pancreatic insufficiency is particularly common in German shepherd dogs. These patients are usually young adults at the time of presentation.
- No other breed, sex, or age predilections are known for canine or feline patients with cobalamin deficiency.

SIGNS

- Clinical signs attributable to the underlying disease process:
 - Chronic enteropathy: diarrhea, weight loss, vomiting, poor appetite, or others.
 - EPI: weight loss, failure to thrive, loose stools, steatorrhea, polyphagia or even pica, borborygmus, flatulence.
- Clinical signs attributable to cobalamin deficiency: weight loss, failure to thrive, poor hair coat, lethargy, anorexia; rarely stupor and encephalopathy.

CAUSES & RISK FACTORS

- Intestinal disease involving the distal small intestine (i.e., the ileum): inflammatory bowel disease, food responsive enteropathy, lymphoma, others.

- Exocrine pancreatic insufficiency.
- Short bowel syndrome.
- Hereditary (Chinese Shar Pei, giant schnauzer).
- Dietary; being fed an exclusively vegan or vegetarian diet without concurrent supplementation.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other diseases causing chronic gastrointestinal disease, immunosuppression, central neuropathies, or peripheral neuropathies.

CBC/BIOCHEMISTRY/URINALYSIS

- May be within normal limits.
- May show changes associated with an underlying disease process (e.g., hypoalbuminemia in patients with severe inflammatory bowel disease).
- May show anemia, neutrophilia with left shift, or neutropenia. Rubricytes have been documented in cobalamin-deficient dogs and have been interpreted as evidence of ineffective erythropoiesis. Hypersegmented neutrophils can also be observed.

OTHER LABORATORY TESTS

- Serum and urine methylmalonic acid concentration are increased in patients with cobalamin deficiency. However, analysis (by GC/MS) is time-consuming and expensive and is not available for routine clinical use.
- Decreased or low normal serum cobalamin concentrations. Studies measuring methylmalonic acid in serum from dogs and cats have shown that patients with low normal serum cobalamin concentrations may be cobalamin-deficient on a cellular level. Note that all assays used for the measurement of serum cobalamin concentration in dogs and cats have been developed for use in humans and thus must be analytically validated for dogs and cats before routine clinical use. In addition, each lab should develop specific reference intervals.

IMAGING

Not useful

DIAGNOSTIC PROCEDURES

None for the diagnosis of cobalamin deficiency. However, intestinal biopsies may be useful to confirm and characterize chronic enteropathies.



TREATMENT

Treatment of the underlying disease process if identified (e.g., inflammatory bowel disease, EPI, lymphoma, small intestinal dysbiosis).



MEDICATIONS

DRUG(S)

- Cobalamin supplements:
 - cyanocobalamin (usually at 1,000 μ g/mL; for parenteral use or 1 mg tablet for oral use)
 - hydroxocobalamin (usually at 1,000 μ g/mL; for parenteral use)
 - methylcobalamin (usually 1 mg capsule; mainly for oral use).
- Traditionally, cobalamin supplementation in cobalamin-deficient patients has been administered parenterally (usually subcutaneously) using most commonly cyanocobalamin or rarely hydroxocobalamin.
- Cats receive 250 μ g/injection; dogs receive between 250 μ g (small dog) and 1,500 μ g (giant dog) per injection.
- In either species there are 6 weekly injections, one more injection a month later, and reevaluation of serum cobalamin concentration a month later.
- Continue therapy weekly or bi-weekly if serum cobalamin is still low; continue monthly or bi-monthly if cobalamin is in the mid-normal range; discontinue if serum cobalamin is in the high end of the normal range.
- Recently, two reports have suggested that oral supplementation may be effective as well at 1 mg q24h for 2–3 months. Re-evaluation suggested as above.



FOLLOW-UP

Depending on the severity of the underlying disease process, the complications from cobalamin deficiency, and treatment response.

PATIENT MONITORING

- See above; re-evaluation of serum cobalamin concentration 1 month after either the last cobalamin injection or the last oral dose of cobalamin.
- Additional monitoring as required for the underlying disease process.



MISCELLANEOUS

ABBREVIATION

- EPI = exocrine pancreatic insufficiency

INTERNET RESOURCES

<http://vetmed.tamu.edu/gilab>

Suggested Reading

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COBALAMIN DEFICIENCY

(CONTINUED)

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Consulting Editor Stanley L. Marks

Coccidioidomycosis

C



BASICS

DEFINITION

A systemic mycosis caused by the inhalation of infective arthroconidia of the soil-borne fungus *Coccidioides immitis*.

PATHOPHYSIOLOGY

- Grows in soil in the mycelial state.
- Inhalation of infective arthroconidia is the primary route of infection; at body temperature, all but one nucleus is shed and an immature spherule is produced within 2–3 days.
- Spherule matures and ruptures releasing 200–300 endospores which can produce new spherules.
- Neutrophils cannot penetrate the spherule wall but can phagocytize the endospores.
- Fewer than 10 inhaled arthrospores are sufficient to cause disease in susceptible animals.
- Respiratory signs are often noted 1–3 weeks after exposure; signs of dissemination may not be evident for several months.
- Most infections are mild or subclinical although dogs appear more susceptible to the development of disseminated disease.
- Fever, lethargy, inappetence, coughing, and joint pain or stiffness may be noticed. Dissemination may occur within 10 days, resulting in signs related to the organ system involved; skin lesions are usually associated with dissemination, but penetrating wounds have rarely been associated with skin lesions.

SYSTEMS AFFECTED

- Respiratory—the site of initial infection.
- Extrapulmonary spread may occur to long bones and joints, eyes, pericardium and myocardium, skin, CNS, testes, and visceral organs.

INCIDENCE/PREVALENCE

Not an uncommon disease in endemic areas, rare in non-endemic areas. It occurs more commonly in dogs and rarely in cats.

GEOGRAPHIC DISTRIBUTION

- *C. immitis* is found in the southwestern United States in the geographic Lower Sonoran life zone.
- More common in Southern California, Arizona, and southwest Texas and is less prevalent in New Mexico, Nevada, and Utah.

SIGNALMENT

Species

Dog and cat

Breed Predilections

None

Mean Age and Range

Though most commonly diagnosed in young animals (< 4 years of age), it is seen in animals of all ages.

Predominant Sex

None

SIGNS

Historical Findings

- Coughing (ranges from dry/harsh to wet/productive)
- Fever unresponsive to antibiotics
- Anorexia, weight loss
- Weakness, lameness
- Seizures, paraparesis, back and neck pain
- Visual changes

Physical Examination Findings

Dogs

- Signs with pulmonary involvement:
- Coughing and dyspnea
- Fever, lethargy
- Signs with disseminated disease:
- Bone swelling, joint enlargement, and lameness.
- Lymphadenomegaly, skin lesions, and draining tracts.
- Neurologic dysfunction can include seizures, ataxia, and behavioral changes.
- Uveitis, keratitis, and iritis.

Cats

- Similar to dogs although skin lesions are most common type of infection in cats.
- Dyspnea
- Lameness caused by bone involvement
- Uveitis

CAUSES

C. immitis grows several inches deep in the soil, where it survives high ambient temperatures and low moisture. After a period of rainfall, the organism returns to the soil surface where it sporulates, releasing many arthroconidia that are disseminated by wind and dust storms.

RISK FACTORS

- Aggressive nosing in contaminated soil and underbrush may expose susceptible animals to large numbers of arthroconidia.
- Dust storms after the rainy season; increased incidence noted after earthquakes.
- Land development with earth disruption may lead to increased exposure.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pulmonary lesions may resemble those of other systemic mycoses (e.g., histoplasmosis, blastomycosis).
- Lymphadenomegaly may be seen in lymphoma, other systemic mycoses, and localized bacterial infections.
- Bone lesions may resemble those caused by primary or metastatic bone tumors or bacterial osteomyelitis.
- Skin lesions must be differentiated from routine abscesses or other infective processes.
- For seizures and ataxia, consider inflammatory and oncologic etiologies.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram—mild nonregenerative anemia, neutrophilic leukocytosis, monocytosis.
- Serum chemistry profile—hyperglobulinemia, hypoalbuminemia, other changes may be consistent with organ of involvement.

- Urinalysis—proteinuria with inflammatory glomerulonephritis.

OTHER LABORATORY TESTS

Serologic tests (generally by AGID or ELISA) for antibody to *C. immitis* may provide a presumptive diagnosis; may aid in monitoring response to therapy.

IMAGING

- Radiography of lung (interstitial infiltrates) and bone lesions (osteolysis) may aid in diagnosis.
- MRI may help in diagnosing granulomas in the CNS.

DIAGNOSTIC PROCEDURES

- Serologic testing; repeat serology titers in 4–6 weeks when low titers are accompanied by clinical signs.
- Microscopic identification of the large spherule form of *C. immitis* in lesion or biopsy material is the definitive method of diagnosis (large 10–80 μm round, double-walled structure containing endospores).
- Lymph node aspirates and impression smears of skin lesions or draining exudate may yield organisms.
- Cultures should be performed by trained laboratory personnel using protective hoods.
- Biopsy of infected tissue often is preferred to avoid false-negative results.
- Tissues involved, however, may not be readily accessible and finding the organism can be challenging; therefore, serologic testing can be a more logical approach.

PATHOLOGIC FINDINGS

- Granulomatous, suppurative, or pyogranulomatous inflammation present in many tissues.
- Presence of the characteristic spherule forms in affected tissues.



TREATMENT

APPROPRIATE HEALTH CARE

- Generally treated as outpatient.
- Concurrent clinical symptoms (e.g., seizures, pain, coughing) should be treated appropriately.

ACTIVITY

Restrict activity until clinical signs begin to subside.

DIET

Feed a high-quality palatable diet to maintain body weight.

CLIENT EDUCATION

- Treatment is potentially long (> 6 months) and expensive.
- Relapse (especially with disseminated disease) is common.
- Reassure client that the infection is not zoonotic.

SURGICAL CONSIDERATIONS

In cases of focal granulomatous organ involvement (e.g., consolidated pulmonary lung lobe, eye, kidney), surgical removal of the affected organ may be indicated.

Coccidioidomycosis

(CONTINUED)



MEDICATIONS

DRUG(S) OF CHOICE

Coccidioidomycosis is considered one of the most severe and life threatening of the systemic mycoses. Treatment of disseminated disease often requires at least 1 year of aggressive antifungal therapy.

Dogs

- Ketoconazole—5–10 mg/kg PO q12h; ideally given with food; treatment typically requires at least 1 year of therapy; if titers rise or clinical signs deteriorate over the first 4–6 weeks of treatment, alternative therapy should be considered.
- Fluconazole—5 mg/kg PO q12h; noted to greatly increase the success of treatment; neurologists recommend 10 mg/kg to increase penetration in neurologic infections; cost of the drug has significantly decreased with the availability of a medical-grade generic compound; treatment failures have been noted with the use of chemical-grade compounded formulations.
- Itraconazole—5 mg/kg PO q12h; administered similarly as KTZ it has been reported to have a higher penetration rate than ketoconazole; some suggest greater efficacy of itraconazole over fluconazole.
- Amphotericin B is rarely recommended because of the risk of renal damage and the availability of effective oral medications; AMB can be administered at a dosage of 0.5 mg/kg IV 3 times per week, for a total cumulative dosage of 8–10 mg/kg; given IV either as a slow infusion (in dogs that are gravely ill) or as a rapid bolus (in fairly healthy dogs); for slow infusion, add AMB to 250–500 mL of 5% dextrose solution and administer as a drip over a period of 4–6 hours; for a rapid bolus, add AMB to 30 mL of 5% dextrose solution and administer over a period of 5 minutes through a butterfly catheter; to lessen the adverse renal effects of AMB, consider 0.9% NaCl (2 mL/kg/h) for several hours before initiating AMB therapy.

Cats

- Any of the following azoles may be used in cats:
 - Ketoconazole 50 mg total dose PO q12h
 - Fluconazole 25–50 mg total dose PO q12h
 - Itraconazole 25–50 mg total dose PO q12h

CONTRAINdications

- Drugs metabolized primarily by the liver should be used with caution alongside any azole drugs. • Drugs metabolized primarily by the kidneys should be used with caution along with AMB.

PRECAUTIONS

- Side effects of azoles include inappetence, vomiting, and hepatotoxicity (typically ALT > ALP); liver values should be monitored; drugs may be stopped until signs abate and restarted at a lower dose, which may be slowly increased to the recommended dose if the animal is able to tolerate the drug; newer azoles (ITZ and FCZ) have fewer side effects.
- Side effects of AMB therapy can be severe, especially renal dysfunction, fever; use with caution if patient is azotemic but not an absolute contraindication if the infection is life-threatening.



FOLLOW-UP

PATIENT MONITORING

- Serologic titers should be monitored every 3–4 months; animals should be treated until their titers fall to less than 1:4; consider itraconazole levels (2–4 hour post-pill) in patients showing a poor response to itraconazole therapy, especially if using a generic or compounded formulation.
- Creatinine and urinalysis should be monitored in all animals treated with AMB; treatment should be temporarily discontinued if the creatinine rises above the reference range or greater than 20% above baseline or if granular casts are noted in the urine.

PREVENTION/AVOIDANCE

- No vaccine is available for dogs or cats.
- Contaminated soil in endemic areas should be avoided, particularly during dust storms after the rainy season.

POSSIBLE COMPLICATIONS

Pulmonary disease resulting in severe coughing may temporarily worsen after therapy is begun owing to inflammation in the lungs. Low-dose short-term oral prednisone and cough suppressants may be required to alleviate the respiratory signs.

EXPECTED COURSE AND PROGNOSIS

- The prognosis for localized respiratory disease is good. • The prognosis for disseminated disease is more guarded; many dogs will improve following oral therapy with resolution of signs reported in up to 90% cases; however, relapses may be common, especially if therapy is shortened; overall recovery rate has been estimated at 60%.
- The prognosis with CNS involvement may be guarded to poor. • The prognosis for cats is not well documented, but long-term therapy should be anticipated and relapses are common. • Serologic testing every 3–4 months after completion of therapy is recommended to monitor the possibility of relapse. • Spontaneous recovery from disseminated coccidioidomycosis without treatment is extremely rare.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- The spherule form of the fungus, as found in animal tissues, is not directly transmissible to humans or to other animals. • Under certain rare circumstances, however, there could be reversion to growth of the infective mold form of the fungus on or within bandages placed over a draining lesion or in contaminated bedding; draining lesions can lead to contamination of the environment with arthrospores; care should be exercised whenever handling an infected draining lesion. • Special precautions should be recommended to households in which the owners may be immunosuppressed.

PREGNANCY/FERTILITY/BREEDING

Azole drugs can be teratogenic and should be used in pregnant animals only if the potential benefit justifies the potential risk to offspring.

SYNONYMS

- Desert rheumatism (in humans) • San Joaquin Valley fever • Valley fever

ABBREVIATIONS

- AGID = agar gel immunodiffusion • AMB = amphotericin B • CNS = central nervous system • ELISA = enzyme-linked immunosorbent assay • FCZ = fluconazole
- ITZ = itraconazole • KTZ = ketoconazole
- MRI = magnetic resonance imaging

Suggested Reading

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Client Education Handout
available online

Coccidiosis

C



BASICS

OVERVIEW

- An enteric infection, traditionally associated with *Cystoisospora canis* (dogs) and *Cystoisospora felis* (cats) as potential pathogens; other species of *Cystoisospora* may be present.
- Strictly host-specific (i.e., no cross-transmission).
- Eimeria* spp. are not parasitic for dogs or cats.
- Toxoplasma gondii* in cats and *Cryptosporidium parvum* in neonatal pups and kittens are coccidians in a non-traditional sense.
- Toxoplasma* infection in cats may cause clinical signs similar to those with *Cystoisospora* infections; oocysts shed in the environment may potentially cause a public health problem.
- Cryptosporidium* is still being assessed as an acute, life-threatening coccidiosis (cryptosporidiosis) of neonatal pups and kittens, but can also cause non-life-threatening small bowel diarrhea in dogs and cats, particularly those housed in crowded environments.
- Voluminous watery diarrhea is characteristic; auto-infection and continuing recycling within the intestinal tract result in a rapid loss of mucosal lining with cryptosporidiosis.

SIGNALMENT

Dog and cat (especially puppies and kittens)

SIGNS

- Watery-to-mucoid, sometimes blood-tinged, diarrhea; vomiting; abdominal discomfort; inappetance
- Weak puppies and kittens
- Immunocompromised animals

CAUSES & RISK FACTORS

- Infected dogs or cats contaminating environment with oocysts of *Cystoisospora* spp. or *Cryptosporidium* spp.
- Stress
- Immunocompromise



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Enteric viral infections and other intestinal parasites

CBC/BIOCHEMISTRY/URINALYSIS

Usually unremarkable; may be hemoconcentrated if dehydrated

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Fecal flotation (preferably centrifugation flotation technique) for oocysts (distinguish from pseudoparasitic *Eimeria* sp.); use sucrose solution (s.g., 1.27); zinc sulfate (s.g., 1.18). Acid-fast stains should be considered for detection of *Cryptosporidium* spp.
- Direct fluorescent antibody (DFA) assay is a sensitive dual assay (can detect *Giardia* cysts and *Cryptosporidium* oocysts very well) and can be performed at reference laboratories or university parasitology laboratories.
- Cystoisospora* oocysts should be 40 μm long; cysts of *Cryptosporidium* are approximately 5 μm diameter.



TREATMENT

- Usually treated as an outpatient
- Inpatient if debilitated
- Fluid therapy if dehydrated



MEDICATIONS

DRUG(S)

- Sulfadimethoxine—55 mg/kg PO on the first day, then 25–50 mg/kg once daily for up to 10–14 days or until dog is asymptomatic for *Cystoisospora* and fecal examination is negative for oocysts.
- Sulfadiazine/trimethoprim 15–30 mg/kg sulfadiazine PO daily up to 10 days; for toxoplasmosis in cats 15 mg/kg sulfadiazine PO q12h for 28 days.
- Amprolium (extra-label) for prevention: dogs, 30 mL of 9.6% solution in 1 gallon of drinking water or 1.25 grams of 20% powder in food to feed four puppies daily. Give as a sole source of food or water for 7 days prior to shipping; bitches can be given 9.6% solution as the sole source of water 10 days prior to whelping; or treatment: dogs, 100 mg q24h PO for 7 days; cats with *Cystoisospora* 60–100 mg total dose PO once daily for 7 days.
- No effective or approved treatment for *Cryptosporidium*; paromomycin 165 mg/kg q12h for 5 days has been suggested (extra-label); however, the drug is potentially nephrotoxic and ototoxic in cats and should not be used. Azithromycin has been used at a dosage of 7–10 mg/kg PO q12h for 7 days for eradication of *Cryptosporidium* spp. in dogs and cats; however, efficacy is unknown.
- Efficacy of tylosin at a dosage of 10–20 mg/kg PO q12h for 2–4 weeks is questionable.

- Clindamycin at 10 mg/kg PO q12h for 2–4 weeks recommended for toxoplasmosis.
- Ponazuril at 30–50 mg/kg for 3 consecutive days. Treatment can be repeated after 3- to 5-day break to increase efficacy. Single dosages of the drug are generally ineffective.

PRECAUTIONS

- As with most antibiotics, mild gastrointestinal upset can be seen with the antibiotics presented here.
- Amprolium—not recommended to be used over 12 days in puppies, exogenous thiamine in high doses may decrease efficacy; neurologic signs have been reported in some dogs—if observed, discontinue medication and begin thiamine supplementation.
- Sulfadimethoxine—diminished hepatic or renal function or urinary obstruction.
- Sulfadiazine/trimethoprim—potentially teratogenic; dog: irreversible KCS, Type 1 or Type 3 hypersensitivity (especially in larger breed dogs); cat: anorexia, leukopenia, anemia, hematuria.

CONTRAINdications/POSSIBLE INTERACTIONS

Sulfa medications—preexisting renal or hepatic disease.



FOLLOW-UP

Fecal flotation (for *Cystoisospora* spp. oocysts) or DFA (for *Cryptosporidium* spp. oocysts) 1–2 weeks following treatment.



MISCELLANEOUS

AGE-RELATED FACTORS

More severe disease in young or immunocompromised patients

SEE ALSO

- Cryptosporidiosis
- Toxoplasmosis

ABBREVIATIONS

- DFA = direct fluorescent antibody
- KCS = keratoconjunctivitis sicca

Suggested Reading

- Bowman DD, Lynn RC, Eberhard ML. Georgis' Parasitology for Veterinarians, 8th ed. St. Louis, MO: Saunders (Elsevier Science), 2003, pp. 92–100.
Lappin, MR. Update on the diagnosis and management of *Iospora* spp. infections in dogs and cats. Top Companion Anim Med 2010, 25(3):133–135.

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COGNITIVE DYSFUNCTION SYNDROME



BASICS

DEFINITION

Syndrome associated with brain aging. Leads to alterations in awareness, decreased responsiveness to stimuli, deficits in learning and memory and agitation and anxiety. Subtle signs seen in early stages, referred to as cognitive decline may include alterations in activity and play and increasing anxiety.

PATHOPHYSIOLOGY

- Unclear which changes are associated with the clinical signs. • Decline in neurons, decrease in frontal lobe volume, increase in ventricular volume and neurotoxic deposits including lipofuscin, ubiquitin, and beta-amyloid. • Toxic free radicals (reactive oxygen species) increase with age because of chronic illness and stressors, age-related decline in mitochondrial efficiency, and decreased clearance mechanisms. • Possible correlation between cognitive decline and amount of beta-amyloid in the cerebral cortex and with increases in toxic free radicals.
- Compromised cerebral vascular blood flow and infarcts may be contributory.
- Neurotransmission is compromised. May be a decline in catecholamine and cholinergic transmission.

SYSTEMS AFFECTED

- Behavioral • Nervous

GENETICS

May be genetic correlation with respect to the distribution of beta-amyloid and the age at which it begins to accumulate.

INCIDENCE/PREVALENCE

- Clinical signs of cognitive dysfunction have been reported to arise in 41% of dogs over 14.
- Prevalence in dogs over 10 estimated at 14.2%. • Clinical signs reported to arise in 50% of cat over 15. • Prevalence in cats over 10 estimated at 35%. • Progressive—pets with existing signs more likely to develop additional signs over next 12 months.

SIGNALMENT

Species

Dogs and cats

Mean Age and Range

- Increased prevalence with increasing age.
- Neuropsychological testing in dogs and cats can identify a decline in memory and learning as early as 6 to 8 years of age. • Clinical signs may not be noticed by pet owners until several years after initial decline except in dogs trained to perform more specialized tasks (e.g., hearing ear, seeing eye, drug detection, agility).

SIGNS

Historical Findings

- Clinical signs have been categorized using the acronym DISHA. • Disorientation,

including getting lost in familiar environments, confusion, or inability to navigate through familiar routes (e.g., goes to the wrong side of door). • Interactions with humans or other animals may be altered (increased irritability, decreased interest in play/affection or increased attention seeking). • Sleep-wake cycle alterations (temporal disorientation), including night waking, vocalization and/or increased sleep during the day. • Housetraining and other previously learned behaviors might deteriorate. • Activity may be altered—including a decline in activity level, exploration, self-care, or even eating. However, as the condition progresses, activity levels may increase with signs of restlessness, pacing, aimless wandering, or compulsive activity disorders such as excessive licking. • Anxiety and agitation – signs may increase in pets with cognitive dysfunction.

Physical Examination

- No specific abnormalities associated with cognitive dysfunction. • Other age-related medical disorders might be noted.

CAUSES

- Exact cause is unknown and animals are variably affected. • Environmental factors may contribute to age related degeneration
- May also be predisposing genetic factors
- Diet, enrichment, and stress management may be in part preventive.
- See "Pathophysiology."

RISK FACTORS

- Chronic or recurrent illness or stress might lead to increased accumulation of reactive oxygen species. • Conditions that affect the cerebral vascular blood supply (e.g., systemic hypertension, anemia).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Any medical condition or disease process that affects the pet's mental attitude or behavior must be ruled out. • Pain (e.g., arthritis, dental disease) can lead to increased irritability, anxiety, and altered response to stimuli • If mobility is affected, the pet may become increasingly aggressive rather than retreat and may be less able to access its elimination area. • Impaired sight or hearing might lead to a decreased responsiveness or increased reactivity to stimuli. • Diseases of the urinary tract can cause inappropriate urination. • Organ failure, tumors, and immune diseases can also affect behavior.
- Endocrinopathies such as hypothyroidism can lead to behavior changes ranging from lethargy to aggression, while hyperadrenocorticism may be associated with altered sleep-wake cycles, housesoiling, panting, and polyphagia. Hyperthyroidism in cats can lead to increased irritability and

increased activity. • Diseases that affect the central nervous system or its circulation can affect behavior.

CBC/BIOCHEMICAL/URINALYSIS

Normal with CDS but concurrent disease processes common in aged dogs.

OTHER LABORATORY TESTS

Normal with CDS

IMAGING

- Used to rule out primary organic/structural cause. • Most important when there are abnormalities on the neurologic examination or when the onset is sudden; less likely to be of diagnostic value if signs are slowly progressive in the absence of other neurologic findings. • Pets with cognitive dysfunction may have increased ventricular volume and an overall decline in brain mass, but these findings alone are not diagnostic.

DIAGNOSTIC PROCEDURES

- Endoscopy, radiography, ultrasound, and other specialized diagnostic procedures may be necessary to rule out other causes of the clinical signs. • BAER testing or ophthalmologic referral might be indicated if sensory dysfunction is a suspected cause of the signs. • A therapeutic trial might be a useful diagnostic aid, for example, to determine the effects of pain management on the resolution of clinical signs.

PATHOLOGIC FINDINGS

Evaluation for brain pathology and staining for β -amyloid deposition might be indicative of the degree of cognitive dysfunction. This type of assessment is available only on postmortem samples.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient care

NURSING CARE

Depends on the type and severity of the clinical signs of cognitive dysfunction.

ACTIVITY AND TRAINING

- Maintain as much exercise, play, training, work, and other daily routines as is practical for the pet's age and health. • Maintaining mental and physical stimulation has been shown to reduce or slow progression of cognitive decline.

DIET AND NEUTRACEUTICALS

- Selected based on the pet's health assessment. • If the pet's health does not require the need for a special therapeutic diet, then a senior diet that has demonstrated efficacy in improving cognitive function should be used. • Hill's Prescription Diet b/d has been shown to improve memory, learning ability, and clinical signs of cognitive dysfunction syndrome. The diet is

(CONTINUED)

COGNITIVE DYSFUNCTION SYNDROME

supplemented with antioxidants such as vitamins E and C, selenium, beta carotene, and flavonoids and carotenoids, omega-3 fatty acids EPA and DHA, and carnitine and alpha lipoic acid, which may improve mitochondrial health. • A canine diet (Purina ProPlan Bright Minds 7+), which is supplemented with medium-chain triglycerides to provide ketones to aging neurons as an alternative energy source has also been shown to improve signs of cognitive function in older dogs. • Some natural supplements may help to improve the signs or slow the decline of cognitive dysfunction. ° Supplements containing phosphatidylserine (Senilife, CEVA Animal Health and Activait, VetPlus), apoaequorin (Neutricks, LLC), and SAMe (Novifit, Virbac Animal Health) have demonstrated some evidence of efficacy. ° For cats, SAMe and a diet containing fish oil, arginine, and antioxidants (not presently available commercially) has demonstrated a beneficial effect.

CLIENT EDUCATION

- Lifelong therapy is required, and concurrent medications may be necessary if the pet has multiple problems. • Any changes in the pet's health or behavior should be reported immediately, as this may be due to cognitive dysfunction or new health problems.
- Considering the pet's health and cognitive status, the owner must be advised on any limitations on what might be achieved.
- Signs are generally progressive; treatment is aimed at slowing the progression of the disease, not cure.

**MEDICATIONS****DRUG(S) OF CHOICE****Selegiline**

- Licensed for use in dogs in North America.
- Monoamine oxidase B inhibitor, in dogs, may contribute to improved catecholamine transmission, a decrease in free radicals, and a neuroprotective effect.
- Dog dose: 0.5–1 mg/kg PO q24h in the morning and maintained if effective.
- Reevaluate clinical signs for improvement after 1–2 months.
- Side effects might include occasional gastrointestinal upset and restlessness, and repetitive behavior at higher doses.

Propentofylline

- Not licensed in North America but is licensed in other countries.
- Methylxanthine.
- Purported to inhibit platelet aggregation and thrombus formation, make the red cells more pliable, and increase blood flow.
- For use in the treatment of dullness and lethargy in old dogs.

- May increase oxygen supply to the CNS without increasing glucose demand.
- Dog: 3 mg/kg PO q12h.

Nicergoline

- Alpha-adrenergic antagonist that may improve cognitive function through vasodilatory effects on cerebral circulation
- Dog: 0.25–0.5 mg/kg PO q12h.

Cats

- No therapeutic agents licensed for treatment of CDS.
- Selegiline (0.5–1 mg/kg PO q24h), propentofylline (1/4 of 50 mg tablet PO q24h) and nicergoline (0.25–0.5 mg/kg PO q24h) have been used off label in cats with anecdotal evidence of effect

CONTRAINdicATIONS

- Selegiline should not be used concurrently with MAO inhibitors such as amitraz, narcotics, alpha-adrenergic agents such as phenylpropanolamine or ephedrine, or selective serotonin reuptake inhibitors (e.g., fluoxetine) or tricyclic antidepressants (e.g., clomipramine). • A 2-week washout is suggested following most tricyclic antidepressants and up to 5 weeks following fluoxetine before starting selegiline.

PRECAUTIONS

- Choose medications that are least sedating and least anticholinergic. • Potential drug interactions must be considered with concurrent use of drugs and over-the-counter medications.

POSSIBLE INTERACTIONS

See "Contraindications."

ALTERNATIVE DRUG(S)

- Enhancement of the noradrenergic system with drugs such as adrafinil and modafinil to improve alertness and exploration.
- Anti-inflammatory medication, and natural supplements such as gingko biloba and curcumin might be considered based on preliminary work in other species.
- Medication used in humans for Alzheimer's disease to enhance cholinergic transmission might be useful, but doses and pharmacokinetics in dogs have not been determined. Potential side effects include nausea, vomiting, diarrhea, and sleep-wake disturbances. • Anxiolytics such as buspirone, drugs to help induce sleep such as benzodiazepines, or antidepressants such as fluoxetine (not in conjunction with selegiline) might be considered to treat anxiety and apathy. • Natural supplements might help to normalize sleep-wake cycles or reduce anxiety (e.g. melatonin, valerian, L-theanine, alpha-casozepine, Harmonease [VPL], Adaptil and Feliway [CEVA]).

**FOLLOW-UP****PATIENT MONITORING**

- If a drug or diet is dispensed, then therapeutic response should be evaluated after 30–60 days and the dose adjusted or treatment changed if there is insufficient improvement. • If the pet is stable, twice-yearly checkups are recommended for senior pets unless new problems arise before a reassessment is due.

PREVENTION/AVOIDANCE

- Providing an enriched environment and as much physical activity as is practical for the pet's age and health may help to prevent or delay the onset of cognitive decline. • Early intervention is the best way to slow the progress or prevent complications.

EXPECTED COURSE AND PROGNOSIS

- Diet and medication should control the clinical signs and slow progression in a majority of cases. • Because of the pet's increasing age, cognitive decline may advance and other concurrent health problems are likely to arise.

**MISCELLANEOUS****SYNOMYMS**

- Age-related cognitive and affective disorders, involutive depression, dysthymia
- Dementia • Senility

ABBREVIATIONS

- BAER = brainstem auditory evoked response • CDS = cognitive dysfunction syndrome • CNS = central nervous system
- MAO = monoamine oxidase • SAMe = S-adenosyl-L-methionine-tosylate disulfate

Suggested Reading

Landsberg GM, Denenberg S, Araujo J. Cognitive dysfunction in cats: a syndrome we used to dismiss as old age. *J Fel Med Surg* 2010; 12:837–848.

Landsberg GM, Hunthausen W, Ackerman L. Behavior Problems of the Dog and Cat, 3rd ed. Edinburgh: Elsevier Saunders, 2013.

Landsberg GM, Nichol J, Araujo JA. Cognitive dysfunction syndrome: a disease of canine and feline brain aging. *Vet Clin Small Anim* 2012; 42:749–768.

Salvin HE, McGreevy PD, Sachdev PS, Valenzuela MJ. Underdiagnosis of canine cognitive dysfunction: a cross-sectional survey of older companion dogs. *Vet J* 2010; 184:277–281.

Authors Gary M. Landsberg and Sagi Denenberg

Consulting Editor Gary M. Landsberg



Client Education Handout
available online

COLD AGGLUTININ DISEASE



BASICS

OVERVIEW

- A rare Type II autoimmune disorder in which antierythrocyte antibodies have enhanced activity at temperatures < 99°F (37.2°C) and usually < 88°F (31.1°C).
- Cold agglutinins are typically IgM, although IgG and IgG-IgM mixed have been reported. • Cold agglutinins with low thermal amplitude usually associated with direct erythrocyte agglutination at low body temperatures in the peripheral microvasculature and with acro-cyanotic disease or other peripheral vaso-occlusive phenomena, all initiated or intensified by cold exposure.
- Fixation of complement and hemolysis is a warm reactive process occurring at higher body temperatures; at those temperatures cold agglutinins have eluted off the RBC, lowering the rate of complement binding. Therefore, acute hemolytic anemias are uncommon.
- Most cold agglutinins cause little or no shortening of erythrocyte lifespan.
- High thermal amplitude cold agglutinins (rare)—may cause chronic hemolysis; the resulting anemia is often mild and stable, but exposure to cold may greatly augment binding of cold agglutinins and complement-mediated intravascular hemolysis.

SIGNALMENT

- Rare disorder in dogs and cats.
- Low titer of naturally occurring cold agglutinins (usually 1:32 or less) may be found in healthy dogs and cats; this is without clinical significance.
- Genetic basis, mean age and range, breed, and sex predilections unknown.
- More likely to occur in colder climates.

SIGNS

- Often a history of cold exposure.
- Acrocyanosis associated with sludging of erythrocyte agglutinates in cutaneous microvasculature.
- Erythema.
- Skin ulceration with secondary crusting.
- Dry, gangrenous necrosis of ear tips, tail tip, nose, and feet.
- Affected areas may be painful.
- Anemia may or may not be an important feature; clinical signs include pallor, weakness, tachycardia, tachypnea, icterus, pigmenturia, mild splenomegaly, and soft heart murmur.

CAUSES & RISK FACTORS

- Primary disease—idiopathic.
- Secondary disease—associated with upper respiratory infection (cats), neonatal isoerythrolysis, lead intoxication (dogs), and neoplasia.
- Cold exposure a risk factor.
- In humans, cold agglutinin disease has been described in liver transplant cases after tacrolimus administration.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Diagnosis made by historical findings (cold exposure), results of physical examination, demonstrating cold agglutination in vitro.
- Skin lesions—cutaneous vasculitis, hepatocutaneous syndrome, erythema multiforme, toxic epidermic necrolysis, dermatomyositis, DIC, SLE, lymphoreticular neoplasms, frostbite, lead poisoning, and pemphigus.
- Anemia—warm antibody hemolytic anemia; other causes of anemia.
- Macroscopic hemagglutination in vitro—dysproteinemias may lead to rouleaux formation, mimicking erythrocyte agglutination on a glass slide.

CBC/BIOCHEMISTRY/URINALYSIS

- Autoagglutination at room temperature.
- Laboratory abnormalities secondary to hemolysis.

OTHER LABORATORY TESTS

- Cold agglutinins should be suspected when blood in heparin or EDTA on a glass slide agglutinates spontaneously at room temperature with enhancement at 39°F (3.9°C), and the erythrocytes disperse again upon warming to 99°F (37.2°C).
- If no agglutination can be induced in vitro, it is inconceivable for it to occur in vivo in extremities.
- Doubtful cases can be confirmed by Coombs' test at 39°F and 99°F.
- Coombs' test at 99°F—cold agglutinins usually not detected because they may be eluted off the erythrocytes during washing; thus test requires the use of anti-complement factor serum.
- Coombs' test at 39°F—incidence of a positive result in healthy dogs has been reported to be > 50%, which may be caused by unspecific binding of the reagent itself or by binding of naturally occurring non-pathogenic low-titer cold agglutinins.
- The globulin class can be established by immunolectrophoresis of a concentrated eluate of the patient's erythrocytes, which may be important for prognosis and treatment.

PATHOLOGIC FINDINGS

- Dermal necrosis.
- Ulceration with secondary features of opportunistic infections.
- Vascular thrombosis with evidence of ischemic necrosis.



TREATMENT

- The patient should be hospitalized in a warm environment until the disease is non-progressive.
- Supportive care and

wound management depend on clinical signs; if necrosis involving the tail tip or feet is severe, amputation may be required.

- Splenectomy is of little assistance in patients with IgM-mediated hemolytic disorders but may be helpful in those with therapy-resistant IgG-mediated hemolytic anemia.
- Inform the client to keep the patient in a warm environment at all times to prevent relapse.
- Exercise restriction.
- In humans, therapy is often ineffective. Plasmapheresis, intravenous gamma globulins, and rituximab ± fludarabine have been beneficial in some patients.



MEDICATIONS

DRUG(S)

IgM Cold Agglutinins

- Immunosuppressive therapy is not very effective against IgM-mediated disorders but can be tried (i.e., corticosteroids, leflunomide, cyclosporine).
- Plasmapheresis.
- Folic acid supplementation.

IgG Cold Agglutinins

Immunosuppressive therapy

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Monitor patient for signs of infection secondary to immunosuppressive therapy.
- Do not use cold IV fluids.



FOLLOW-UP

- A patient with known cold agglutinin disease should be kept in warm environments at all times.
- Cold agglutinin disease usually characterized by acute onset and rapid progression.
- Prognosis is guarded to fair.
- Recovery may take weeks.



MISCELLANEOUS

SEE ALSO

Anemia, Immune-Mediated

ABBREVIATIONS

- DIC = disseminated intravascular coagulation
- EDTA = ethylene diamine tetra-acetic acid
- SLE = systemic lupus erythematosus

Suggested Reading

Dickson NJ. Cold agglutinin disease in a puppy associated with lead intoxication. J Small Anim Pract 1990, 31:105–108.

Author Jörg Bucheler

Consulting Editor Alan H. Rebar

COLIBACILLOSIS



BASICS

DEFINITION

- *Escherichia coli*—Gram-negative member of the *Enterobacteriaceae*; normal inhabitant of the intestine of most mammals; along with other infectious agents, may increase the severity of parvovirus infections.
- Acute infection of puppies and kittens in the first week of life; characterized by septicemia and multiple organ involvement.
- Isolation from stool of young animals— inconclusive evidence of pathogenic potential because it is normal flora; need to assess virulence potential using molecular methods.
- Isolation from blood cultures or internal organs—constitutes better evidence of causality.
- Infection of older dogs and cats— documented; individual strains poorly characterized in regard to virulence attributes.

PATHOPHYSIOLOGY

- Virulence factors—not well defined; likely *E. coli* as a cause of septicemia in neonatal dogs and cats reflects a balance between immunologic immaturity and intestinal barrier function of the host and resident enteric *E. coli* rather than a single virulent strain.
- ETEC, AEEC, UPEC, and CNF+ *E. coli* strains—recovered from dogs.
- Similar *E. colis* isolated from cats (strains poorly characterized).
- Intestinal strains colonize and multiply in the small intestine; ETEC then elaborates uncharacterized adhesins and enterotoxins (STa); the attaching and effacing factor of AEEC (EAE+).
- Many strains of *E. coli* from dogs and cats are hemolytic.
- A new type of *E. coli* has been found in boxer dogs with IBD (granulomatous colitis) characterized by ability to adhere, to invade, and to replicate in macrophages, resulting in a tremendous inflammatory response within the intestinal wall.

SYSTEMS AFFECTED

- Neonates—small intestine (enteritis); multiple body systems (septicemia).
- Puppies/kittens and adults—small intestine (enteritis); urogenital (cystitis, endometritis, pyelonephritis, prostatitis); mammary gland (mastitis); large intestine (colitis).

GENETICS

Boxer dogs may be predisposed to large bowel colitis.

INCIDENCE/PREVALENCE

- Few statistics available.
- More common in neonatal puppies and kittens < 1 week old that have not received any or adequate amounts of colostrum.

- Problem in overpopulated kennels and catteries.
- Sporadic accounts in older dogs and cats (mainly diarrhea and urogenital problems).
- Purulent skin disease and otitis and meningoencephalomyelitis.

Dogs

- ETEC—2.7–29.5% of diarrheic dogs; strains: STa/STb+/-, and CNF+ isolated from diarrheic dogs along with hemolysin.
- AEEC/EPEC—diarrheic cats; strains: EAE+, hemolysin.
- *E. coli* (usually β -hemolytic)—major cause of septicemia in newborn puppies exposed *in utero*, during birth, or from mastitic milk.

Cats

- AEEC/EPEC—diarrheic cats; strains: EAE+, hemolytic.
- ExPEC—acute necrotizing and hemorrhagic pneumonia and pleuritis; strains: CNF-1 plus other adhesions.
- UPEC—cystitis; strains: CNF-1+, P-fimbria, hemolysin.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog and cat

Breed Predilections

Boxer dogs may be predisposed to large bowel colitis.

Mean Age and Range

- Neonatal infections common (diarrhea, septicemia) up to 2 weeks of age.
- Puppies/kittens and adult animals—sporadic disease often associated with other infectious agents.

Predominant Sex

None

SIGNS

General Comments

E. coli—one of the most common causes of septicemia and death in puppies and kittens.

Historical Findings

- Neonates—sudden-onset vomiting, weakness/lethargy, diarrhea, cold skin; one or more animals affected in a litter.
- Puppies/kittens and adults—vomiting and diarrhea.

Physical Examination Findings

- Neonates—acute depression, anorexia, vomiting, tachycardia, weakness, hypothermia, cyanosis, watery diarrhea.
- Puppies/kittens and adults—ETEC associated with acute vomiting, diarrhea, anorexia, rapid dehydration, fever.

CAUSES

- *E. coli*—member of the endogenous microbial flora of the adult's gastrointestinal tract, prepuce, and vagina.
- Many strains isolated from case material are poorly characterized in regard to virulence

factors; strains need to be evaluated by molecular methods to assess virulence potential.

- Often found in older dogs and cats concurrently with other infectious agents.

RISK FACTORS

Neonates

- Bitch/queen in poor health and nutritional status—unable to provide good care and colostrum to offspring.
- Lack of colostrum or insufficient colostrum.
- Dirty birthing environment.
- Difficult or prolonged labor and birth.
- Crowded facilities—buildup of feces in environment, greater chance for fecal-oral spread of infection.

Puppies/Kittens and Adults

- Concurrent disease—parvovirus; heavy parasitism
- Antimicrobial drugs—upset microbial flora of gastrointestinal tract
- Immunosuppression
- Post-parturient mastitis
- Venous catheterization



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infectious enteritis—viral: feline panleukopenia, FeLV, FIV, enteric coronavirus, canine parvovirus, rotavirus, canine distemper; bacterial: *Salmonella*, *E. coli*, *Campylobacter jejuni*, *Yersinia enterocolitica*, bacterial overgrowth syndrome, *Clostridium difficile*, *Clostridium perfringens*; parasitic: hookworms, ascarids, whipworms, *Strongyloides*, *Giardia*, coccidia, cryptosporidia, rickettsiae (salmon poisoning).
- Dietary-induced enteritis—overeating; abrupt changes; starvation; thirst; food intolerance or allergy; indiscretions (e.g., foreign material or garbage).
- Drug- or toxin-induced enteritis—antimicrobial agents; antineoplastic agents; anthelmintics; heavy metals; organophosphates.
- Extra-intestinal disorders or metabolic diseases—acute pancreatitis; hypoadrenocorticism; liver or kidney disease; pyometra; peritonitis.
- Functional or mechanical ileus—gastric-dilatation volvulus; intussusception; electrolyte disorder; gastrointestinal foreign body.
- Neurologic disorders—vestibular disease; psychogenic such as fear, excitement, pain.
- Fading neonates.

CBC/BIOCHEMISTRY/URINALYSIS

- Few abnormalities noted, owing to rapidity of death in puppies.

COLIBACILLOSIS

C

- Adults with enteritis may show chemistry abnormality, depending on the state of dehydration.

DIAGNOSTIC PROCEDURES

- Antimicrobials—produce false-negative results if used before obtaining bacterial cultures.
- Routine bacterial culture and identification of *E. coli* from blood (antemortem) or necropsy tissue (bone marrow, heart blood, liver/spleen, brain, mesenteric lymph node) required.
- Appropriate testing of strains—identify adhesins and toxins (by DNA colony hybridization, PCR) in ETEC and VTEC strains.

PATHOLOGIC FINDINGS

- Acute enteritis
- Mucosal inflammation of small intestine
- Petechiae and hemorrhagic lesions on serosal surface of gastrointestinal mucosae and all body cavities
- Fibrin on abdominal wall
- Necrosis of liver/spleen



TREATMENT

APPROPRIATE HEALTH CARE

Acutely ill puppies/kittens—inpatients; good nursing care.

NURSING CARE

- Balanced parenteral polyionic isotonic solution (lactated Ringer's)—restore fluid balance.
- Oral hypertonic glucose solution—for secretory diarrhea, as required.

ACTIVITY

Acutely ill immature puppies/kittens (bacteremic/septicemic)—restricted activity, cage rest, monitoring, and warmth.

DIET

Puppies—likely to still be nursing when affected; good nursing care needed with bottle-feeding and/or IV nutrients.

CLIENT EDUCATION

Neonates—life-threatening with poor prognosis.



MEDICATIONS

DRUG(S) OF CHOICE

- Antimicrobial therapy—*septicemia*.
- Guided by culture and susceptibility (MIC) testing of *E. coli*; empiric therapy until results available.
- Amikacin: dog and cat, 20 mg/kg IV q24h.
- Cefazolin: dog and cat, 5–15 mg/kg IV q6–8h.
- Cefoxitin: dog and cat, 30 mg/kg once, then 15 mg/kg IV q4h.

- Enrofloxacin: dog, 10 mg/kg IV q24h; cat, 5 mg/kg IV q24h; avoid use in pregnant, neonatal, or growing animals (medium-sized dogs < 8 months of age; large or giant breeds < 12–18 months of age) because of cartilage lesions.
- Ticarcillin-clavulanate: dogs and cats, 50 mg/kg PO q6h.

CONTRAINdications

- Fluoroquinolones—enrofloxacin: avoid use in pregnant, neonatal, or growing animals (medium-sized dogs < 8 months of age; large or giant breeds < 12–18 months of age) because of cartilage lesions.
- Chloramphenicol and trimethoprim-sulfa are likely ineffective for *E. coli* septicemia.

PRECAUTIONS

Ensure adequate hydration and perfusion when using aminoglycosides.



FOLLOW-UP

PATIENT MONITORING

- Blood culture—puppies/kittens with fever and/or diarrhea.
- Monitor temperature—with signs of lethargy and/or depression.
- Monitor behavior—eating, drinking, and/or nursing; adequate weight gain.

PREVENTION/AVOIDANCE

- Bitch/queen—good health; vaccinated; good nutritional status.
- Clean and disinfect parturition environment (1:32 dilution of bleach); clean bedding after birth frequently.
- Ensure adequate colostrum intake of all littermates.
- Separate mother with nursing litter from other cats or dogs.
- Keep the density low in kennel or cattery rooms.
- Wash hands and change clothes and shoes after handling other cats/dogs and before dealing with neonates.

EXPECTED COURSE AND PROGNOSIS

- Neonates—life-threatening; prognosis often poor; neonate may rapidly succumb; quick treatment with supportive care essential for survival.
- Adults—self-limiting with supportive care, depending on the degree of dehydration and existence of other diseases.



MISCELLANEOUS

AGE-RELATED FACTORS

Neonates—greatest risk of infection and subsequent septicemia.

ZOONOTIC POTENTIAL

- Little documented information of the virulence potential of *E. coli* strains from dogs or cats for humans, although recently, similarities have been found between canine fecal and UTI *E. coli* and human *E. coli* associated with UTI, sepsis, and meningitis; growing concern for the presence of multidrug resistance determinants in *E. coli* strains from companion animals.
- Always wash hands after handling animals (especially patients with diarrhea) because of the risk of acquiring other infectious agents (e.g., salmonellae, *Giardia*).
- Caution: keep children and immunosuppressed persons away from pets with diarrhea.

SYNONYMS

- *E. coli* septicemia
- Neonatal enteritis

ABBREVIATIONS

- AEEC = attaching and effacing *E. coli*
- CNF = cytotoxic necrotizing factor
- EAE = experimental autoimmune encephalomyelitis
- EPEC = enteropathogenic *E. coli*
- ETEC = enterotoxigenic *E. coli*
- ExPEC = extraintestinal pathogenic *E. coli*
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- IBD = inflammatory bowel disease
- MIC = minimal inhibitory concentration
- PCR = polymerase chain reaction
- UPEC = uropathogenic *E. coli*
- UTI = urinary tract infection
- VTEC = verotoxigenic *E. coli*

Suggested Reading

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Weese JS. Bacterial enteritis in dogs and cats: diagnosis, therapy, and zoonotic potential. Vet Clin North Am Small Anim Pract 2011, 41:287–309.

Author Patrick L. McDonough

Consulting Editor Stephen C. Barr



Client Education Handout
available online

(CONTINUED)

COLITIS AND PROCTITIS

C



BASICS

DEFINITION

- Colitis—inflammation of the colon (large intestine). Colitis may be acute and self-limiting or chronic.
- Colitis does not infer causality, and an underlying cause of the colitis should be investigated, particularly in chronic cases.
- Proctitis—inflammation of the rectum.

PATHOPHYSIOLOGY

- Inflammation of the colon causes accumulation of inflammatory cytokines, disrupts tight junctions between epithelial cells, stimulates colonic secretion, stimulates goblet cell secretion of mucus, and disrupts motility.
- These mechanisms reduce the ability of the colon to absorb water and electrolytes, and store feces, which causes frequent diarrhea, often with mucus and/or frank blood.

SYSTEMS AFFECTED

Gastrointestinal

GENETICS

- Breeds predisposed to histiocytic ulcerative colitis (granulomatous colitis) include boxers, French bulldogs, and perhaps border collies.
- German shepherd dogs are predisposed to perianal fistulae that can be associated with colitis.

INCIDENCE/PREVALENCE

- Approximately 30% of dogs with chronic diarrhea examined at one university hospital.
- 75% of dogs with a food-responsive enteropathy had clinical signs of colitis.
- Prevalence of colitis is probably higher than perceived, because many diarrheic dogs and cats can have mixed bowel diarrhea (component of small and large bowel diarrhea).

GEOGRAPHIC DISTRIBUTION

N/A except for certain infectious diseases (pythiosis: predominantly Gulf Coast and southeast United States although becoming more widespread; histoplasmosis: Midwest, eastern United States).

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Boxer dogs, French bulldogs, border collies (granulomatous colitis).
- German shepherd dogs: perianal fistulas and concurrent colitis.

Mean Age and Range

Any age; boxers, French bulldogs usually younger (< 2 years of age).

SIGNS

Historical Findings

- Fecal consistency can be variable from semiformed to liquid.

- Marked increase in frequency of defecation (6–15 times per day) with small fecal volume.
- Tenesmus.
- Increased fecal mucus.
- Hematochezia; cats may have formed feces with hematochezia.
- Occasional dyschezia (painful defecation).
- Vomiting in approximately 30% dogs.
- Weight loss is less common, but can be seen with colonic lymphoma, histoplasmosis, and pythiosis.

Physical Examination Findings

- Usually unremarkable.
- Rectal examination may reveal a thickened and irregular colorectal mucosa.
- Dogs with GC may show systemic signs of weight loss and anorexia.

CAUSES

- Dietary: food-responsive enteropathy is a common and important cause of colitis; dietary indiscretion; food intolerance.
- Drug administration (antibiotics, NSAIDs).
- Infectious—*Trichuris vulpis*, *Entamoeba histolytica*, *Balantidium coli*, *Tritrichomonas foetus*, *Clostridium perfringens* and *Clostridium difficile*, *Campylobacter jejuni* and *Campylobacter coli*, *Yersinia enterocolitica*, *Prototheca*, *Histoplasma capsulatum*, and pythiosis/phycomycosis.
- Traumatic—foreign body, abrasive material.
- Inflammatory—secondary to pancreatitis (transverse colitis).
- Inflammatory/immune—IBD (lymphoplasmacytic, eosinophilic, granulomatous) colitis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Neoplasia—colonic lymphoma, adenocarcinoma, sarcomas.
- Irritable bowel syndrome.
- Colorectal polyps do not typically cause signs of colitis, but instead cause hematochezia in association with formed stool that is defecated at normal frequency.
- Cecal inversion.
- Ileoceccocolic intussusception.

CBC/BIOCHEMISTRY/URINALYSIS

- Results usually unremarkable; neutrophilia with a left shift can be seen with severe inflammatory causes; eosinophilia secondary to eosinophilic colitis, parasitism, histoplasmosis, and pythiosis/phycomycosis.
- Mild microcytic, hypochromic anemia may occur secondary to chronic intestinal bleeding and iron deficiency.
- Hyperglobulinemia in some patients (especially cats) with chronic disease.

OTHER LABORATORY TESTS

- Examination of fecal centrifugation flotation, direct fecal smear (only on fresh diarrheic feces), fecal bacterial toxin

immunoassays (*C. perfringens* enterotoxin and *C. difficile* toxins A and B), and PCR for bacteria and toxin genes when indicated, serum ELISA test for *Pythium* when indicated.

- Rectal scraping for cytology for *Histoplasma* organisms.
- Fecal PCR or In Pouch TF medium for culture of *Tritrichomonas foetus*.

IMAGING

- Abdominal radiographs—usually unremarkable.
- Abdominal ultrasonography—may reveal masses, diffuse thickening or altered architecture of the colon, or enlarged associated lymph nodes.
- Contrast studies—barium may be administered transcolonically to evaluate the colorectal mucosa for irregularities or filling defects and colorectal strictures; however, the procedure is rarely indicated in dogs and cats with colitis and is of low sensitivity in general.

OTHER DIAGNOSTIC PROCEDURES

- Colonoscopy with biopsy—procedure of choice for diagnosis of chronic or refractory cases. Animals must be adequately prepared for colonoscopy by being fasted and administered osmotic cathartics such as Osmoprep or Golytely; mucosal changes visible grossly in animals with colitis include disappearance of submucosal blood vessels, granular appearance of mucosa, hyperemia, excessive mucus, ulceration, pinpoint hemorrhage (small ulcerations), or mass(es).
- One should always obtain multiple biopsy specimens from multiple locations (ascending colon, transverse colon, descending colon, and rectum) because the extent of mucosal change assessed histologically does not necessarily reflect the severity of the colitis or proctitis.

PATHOLOGIC FINDINGS

Histopathologic findings depend on the histologic type of colitis—lymphoplasmacytic, eosinophilic, or histiocytic represent the most common subtypes; hyperplastic mucosa may be seen with irritable bowel syndrome; various infectious agents may be seen with special stains.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient medical management unless diarrhea is severe enough to cause dehydration and warrant hospitalization.

NURSING CARE

Give dehydrated patients balanced electrolyte solution with potassium IV or SC.

DIET

- There is no inherent benefit to fasting patients with diarrhea, unless the cause of the diarrhea has an osmotic component.

COLITIS AND PROCTITIS

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- Animals that do not have severe clinical signs can be managed with an elimination diet or hypoallergenic diet for 2 weeks. The response to dietary therapy is typically seen within the first 5–7 days following dietary implementation. Obtain a comprehensive dietary history to optimize selection of a novel, single protein source diet. Strict dietary compliance is pivotal during this trial period to optimize interpretation of response.
- Fiber supplementation with poorly fermented fiber (e.g., bran and alpha-cellulose) is recommended to increase fecal bulk, improve colonic muscle contractility, and bind fecal water to produce formed feces.
 - Some fermentable fiber sources (e.g., psyllium or a diet containing beet pulp or fructooligosaccharides) may be beneficial—short-chain fatty acids produced by fermentation may be beneficial for colonocyte function.

CLIENT EDUCATION

Treatment may be intermittent and long-term in patients with inflammatory/immune-mediated colitis. Recurrences can be seen, particularly when drug therapy is being tapered.

SURGICAL CONSIDERATIONS

Segments of colon severely affected by fibrosis from chronic inflammation and subsequent stricture formation may need surgical excision, especially in patients with the granulomatous form of the disease; cecal inversion and ileoceccocolic intussusception require surgical intervention; pythiosis/phymomycosis often requires surgical excision or debulking.



MEDICATIONS

DRUG(S) OF CHOICE

Antimicrobial Drugs

- *Trichuris*—fenbendazole (50 mg/kg PO q24h for 5 consecutive days, repeat in 3 months).
- *Entamoeba, Balantidium*—metronidazole (25 mg/kg PO q12h for 5–7 days).
- *Tritrichomonas foetus*—Ronidazole (30 mg/kg q24h for 14 days).
- *Clostridium perfringens*—metronidazole (10 mg/kg PO q12h for 5 days), tylosin (5–10 mg/kg PO q24h for 5 days), ampicillin or amoxicillin (20 mg/kg PO q8h for 5 days).
- *Clostridium difficile*—metronidazole (10 mg/kg PO q12h for 5 days),
- *Campylobacter* spp.—Erythromycin (10–15 mg/kg PO q8h), or azithromycin (5–10 mg/kg PO q24h) can be given for 7–10 days. Azithromycin is better tolerated than erythromycin,
- *Yersinia* spp.—select the drug on the basis of bacterial culture and sensitivity testing.
- *Prototheca*—no known treatment.

- *Histoplasma*—itraconazole (dogs, 10 mg/kg PO q24h; cats, 5 mg/kg PO q12h; several months of therapy is necessary); amphotericin B (0.25–0.5 mg/kg slow IV q48h up to cumulative dose of 4–8 mg/kg) in advanced cases.
- Pythiosis—itraconazole (10 mg/kg PO q24h) and terbinafine (10 mg/kg PO q24h) are the drugs of choice following surgical debridement of affected portions of bowel. Antifungal therapy is often administered for 3–4 months or longer in affected animals.

Anti-inflammatory and Immunosuppressive Drugs for Inflammatory/Immune Colitis

- Sulfasalazine (dogs, 25–40 mg/kg PO q8h for 3–6 weeks with a progressive tapering of the dose throughout the course of drug therapy; cats, 20 mg/kg PO q12h for 3 weeks). Use with caution, particularly in cats, in which adverse effects on the gastrointestinal tract and kidneys can be observed. Sulfasalazine has been associated with irreversible KCS.
- Corticosteroids—prednisone for dogs and prednisolone for cats: 1–2 mg/kg PO q12h for 5–7 weeks with gradual, progressive tapering of dose. Most cats can be started off on 5 mg (per cat) q12h with gradual taper. Never use more than 50 mg total of prednisone (per day) for any animal, regardless of size.
- Azathioprine (dogs) 1–2 mg/kg PO q24h for 10–14 days followed by a taper to 1–2 mg/kg q48h for 4–6 weeks. The drug is markedly myelosuppressive in cats and should be avoided even though a lower dose (0.3 mg/kg PO q48h) for this species has been published.

- Chlorambucil is an effective immunomodulator in both dogs and cats and is usually administered in conjunction with prednisone or prednisolone. Several dosing regimes have been published: cats, 2 mg per cat q3–4 days for 2–3 months (or longer if managing lymphoma) or 15 mg/m² given for 4 consecutive days every 3 weeks for 2–3 months; dogs, 0.1–0.2 mg/kg PO q24h for 8–12 weeks for immune disease, with gradual tapering of dose over the course of therapy.
- Cyclosporine (5 mg/kg PO q12–24h for 6 weeks for immune disease).
- Sulfasalazine or other 5-ASA drugs—may be a reasonable consideration following assessment to dietary therapy for 2 weeks, and is typically reserved for cases with mild colitis before considering prednisone therapy.
- Granulomatous colitis is managed with fluoroquinolones such as enrofloxacin at 10 mg/kg q 24h for 6–8 weeks.
- Reconsider the diagnosis carefully in dogs that do not respond to dietary therapy, fenbendazole administration, and tylosin therapy.

Motility Modifiers (Indicated for symptomatic relief only in animals with intractable diarrhea and must be avoided in all animals with a suspected infectious enteropathy)

- Loperamide (0.1 mg/kg PO q8–12h).
- Diphenoxylate (0.1–0.2 mg/kg PO q8h).
- Propantheline bromide (0.25–0.5 mg/kg PO q8h) if colonic spasm is contributing to clinical signs.

Anthelmintics

- Broad-spectrum anthelmintics such as fenbendazole (50 mg/kg q24h for 5 consecutive days) in conjunction with dietary therapy (elimination diet) for the first 2 weeks is the mainstay of therapy for most patients with chronic colitis, unless the animal is a boxer breed that should have endoscopy and biopsy to confirm the granulomatous colitis that has a different therapy and prognosis.
- Tylosin is a highly effective antimicrobial that can be administered following assessment of response to dietary and anthelmintic therapy.

CONTRAINDICATIONS

Anticholinergics

PRECAUTIONS

- Monitor patients on sulfasalazine for signs of keratoconjunctivitis sicca. Measure tear production (Schirmer tear test) at baseline and every 2 weeks throughout the course of therapy. Discontinue drug if tear production decreases.
- Monitor patients on azathioprine for bone marrow suppression—CBC every 2–3 weeks; stop treatment or go to alternate day if WBC count falls below 3,000 cells/ μ L.
- Azathioprine can also increase the risk of pancreatitis and should be used extremely cautiously in any dog at increased risk for pancreatitis. Azathioprine can also cause a hepatopathy.
- Chlorambucil can cause a progressive neutropenia and a CBC should be repeated q2–3 weeks in all animals receiving this drug.
- Cyclosporine can cause hepatotoxicity and a chemistry panel should be performed as baseline before starting the drug and repeated q2–3 months.
- Amphotericin B is nephrotoxic and requires close assessment of renal function via urinalyses and serum biochemistry panels.
- Enrofloxacin-resistant cases of granulomatous colitis are increasing in prevalence due to antimicrobial resistance, necessitating alternative antimicrobial therapy in select cases.



FOLLOW-UP

PATIENT MONITORING

Infrequent recheck examinations or client communication by phone. Recheck of CBC is

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important for animals on immunomodulatory therapy.

PREVENTION/AVOIDANCE

- Avoid exposure to infectious agents (e.g., other dogs, contaminated foods, moist environments).
- Avoid abrupt dietary changes.

POSSIBLE COMPLICATIONS

Recurrence of signs without treatment, when treatment is tapered, and with progression of disease.

EXPECTED COURSE AND PROGNOSIS

- Most bacterial and parasitic infectious causes have an excellent prognosis with a high likelihood of cure following therapy.
- *Protorheca*—grave; no known treatment except excision.
- *Histoplasma* spp.—poor in advanced or disseminated disease; mild-to-moderate cases generally respond to therapy.
- Pythiosis/phycomycosis—poor long-term prognosis in most animals, despite surgical intervention, given advanced stage of disease at diagnosis.
- Cecal inversion, ileoceccolic intussusception—good with surgical resection if diagnosed in a timely fashion.
- Inflammatory—fair to good with treatment in patients with lymphoplasmacytic, eosinophilic, and granulomatous colitis.

- Most dogs with mild to moderate nonspecific colitis respond favorable to a combination of fenbendazole, feeding of an elimination or hypoallergenic diet, and tylosin therapy.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Inflammatory/immune disease and infectious agents may also affect the small intestine concurrently.

ZOONOTIC POTENTIAL

Entamoeba, *Balantidium*, *Campylobacter jejuni*, *Yersinia* in immunosuppressed individuals.

PREGNANCY/FERTILITY/BREEDING

Caution with drug use—corticosteroids, azathioprine, cyclosporine, antifungals, and antibiotics.

SYNOMYS

- Inflammatory bowel disease (IBD)
- Large bowel diarrhea

SEE ALSO

- Colitis, Histiocytic Ulcerative
- Inflammatory Bowel Disease
- Individual chapters on infectious and parasitic agents

ABBREVIATIONS

- 5-ASA = 5-aminosalicylic acid
- GC = granulomatous colitis
- KCS = keratoconjunctivitis sicca
- NSAID = nonsteroidal anti-inflammatory drug
- WBC = white blood cell

Suggested Reading

Marks SL, Kather EJ, Kass PH, et al.

Genotypic and phenotypic characterization of *Clostridium perfringens* and *Clostridium difficile* in diarrheic and healthy dogs. J Vet Intern Med 2002, 16:533–540.

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**Client Education Handout
available online**

COLITIS, HISTIOCYTIC ULCERATIVE



BASICS

OVERVIEW

- Relatively common cause of colitis in boxer breeds and infrequently seen in French bulldogs and border collies.
- Boxer colitis is also referred to as granulomatous colitis (GC) in light of the granulomatous inflammation (macrophages) in the colon.
- Etiology of GC is an adherent-invasive *E. coli* (AIEC) strain.

SIGNALMENT

- Dogs; primarily affects young boxers, usually less than 3 years of age.
- Reported in French bulldogs and border collies less frequently.

SIGNS

- Bloody, mucoid diarrhea with marked increase in the frequency of defecation.
- Tenesmus.
- Weight loss and anorexia can occur and debilitation may develop.

CAUSES & RISK FACTORS

- GC appears to be a genetic disorder in boxer breeds associated with reduced macrophage phagocytic function and an inability to kill adherent-invasive *E. coli*.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of colitis—non-histiocytic IBD (lymphocytic plasmacytic, eosinophilic colitis), other infectious causes of colitis (pythiosis), parasitic colitis (whipworms), food-responsive diarrhea.
- Cecal inversion.
- Ileocolic intussusception.
- Neoplasia—lymphoma, adenocarcinoma.
- Foreign body.
- Colorectal polyps. Dogs with colorectal polyps do not have diarrhea or increased mucus in their stools, and instead have a normal defecation frequency with formed stools coated with frank blood.
- Irritable bowel syndrome.
- Differentiate by clarifying the history (colitis vs. colorectal neoplasia), fecal floatations, abdominal imaging, and colonoscopy or proctoscopy and biopsy.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually unremarkable; microcytic anemia may be present in boxer dogs with GC secondary to intestinal bleeding.
- Chemistry panel may reveal hypoalbuminemia, electrolyte abnormalities, and prerenal azotemia in dogs with severe diarrhea and anorexia.

OTHER LABORATORY TESTS

N/A

IMAGING

Abdominal ultrasound in boxer dogs with GC often reveals mild or moderate mesenteric or sublumbar lymphadenomegaly, and the colonic wall can appear thickened.

DIAGNOSTIC PROCEDURES

- Proctoscopy or colonoscopy to obtain colonic biopsies.
- Most boxer dogs with GC have involvement of the descending colon, underscoring the diagnostic utility of proctoscopy.
- Common changes in appearance to the colonic wall include erythema, irregularity, and ulceration of the colonic and rectal wall.

MICROBIOLOGIC TESTING

E. coli is commonly isolated on routine bacteriologic media from feces of both healthy dogs and dogs with diarrhea. However, attempts to isolate *E. coli* from colonic biopsies is recommended for sensitivity testing and optimization of antimicrobial therapy.

PATHOLOGIC FINDINGS

- Histopathologic lesions include neutrophilic inflammation, epithelial ulceration, crypt hyperplasia and distortion, decreased numbers of goblet cells, and large numbers of macrophages that stain positive with periodic acid-Schiff (PAS) stain.
- The presence of *E. coli* within macrophages can be confirmed using fluorescent in-situ hybridization (FISH).



TREATMENT

- Outpatient medical management following confirmation of the diagnosis.
- Antimicrobial therapy utilizing fluoroquinolones is the mainstay of therapy.
- Diet change to include a moderately fermentable fiber source can be used in cases that do not show complete resolution of diarrhea.



MEDICATIONS

DRUG(S)

Antimicrobials—First-Line Therapy

- Enrofloxacin (10 mg/kg q24h), for a minimum duration of 6–8 weeks is typically associated with rapid resolution of clinical signs and resolution of histopathologic abnormalities.
- Because enrofloxacin resistance has been documented in some isolates from dogs with GC, attempts to isolate *E. coli* from colonic biopsies before treatment is recommended such that antimicrobial susceptibility testing can be performed.
- Antimicrobials that penetrate intracellularly, such as fluoroquinolones, chloramphenicol, rifampin, or trimethoprim-sulfonamides, should be preferentially chosen for treatment based on the results of antimicrobial susceptibility testing.
- Chloramphenicol and trimethoprim-sulfonamide should be considered for cases resistant to fluoroquinolones.

Anti-inflammatory/Immunosuppressive Drugs

- Rarely indicated in dogs with GC, and used at anti-inflammatory dose in conjunction with appropriate antimicrobial therapy.
- Diagnosis must be reconsidered if there is no dramatic improvement in clinical signs following administration of fluoroquinolone therapy because not all boxers with signs of colitis have GC.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Avoid anticholinergics or other motility modifiers such as Imodium in dogs with an infectious cause of their diarrhea.



FOLLOW-UP

PATIENT MONITORING

- Monitor clinical signs, stool consistency and frequency, and body weight.
- Dogs showing a favorable response should improve within 3–5 days of starting fluoroquinolone therapy.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Colonic stricture if inflammation is uncontrolled for long periods.

EXPECTED COURSE AND PROGNOSIS

- Generally good prognosis following appropriate antimicrobial therapy.
- Increasing injudicious administration of fluoroquinolones to dogs is increasing the resistance of *E. coli* to this class of antimicrobials, necessitating the use of alternative antimicrobials in a subset of dogs.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

- Boxers, French bulldogs and border collies with GC should not be bred.

SEE ALSO

Colitis and Proctitis

ABBREVIATIONS

- IBD = inflammatory bowel disease
- GC = granulomatous colitis
- FISH = fluorescent in-situ hybridization
- PAS = periodic acid-Schiff

Suggested Reading

Craven M, Dogan B, Schukken A, et al. Antimicrobial resistance impacts clinical outcome of granulomatous colitis in boxer dogs. J Vet Intern Med 2010, 24(4):819–824.

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COMPULSIVE DISORDERS—CATS



BASICS

DEFINITION

- Compulsive disorders are relatively invariant exaggerated behavior patterns, often derived from normal behaviors but out of context and repetitive, without apparent function. May be performed to the exclusion of other normal behaviors or to the detriment of the animal.
- May be a heterogeneous group of conditions with differing pathologies including compulsive, stereotypic and neurologic; therefore abnormal repetitive behaviors might be used to describe the clinical presentation until a diagnosis is made.
- Considered here are psychogenic dermatitis/alopecia, compulsive fabric chewing, and hyperesthesia syndrome.

PATOPHYSIOLOGY

- Diagnosis of exclusion; must rule out pathophysiologic causes, including psychomotor seizures, before a presumptive diagnosis is made.
- Can be a behavioral response to confinement, specific anxiety-producing event, or undefined environmental conditions (e.g., conflict, stress, anxiety, frustration); over time, can become fixed and independent of the environment.
- Behaviors may be self-reinforcing—allowing some animals to cope with conditions that do not meet their species-specific needs.

SYSTEMS AFFECTED

- Behavioral
- Gastrointestinal—fabric chewing
- Musculoskeletal—feline hyperesthesia (involves cutaneous trunci muscle), tail attack/mutilation
- Skin/Exocrine—psychogenic dermatitis/alopecia
- Nervous—feline hyperesthesia syndrome

GENETICS

None identified, although the association of compulsive fabric chewing with Asian breeds suggests a heritable component.

INCIDENCE/PREVALENCE

Unknown, uncommon

GEOGRAPHIC DISTRIBUTION

None identified

SIGNALMENT*Species*

Cat

Breed Predispositions

Siamese, Burmese, other Asian breeds and crosses overrepresented for fabric chewing and sucking.

Mean Age and Range

- Compulsive disorders can develop at any time, generally not seen in kittens.
- Psychogenic dermatitis/alopecia: 6 months to 12 years.
- Fabric chewing: 12 to 49 months; generally around 24 months.
- Hyperesthesia syndrome: 1 to 5 years.

Predominant Sex

None

SIGNS*General Comments*

- Behaviors may quickly increase in frequency if reinforced with attention by owner.
- Scolding or punishment may increase cat anxiety and worsen expression of behavior.

Historical Findings

- Onset may be coincident with an environmental change (e.g., move or new household member) suggesting stress effect, cat may hide to avoid punishment.
- Psychogenic dermatitis/alopecia—may be associated with excessive grooming to the exclusion of other activities; may be history of flea exposure or diet change.
- Compulsive fabric chewing—some patients show preference for a specific fabric type such as wool or may have general texture preference. Grind fabric with molars; may ingest fabric leading to foreign body obstruction.
- Hyperesthesia syndrome—may be triggered by tactile contact (petting along the dorsum and rump), may be episodic; flea exposure.

Physical Examination Findings

- Psychogenic dermatitis/alopecia—focal, partial, and bilateral dermatitis or alopecia; most common locations: groin, ventrum, and medial or caudal thigh regions; appearance of the skin variable (normal or abnormal; erythematous to abraded).
- Fabric chewing—often normal; secondary gastrointestinal inflammation or obstruction may occur if cat ingests material.
- Hyperesthesia syndrome—may be normal. Episode may be prompted by petting or scratching dorsum; signs may include dilated pupils, salivation, alarming vocalization, “rippling skin” (hyperresponsive cutaneous trunci muscle), inappropriate urination or defecation, tail twitching, frantic grooming, self-directed (especially to tail) or owner-directed aggression, escape behavior.

CAUSES

Unidentified

RISK FACTORS

- Changes in surroundings might predispose cat to compulsive disorder.
- More commonly reported in indoor cats.

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

Rule out medical differentials, including psychomotor seizures, before a behavioral diagnosis is made.

Psychogenic Dermatitis/Alopecia

- Skin conditions—especially those associated with pruritis.
- External parasites, especially fleas.
- Fungal or bacterial dermatitis.
- Food hypersensitivity, atopy.
- Cutaneous neoplasia.

- Eosinophilic granuloma complex
- Nervous system disorders
- Disk rupture and associated neuritis
- Feline hyperesthesia syndrome
- Pain/neuropathy

Fabric Chewing

- Lead intoxication
- Hyperthyroidism
- Thiamin deficiency

Hyperesthesia Syndrome

- Seizure disorder
- Skin disorders (external parasites)
- Food hypersensitivity
- Flea bite hypersensitivity
- Spinal disorder/neuropathy
- Myositis, myopathy

CBC/BIOCHEMISTRY/URINALYSIS

Minimum database to rule out metabolic abnormalities. No consistent clinicopathologies are associated with compulsive disorders.

OTHER LABORATORY TESTS*Psychogenic Alopecia*

Microscopic examination of hairs (trichogram), skin scraping, skin biopsy, fungal culture, bacterial culture, examination for external parasites, intradermal allergy testing—rule out dermatologic condition

Fabric Chewing

- Serum lead level—if indicated for pica
- Serum T4

Hyperesthesia Syndrome

Rule out dermatologic condition as above

IMAGING

CT or MRI—if indicated by abnormalities on the neurologic examination. Fabric chewing—imaging GIT if obstruction or foreign body suspected.

DIAGNOSTIC PROCEDURES*Psychogenic Alopecia*

Complete dermatologic evaluation (see “Other Laboratory Tests”)

Hyperesthesia Syndrome

Skin and/or muscle biopsy (as necessary)

PATHOLOGIC FINDINGS*Psychogenic Alopecia*

- Microscopic examination of hairs—typically shafts are cleanly broken off at variable length as a result of trauma from the tongue.
- If primarily behavioral, results of other dermatologic testing will be generally normal.

**TREATMENT****APPROPRIATE HEALTH CARE**

Supportive care

NURSING CARE*Fabric Chewing*

Create a “safe place” for when the cat is left alone, devoid of fabric of the sort favored for chewing.

ACTIVITY

Increase opportunities for play and social interactions by providing outlets favored by the affected cat.

COMPULSIVE DISORDERS—CATS

(CONTINUED)

Table 1

Drugs and dosages used to manage feline compulsive disorder.				
Drug	Drug Class	Oral Dosage in Cats	Frequency	Side Effects (Usually Transient)
Fluoxetine	SSRI	0.5–1.0 mg/kg	q24h	Decreased appetite, sleepiness
Paroxetine	SSRI	0.25–0.50 mg/kg	q24h	Constipation
Clomipramine	TCA	0.25–0.50 mg/kg	q24h	Sleepiness, urine retention
Amitriptyline	TCA	0.25–1.0 mg/kg	q24h	Sleepiness, urine retention
Gabapentin	Anticonvulsant	3–10 mg/kg	q12h	Sleepiness, sedation

DIET

- *Fabric chewing*: increasing fiber in the diet has been suggested
- *Presumptive psychogenic alopecia*: Exclusion diet

CLIENT EDUCATION

- Identify and remove triggers for the behavior, if applicable.
- Do not reward the behavior.
- Ignore the behavior as much as possible; distract the cat and initiate an acceptable behavior.
- Note details of the time, place, and social milieu so that an alternative behavior (play or feeding or food-dispensing toy) may be scheduled prior to initiation of the compulsive behavior.
- Punishment is contraindicated and can increase the unpredictability of the patient's environment, increase the patient's fear or aggressive behavior, and disrupt the human-animal bond.
- Reduce environmental stress—increase the predictability of household events (feeding, play, exercise, and social time with the client); eliminate unpredictable events as much as possible.

SURGICAL CONSIDERATIONS

N/A

**MEDICATIONS****DRUG(S) OF CHOICE**

- If a specific etiology cannot be identified, drugs may be helpful (Table 1).
- Goal—use the drugs until control is achieved for 2 months; attempt gradual withdrawal by decreasing dosage at 2-week intervals. Treatment should be resumed at the last effective dose at the first sign of relapse; may be life-long.
- Drugs are listed with dosage used to manage behavior and common side effects.
- Hyperesthesia syndrome: gabapentin has been reported anecdotally to reduce the frequency and intensity of bouts.

CONTRAINdications

- SSRIs—depending on agent: poor appetite, constipation, sedation.
- TCAs—cardiovascular abnormalities (cardiac conduction disturbances), glaucoma, urinary and fecal retention.
- Transdermal route does not produce satisfactory drug levels.

PRECAUTIONS

- Start behavioral drugs at low dose to avoid side effects. May give at bedtime to reduce complaints of sedation, may be given with food.
- No drugs are approved by the FDA for the treatment of these disorders in cats; inform client of the extra-label use and the risks involved; document the discussion in the medical record or with a release form.

POSSIBLE INTERACTIONS

Do not use TCAs or SSRIs with monoamine oxidase inhibitors, including selegiline.

ALTERNATIVE DRUG(S)

Phenobarbital if seizure disorder suspected. Selegiline if cognitive dysfunction. *Presumptive psychogenic alopecia*: exclusion diet, parasiticide trial course of steroids.

**FOLLOW-UP****PATIENT MONITORING**

- Before initiating treatment, record the frequency of compulsive behavior so that progress can be monitored.
- Successful treatment requires a schedule of follow-up examinations; a recommended schedule is a phone check 1 week after the initial consultation and an office recheck 4–6 weeks later. If improvement is evident, the treatment regime should be continued. If there is no improvement, differential diagnoses should be considered or an alternative drug should be considered.
- If a medication is not effective after dosage adjustment, select an agent from another drug class.

PREVENTION/AVOIDANCE

Create an enriched environment with distributed resources, safe and accessible elevated resting sites, exercise and play opportunities, and predictable social interactions with people.

POSSIBLE COMPLICATIONS

- Treatment failure.
- Realistic expectations must be made; immediate control of a long-standing problem is unlikely.

EXPECTED COURSE AND PROGNOSIS

With treatment, prognosis for improvement is good; treatment can be life-long.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Avoidance behavior or aggression toward the owner—if the owner punishes the patient when it exhibits a compulsive behavior.

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

- Do not breed animals that display compulsive behavior.
- Tricyclic antidepressants—contraindicated in pregnant animals.

SYNOMYS

Hyperesthesia syndrome: rippling skin disease, neurodermatitis

SEE ALSO

Compulsive Disorders—Dogs

ABBREVIATIONS

- GIT = gastrointestinal tract
- OCD = obsessive-compulsive disorder
- SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant

INTERNET RESOURCES

Cornell University Feline Health Center

- http://www.vet.cornell.edu/fhc/health_resources/CW_lick.cfm
- http://www.vet.cornell.edu/FHC/health_resources/HyperesthesiaSyndrome.cfm

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Client Education Handout
available online

COMPULSIVE DISORDERS—DOGS



BASICS

DEFINITION

- Heterogeneous group of conditions with differing pathologies including compulsive, stereotypic, and neurologic; therefore “abnormal repetitive behaviors” might be used to describe the clinical presentation until a diagnosis is made.
- Can be categorized as locomotor (spinning, tail chasing, circling, fence running, pacing, light/shadow chasing); oral (licking, sucking/mouthing an object/body part [e.g., flank, tail, limb], pica, excessive drinking, “fly biting”); or hallucinatory (“fly biting,” hind end checking, freezing, staring), with or without vocal and affective responses.
- Compulsive disorders are abnormal, repetitive, exaggerated and/or sustained, variable in form and fixated on a goal. They are derived from normal maintenance behaviors such as grooming, predation, and ingestion. Motivational conflict or frustration appears to trigger the behaviors in specific contexts often associated with high arousal; over time, with repeated/sustained conflict, the behavior becomes emancipated from the original trigger stimuli and is displayed in diverse contexts.
- Stereotypes are repetitive behaviors that are unvaried in sequence and have no obvious function or purpose. They may arise in situations of conflict or frustration related to confinement or husbandry practices, when the environment lacks sufficient outlets for the normal behavior repertoire, and with maternal deprivation.

PATOPHYSIOLOGY

- Likely associated with alterations in brain neurotransmitter functions: primarily serotonin; also dopamine, endorphins. Different CDs may preferentially involve different brain regions.
- Abnormal serotonin transmission has been identified as a primary mechanism by which compulsive disorders are induced; stereotypes might be induced by dopaminergic stimulation.

SYSTEMS AFFECTED

- Behavioral—fear, anxiety, aggression.
- Cardiovascular—tachycardia.
- Endocrine/Metabolic—HPA axis upregulation.
- Gastrointestinal—inappetence, gastroenteritis, foreign body obstruction
- Hemic/Lymphatic/Immune—stress leukogram
- Musculoskeletal—weight loss, self-injury.
- Respiratory—tachypnea.
- Skin/Exocrine—abrasions/lacerations/; wounds/infections secondary to self-trauma.

GENETICS

- Likely genetic predisposition/susceptibility: higher than expected occurrence among first-generation relatives (though manifestations may differ).
- Certain breeds overrepresented for specific CDs.

INCIDENCE/PREVALENCE

Generally uncommon; more common in certain breeds/families.

SIGNALMENT

Species

Dog

Breed Predispositions

Bull terrier—spinning, freezing; German shepherd—spinning, tail chasing; Great Dane, German shorthaired pointer—self-directed oral behaviors, fence running, hallucinations; Doberman—flank/blanket sucking; miniature schnauzer—hind end checking; border collie—light/shadow chasing.

Mean Age and Range

May be presented at any age; usually develops from onset of sexual (6 months) to social (12–24 months) maturity; earlier onset (3–6 months) reported for some CDs.

Predominant Sex

Some CDs may be more common in males.

SIGNS

General Comments

- Wide variety of manifestations: behaviors may be repetitive or static (e.g., freezing).
- Signs may or may not be observed during examination. Descriptions may be unclear; videotape aids diagnosis and treatment planning.

Historical Findings

- May be other signs of anxiety/concurrent behavioral diagnoses (e.g., separation anxiety, fears, aggression) and/or a history of stress (e.g., inadequate stimulation, punishment, schedule/routine/household change).
- Behavior may first be displayed as part of play or in situations of high arousal or stress; eventually may occur in multiple contexts independent of identifiable triggers.
- Certain repetitive behaviors are expressed in situations with little to no external stimulation or evidence of arousal (e.g., blanket sucking).
- Occurs whether or not the owner is present. If punished, pet may avoid detection.
- Hallmarks—behavior is ritualized, often exaggerated in form, and with time increases in frequency, intensity, and duration.
- Behavior may be difficult or impossible to interrupt (even with physical restraint).
- Behavior may interfere with normal functioning (e.g., eating, sleeping, social interactions).

Physical Examination Findings

- May be unremarkable.
- May see skin lesions and injuries related to self-trauma (especially to tail, forelimbs, distal extremities); excessive tooth wear/damage; lameness or loss of/poor body condition.

CAUSES

No direct cause

RISK FACTORS

- Environmental stress (e.g., kenneling—spinning), management, illness, other.
- Owner/environmental reinforcement of the behavior.
- Medical disease, pain, or neuropathy—may increase anxiety or may be primary cause of behavior.
- Sensory abnormalities (e.g., visual deficits) may contribute.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Dermatologic disease (e.g., atopy)
- Gastrointestinal disease (e.g., IBD)
- Metabolic/endocrine disease (e.g., Cushing's)
- Neurologic disease (e.g., seizure focus, forebrain neoplasia)
- Orthopedic disease (e.g., DJD)
- Any disorder causing abnormalities of sensation such as dysesthesia, paresthesia, (sensory neuropathy)
- Other problem behaviors: displacement or conflict behaviors, play and attention seeking, and behaviors occurring secondary to lack of stimulation or due to resource restriction (e.g., water restriction—excessive drinking),
- Diagnostics needed to rule out physical causes of behavior, especially self-mutilation.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually within the laboratory's reference range—use for general health screening; prior to drug use.
- Hematocrit, cholesterol, triglyceride increases have been reported.

OTHER LABORATORY TESTS

Various; specific to differential diagnoses.

IMAGING

- For neurologic differentials, CT and MRI to rule out structural brain disease; altered brain/gray matter volume/density reported in CD.
- Radiography, ultrasound if needed to rule out underlying physical causes.

DIAGNOSTIC PROCEDURES

- None specific for CD.
- Indications based on other differentials (e.g., endoscopy, biopsy, echocardiography).



TREATMENT

Not all repetitive behavior is abnormal; it may represent a coping mechanism. If not harmful nor interfering with normal functioning, health, or human-animal bond, intervention may be unnecessary or contraindicated.

APPROPRIATE HEALTH CARE

- Outpatient unless severe self-mutilation/self-injury; hospitalization may exacerbate CD.
- Sedation—stop-gap measure; if needed to stop serious self-mutilation, increases suspicion of underlying physical abnormality.
- Treat associated physical conditions (primary or

COMPULSIVE DISORDERS—DOGS

(CONTINUED)

C

secondary). • Combination of environmental modification, behavior modification, and pharmacologic treatment. • Pharmacologic intervention—implement early; reduction of anxiety facilitates behavioral therapy.

- Environmental modification—reduce stress and anxiety; identify and remove sources (e.g., triggers) and/or begin desensitization and counter-conditioning exercises.
- Punishment—contraindicated; increases anxiety, may worsen behavior and increase patient secrecy. • Provide structured, consistent interactions, routine, and sufficient exercise, enrichment/mental stimulation appropriate to the species and individual; includes interactive play and reward-based training.
- Behavior modification—teach the patient to relax in a variety of settings; also teach a calm, desirable behavior incompatible with the stereotypic one, coupled to a verbal cue (e.g., for circling, teach to lie down with head and neck outstretched in response to “Head down”). In some cases, a head collar (e.g., Gentle Leader, Halti) left on the dog (when the owner is home) in the problem contexts may allow the owner to use gentle physical guidance along with verbal encouragement/cues to interrupt the behavior and redirect it more effectively. Monitor for situation in which behavior occurs and pre-empt it by engaging the pet in an incompatible activity; if behavior occurs, disrupt immediately, redirect the animal to alternative incompatible activity and reward (food, play, other reinforcer).
- Have clients monitor behaviors via videos and written logs for objective assessment of response to therapy. Improvement may be seen in frequency and/or intensity of bouts.

Discussion of a rating scale and how to judge changes may help in assessing response to therapy.

- Bandages, collars, braces, and crates increase distress, do not address the behavioral condition, and may worsen it. If needed to ensure healing, use as briefly as possible.

ACTIVITY

Environmental enrichment

DIET

N/A

CLIENT EDUCATION

• Cure is unlikely; usually requires life-long management.

- Teach client to recognize all body language/behaviors reflecting anxiety.

SURGICAL CONSIDERATIONS

Tail/limb mutilation: avoid amputation; it is unlikely to resolve the CD.



MEDICATIONS

DRUG(S) OF CHOICE

- SSRIs and TCAs—effects are via CNS serotonin effects.
- Generally treat at low end of dose range for 4–6 weeks; gradually

increase dosage if ineffective and no adverse events.

- SSRIs: fluoxetine 1–2 mg/kg q24h; sertraline 1–3 mg/kg q24h; paroxetine 1–2 mg/kg q24h.
- TCAs: clomipramine is most serotonergic (most effective, fewest side effects)—2–3 mg/kg q12h.
- If symptoms resolve, continue medication for >1 month, then reduce dose no faster than 25% every two weeks. Recurrence common.

CONTRAINDICATIONS

- Hepatic or renal compromise—medications metabolized by these organs.
- Cardiac conduction anomalies—TCAs.
- Use extreme care combining serotonergic drugs (e.g., SSRI with tramadol); risk of serotonin syndrome (potentially fatal).
- Do not use SSRIs or TCAs within 2 weeks of MAOIs (e.g., selegiline, amitriptyline).

PRECAUTIONS

- Use of listed medications for CD is extra- or off-label.
- TCA overdose—cardiac conduction disturbances.
- TCA/SSRI overdose—serotonin syndrome.
- Most common side effects of SSRIs and TCAs: lethargy, appetite change; less common: increased anxiety/reactivity, vomiting/diarrhea; severe side effects may necessitate drug discontinuation.

POSSIBLE INTERACTIONS

SSRIs competitively inhibit CYP450 enzymes: may increase warfarin, many TCAs, some benzodiazepines and anticonvulsants, other medications; check compatibility and adjust dosage if necessary.

ALTERNATIVE DRUG(S)

- Synthetic pheromones (Adaptil), l-theanine or alpha-casozepine may reduce anxiety (see label for dosing).
- Second-line TCAs, e.g., amitriptyline 1–6 mg/kg q12h.
- Selegiline (MAOI) 0.5–1 mg/kg q24h: may be effective in some cases.
- Memantine (NMDA receptor antagonist) 0.3–1 mg/kg q12h.
- Narcotic antagonists (e.g., naltrexone, naloxone) may be effective but not a practical therapeutic option. Antipsychotics (e.g., thioridazine, haloperidol) not recommended due to risk of adverse effects, efficacy undocumented.



FOLLOW-UP

PATIENT MONITORING

- CBC, biochemistry, T₄ (TCAs may artificially lower) and urinalysis—semiannually to yearly if chronic treatment; adjust dosages accordingly.
- Medications may take 8–12 weeks or longer to affect CDs; first sign of efficacy may be change in bout duration/frequency.
- Relapses common during stressful situations; manage with increased intensity of behavior modification, addition of short-term, shorter-acting anxiolytics (e.g., benzodiazepines).

PREVENTION/AVOIDANCE

Monitor animals with affected relatives; early recognition and intervention.

POSSIBLE COMPLICATIONS

Dermatologic/musculoskeletal injury; gastrointestinal disorders.

EXPECTED COURSE AND PROGNOSIS

- Untreated CDs almost always progress.
- > 50% reduction in CD in approximately two-thirds of cases with appropriate medication and behavioral and environmental modification.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Various; specific to type of CD.

PREGNANCY/FERTILITY/BREEDING

- Listed medications not evaluated/contraindicated in pregnant animals; avoid use.
- Do not breed affected animals.

SYNOMYMS

Obsessive-compulsive disorder

SEE ALSO

Acral Lick Dermatitis

ABBREVIATIONS

- CD = compulsive disorder
- CNS = central nervous system
- CT = computed tomography
- CYP450 = cytochrome P450
- DJD = degenerative joint disease
- HPA = hypothalamic-pituitary-adrenal
- IBD = inflammatory bowel disease
- MAOI = monoamine oxidase inhibitor
- MRI = magnetic resonance imaging
- NMDA = N-methyl-D-aspartate
- SSRI = selective serotonin reuptake inhibitor
- T₄ = thyroxine
- TCA = tricyclic antidepressant

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Client Education Handout available online

CONGENITAL AND DEVELOPMENTAL RENAL DISEASES



BASICS

DEFINITION

- Functional or morphologic abnormalities resulting from heritable (genetic) or acquired disease processes affecting differentiation and growth of the developing kidney before or shortly after birth.
- Renal agenesis—complete absence of one or both kidneys.
- Renal dysplasia—disorganized renal parenchymal development.
- Renal ectopia—congenital malposition of one or both kidneys; ectopic kidneys may be fused.
- Glomerulopathy—glomerular disease of any type.
- Tubulointerstitial nephropathy—a non-inflammatory disorder of renal tubules and interstitium.
- Polycystic renal disease—formation of multiple, variable-sized cysts throughout the renal medulla and cortex.
- Renal telangiectasia—multifocal vascular malformations involving the kidneys and other organs.
- Renal amyloidosis—extracellular deposition of amyloid in glomerular capillaries, glomeruli, and interstitium.
- Nephroblastoma—a congenital renal neoplasm arising from the pluripotent metanephric blastema.
- Multifocal renal cystadenocarcinoma—a hereditary renal neoplasm in dogs.
- Fanconi syndrome—a generalized renal tubular functional anomaly characterized by impaired reabsorption of glucose, phosphate, electrolytes, amino acids, and uric acid.
- Primary renal glucosuria—an isolated functional defect in renal tubular reabsorption of glucose.
- Cystinuria—excessive urinary excretion of cystine because of an isolated functional defect in renal tubular reabsorption of cystine and other dibasic amino acids.
- Xanthinuria—excessive urinary excretion of xanthine caused by a deficiency in xanthine oxidase.
- Hyperuricuria—excessive urinary excretion of uric acid, sodium urate, or ammonium urate.
- Primary hyperoxaluria—intermittent hyperoxaluria, l-glyceric aciduria, oxalate nephropathy, and acute renal failure.
- Congenital nephrogenic diabetes insipidus—polyuria caused by diminished renal responsiveness to antidiuretic hormone.

PATHOPHYSIOLOGY

- Many congenital and developmental renal disorders are caused by genetic abnormalities that disrupt the normal sequential and coordinated development and interaction of multiple embryonic tissues involved in formation of the mature kidney.
- Congenital and developmental renal disorders may also be caused by non-genetic factors affecting the developing kidney before or shortly after birth.

SYSTEMS AFFECTED

Renal/Urologic

GENETICS

- Familial renal disorders have been reported in the following breeds of dogs and cats:
- Renal agenesis in beagle and Doberman pinscher
- Renal dysplasia in Alaskan malamute, border terrier, boxer, chow chow, Dutch kooiker, golden retriever, keeshond, Lhasa apso, miniature schnauzer, Rhodesian ridgeback, shih tzu, soft-coated Wheaten terrier, and standard poodle dogs
- Glomerulopathy in beagle, Belgian shepherd, Bernese mountain dog, Brittany spaniel, bull terrier, bullmastiff, Dalmatian, Doberman pinscher, English cocker spaniel, Newfoundland, Pembroke Welsh corgi, rottweiler, Samoyed, and soft-coated Wheaten terrier dogs
- Tubulointerstitial nephropathy in Norwegian elkhound dogs
- Polycystic renal disease in beagle, bull terrier, cairn terrier, and West Highland white terrier dogs, and in Persian, exotic shorthair, and Himalayan cats
- Renal telangiectasia in Pembroke Welsh corgi
- Renal amyloidosis in Abyssinian, Oriental shorthair, and Siamese cats, and in beagle, English foxhound, and shar-pei dogs
- Renal cystadenocarcinoma in German shepherds
- Fanconi syndrome in basenji and border terrier dogs
- Primary renal glucosuria in Norwegian elkhound, Scottish terrier, and basenji dogs
- Cystinuria in Australian cattle, Australian shepherd, basenji, basset hound, bullmastiff, Chihuahua, English bulldog, dachshund, French bulldog, Irish terrier, mastiff, Newfoundland, Scottish deer hound, Staffordshire bull terrier, and Welsh corgi dogs and in domestic cats
- Xanthinuria in Cavalier King Charles spaniel and wirehaired dachshund dogs, and in domestic shorthair cats
- Hyperuricuria in Dalmatians, black Russian terriers, and English bulldogs
- Primary hyperoxaluria in domestic shorthair cats and in Tibetan spaniels.

INCIDENCE/PREVALENCE

Uncommonly recognized, but occur more frequently in related animals from more than one generation than in the general population.

SIGNALMENT

Species

Dog and cat

Breed Predilections

Sporadic cases can occur without an apparent familial predisposition in any breed of dog or cat.

Mean Age and Range

Most patients are < 5 years old at time of diagnosis.

Predominant Sex

- Familial cystinuria occurs primarily in male dogs.
- Samoyed hereditary glomerulopathy more common in males than females.
- Familial glomerulonephropathy of Bernese mountain dogs is more common in females.

SIGNS

General Comments

Most congenital and developmental disorders cannot be distinguished from acquired renal diseases on the basis of history or physical examination.

Historical Findings

- Indicate chronic renal failure.
- Some glomerulopathies associated with abdominal distension, edema, or other signs of the nephrotic syndrome.
- Abdominal distension in some patients with polycystic kidneys or renal neoplasms.
- Hematuria or abdominal pain in some patients with renal telangiectasia or renal neoplasms.
- Patients with unilateral renal agenesis, ectopic kidneys, and isolated renal tubular transport defects are frequently asymptomatic.

Physical Examination Findings

- Signs associated with chronic renal failure.
- Ascites or pitting edema in some patients with protein-losing glomerulopathies or amyloidosis.
- Renomegaly or abdominal mass lesions in some patients with polycystic kidneys, renal neoplasms, or fused ectopic kidneys.

CAUSES

Non-hereditary

- Infectious agents—feline panleukopenia virus and canine herpesvirus infection associated with renal dysplasia.
- Drugs—corticosteroids, diphenylamine, and biphenyls associated with polycystic kidneys; chlorambucil and sodium arsenite associated with renal agenesis.
- Dietary factors—hypovitaminosis A associated with renal ectopia.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Rule out acquired and non-developmental causes of primary renal disease.
- Rule out non-renal causes of hematuria, proteinuria, glucosuria, abdominal distention, or ascites.

CBC/BIOCHEMISTRY/URINALYSIS

- Nonregenerative anemia in patients with chronic renal failure.
- Azotemia and urine specific gravity < 1.030 observed in dogs and < 1.035 observed in cats if renal failure develops.
- Proteinuria, hypoalbuminemia, and hypercholesterolemia in patients with the nephrotic syndrome.
- Normoglycemic glucosuria in animals with Fanconi syndrome or primary renal glucosuria.
- Hematuria in patients with congenital renal neoplasia or renal telangiectasia.
- Cystine crystalluria in patients with cystinuria.
- Xanthine crystalluria in patients with xanthinuria.
- Urine crystalluria in patients with hyperuricuria.

CONGENITAL AND DEVELOPMENTAL RENAL DISEASES

(CONTINUED)

OTHER LABORATORY TESTS

Direct genetic tests are available for detection of specific genetic mutations associated with familial nephropathy in English cocker spaniel dogs, familial cystinuria in Newfoundland dogs, and familial polycystic renal disease in Persian and Persian-derived breeds of cats.

IMAGING

Survey abdominal radiography, renal ultrasonography, and excretory urography are important means of identifying and characterizing congenital and developmental renal disorders and their associated sequelae.

DIAGNOSTIC PROCEDURES

Consider light microscopic evaluation of kidney biopsy specimens from patients with morphologic or functional abnormalities of the kidney for which a definitive diagnosis has not been established by other, less invasive means.

PATHOLOGIC FINDINGS

- Renal dysplasia—end-stage kidneys; primary lesions include immature (“fetal”) glomeruli, persistent mesenchyme, persistent metanephric ducts, atypical tubular epithelium, and dysontogenic metaplasia; primary lesions usually associated with, and may be obscured by, secondary degenerative, inflammatory, and compensatory lesions.
- Glomerulopathies—usually normal-to-small kidneys; most are characterized by a primary membranoproliferative glomerulonephritis with variable degrees of tubulointerstitial disease, but cystic atrophic membranous glomerulopathy is the characteristic lesion in affected rottweilers.
- Tubulointerstitial nephropathy—end-stage kidneys; renal lesions include periglomerular fibrosis, parietal epithelial cell hyperplasia and hypertrophy, interstitial fibrosis, and interstitial mononuclear cell infiltrate.
- Polycystic renal disease—see specific chapter.
- Renal amyloidosis—see specific chapter.
- Renal telangiectasia—lesions include multiple, variable-sized, red-black, blood-filled nodules and clots in the renal cortex and medulla, interstitial fibrosis, interstitial mononuclear cell infiltrate, and hydronephrosis.
- Nephroblastoma—unilateral renal mass; microscopically characterized by both embryonic mesenchymal and epithelial tissue components.
- Multifocal renal cystadenocarcinoma—bilaterally enlarged kidneys with irregular protruding cystic structures or multifocal neoplastic renal tubular epithelial cell proliferations.
- Renal ectopia—kidneys abnormally located in the retroperitoneal space or abdomen; horseshoe

kidneys are symmetrically fused along the medial border of either pole.

- Fanconi syndrome—inconsistent microscopic findings of tubular atrophy, interstitial fibrosis, and acute papillary necrosis.
- Primary hyperoxaluria—large, irregularly shaped kidneys; microscopic lesions include renal tubular deposition of calcium oxalate crystals and variable interstitial and periglomerular fibrosis.



TREATMENT

- The nature of congenital and developmental renal disorders often precludes specific treatment.
- Supportive or symptomatic treatment may improve quality of life and minimize progression in patients with renal dysfunction.
- Refer to chapters describing specific renal diseases or clinical syndromes.



MEDICATIONS

DRUG(S) OF CHOICE

Refer to chapters describing specific renal diseases or clinical syndromes.

CONTRAINDICATIONS

Avoid potentially nephrotoxic drugs (e.g., gentamicin, nonsteroidal anti-inflammatory drugs) or anesthetic agents that decrease renal function when possible.

PRECAUTIONS

Avoid drugs requiring renal excretion in patients with renal failure; if necessary, modify dosage regimens to compensate for decreased renal clearance of drugs and other metabolites.



FOLLOW-UP

PATIENT MONITORING

Refer to chapters describing specific renal diseases or clinical syndromes.

PREVENTION/AVOIDANCE

Congenital and developmental renal disorders are irreversible, so control lies in preventing breeding of affected animals. Always consider early identification and correction of predisposing factors (genetic and non-genetic) that may affect future offspring.

POSSIBLE COMPLICATIONS

- Acute or chronic renal failure
- Nephrotic syndrome
- Urolithiasis
- Hydronephrosis
- Urinary tract infection

EXPECTED COURSE AND PROGNOSIS

- Highly variable; depends on the specific disorder, the extent of primary lesions, and the severity of renal dysfunction.
- Most congenital and developmental disorders are irreversible and may result in advanced chronic renal failure, but some patients with mild-to-moderate renal dysfunction may remain stable for long periods.
- Patients with some disorders (e.g., unilateral renal agenesis, renal ectopia, cystinuria, hyperuricuria, primary renal glucosuria) may remain asymptomatic unless the disorder is complicated by urolithiasis, urinary tract infection, or other disease processes that promote progressive renal dysfunction.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Polycystic renal disease associated with hepatic biliary cysts.
- Cystinuria, xanthinuria, and hyperuricuria associated with formation of uroliths.
- Amyloidosis in Chinese shar-pei dogs associated with intermittent pyrexia or swelling of the hocks.
- Renal neoplasms associated with hypertrophic osteoarthropathy, polycythemia, or other paraneoplastic syndromes.

SYNOMYMS

Familial renal disease, juvenile renal disease

SEE ALSO

- Amyloidosis
- Anemia of Chronic Renal Disease
- Fanconi Syndrome
- Hematuria
- Hyperparathyroidism, Renal Secondary
- Nephrotic Syndrome
- Oliguria and Anuria
- Polycystic Kidney Disease
- Polyuria and Polydipsia
- Renal Failure, Acute
- Renal Failure, Chronic
- Renal Tubular Acidosis
- Renomegaly
- Urolithiasis, Cystine

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CONGENITAL OCULAR ANOMALIES

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BASICS

DEFINITION

Solitary or multiple abnormalities that affect the globe or its adnexa; observed in young dogs and cats at birth or within the first 6–8 weeks of life.

PATHOPHYSIOLOGY

- Breed-related inherited defects.
- Spontaneous malformations. • *In utero* systemic infections and inflammations, exposure to toxic compounds, and lack of specific nutrients in pregnant dams or bitches.

SYSTEMS AFFECTED

Ophthalmic—entire eye or any part; unilateral or bilateral.

GENETICS

- Known, suspected, or unknown mode of inheritance. • PPM in basenjis—dominant trait. • PHTVL and PHPV in Doberman pinschers—dominant allele with variable expression. • Multifocal retinal dysplasia in English springer spaniels—recessive trait.
- CEA—recessive trait. • MOD in Australian shepherds—autosomal recessive trait with incomplete penetrance. • Retinal dystrophy in briards—recessive trait. • Rod cone dysplasia in collies, Irish setters, Cardigan Welsh corgi and Sloughi dogs—recessive traits; non-allelic disease. • Cone rod dystrophy in pit bull terriers and in long- and shorthaired dachshund breeds; recessive traits; non-allelic disease. • Photoreceptor dysplasia in Abyssinians, Persian, and domestic shorthair cats—dominant trait in Abyssinians and in domestic shorthair cats, recessive in Persians.

INCIDENCE/PREVALENCE

- Incidence—low; dogs > cats.
- CEA—> 50% in collies, lower in other breeds.

SIGNALMENT

Species

Dog and cat

Breed Predilections

See “Genetics”

Mean Age and Range

See “Definition”

SIGNS

General Comments

- Depends on defect. • May cause no signs of disease; often incidental finding. • May be congenitally blinding disease.

Historical Findings

Ranges from none to severe visual impairment to blindness.

Physical Examination Findings

- Anophthalmos—congenital lack of the globe; exceedingly rare. • Microphthalmos—congenitally small eye; often associated with other hereditary defects. • Eyelid agenesis or

colobomas of the eyelids—may result in congenitally open eyelids; affects the temporal portion of the upper eyelid; may cause blepharospasm and epiphora.

- Dermoids—islands of aberrant skin tissue involving either eyelids, conjunctiva, or cornea; blepharospasm and epiphora.
- Atresia and imperforate puncta of the lacrimal system—common in dog breeds; results in a tear streak at the nasal canthus; usually not associated with other ocular findings.
- Congenital KCS—sporadically in any dog or cat breed; usually unilateral; affected eye appears smaller than the normal eye; thick mucous discharge from a red and irritated eye.
- PPM—remnants of the pupillary membrane spanning from the iris collarette to another portion of the iris, lens or cornea; may coexist with other defects; numerous dog breeds, especially basenjis.
- Iris cysts—pigmented or non-pigmented ball-like structures may float freely in the anterior chamber or be attached to the posterior iris, ciliary body or corneal endothelium.
- Congenital glaucoma—in dogs and cats; rare; note enlarged, red, and typically painful eye.
- Pupillary abnormalities—polycoria, acorea, aniridia, or dyscoria.
- Congenital cataracts—primary, often inherited or secondary to other developmental defects; associated with other anomalies of the lens, including microphakia, lenticonus or lentiglobus, and coloboma.
- PHTVL and PHPV—persistence of parts of the hyaloid vasculature; developmental aberrations of the vitreous, lens, and lens capsule; may show cataract, leukocoria, and/or a reddish sheen from the pupillary area with intralenticular bleeding.
- Retinal dysplasia—in several dog breeds; sporadically in cats; effect on retinal structure depends on severity; ranges from focal folds to geographic focal detachment to complete retinal detachment.
- CEA—bilateral area of choroidal hypoplasia temporal to optic nerve; visual impairment or blindness can be caused by optic nerve coloboma and retinal detachment.
- MOD—microphthalmia, microcornea, heterochromia irides, pupillary abnormalities, cataract, fundus coloboma, retinal detachment, intraocular hemorrhage.
- Coloboma of the posterior segment—primary or in conjunction with CEA or MOD; typically seen in optic nerve head in CEA, usually at the 6 o'clock position, or in the fundus periphery in MOD; may be in other locations of the fundus near the optic nerve head.
- Rod and cone dysplasia in Irish setters, and collie dogs, Persian and Abyssinians cats; rod dysplasia and early rod degeneration in Norwegian elkhounds; cone degeneration or hemeralopia in Alaskan malamutes and cone rod dystrophies in dogs; often show pupillary abnormalities and visual impairment in the first few months of life.
- Retinal dystrophy in briards; RPE65 null

mutation; congenital night blindness; nystagmus, dilated pupils; but normal fundus until middle age. • Retinal detachment—often seen in conjunction with other hereditary ocular diseases (e.g., retinal dysplasia, CEA, MOD); found in Labrador retrievers, Bedlington terriers, Sealyham terriers, and collies with CEA; signs include widely dilated pupils, weak to absent pupillary light reflexes; blindness with complete detachment.

CAUSES

- Genetic. • Spontaneous malformations.
- Infections and inflammations during pregnancy. • Toxicity during pregnancy.
- Nutritional deficiencies.

RISK FACTORS

Breeding dogs or cats that are homozygous or heterozygous for a hereditary disease with recessive inheritance or affected animals where the disease has a dominant inheritance.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infectious and inflammatory processes in adnexa—may mimic and mask congenital abnormalities.
- Cataracts induced at an early age and especially those that progress quickly may seem to be congenital.
- Post-inflammatory ophthalmic lesions with synechia—easily confused with PPM.
- Tumors of the anterior segment—may be confused with iris cysts.
- Generalized retinopathy of inflammatory origin—may appear to be photoreceptor dysplasia with retinal atrophy; usually unilateral.
- Retinal detachment as a result of trauma or uveitis in young dogs—may appear to be a congenital abnormality of neural retina.
- Optic nerve atrophy due to inflammatory process—may be difficult to differentiate from congenital optic nerve hypoplasia.

IMAGING

Ultrasound—diagnosis of abnormalities of the lens and the posterior segment.

DIAGNOSTIC PROCEDURES

- Examination with diffuse illumination—permits for diagnosis of adnexal and anterior and posterior segment anomalies.
- Evaluation of tear production (Schirmer tear strips)—performed routinely with chronic adnexal inflammatory and infectious processes.
- Tonometry when glaucoma is suspected.
- Direct and/or indirect ophthalmoscopy and biomicroscopy—necessary to diagnose abnormalities of the internal structures; examination after pupil dilation; difficult to perform in patients

CONGENITAL OCULAR ANOMALIES

(CONTINUED)

younger than 5 weeks. • ERG—objective evaluation of retinal function.

C PATHOLOGIC FINDINGS

- Congenital KCS—usually keratitis with corneal neovascularization, scarring, and pigmentation; inflammatory changes of conjunctiva; abnormally developed or atrophied lacrimal glands.
- Congenital glaucoma—buphthalmos common, sometimes secondary lens luxation and neuroretinal thinning; abnormally developed iridocorneal filtration angle.
- PHTVL and PHPV—range of defects; retrorenal pigmented dots and plaques, strands of vascular tissue from the optic nerve head to the posterior lens capsule; often posterior lens capsule defects with cataracts.
- Retinal dysplasia—abnormal folding of the neuroretina; multifocal defects often along the major blood vessels in central tapetal fundus; with geographic defects—usually large, abnormal area with elevated retina and surrounding area of hyperpigmentation and scarring; sometimes completely detached retina.
- Rod cone dysplasia—abnormalities in rod and/or cone outer and inner segments; degeneration of photoreceptor nuclei.
- Retinal dystrophy in briards—large lipoid-like inclusions in the retinal pigment epithelium and disorganization and degeneration of photoreceptors with time.
- Coloboma—notch in affected tissue; thinning of the neural retina in region of the optic nerve head or near its border with posterior segment defects.
- Retinal detachment—neural retina detached from the retinal pigment epithelium; neural retina often atrophic.
- Optic nerve hypoplasia—avascular, dark, abnormally small, circular optic nerve head.



TREATMENT

APPROPRIATE HEALTH CARE

- Patients usually referred to an ophthalmologist.
- No medical treatment for most congenital abnormalities, except symptomatic treatment or surgery.

NURSING CARE

- In KCS—removing of discharge and flushing with saline.
- Accommodate handicap of blind animals: leash walking, supervision.

ACTIVITY

Visually impaired or blind animals need adequate exercise.

DIET

Provide a diet adequate in vitamins, antioxidants, and omega-3 fatty acids, especially in photoreceptor degenerations.

CLIENT EDUCATION

- Depends on abnormality.
- Discuss visual capacity, possible progression, and sequelae.

SURGICAL CONSIDERATIONS

- Depends on abnormality.
- Adnexal abnormalities—surgery as soon as possible.
- Congenital KCS—parotid duct transposition.
- Cataract extraction—congenital cataract may be associated with other anomalies, decreasing the chances for visual rehabilitation or causing surgical complications; careful presurgical evaluation needed: imaging, ERG.
- Congenital glaucoma—enucleation or intrascleral prosthesis treatments of choice; consider euthanasia if bilateral.



MEDICATIONS

DRUG(S) OF CHOICE

- Congenital KCS—tear substitutes, frequent application, antibiotics may be added; cyclosporin ophthalmic ointment q12h.
- Congenital cataracts—if only in nuclear region of the lens, mydriatics used to increase visual capability.

PRECAUTIONS

Cats are sensitive to systemic administration of enrofloxacin, shown to cause retinal degeneration and blindness in cats when exceeding normal dose.



FOLLOW-UP

PATIENT MONITORING

- Depends on defect.
- Congenital KCS—repeated monitoring of tear production and status of external eye.
- Congenital cataracts and severe PHTVL and PHPV—regular checkups, usually on a 6-month basis; monitor progression.
- Large colobomatous defects of the fundus and geographic retinal dysplasia—regular checkups to monitor possible retinal detachment.

PREVENTION/AVOIDANCE

Restrict breeding of affected animals and of known carriers of documented hereditary defects; note that DNA-based tests are available for various diseases (see list of diagnostic facilities offering genetic testing below).

POSSIBLE COMPLICATIONS

- In congenital KCS with parotid duct transposition, keratitis and dermatitis may occur due to excessive deposition of minerals from saliva.
- Cataract surgery can result in glaucoma, retinal detachment, and corneal scarring in puppies and kittens; surgery seldom recommended before age 8–12 weeks.

EXPECTED COURSE AND PROGNOSIS

- Most abnormalities affecting adnexa can be corrected in young dogs and cats.
- In congenital KCS with parotid duct transposition prognosis is good.
- Prognosis for most anterior segment abnormalities is good to fair.
- Prognosis in glaucoma is poor.
- For photoreceptor abnormalities the prognosis for vision is poor, but the eyes should remain comfortable.
- For most other abnormalities the prognosis depends on the severity of the condition.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Retinal dysplasia—described with chondrodysplastic skeletal abnormalities in field-trial Labradors and Samoyeds.

PREGNANCY/FERTILITY/BREEDING

- Depends on defect.
- Dogs and cats affected with congenital ocular anomalies with blindness and/or pain should not be used for breeding.
- Many congenital ocular anomalies are hereditary and the use of affected animals in breeding should be prohibited or severely restricted. Breeding advice should be sought from a kennel club and breed associations.

ABBREVIATIONS

- CEA = collie eye anomaly
- ERG = electroretinography
- KCS = keratoconjunctivitis sicca
- MOD = merle ocular dysgenesis
- PHPV = persistent hyperplastic primary vitreous
- PHTVL = persistent hyperplastic tunica vasculosa lentis
- PPM = persistent pupillary membranes

INTERNET RESOURCES

The following laboratories offer DNA-based tests:

- www.antagene.com
- www.CatDNAtest.org
- www.aht.org.uk
- www.laboklin.co.uk
- www.optigen.com
- www.vgl.ucdavis.edu/services
- www.vetgen.com
- www.caninegeneticdiseases.net
- www.cvm.msu.edu/PRA1test

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**Client Education Handout
available online**

CONGENITAL SPINAL AND VERTEBRAL MALFORMATIONS



BASICS

DEFINITION

Anomalous development of spinal structures, which are apparent at birth or within the first weeks of life.

PATHOPHYSIOLOGY

- Malformation of the occipital bones, atlas, and axis; malformation of the odontoid process; occipitoatlantoaxial malformation; and occipital dysplasia—may cause atlantoaxial subluxation with secondary compression and trauma to the first segments of the cervical spinal cord.
- Other embryonic or developmental anomalies of the vertebrae such as hemivertebra, transitional vertebra, block vertebra, and butterfly vertebra—these defects cause deformity and instability of the vertebral canal and, in rare occasions, compression of the associated spinal cord or nerve roots.
- Sacrococcygeal dysgenesis—characterized by absence or partial development of the sacrocaudal spinal cord segments; often associated with additional malformations (e.g., spina bifida).
- Spina bifida—caused by failure of fusion of the vertebral arches; may be associated with protrusion of the spinal cord and meninges; other malformations often linked to this syndrome include spinal dysplasia, dysraphism, syringomyelia/hydromyelia, and myelodysplasia.
- Congenital spinal stenosis—can occur when vertebral malformations cause segmental or diffuse narrowing of the spinal cord; inborn errors in skeletal growth, hypertrophy of ligamentum flavum, and bony proliferation may also contribute to the stenosis.

SYSTEMS AFFECTED

Nervous—spinal cord; spinal nerve roots; and vertebral column.

GENETICS

- A genetic background, with unknown mode of inheritance, is suspected in most congenital spinal diseases.
- Sacrococcygeal dysgenesis—autosomal dominant.
- Thoracic hemivertebra of German shorthaired pointers—autosomal recessive.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species and Breed Predilections

- Malformation of the occipital bones, atlas, and axis—most common in small-breed dogs.
- Hemivertebra, transitional vertebra, block vertebra, and butterfly vertebra—most common in brachycephalic, “screw-tailed” breeds (e.g., French and English bulldog, pug, Boston terrier).
- Sacrococcygeal dysgenesis—Manx cat.

- Spina bifida—bulldog, Manx cat, and other screw-tailed breeds.
- Spinal dysraphism—Weimaraner.
- Congenital spinal stenosis—Doberman pinscher; chondrodystrophic breeds.

Mean Age and Range

- Often silent, vertebral malformation may cause clinical disease during the rapid growth of the animal (e.g., 5–9 months of age).
- Spinal cord anomalies cause clinical disease from birth on.

SIGNS

- Distortion of the spinal column—lordosis; kyphosis; and scoliosis in cases of vertebral malformations.
- Ataxia and paresis associated with spinal cord compression and trauma.
- Signs vary with spinal cord segment(s) involved.

CAUSES

Breed-related inherited defects are suspected for most congenital spinal abnormalities, although interactions between several genes and environmental factors (e.g., teratogenic compounds, nutritional deficiencies) are likely involved and would explain some of these complex pathologic changes.

RISK FACTORS

- Teratogenic compounds
- Toxins
- Nutritional deficiencies
- Stress



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Metabolic disease (e.g., storage diseases).
- Nutritional disease (e.g., hypovitaminosis and hypervitaminosis A, thiamine deficiency).
- Early onset inflammatory or infectious processes (e.g., viral, protozoal, and rarely bacterial).
- Toxin exposure (e.g., lead, organophosphates, hexachlorophene, organochlorine).
- Trauma.

CBC/BIOCHEMISTRY/URINALYSIS

Usually within normal limits.

OTHER LABORATORY TESTS

N/A

IMAGING

- Survey radiography—reveal vertebral malformation(s) and deviation of the spinal column.
- Myelography—to determine the level(s) of spinal cord compression; flexed and extended views may cause neurologic deterioration if instability present.
- CT myelography, and 3-D reconstructed imaging—to characterize bony abnormalities and associated spinal cord compression.

- MRI—sensitive modality to visualize abnormalities of spinal cord parenchyma, cauda equina, nerve roots and surroundings soft tissues.

DIAGNOSTIC PROCEDURES

Cerebrospinal fluid analysis to rule out infectious/inflammatory conditions.

PATHOLOGIC FINDINGS

- Multiple congenital malformations—often present concomitantly; pathologic changes reflect several disease processes.
- Acute compression of the spinal cord secondary to congenital malformation(s)—may result in spinal cord ischemia, hemorrhage, ballooning of the myelin sheath at the point of compression or trauma, and axonal swelling or loss; in chronic spinal cord compression, myelin degeneration, astrocytosis, and fibrosis are more prominent; at spinal sites, cranial and caudal to the primary injury, Wallerian degeneration can be observed in ascending or descending pathways, respectively.
- Chronic changes—may result from vertebral malformations secondary to bony proliferation, thickening of the joint capsule, hypertrophy of articular processes, and thickening of the ligaments surrounding the spinal cord.
- Atlantoaxial subluxation—congenital aplasia or hypoplasia of the odontoid process and surrounding ligaments.
- Occipitoatlantoaxial malformations—fusion of the atlas to the occipital bone (cats) and dorsal angulation of the dens (dogs).
- Occipital dysplasia—anomaly of the foramen magnum in which the occipital bone is incompletely formed and fibrous tissue membrane covers the caudal cerebellum.
- Sacrococcygeal dysgenesis—caudal vertebral aplasia or hypoplasia.
- Spina bifida—incomplete fusion of the dorsal vertebral arches where the meninges or spinal cord can protrude; most commonly seen in the caudal lumbar or sacral area; a dimple can be observed in few cases secondary to the lack of separation between the neuroectoderm and other ectodermal structures, leaving a small attachment between the spinal cord or meninges and the skin; often seen with myelodysplasia, central canal defects, syringomyelia or hydromyelia, and abnormal gray-matter differentiation.
- Spinal stenosis—pathologic changes observed within the spinal cord are most commonly chronic and are caused by focal or diffuse narrowing of the spinal canal.



TREATMENT

APPROPRIATE HEALTH CARE

- Depends on severity of neurologic deficits.
- Outpatient—if animal is ambulatory.

CONGENITAL SPINAL AND VERTEBRAL MALFORMATIONS (CONTINUED)

- Inpatient—if animal is non-ambulatory or requires emergency surgical treatment (e.g., for atlantoaxial subluxation).

NURSING CARE

- Restricted activity combined with physical therapy—may help neurologically disabled patients in the postoperative period; a cart may be necessary for severely affected patients.
- Management of urination—essential for cases in which disorders of micturition accompany the spinal injury.

ACTIVITY

Restricted, especially if vertebral subluxation is present.

DIET

Maintaining a lean body weight limits stress on the spinal column.

CLIENT EDUCATION

- Many congenital vertebral malformations are clinically silent.
- Perform a thorough workup when a congenital malformation results in neurologic abnormalities.
- Heritability is suspected and breeding must be performed only with serious consideration.
- Many neurologically affected dogs and cats left untreated are euthanized.
- Early surgical intervention often necessary to alleviate compression of the spinal cord and prevent further damage.

SURGICAL CONSIDERATIONS

- In general, surgical decompression is required when congenital malformation(s) cause narrowing of the spinal canal and compression of the spinal cord. In cases of chronic or diffuse spinal cord compression, improvement following surgery is minimal.
- Atlantoaxial subluxation—surgical ventral decompression combined with stabilization of the atlantoaxial joint with pins or screws is the treatment of choice.
- Spina bifida—meningoceles can be closed surgically to prevent leakage of cerebrospinal fluid and infections; surgery usually not attempted when the spinal cord parenchyma is involved.



MEDICATIONS

DRUG(S) OF CHOICE

Corticosteroids may be used in some cases, with questionable results.

CONTRAINDICATIONS

Avoid steroids with concomitant infections.

PRECAUTIONS

Steroids may cause ulcerations of the gastrointestinal tract and inhibit bone growth.

POSSIBLE INTERACTIONS

Steroids reduce immune response following vaccination.

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Frequent neurologic examinations—to monitor the progression of clinical signs in developing animals (e.g., every 4–6 weeks).
- Neuroimaging—repeat as needed.

PREVENTION/AVOIDANCE

Avoid breeding affected animals.

POSSIBLE COMPLICATIONS

- Depend on the type and severity of neurologic signs. In cases of subluxation of the atlantoaxial joint, acute death may occur.
- Acute paralysis can also be seen with vertebral subluxation, with further trauma and spinal cord compression.
- Implant failure may be observed after surgical decompression/stabilization.

EXPECTED COURSE AND PROGNOSIS

- Prognosis varies depending on the type of malformation, degree of spinal cord compression or injury, and surgical decompression or stabilization techniques.
- Vertebral malformation without compression of the spinal cord—prognosis is good.
- Atlantoaxial subluxation following surgical decompression or stabilization—prognosis is fair to good.
- Spinal cord compression treated surgically—prognosis is fair.
- Spina bifida associated with spinal cord malformation, chronic neurologic disease despite surgical treatment, and lower motor neuron incontinence—prognosis is poor.

- Medical treatment usually is insufficient to alleviate moderate to severe neurologic signs caused by spinal cord compression secondary to congenital vertebral malformation(s).



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Ataxia
- Atlantoaxial Instability
- Cervical Spondylomyelopathy (Wobbler Syndrome)
- Paralysis
- Spinal Dysraphism

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging

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Client Education Handout
available online

CONGESTIVE HEART FAILURE, LEFT-SIDED



BASICS

DEFINITION

Failure of the left side of the heart to advance blood at a sufficient rate to meet the metabolic needs of the patient or to prevent blood from pooling within the pulmonary venous circulation.

PATHOPHYSIOLOGY

- Low cardiac output causes lethargy, exercise intolerance, syncope, and prerenal azotemia.
- High hydrostatic pulmonary venous pressure causes leakage of fluid from pulmonary venous circulation into pulmonary interstitium and alveoli. When fluid leakage exceeds ability of lymphatics to drain the affected areas, pulmonary edema develops.

SYSTEMS Affected

- All organ systems can be affected by poor perfusion. • Respiratory increased rate and effort because of edema. • Cardiovascular.

GENETICS

Some congenital heart defects, cardiomyopathies, and valvular heart disease have a genetic basis in some breeds.

INCIDENCE/PREVALENCE

Common

GEOGRAPHIC DISTRIBUTION

Seen everywhere, but prevalence of causes varies with location.

SIGNALMENT

Species

Dog and cat

Breed Predilections

Varies with cause

Mean Age and Range

Varies with cause

Predominant Sex

Varies with cause

SIGNS

General Comments

Signs vary with underlying cause and species.

Historical Findings

- Weakness, lethargy, exercise intolerance.
- Coughing (dogs) and dyspnea (increased respiratory rate and effort); respiratory signs often worsen at night and can be partially relieved by assuming a standing, sternal, or “elbows abducted” position (orthopnea).
- Cats rarely cough from heart failure, and a client complaint of coughing should prompt a search for primary airway disease.

Physical Examination Findings

- Tachypnea. • Coughing, often soft in conjunction with tachypnea (dogs).
- Dyspnea and tachypnea. • Pulmonary crackles and wheezes. • Pale/gray/cyanotic mucous membranes. • Prolonged capillary refill time. • Possible murmur or gallop.
- Weak femoral pulses.

CAUSES

Pump (Muscle) Failure of Left Ventricle

- DCM • Trypanosomiasis (rare)
- Doxorubicin cardiotoxicity (dogs)
- Hypothyroidism (rare) • Hyperthyroidism (rarely causes pump failure; more commonly causes high output failure) • Pacing-induced cardiomyopathy (muscle failure caused by persistent pathologic supraventricular or ventricular tachyarrhythmia)

Pressure Overload of Left Heart

- Systemic hypertension (uncommon cause of heart failure in animals) • Subaortic stenosis
- Coarctation of the aorta (rare; Airedales predisposed) • Left ventricular tumors (rare)

Volume Overload of Left Heart

- Mitral valve endocardiosis (dogs) • Mitral valve dysplasia (cats and dogs) • PDA (dogs)
- Ventricular septal defect • Aortic valve insufficiency secondary to endocarditis (dogs)

Impediment to Filling of Left Heart

- Pericardial effusion with tamponade
- Restrictive pericarditis • Restrictive cardiomyopathy • Hypertrophic cardiomyopathy • Left atrial masses (e.g., tumors and thrombus) • Pulmonary thromboembolism • Mitral stenosis (rare)
- Cor triatriatum sinister (cats, rare)

Rhythm Disturbances

- Bradycardia (high-grade AV block)
- Tachycardia (e.g., atrial fibrillation, sustained supraventricular tachycardia, and ventricular tachycardia; see pacing-induced cardiomyopathy under pump failure)

RISK FACTORS

Conditions causing chronic high cardiac output (e.g., hyperthyroidism and anemia).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Must differentiate from other causes of coughing, dyspnea, and weakness.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC usually normal; maybe stress leukogram. • Mild-to-moderate liver enzyme elevation; bilirubin generally normal.
- Prerenal azotemia in some animals.

OTHER LABORATORY TESTS

- Thyroid disorders may be detected. • Serum NT-proBNP and troponin I concentrations are higher in animals with L-CHF than in normal animals.

IMAGING

Radiographic Findings

- Left heart and pulmonary veins enlarged.
- Pulmonary edema, often hilar, especially involving the right caudal lung lobe in acute edema of dog, but may be patchy, especially in cats; acute pulmonary edema may begin in right caudal lung lobe.

Echocardiography

- Findings vary markedly with cause, but left atrial enlargement a relatively consistent finding in cardiogenic pulmonary edema.
- Diagnostic test of choice for documenting congenital defects, cardiac masses, and pericardial effusion.

DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

- Atrial or ventricular arrhythmias.
- Evidence of left heart enlargement (e.g., wide P waves, tall and wide QRS complexes, and left axis orientation). • May be normal.

PATHOLOGIC FINDINGS

Cardiac findings vary with disease.



TREATMENT

APPROPRIATE HEALTH CARE

- Usually treat as outpatient unless animal is dyspneic or severely hypotensive. • Identify and correct underlying cause whenever possible. • Minimize handling of critically dyspneic animals. Stress can kill!

NURSING CARE

Oxygen in dyspneic patients.

ACTIVITY

Restrict activity when dyspneic or tachypneic.

DIET

Initiate moderately sodium-restricted diet. Severe sodium restriction is indicated in animals with advanced disease.

CLIENT EDUCATION

With few exceptions (e.g., animals with thyroid disorders, arrhythmias, nutritionally responsive heart disease), left congestive heart failure is not curable.

SURGICAL CONSIDERATIONS

- Surgical intervention, coil embolization, Amplatz occluder placement or balloon valvuloplasty may benefit selected patients with some forms of congenital and acquired valvular heart disease. Response to these interventions varies. • Pericardiocentesis in animals with pericardial effusion.



MEDICATIONS

DRUG(S) OF CHOICE

Diuretics

- Furosemide (1–2 mg/kg q8–24h) or other loop diuretic is the initial diuretic of choice; diuretics are indicated to reduce preload and remove pulmonary edema. Critically dyspneic animals often require high doses (4–8 mg/kg) given IV to stabilize; this dose can be repeated in 1 hour if animal is still severely dyspneic. An IV bolus of 0.66 mg/kg followed by a CRI of 0.66–1 mg/kg/h for 1–4 hours causes

CONGESTIVE HEART FAILURE, LEFT-SIDED

(CONTINUED)

greater diuresis than an equal dose divided into two IV boluses given 4 hours apart. Once edema resolves, taper to the lowest effective dosage. • Spironolactone (0.5–2 mg/kg PO q12–24h) increases survival in humans with CHF and is in current clinical trials in dogs. Use in combination with furosemide.

- Thiazide diuretics can be added to furosemide and spironolactone in refractory heart failure cases. • Torsemide may be useful as a substitute for furosemide in animals requiring chronic furosemide dosing in excess of 12 mg/kg (total daily dose).

ACE Inhibitors

- ACE inhibitor such as enalapril (0.5 mg/kg q12–24h) or benazepril (0.25–0.5 mg/kg q24h) indicated in most animals with L-CHF.
- ACE inhibitors improve survival and quality of life in dogs with L-CHF secondary to degenerative valve disease and DCM.

Positive Inotropes

- Pimobendan (0.25–0.3 mg/kg PO q12h) is a calcium channel sensitizer that dilates arteries and increases myocardial contractility. First-line agent in treating DCM or CHF due to chronic valve disease. Efficacy in cats with CHF is not known, but possibly beneficial.
- Dobutamine (dogs, 2.5–10 µg/kg/minute; cats, 0.5–5 µg/kg/minute) is a potent positive inotropic agent that may provide valuable short-term support of a heart failure patient with poor cardiac contractility. • Positive inotropes in general are potentially arrhythmogenic, monitor carefully.

Venodilators

- Nitroglycerin ointment (one-fourth inch/5 kg q6–8h) causes venodilation, lowering left atrial filling pressures. • Used for acute stabilization of patients with severe pulmonary edema and dyspnea. • May be useful in animals with chronic L-CHF; to avoid tolerance, use intermittently and with 12-hour dose-free interval between the last dose of 1 day and the first dose of the next.

Antiarrhythmic Agents

Treat arrhythmias if clinically indicated.

CONTRAINDICATIONS

Avoid vasodilators in patients with pericardial effusion or fixed outflow obstruction.

PRECAUTIONS

- ACE inhibitor and arterial dilators must be used with caution in patients with possible outflow obstruction. • Pulmonary hypertension, hypothyroidism and hypoxia increase risk for digoxin toxicity; hyperthyroidism diminishes effects of digoxin. • ACE inhibitor and digoxin—use cautiously in patients with renal disease. • Dobutamine—use cautiously in cats. • Spironolactone—may cause facial pruritis in cats.

POSSIBLE INTERACTIONS

- Combination of high-dose diuretics and ACE inhibitor may cause azotemia, especially in animals with severe sodium restriction.

- Combination diuretic therapy adds to risk of dehydration and electrolyte disturbances.
- Combination vasodilator therapy predisposes animal to hypotension.

ALTERNATIVE DRUG(S)

Arterial Dilators

- Hydralazine (0.5–2 mg/kg PO q12h; 0.5 mg/kg PO to start when added to ACEI) or amlodipine (0.05–0.2 mg/kg PO q24h) can be substituted for an ACE inhibitor in patients that do not tolerate the drug or have advanced renal failure. Monitor for hypotension and tachycardia; can be cautiously added to an ACE inhibitor in animals with refractory L-CHF.
- Nitroprusside (1–10 µg/kg/minute) is a potent arterial dilator that is usually reserved for short-term support of patients with life-threatening edema.

Digoxin

- Digoxin (dogs, 0.22 mg/m² q12h; cats, 0.01 mg/kg q48h) is used in animals with atrial fibrillation and myocardial failure (e.g., dilated cardiomyopathy). Commonly used in combination with diltiazem to control the rate of atrial fibrillation. • Digoxin is also indicated to treat dogs with refractory heart failure from either myocardial failure or volume loads. However, its use as a primary agent in myocardial failure has been replaced by pimobendan. • In humans, digoxin has no effect on mortality but decreases hospitalization due to heart failure.

Calcium Channel Blockers

- Diltiazem (0.5–1.5 mg/kg PO q8h) is frequently used in L-CHF patients for rate control in animals with supraventricular arrhythmias not controlled by digoxin and in cats with hypertrophic cardiomyopathy.

Beta-Blockers

- Atenolol and metoprolol are used for rate control in animals with supraventricular tachycardia, hypertrophic cardiomyopathy, and hyperthyroidism. • Used alone or with a class 1 antiarrhythmic drug for control of ventricular arrhythmias; these drugs depress contractility (negative inotropes), so use cautiously in patients with myocardial failure or active signs of CHF. • On basis of human studies, may enhance survival in animals with idiopathic DCM; treatment is best initiated under the guidance of a cardiologist, starting with very low dosage and gradually increasing the dosage. Carvedilol is sometimes used for this purpose, starting at 0.1 mg/kg q24h and titrating to 0.5 mg/kg q12h.

Nutritional Supplements

- Potassium and magnesium supplementation if deficiency is documented; use potassium supplements cautiously in animals receiving an ACE inhibitor or spironolactone.
- Taurine supplementation in cats with DCM and dogs with DCM and taurine deficiency (e.g., American cocker spaniels) • L-carnitine supplementation may help some dogs with

DCM. • Coenzyme Q₁₀ is of potential value based on the results in humans with DCM.



FOLLOW-UP

PATIENT MONITORING

- Monitor renal status, electrolytes, hydration, respiratory rate and effort, heart rate, body weight, and abdominal girth (dogs). • If azotemia develops, reduce the dosage of diuretic. If azotemia persists and the animal is also on an ACE inhibitor, reduce or discontinue the ACE inhibitor. Use digoxin with caution if azotemia develops. • Monitor ECG if arrhythmias are suspected. • Check digoxin concentration periodically. Recommended range is 0.5–1.5 ng/mL, 8–10 hours after a dose.

PREVENTION/AVOIDANCE

- Minimize stress, exercise, and sodium intake in patients with heart disease. • Prescribing an ACE inhibitor early in the course of heart disease in patients with DCM may slow the progression of heart disease and delay onset of CHF. Their role in asymptomatic animals with mitral valve disease remains controversial. Pimobendan delays the onset of CHF in Doberman pinschers, and in dogs with hemodynamically significant mitral valve regurgitation.

POSSIBLE COMPLICATIONS

- Syncope • Aortic thromboembolism (cats)
- Arrhythmias • Electrolyte imbalances
- Digoxin toxicity • Azotemia and renal failure

EXPECTED COURSE AND PROGNOSIS

Prognosis varies with underlying cause; cats and dogs that survive their initial episode of pulmonary edema and can be reliably medicated often survive months to more than a year with a good quality of life.



MISCELLANEOUS

AGE-RELATED FACTORS

- Congenital causes seen in young animals.
- Degenerative heart conditions and neoplasia generally seen in old animals.

SEE ALSO

- Pulmonary Edema, Non-cardiogenic

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- AV = atrioventricular • DCM = dilated cardiomyopathy • ECG = electrocardiogram
- L-CHF = left-sided congestive heart failure
- PDA = patent ductus arteriosus

Authors Francis W.K. Smith, Jr. and Bruce W. Keene



Client Education Handout
available online

CONGESTIVE HEART FAILURE, RIGHT-SIDED



BASICS

DEFINITION

Failure of the right side of the heart to advance blood at a sufficient rate to meet the metabolic needs of the patient or to prevent blood from pooling within the systemic venous circulation.

PATOPHYSIOLOGY

- High hydrostatic pressure leads to leakage of fluid from venous circulation into the pleural and peritoneal space and potentially into the pericardium and interstitium of peripheral tissue.
- When fluid leakage exceeds ability of lymphatics to drain the affected areas, pleural effusion, ascites, pericardial effusion, and peripheral edema develop.

SYSTEMS AFFECTED

All organ systems can be affected by either poor delivery of blood or the effects of passive congestion from backup of venous blood.

GENETICS

- Some congenital cardiac defects have a genetic basis in certain breeds.
- Arrhythmogenic right ventricular cardiomyopathy appears to have a genetic basis in boxer dogs.

INCIDENCE/PREVALENCE

Common

GEOGRAPHIC DISTRIBUTION

Syndrome seen everywhere, but prevalence of various causes varies with location.

SIGNALMENT

Species

Dog and cat

Breed Predilections

Varies with cause

Mean Age and Range

Varies with cause

Predominant Sex

Varies with cause

SIGNS

General Comments

- Signs vary with underlying cause and between species.
- Pleural effusion without ascites and hepatomegaly is rare in dogs with R-CHF.
- Ascites without pleural effusion is rare in cats with R-CHF.
- Small volume pericardial effusion without tamponade is relatively common in cats with R-CHF.
- Interstitial peripheral edema is a rare manifestation of R-CHF in both species.

Historical Findings

- Weakness
- Lethargy
- Exercise intolerance
- Abdominal distension
- Dyspnea, tachypnea

Physical Examination Findings

- Jugular venous distention
- Hepatojugular reflex
- Jugular pulse in some animals

- Hepatomegaly
- Ascites common in dogs and rare in cats with R-CHF
- Possible regurgitant murmur in tricuspid valve region or ejection murmur at left heart base (pulmonic stenosis)
- Muffled heart sounds if animal has pleural or pericardial effusion
- Weak femoral pulses
- Rapid, shallow respiration if animal has pleural effusion or severe ascites
- Peripheral edema (infrequent)

CAUSES

Pump (Myocardial) Failure of Right Ventricle

- Idiopathic dilated cardiomyopathy
- ARVC
- Hypertrophic cardiomyopathy (cats)
- Restrictive cardiomyopathy (cats)
- Trypanosomiasis
- Doxorubicin cardiotoxicity
- Chronic hyperthyroidism

Volume Overload of Right Ventricle

- Chronic AV valve (mitral \pm tricuspid) insufficiency caused by endocardiosis
- Tricuspid valve dysplasia

Pressure Overload of Right Ventricle

- Heartworm disease
- Chronic obstructive pulmonary disease with pulmonary hypertension
- Pulmonary thromboembolism
- Pulmonic stenosis
- Tetralogy of Fallot
- Right ventricular tumors
- Primary pulmonary hypertension

Impediment to Right Ventricular Filling

- Pericardial effusion (tamponade)
- Constrictive/restrictive pericarditis
- Right atrial or caval masses
- Tricuspid stenosis
- Cor triatriatum dexter

Rhythm Disturbances

- Bradycardia, generally complete atrioventricular block
- Tachyarrhythmias, generally sustained supraventricular tachycardia

RISK FACTORS

- No heartworm prophylaxis
- Offspring of animal with right-sided congenital cardiac defect
- Conditions that augment demand for cardiac output (e.g., hyperthyroidism, anemia, pregnancy)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Must differentiate from other causes of pleural effusion and ascites; generally requires a complete diagnostic work-up that includes CBC, biochemistry profile, heartworm test, thoracentesis or abdominocentesis with fluid analysis and cytologic examination, and, sometimes, thoracic and abdominal ultrasound.
- Animals with ascites or pleural effusion due to heart failure should have jugular venous distension.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC usually normal; animals with heartworm disease may have eosinophilia.

- Mild to moderately high ALT, AST, and ALP because of passive congestion of the liver; bilirubin generally normal.
- Prerenal azotemia in some animals.

OTHER LABORATORY TESTS

Heartworm test may be positive.

IMAGING

Thoracic Radiographic Findings

- Right heart enlargement in some animals
- Dilated caudal vena cava (diameter greater than the length of the vertebra directly above the heart)
- Pleural effusion (especially cats)
- Hepatosplenomegaly and possible ascites (especially dogs)

Echocardiography

- Findings vary with underlying cause.
- Especially useful for documenting congenital defect, cardiac mass, and pericardial effusion.
- Abdominal ultrasound reveals hepatomegaly with hepatic vein dilation, flow reversal in the hepatic veins (Doppler) and, possibly, ascites.

DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

- Small ($< 1 \text{ mV}$) QRS complexes in all frontal axis leads if animal has pericardial or pleural effusion.
- Electrical alternans or elevated ST segment in animal with pericardial effusion.
- Evidence of right heart enlargement (e.g., tall [$> 0.4 \text{ mV}$] P waves in lead II, deep S waves in leads I, II, aVF, and right axis deviation).
- Atrial or ventricular arrhythmias.
- ECG may be normal.

Abdominocentesis

Analysis of ascitic fluid in patients with R-CHF generally reveals modified transudate with a total protein $> 2.5 \text{ mg/dL}$.

Thoracentesis

- Cats with pleural effusion associated with R-CHF may have transudate, modified transudate, or chylous effusion.
- Dogs with pleural effusion and R-CHF may have transudate or modified transudate.

Central Venous Pressure

Central venous pressure is high ($> 9 \text{ cmH}_2\text{O}$) or rises dramatically to that level and remains elevated for more than an hour following a fluid bolus (e.g., 5–10 mL/kg IV).

PATHOLOGIC FINDINGS

- Cardiac findings vary with disease.
- Hepatomegaly in animals with centrilobular necrosis (chronic condition).



TREATMENT

APPROPRIATE HEALTH CARE

Most animals treated as outpatients unless dyspneic or collapsed (e.g., significant pleural or pericardial effusion).

CONGESTIVE HEART FAILURE, RIGHT-SIDED

(CONTINUED)

NURSING CARE

Thoracentesis and abdominocentesis may be required periodically for patients no longer responsive to medical management or for those with severe dyspnea due to pleural effusion or ascites.

ACTIVITY

Restrict activity

DIET

Restrict sodium moderately; severe sodium restriction is indicated for animals with advanced disease.

CLIENT EDUCATION

- With few exceptions (e.g., in heartworm disease, arrhythmias, hyperthyroidism, and idiopathic pericardial effusion), R-CHF is not curable.
- Most patients improve with initial treatment but often have recurrent failure.

SURGICAL CONSIDERATIONS

- Surgical intervention or balloon valvuloplasty is indicated to treat certain congenital defects such as pulmonic stenosis or cor triatriatum dexter and Amplatz occluder placement for morphologically appropriate atrial septal defects.
- Pericardiocentesis or pericardectomy is done if animal has pericardial effusion.
- Removal of heartworms from the heart via the jugular vein in dogs with caval syndrome.



MEDICATIONS

DRUG(S) OF CHOICE

Drugs should be administered only after a definitive diagnosis is made.

Diuretics

- Furosemide (1–2 mg/kg q8–24h) or another loop diuretic is the initial diuretic of choice. Diuretics are indicated to remove excess fluid accumulation.
- Spironolactone (2 mg/kg PO q12–24h) increases survival in humans with heart failure. Use in combination with furosemide.

Vasodilators

- ACE inhibitors such as enalapril (0.5 mg/kg q12–24h) or benazepril (0.25–0.5 mg/kg q24h) are helpful in DCM and chronic AV valve insufficiency.
- Sildenafil (0.5–1 mg/kg PO q12h up to 2–3 mg/kg q8h) may be beneficial in the setting of pulmonary hypertension.

Pimobendan

- Calcium sensitizer that acts as an inodilator, causing arterial vasodilation and increases myocardial contractility.
- Especially useful in myocardial failure.
- Dose—0.25–0.3 mg/kg PO q12h.

Digoxin

- Digoxin (dogs, 0.22 mg/m² q12h; cats, 0.01 mg/kg q48 h) is used in animals with myocardial failure (e.g., dilated cardiomyopathy) and atrial fibrillation.
- Digoxin is also indicated in animals with refractory CHF that have supraventricular arrhythmias (e.g., sinus tachycardia, atrial fibrillation, and atrial or junctional tachycardia).

CONTRAINDICATIONS

- Avoid diuretics in patients with pericardial effusion/tamponade.
- Avoid vasodilators in patients with pericardial effusion or fixed outflow obstructions.

PRECAUTIONS

- ACE inhibitors and arterial dilators must be used with caution in patients with possible outflow obstructions.
- Pulmonary hypertension, hypothyroidism and hypoxia increase risk for digoxin toxicity; hyperthyroidism diminishes effects of digoxin.
- ACE inhibitor and digoxin—use cautiously in patients with renal disease.
- Dobutamine—use cautiously in cats.
- Spironolactone—may cause facial pruritis in cats.

POSSIBLE INTERACTIONS

- Combination of high-dose diuretics and ACE inhibitor may alter renal perfusion and cause azotemia.
- Combination diuretic therapy promotes risk of dehydration and electrolyte disturbances.

ALTERNATIVE DRUG(S)

- Patients unresponsive to furosemide, spironolactone, vasodilator, pimobendan and digoxin (if indicated) may benefit from triple diuretic therapy by adding a thiazide diuretic, or substitution of torsemide for furosemide, generally at 0.1–0.2 mg of torsemide for each 1 mg of furosemide previously administered.
- Potassium and magnesium supplementation if deficiency documented; use potassium supplements cautiously in animals receiving ACE inhibitor or spironolactone.
- Treat arrhythmias if clinically indicated.
- Taurine supplementation in cats with DCM and dogs with DCM and taurine deficiency.
- Carnitine supplementation may help some dogs with DCM (e.g., cocker spaniels and boxers).



FOLLOW-UP

PATIENT MONITORING

- Monitor renal status, electrolytes, hydration, respiratory rate and effort, body weight, and abdominal girth (dogs).
- If

azotemia develops, reduce the diuretic dosage. If azotemia persists and the animal is also on an ACE inhibitor, reduce or discontinue this drug. If azotemia develops, reduce the digoxin dosage to avoid toxicity.

- Monitor ECG periodically to detect arrhythmias.
- Monitor digoxin concentrations. Normal values are 0.5–1.5 ng/mL for a serum sample obtained 8–10 hours after a dose is administered.

POSSIBLE COMPLICATIONS

- Pulmonary thromboembolism
- Arrhythmias
- Electrolyte imbalances
- Digoxin toxicity
- Azotemia and renal failure

EXPECTED COURSE AND PROGNOSIS

Prognosis varies with underlying cause.



MISCELLANEOUS

AGE-RELATED FACTORS

- Congenital causes seen in young animals.
- Degenerative heart conditions and neoplasia generally seen in old animals.

SEE ALSO

- Ascites
- Chylothorax
- Chapters on diseases causing R-CHF
- Pleural Effusion

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- ARVC = arrhythmogenic right ventricular cardiomyopathy
- AST = aspartate aminotransferase
- AV = atrioventricular
- DCM = dilated cardiomyopathy
- ECG = electrocardiogram
- L-CHF = left-sided congestive heart failure
- R-CHF = right-sided congestive heart failure

Suggested Reading

Stickland KN. Pathophysiology and therapy of heart failure. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., *Manual of Canine and Feline Cardiology*, 5th ed. St. Louis, MO: Saunders Elsevier, 2015 (in press).

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Client Education Handout
available online

CONJUNCTIVITIS—CATS

C



BASICS

DEFINITION

Inflammation of the conjunctiva, the vascularized mucous membrane that covers the anterior portion of the sclera (bulbar conjunctiva) and lines the eyelids (palpebral conjunctiva) and third eyelid.

PATHOPHYSIOLOGY

May be primary or secondary to adnexal or ocular disease.

SYSTEMS AFFECTED

Ophthalmic—ocular with possible eyelid involvement.

GENETICS

N/A

INCIDENCE/PREVALENCE

Common

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Cat

Breed Predilections

Infectious—purebred cats may be predisposed.

Mean Age and Range

Infectious—commonly affects young animals.

Predominant Sex

N/A

SIGNS

- Blepharospasm • Conjunctival hyperemia
- Ocular discharge—serous, mucoid, or mucopurulent • Chemosis • Conjunctival follicles • Upper respiratory infection—possible with infectious etiologies

CAUSES

Viral

- FHV—most common infectious cause; only one that leads to corneal changes (e.g., dendritic or geographic ulcers).
- Calicivirus—may cause conjunctival ulcerations.

Bacterial

- *Chlamydophila felis*—chemosis is a common clinical sign.
- *Mycoplasma* spp.—may represent overgrowth of normal flora.
- Conjunctivitis neonatorum—accumulation of exudates under closed eyelids prior to natural opening; bacterial or viral component (see Ophthalmia Neonatorum).

Immune-Mediated

- Eosinophilic • Lipogranulomatous
- Allergic • Related to systemic immune-mediated diseases

Trauma or Environmental Causes

- Conjunctival foreign body • Irritation from dust, smoke, chemicals, or ophthalmic medications

Secondary to Adnexal Disease

- May develop KCS as a result of scarring (see Keratoconjunctivitis Sicca).
- Eyelid diseases (e.g., entropion, trichiasis, distichia, or eyelid agenesis)—cause frictional irritation or exposure.
- Dacryocystitis or nasolacrimal system outflow obstruction.

Secondary to Other Ocular Diseases

- Ulcerative keratitis • Corneal sequestrum

RISK FACTORS

Stress or immune system compromise (FHV)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Must distinguish primary conjunctivitis from secondary conjunctival hyperemia (see Red Eye).
- Thorough systematic ophthalmic exam allows rule-out of other potential diseases (e.g., ulcers, uveitis, glaucoma, orbital disease); assess pupil size and symmetry, look for aqueous flare, perform IOP and fluorescein staining.
- Deeper, darker, more linear and immobile blood vessel injection indicates episcleral vasculature congested due to intraocular disease.
- Conjunctival mass biopsy will differentiate neoplasia (lymphoma and squamous cell carcinoma most common).

CBC/BIOCHEMISTRY/URINALYSIS

Normal, except with systemic disease

OTHER LABORATORY TESTS

Infectious—consider serologic tests for FeLV and FIV; rule out underlying immunocompromise.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Thorough adnexal examination—rule out eyelid abnormalities and foreign bodies under eyelids or third eyelid.
- Complete ophthalmic examination—rule out other ocular diseases (e.g., uveitis and glaucoma).
- Fluorescein stain—assess for corneal ulceration or dendritic lesions (FHV) and observe nares for stain passage to indicate nasolacrimal system patency.
- Nasolacrimal flush—considered to rule out dacryocystitis or nasolacrimal system obstruction.
- Bacterial culture if initial treatment is unsuccessful; specimen is taken before anything is placed in the eye (e.g., topical anesthetic, fluorescein, flush) to prevent inhibition or dilution of bacterial growth.
- Schirmer tear test—if ocular surface appears visibly dry; performed before anything is placed in the eye.
- Conjunctival cytology—may reveal a cause (rare); eosinophils diagnose eosinophilic conjunctivitis; may see degenerate neutrophils and intracytoplasmic bacteria, which indicate bacterial infection; may see intracytoplasmic inclusion bodies with chlamydial or mycoplasmal infection; rarely see intranuclear

FHV inclusions.

- Conjunctival biopsy—"snip biopsy" may be useful with mass lesions and immune-mediated disease or chronic disease.
- PCR testing for Chlamydia or FHV.
- Virus isolation or IFA testing for FHV; false-positive result if fluorescein staining is done before IFA testing.
- Serologic test for FHV antibodies—not useful due to widespread exposure and vaccination.

PATHOLOGIC FINDINGS

- Biopsy—typical signs of inflammation (e.g., neutrophils and lymphocytes); possibly infectious agents.
- Histopathology of mass lesions may reveal neoplasia (e.g., squamous cell carcinoma and lymphoma).



TREATMENT

APPROPRIATE HEALTH CARE

- Primary—often outpatient.
- Secondary to other diseases (e.g., ulcerative keratitis, uveitis, glaucoma)—may need hospitalization to address a severe underlying ophthalmic issue.

NURSING CARE

Irritant induced conjunctivitis—flush ocular surfaces and remove foreign body if observed.

ACTIVITY

- No restriction for most patients.
- Suspected contact irritant or acute allergic disease—prevent contact with the offending agent.
- Suspected FHV—minimize stress.
- Do not expose patients with infectious disease to susceptible animals.

DIET

- No change for most patients.
- Suspected underlying skin disease and/or food allergy—food elimination diet recommended.

CLIENT EDUCATION

- When solutions and ointments are prescribed, instruct the client to use the solution(s) before the ointment(s) and wait at least 5 minutes between treatments.
- If copious discharge is noted, instruct the client to clean the eyes before giving medication.
- Instruct the client to call for instructions if the condition fails to improve or worsens, which indicates that the condition may not be responsive, may be progressing, or that the animal may be having an adverse reaction to a prescribed medication.

SURGICAL CONSIDERATIONS

- Lipogranulomatous conjunctivitis—surgical incision and curettage of glandular material and inflammatory infiltrates.
- Entropion, distichia, or other eyelid disease—perform temporary or permanent surgery depending on the findings, signalment and history.
- Nasolacrimal duct obstruction—difficult; treatment often not recommended (see Epiphora).
- Conjunctival neoplasia—depending on tumor type and extent of involvement may involve local excision and

CONJUNCTIVITIS—CATS

(CONTINUED)

adjunctive therapy (β -irradiation, cryotherapy), enucleation, or exenteration.

- Symblepharon—conjunctival adhesions may require surgical resection once active infection is controlled.
- Corneal sequestration—keratectomy often recommended (see Corneal Sequestrum).



MEDICATIONS

DRUG(S) OF CHOICE

Herpetic

- Condition usually mild and self-limiting.
- Antiviral treatment—indicated for severe intractable conjunctivitis, herpetic keratitis, and before keratectomy for corneal sequestra suspected to be related to FHV; for all antivirals treat 2 weeks past the resolution of clinical signs.
- 0.5% cidofovir solution (available from compounding pharmacies)—topical q12h.
- 0.1% idoxuridine solution or 0.5% ointment (available from compounding pharmacies)—topical q4h.
- Vidarabine 3% ointment—topical q4h.
- Trifluridine 1% solution—topical q4h; potentially irritating.
- Oral famciclovir found to be effective and safe for use in cats. Dosage is controversial—most commonly used as famciclovir 250 mg tablet—1/2 tab PO q12h for 2–3 weeks; however, used without complication at doses up to 90 mg/kg PO q8h.
- Lysine 500 mg PO q12h for adult cat (250 mg PO q12h for kitten).

Chlamydial or Mycoplasmal

- Tetracycline, erythromycin or chloramphenicol ophthalmic ointment—topically q6–8h; continue for several days past resolution of all clinical signs; recurrence or reinfection common.
- Topical ciprofloxacin ophthalmic solution q6–8h as an alternative to ophthalmic ointment.
- Doxycycline 10 mg/kg PO q24h for 3–4 weeks may be superior to or used along with topical ophthalmic treatment.
- Based on bacterial culture and sensitivity results.

Neonatal

Carefully open the eyelid margins (medial to temporal), establish drainage, and treat with topical antibiotic ointment q6–8h and an antiviral for suspected FHV.

Eosinophilic

- Topical corticosteroid—0.1% dexamethasone sodium

phosphate q6–8h generally effective; taper gradually to the lowest effective dose or transition to cyclosporine.

- Cyclosporine 0.2% ointment or 1–2% compounded solution,—therapy q8–24h.
- Oral megestrol acetate—may help resistant condition but rarely used given possible systemic side effects.

CONTRAINDICATIONS

- Topical corticosteroids—avoid with known or suspected infectious conjunctivitis; may result in FHV recrudescence and predispose to corneal sequestrum formation; never use if corneal ulceration is noted.
- Valacyclovir should never be used in cats.

PRECAUTIONS

- Topical medications may be irritating.
- Monitor all patients treated with topical corticosteroids for signs of corneal ulceration; discontinue agent immediately if corneal ulceration occurs.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Other corticosteroids—1% prednisolone acetate; betamethasone.



FOLLOW-UP

PATIENT MONITORING

Recheck shortly after beginning treatment (at 5 days); then in 2 weeks or as needed.

PREVENTION/AVOIDANCE

- Treat any underlying disease that may be exacerbating the conjunctivitis.
- Minimize stress for patients with herpetic disease.
- Isolate patients with infectious conjunctivitis to prevent spread.
- Prevent reexposure to infectious sources.
- Vaccination recommended; infection is still possible if the cat was exposed to an infectious agent before being vaccinated (e.g., FHV infection from an infected queen).

POSSIBLE COMPLICATIONS

- Corneal sequestration (black lesion representing necrotic cornea and possibly associated with FHV)—usually requires surgical keratectomy.
- Symblepharon (adhesions between the conjunctival surfaces \pm cornea)—may require surgical intervention.
- KCS—most likely from chronic FHV.

EXPECTED COURSE AND PROGNOSIS

- FHV—most patients become chronic carriers; episodes less common as patient matures; may see repeated exacerbations; tend to note more severe clinical signs at times of stress or immunocompromise.
- Bacterial conjunctivitis—usually resolves with appropriate administration of antibiotic.
- Immune-mediated diseases (e.g., eosinophilic)—control not cure; may require chronic treatment at the lowest level possible.
- If an underlying disease is found (e.g., KCS, entropion), resolution may depend on appropriate treatment and resolution of the disease.



MISCELLANEOUS

ASSOCIATED CONDITIONS

FeLV and FIV—may predispose patient to the chronic carrier state of FHV conjunctivitis.

AGE-RELATED FACTORS

FHV—tends to be more severe in kittens and in old cats with waning immunity.

ZOONOTIC POTENTIAL

Chlamydophila felis—low

PREGNANCY/FERTILITY/BREEDING

- Use topical and systemic medications with caution, if at all, in pregnant animals.

SEE ALSO

- Keratoconjunctivitis Sicca • Red Eye
- Ophthalmia Neonatorum • Corneal Sequestrum

ABBREVIATIONS

- FeLV = feline leukemia virus
- FHV = feline herpesvirus
- FIV = feline immunodeficiency virus
- IFA = immunofluorescent antibody test
- KCS = keratoconjunctivitis sicca
- PCR = polymerase chain reaction

Suggested Reading

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Client Education Handout
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CONJUNCTIVITIS—DOGS

C



BASICS

DEFINITION

Inflammation of the conjunctiva, the vascularized mucous membrane that covers the anterior portion of the sclera (bulbar conjunctiva) and lines the eyelids (palpebral conjunctiva) and third eyelid.

PATHOPHYSIOLOGY

- Primary—allergic; infectious; environmental.
- Secondary to other ocular disease—KCS, entropion, distichiasis.

SYSTEMS AFFECTED

Ophthalmic—ocular with possible eyelid involvement.

GENETICS

N/A

INCIDENCE/PREVALENCE

Common

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog

Breed Predilection

Breeds predisposed to allergic or immune-mediated skin diseases (e.g., atopy) tend to have more problems with allergic conjunctivitis or KCS.

Mean Age and Range

N/A

Predominant Sex

None

SIGNS

- Blepharospasm
- Conjunctival hyperemia
- Ocular discharge—serous, mucoid, or mucopurulent
- Chemosis
- Follicle formation on posterior third eyelid surface
- Enophthalmos and third eyelid elevation

CAUSES

Infectious

- Bacterial—rare as a primary condition, most commonly secondary to KCS; conjunctivitis neonatorum involves accumulation of exudates under closed eyelids prior to natural opening.
- Viral—canine herpes virus-1, canine distemper virus, or canine adenovirus-2.
- Parasitic—Leishmania, Onchocerca, or Thelazia.
- Conjunctival manifestation of systemic infectious disease.

Immune-Mediated

- Allergic—especially in atopic patients.
- Follicular conjunctivitis—especially in dogs younger than 18 months, secondary to chronic antigenic stimulation.
- Lymphocytic/plasmacytic conjunctivitis—especially in German shepherds with or

without chronic superficial keratitis (pannus).

- Related to systemic immune-mediated diseases (e.g., pemphigus).

Trauma or Environmental Causes

- Conjunctival foreign body
- Irritation from dust, smoke, chemicals, or ophthalmic medications

Other

Ligneous conjunctivitis—rare, young female Dobermanns may be predisposed.

Secondary to Adnexal Disease

- Aqueous tear film deficiency (see Keratoconjunctivitis Sicca) or qualitative tear deficiency.
- Eyelid diseases—entropion, ectropion, medial canthal pocket syndrome, eyelid mass.
- Hair or eyelash disorders—trichiasis, distichiasis, ectopic cilia.
- Exposure—facial nerve paralysis, lagophthalmos.
- Dacryocystitis or nasolacrimal system outflow obstruction (e.g., obstructed duct or imperforate punctum).

Referred Inflammation from Other Ocular Diseases

- Ulcerative keratitis
- Nodular episcleritis
- Anterior uveitis
- Glaucoma

RISK FACTORS

Atopy and KCS



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Must distinguish primary conjunctivitis from secondary conjunctival hyperemia or referred inflammation.
- Thorough systematic ophthalmic exam allows rule out of other potential diseases (e.g., KCS, ulcers, uveitis, glaucoma, orbital disease); assess pupil size and symmetry, look for aqueous flare, attempt globe retropulsion, perform Schirmer tear test, IOP and fluorescein staining.
- Deeper, darker, more linear and immobile blood vessel injection indicates episcleral vasculature congested due to episcleritis or intraocular disease.
- Mass biopsy will differentiate conjunctival neoplasia (rare: melanoma, hemangioma, hemangiosarcoma, lymphoma, papilloma, mast cell tumor) or nodular episcleritis.

CBC/BIOCHEMISTRY/URINALYSIS

Normal, except with systemic disease.

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Thorough adnexal examination—rule out facial nerve paralysis, lagophthalmos, eyelid abnormalities, hair or eyelash disorders, and foreign bodies in cul-de-sacs or under third

eyelid.

- Schirmer tear test—measures aqueous tears to diagnose or rule out KCS; perform before anything else is placed in the eye.
- Fluorescein stain—no corneal retention rules out ulcerative keratitis; stain flow to nares rules out nasolacrimal disease.
- Tear film breakup time—assesses tear film stability to rule out qualitative tear deficiency.

- Intraocular pressures—rule out glaucoma.
- Globe retropulsion—rule out orbital disease.
- Examine for signs of anterior uveitis (e.g., hypotony, aqueous flare, and miosis) or other intraocular disease (e.g., cataracts, lens luxation).
- Consider a nasolacrimal duct flush—rule out nasolacrimal disease if fluorescein stain did not pass to nares.
- Aerobic bacterial culture and sensitivity—consider with mucopurulent discharge if KCS has been ruled out; ideally, specimens are taken before anything is placed in the eye (e.g., topical anesthetic, fluorescein, and flush) to prevent inhibition or dilution of bacterial growth.
- Conjunctival cytology—may reveal a cause (rare); lymphocytes and plasma cells diagnostic for lymphocytic/plasmacytic conjunctivitis; eosinophils may help diagnose allergic conjunctivitis; may see degenerate neutrophils and intracytoplasmic bacteria indicating bacterial infection; rarely see distemper virus intracytoplasmic inclusion bodies.
- Conjunctival biopsy—may be useful with mass lesions and nodular episcleritis or chronic disease for which a definitive diagnosis has not been made.
- Intradermal skin testing—may be helpful with suspected allergic conjunctivitis.

PATHOLOGIC FINDINGS

- Biopsy—typical signs of inflammation (e.g., neutrophils and lymphocytes); may note infectious agents.
- Histopathology of mass lesions may reveal neoplasia or nodular episcleritis.
- Ligneous conjunctivitis—thick amorphous eosinophilic hyaline-like material.



TREATMENT

APPROPRIATE HEALTH CARE

- Primary—often outpatient.
- Secondary to other diseases (e.g., ulcerative keratitis, uveitis, glaucoma, lens luxation)—may require hospitalization to address a severe underlying ophthalmic issue.

NURSING CARE

- Irritant induced conjunctivitis—flush ocular surfaces and remove foreign body if observed.
- Allergic or follicular conjunctivitis— instruct the client to apply a viscous artificial tear gel to both eyes before the patient is active outdoors (q8–12h) then flush the ocular surface with eye wash when returning indoors to remove “trapped” allergens.

CONJUNCTIVITIS—DOGS

(CONTINUED)

- Secondary to ectropion or medial canthal pocket syndrome— instruct the client to flush the ocular surface with eye wash daily to remove dust, dirt, or other particulate matter that collects ventrally.

ACTIVITY

- No restriction for most patients.
- Suspected contact irritant or acute allergic disease— prevent contact with the offending agent.
- Do not expose patients with infectious viral disease to susceptible animals.

DIET

- No change for most patients.
- Suspected underlying skin disease and/or food allergy— food elimination diet recommended.

CLIENT EDUCATION

- When solutions and ointments are prescribed, instruct the client to use the solution(s) before the ointment(s) and wait at least 5 minutes between treatments.
- If copious discharge is noted, instruct the client to clean the eyes before giving medication.
- Instruct the client to call for instructions if the condition fails to improve or worsens, which indicates that the condition may not be responsive, may be progressing, or that the animal may be having an adverse reaction to a prescribed medication.
- Inform the client that an Elizabethan collar should be placed on the patient if self-trauma occurs.

SURGICAL CONSIDERATIONS

- Follicular conjunctivitis—if follicles are large and unresponsive to medical care, consider follicle debridement.
- Entropion, distichia, or other eyelid disease—perform temporary or permanent surgery depending on the findings, signalment and history.
- Nasolacrimal duct obstruction—if repeated flushing attempts at weekly intervals along with medical therapy is unsuccessful consider contrast study and surgery (see Epiphora).
- Conjunctival neoplasia—depending on tumor type and extent of involvement may involve local excision and adjunctive therapy (β -irradiation, cryotherapy), enucleation, or exenteration.



MEDICATIONS

DRUG(S) OF CHOICE

Bacterial

- Initial treatment— broad-spectrum topical triple antibiotic q6–8h continuing several days past the resolution of clinical signs.
- Based on bacterial culture and sensitivity results if refractory to initial treatment.
- Systemic antibiotic (e.g., cephalosporin)— occasionally indicated, especially for more generalized disease (e.g., pyoderma).

Neonatal

Carefully open the eyelid margins (medial to lateral), establish drainage, and treat with topical antibiotic ointment q6–8h.

Herpetic

- Condition usually mild and self-limiting.
- Antiviral treatment—indicated for severe intractable canine herpes virus-1 conjunctivitis or herpetic keratitis.
- 0.5% cidofovir solution (available from compounding pharmacies) — topical q12h.
- Trifluridine 1% solution—topical q4h.
- 0.1% idoxuridine solution (available from compounding pharmacies)—topical q4h.

Immune-Mediated

- Depends on severity.
- Allergic and follicular conjunctivitis— attempt “Nursing Care” first with viscous artificial tear gel lubricants and ocular flushing q8–12h; if nonresponsive consider antihistamine eye drops (e.g., ketotifen) q8–12h or topical corticosteroid (e.g., dexamethasone) q8–12h.
- Lymphocytic/plasmacytic conjunctivitis— 0.1% dexamethasone q8h then taper gradually to lowest effect dose; could attempt transition to cyclosporine 0.2% ointment or 1–2% compounded solution q12–24h.
- Treatment of any underlying disease (e.g., atopy) often improves clinical signs of allergic conjunctivitis.

Tear Deficiencies

- Aqueous tear film deficiency (see Keratoconjunctivitis Sicca)
- Qualitative tear deficiency—cyclosporine 0.2% ointment or 1–2% compounded solution q12h and viscous artificial tear lubricants q6–12h.

CONTRAINdications

Topical corticosteroids— avoid if corneal ulceration is present, patient is at high risk for ulceration (e.g., entropion, lagophthalmos, severe KCS), and with known or suspected infectious conjunctivitis.

PRECAUTIONS

- Topical medications may be irritating.
- Topical corticosteroids—monitor all patients carefully for signs of corneal ulceration; discontinue agent immediately if corneal ulceration occurs.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Other corticosteroids—1% prednisolone acetate; betamethasone; hydrocortisone.



FOLLOW-UP

PATIENT MONITORING

Recheck shortly after beginning treatment (at 5 days); then recheck in 2 weeks or as needed.

PREVENTION/AVOIDANCE

Treat any underlying disease that may be exacerbating the conjunctivitis (e.g., KCS, allergic or immune-mediated skin disease).

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

- Good prognosis when underlying cause identified and treated (e.g., KCS, adnexal disease, eyelash disorder).
- Bacterial—usually resolves with appropriate antibiotics; may depend on resolution of underlying disease (e.g., KCS).
- Allergic or follicular—nursing care or medical treatment may be needed during peak allergy times.
- Lymphocytic/plasmacytic—tend to be controlled and not cured; may require chronic treatment at the lowest level possible.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Atopy • Pyoderma

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Use topical and systemic medications with caution, if at all, in pregnant animals.

SEE ALSO

- Epiphora • Keratoconjunctivitis Sicca • Red Eye

ABBREVIATION

KCS = keratoconjunctivitis sicca

Suggested Reading

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Client Education Handout
available online

CONSTIPATION AND OBSTIPATION



BASICS

DEFINITION

- Constipation—infrequent, incomplete, or difficult defecation with passage of hard or dry feces.
- Obstipation—intractable constipation caused by prolonged retention of hard, dry feces; defecation is impossible in the obstipated patient.

PATHOPHYSIOLOGY

- Constipation can develop with any disease that impairs the passage of feces through the colon. Potential causes include congenital vertebral malformation, spinal cord disease, pelvic canal narrowing (trauma), rectal mass lesions causing obstruction, and perianal disease causing painful defecation. Often in cats, no underlying etiology can be identified.
- Delayed fecal transit allows removal of additional salt and water, producing drier feces. Clinical signs are attributable to dehydration and potential toxemia resulting from fecal retention.
- Peristaltic contractions may increase during constipation, but eventually motility diminishes because of smooth muscle degeneration secondary to chronic overdistension.

SYSTEMS AFFECTED

Gastrointestinal

GENETICS

N/A

INCIDENCE/PREVALENCE

Common clinical problem in older cats; less common in dogs.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

- Dog and cat
- More common in cat

Breed Predilections

N/A

Mean Age and Range

N/A

Predominant Sex

N/A

SIGNS

Historical Findings

- Straining to defecate with small or no fecal volume
- Hard, dry feces
- Infrequent defecation
- Small amount of liquid, mucoid stool—sometimes with blood present produced after prolonged tenesmus
- Occasional vomiting, inappetence, and/or lethargy

Physical Examination Findings

- Colon filled with hard feces. Severe impaction may cause abdominal distention.
- Other findings depend on the underlying cause.
- Rectal examination may reveal mass, stricture, perineal hernia, anal sac disease, foreign body or material, prostatic enlargement, or narrowed pelvic canal.

CAUSES

Dietary

- Bones
- Hair
- Foreign material
- Excessive fiber
- Inadequate water intake

Environmental

- Lack of exercise
- Change of environment—hospitalization, dirty litter box
- Inability to ambulate

Drugs

- Anticholinergics
- Antihistamines
- Opioids
- Barium sulfate
- Sucralfate
- Antacids
- Kaopectolin
- Iron supplements
- Diuretics

Painful Defecation (Dyschezia)

- Anorectal disease—anal sacculitis, anal sac abscess, perianal fistula, anal stricture, anal spasm, rectal foreign body, rectal prolapse, proctitis.
- Trauma—fractured pelvis, fractured limb, dislocated hip, perianal bite wound or laceration, perineal abscess.

Mechanical Obstruction

- Extraluminal—healed pelvic fracture with narrowed pelvic canal, prostatic hypertrophy, prostatitis, prostatic neoplasia, intrapelvic neoplasia, sublumbar lymphadenopathy.
- Intraluminal and intramural—colonic or rectal neoplasia or polyp, rectal stricture, rectal foreign body, rectal diverticulum, perineal hernia, rectal prolapse, and congenital defect (atresia ani).

Neuromuscular Disease

- Central nervous system—paraplegia, spinal cord disease, intervertebral disc disease, cerebral disease (lead toxicity, rabies).
- Peripheral nervous system—dysautonomia, sacral nerve disease, sacral nerve trauma (e.g., tail fracture/pull injury).
- Colonic smooth muscle dysfunction—idiopathic megacolon in cats.

Metabolic and Endocrine Disease

- Impaired colonic smooth muscle function—hyperparathyroidism, hypothyroidism, hypokalemia (chronic renal failure), hypercalcemia.

- Debility—general muscle weakness, dehydration, neoplasia.

RISK FACTORS

- Drug therapy—anticholinergics, narcotics, barium sulfate
- Metabolic disease causing dehydration
- Intact male—perineal hernia, prostatic disease
- Perianal fistula
- Pica—foreign material
- Excessive grooming—hair ingestion
- Decreased grooming/inability to groom—longhaired cats, pseudocoprostasis
- Pelvic fracture



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Dyschezia and tenesmus (e.g., caused by colitis or proctitis)—unlike constipation, associated with increased frequency of attempts to defecate and frequent production of small amounts of liquid feces containing blood and/or mucus; rectal examination reveals diarrhea and lack of hard stool.
- Stranguria (e.g., caused by cystitis/urethritis)—unlike constipation, can be associated with hematuria and abnormal findings on urinalysis (pyuria, crystalluria, bacteruria).

CBC/BIOCHEMISTRY/URINALYSIS

- Usually unremarkable.
- May detect hypokalemia, hypercalcemia.
- High PCV and total protein in dehydrated patients.
- High WBC in patients with severe obstipation secondary to bacterial or endotoxin translocation, abscess, perianal fistula, prostatic disease.
- Pyuria and hematuria with prostatitis.

OTHER LABORATORY TESTS

- If patient (dog) is hypercholesterolemic, consider a thyroid panel to rule out hypothyroidism.
- If patient is hypercalcemic, consider parathyroid hormone assay.

IMAGING

- Abdominal radiography documents severity of colonic impaction. Other findings may include colonic or rectal foreign body, colonic or rectal mass, prostatic enlargement, fractured pelvis, dislocated hip, or perineal hernias.
- Pneumocolon (after enemas to clean colon) may better define an intraluminal mass or stricture.
- Ultrasonography may help define extraluminal mass and prostatic disease.

DIAGNOSTIC PROCEDURES

Colonoscopy may be needed to identify a mass, stricture, or other colonic or rectal

CONSTIPATION AND OBSTIPATION

(CONTINUED)

lesion; rectal/colonic mucosal biopsy specimens should always be obtained.

C



TREATMENT

APPROPRIATE HEALTH CARE

- Remove or ameliorate any underlying cause if possible.
- Discontinue any medications that may cause constipation.
- May need to treat as inpatient if obstipation and/or dehydration present.

NURSING CARE

Dehydrated patients should receive IV (preferably) or SC balanced electrolyte solutions (with potassium supplementation if indicated).

ACTIVITY

Encourage activity

DIET

Dietary supplementation with a bulk-forming agent (bran, methylcellulose, canned pumpkin, psyllium) is often helpful, though they can sometimes worsen colonic fecal distension; in this case, feed a low-residue-producing diet.

CLIENT EDUCATION

Feed appropriate diet and encourage activity.

SURGICAL CONSIDERATIONS

- Manual removal of feces with the animal under general anesthesia (after rehydration) may be required if enemas and medications are unsuccessful.
- Subtotal colectomy may be required with recurring obstipation that responds poorly to assertive medical therapy.



MEDICATIONS

DRUG(S) OF CHOICE

- Emollient laxatives—docusate sodium or docusate calcium (dogs, 50–100 mg PO q12–24h; cats, 50 mg PO q12–24h).
- Stimulant laxatives—bisacodyl (5 mg/animal PO q8–24h). Ensure that animal is not obstructed prior to use of stimulant laxatives.
- Saline laxatives—isosmotic mixture of polyethylene glycol and poorly absorbed salts; usually administered as a trickle amount via nasoesophageal tube over 6–12 hours.
- Disaccharide laxative—lactulose (1 mL/4.5 kg PO q8–12h to effect).

- Warm water enemas may be needed; a small amount of mild soap or docusate sodium can be added but is usually not needed; sodium phosphate retention enemas (e.g., Fleet; C.B. Fleet Co., Inc.) are contraindicated because of their association with severe hypocalcemia.
- Suppositories can be used as a replacement for enemas; use glycerol, bisacodyl, or docusate sodium products.
- Motility modifiers can be administered—cisapride (dogs, 0.3–0.5 mg/kg PO q8–12h; cats, 2.5–10 mg/cat PO q8–12h) may stimulate colonic motility; indicated with early megacolon.

CONTRAINdications

- Lubricants such as mineral oil and white petrolatum are NOT recommended because of the danger of fatal lipid aspiration pneumonia due to their lack of taste.
- Fleet enemas.
- Anticholinergics.
- Diuretics.

PRECAUTIONS

Cisapride, and cholinergics—can be used with caution; contraindicated in obstructive processes. Avoid the use of metoclopramide because it does not affect the colon.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

- Ranitidine causes contraction of colonic smooth muscle in vitro.
- Newer generation cisapride-like drugs may be available soon.
- Pilot studies in Europe demonstrate improved ease of defecation following the administration of multistrain probiotic bacteria.



FOLLOW-UP

PATIENT MONITORING

Monitor frequency of defecation and stool consistency at least twice a week initially, then weekly or biweekly in response to dietary and/or drug therapy.

PREVENTION/AVOIDANCE

Keep pet active and feed appropriate diet. Subcutaneous fluids to ensure hydration can help reduce the frequency of constipation, particularly in cats.

POSSIBLE COMPLICATIONS

- Chronic constipation or recurrent obstipation can lead to acquired megacolon.
- Overuse of laxatives and enemas can cause diarrhea.
- Colonic mucosa can be damaged by improper enema technique, repeated rough mechanical breakdown of feces, or ischemic necrosis secondary to pressure of hard feces.
- Perineal irritation and ulceration can lead to fecal incontinence.

EXPECTED COURSE AND PROGNOSIS

Varies with underlying cause



MISCELLANEOUS

ASSOCIATED CONDITIONS

Vomiting—with severe/prolonged obstipation

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYS

- Colonic impaction
- Fecal impaction

SEE ALSO

Megacolon

ABBREVIATIONS

- PCV = packed cell volume
- WBC = white blood cell

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Client Education Handout
available online

CONTACT DERMATITIS

C



BASICS

OVERVIEW

- Irritant contact dermatitis and allergic contact dermatitis—rare and possibly different pathophysiologic syndromes with similar clinical signs; differentiation may be more conceptual than practical.
- ICD—results from direct damage to keratinocytes by exposure to a particular compound; damaged keratinocytes induce an inflammatory response directed at the skin without prior sensitization.
- ACD—considered a type IV (delayed) hypersensitivity, an immunologic event requiring sensitization and elicitation: Langerhans cells interact with environmental haptens to create antigens, leading to the sensitization of T-lymphocytes and activation following reexposure with release of cytokines (most notably TNF- α and IFN- γ).
- Recent reports blur the distinction between ICD, ACD, and atopic dermatitis.

SIGNALMENT

- Dogs and cats.
- ICD—occurs at any age as a direct result of the irritant nature of the offending compound.
- ACD—rare in young animals; most animals are chronically exposed to the antigen (months to years); extremely rare in cats, except when exposed to d-limonene-containing insecticides.
- Increased risk of ACD—German shepherd dog, poodle, wirehaired fox terrier, Scottish terrier, West Highland white terrier, Labrador and golden retriever.

SIGNS

Lesions

- Location determined by antigen contact; commonly limited to glabrous skin and regions frequently in direct contact with the environment.
- Thick hair coat of dogs is an effective barrier against contactants.
- Extreme erythroderma stops abruptly at the hairline.
- Initial erythema and papules leading to crusts and excoriations; vesicles uncommon.
- Chronic exposure leads to lichenification and hyperpigmentation.

Others

- Reactions to topical medications (e.g., otic preparations, spot-on flea products) usually localized.
- Generalized reactions, resulting from shampoos or insecticide sprays.
- Pruritus—moderate to severe (most common).
- Seasonal incidence may indicate a plant or outdoor antigen (e.g., ice-melting substance).

CAUSES & RISK FACTORS

- Reported offending substances—plants, mulch, cedar chips, fabrics, rugs, carpets, plastics, rubber, leather, nickel, cobalt, concrete, soaps, detergents, floor waxes, epoxy

resin, carpet and litter deodorizers, herbicides, fertilizers, insecticides (including newer topical flea treatments), flea collars, topical preparations especially neomycin.

- Increased incidence of ACD and ICD in the young and in atopic animals.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Atopy
- Food allergy
- Drug reaction
- Insect bites/hypersensitivity
- Pelodera dermatitis
- Hookworm dermatitis
- Pyoderma
- *Malassezia* dermatitis
- Dermatophytosis
- Demodicosis
- Lupus erythematosus
- Seborrheic dermatitis
- Solar dermatitis
- Thermal injuries
- Trauma from rough surfaces
- Staphylococcal folliculitis

DIAGNOSTIC PROCEDURES

- ACD—closed-patch test sometimes helpful (corticosteroids and NSAIDs must be discontinued 3–6 weeks before testing); use materials taken from the environment or home applied to upper thorax skin under a bandage for 48 hours. Examine for 5 days. Erythema, edema, variable pruritus.
- Best diagnostic test for ICD—eliminate contact irritant or antigen, followed by provocative exposure.
- Open patch test—applying the substance to the inside pinnae causing mild erythema, edema, pruritus. Examine daily for 5 days.
- Skin biopsy.

PATHOLOGIC FINDINGS

- Intraepidermal vesiculation and spongiosis; superficial dermal edema with perivascular mononuclear cell infiltrate in ICD and ACD; polymorphonuclear cell infiltrate in ICD; leukocyte exocytosis common.
- Lymphocytic spongiotic or eosinophilic and lymphocytic spongiotic infiltrate with intraepidermal eosinophilic pustules in canine ACD.



TREATMENT

- Eliminate offending substance(s).
- Bathe with hypoallergenic shampoos to remove antigen from the skin.
- Create mechanical barriers, if possible—socks, shirts, restriction from environment.



MEDICATIONS

DRUG(S)

- Systemic corticosteroids—prednisolone (1 mg/kg PO q24h for 5–7 days then q48h for 2 weeks).

- Topical corticosteroids for focal lesions.
- Pentoxifylline 10–25 mg/kg PO q8-12h initially; may be reduced to q24h to maintain; may cause gastric irritation.
- Cyclosporine 5 mg/kg q24h for ACD.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Pentoxifylline—do not administer with alkylating agents, cisplatin, and amphotericin B; cimetidine may increase serum levels of pentoxifylline.



FOLLOW-UP

PREVENTION/AVOIDANCE

Remove offending substances from the environment.

EXPECTED COURSE AND PROGNOSIS

ICD

- Acute condition—may occur after only one exposure; can be manifested within 24 hours of exposure.
- Corticosteroids rarely helpful.
- Lesions resolve 1–2 days after irritant removal.

ACD

- Requires months to years of exposure for hypersensitivity to develop.
- Reexposure results in development of clinical signs within 1–5 days; signs may persist for several weeks.
- Responds well to corticosteroids; pruritus returns after discontinuation if the antigenic stimulus persists.
- Hypo sensitization not effective.
- Prognosis—good if the allergen is identified and removed; poor if the allergen is not identified; may require life-long treatment.

ABBREVIATIONS

- ACD = allergic contact dermatitis
- ICD = irritant contact dermatitis
- IFN- γ = interferon gamma
- NSAID = nonsteroidal anti-inflammatory drug
- TNF- α = tumor necrosis factor alpha

Suggested Reading

Gross TL, Ihrke PJ, Affolter VK. Skin Disease of the Dog and Cat, 2nd ed. Oxford: Blackwell, 2006, pp. 98–102, 105–109, 214–216.

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Consulting Editor Alexander H. Werner

COONHOUND PARALYSIS (ACUTE POLYRADICULONEURITIS)



BASICS

DEFINITION

- Acute inflammatory disorder involving the axons and myelin of nerve roots, spinal nerves, and peripheral nerves in dogs, with or without a previous history of contact with raccoon saliva, vaccination, or a gastrointestinal or respiratory infection.
- Proposed animal model for Guillain-Barré syndrome in humans.

PATOPHYSIOLOGY

- Etiology uncertain, appears to be immune-mediated.
- Immune-mediated inflammation develops 7–14 days after antecedent event (delayed hypersensitivity reaction?).
- Thought to be the dog's immune system reaction to a cross-reacting antigen (suspect molecular mimicry phenomenon between external antigen and gangliosides from dog's neural tissue, with the development of antiganglioside autoantibodies).
- Coonhound paralysis (CHP)—antecedent event is recent contact with raccoon saliva.
- Acute canine idiopathic polyradiculoneuritis (ACIP)—affected dogs with identical clinical signs than those with CHP but without a history of raccoon exposure; may have history of recent respiratory or gastrointestinal infection.
- Post-vaccinal polyradiculoneuritis—antecedent event is recent vaccination (rare).
- *Toxoplasma gondii* infection—dogs with ACIP more likely to have positive titers than control dogs (possible triggering factor?).

SYSTEMS AFFECTED

- Peripheral nervous system—most severe involvement in the ventral (motor) nerve roots and ventral root components of the spinal nerves; lumbosacral nerve roots affected more severely than cervical and thoracic nerve roots.
- Cranial nerves—nerve VII often affected; nerves IX, X occasionally affected.
- Respiratory failure—secondary to intercostal and/or phrenic nerve involvement in some patients.

GENETICS

No proven basis.

INCIDENCE/PREVALENCE

- Most commonly recognized acute polyneuropathy in dogs.
- Low incidence.

GEOGRAPHIC DISTRIBUTION

- CHP—relative to the distribution of raccoons (e.g., North and Central America; parts of South America).
- ACIP—worldwide.

SIGNALMENT

Species

Dog, very occasionally cat.

Breed Predilections

- CHP—Coonhounds; any breed in contact with raccoons susceptible.
- ACIP, post-vaccinal polyradiculoneuritis—none.

Mean Age and Range

N/A

Predominant Sex

N/A

SIGNS

Historical Findings

- Appear 7–14 days after contact with raccoon saliva (bite or scratch), receipt of a vaccination, or development of a respiratory or gastrointestinal infection.
- Initial signs—stiff, stilted gait in all limbs, typically starting in the pelvic limbs and eventually progressing to the thoracic limbs.
- Rapid progression (2–4 days) to a flaccid, lower motor neuron tetraparesis to tetraplegia.
- Owners may notice loss or change of voice.
- Appetite and water consumption—usually normal.
- Urination and defecation—normal.
- Progressive phase of the disease—clinical signs can continue to worsen up to 5–10 days after onset.

Neurologic Examination Findings

- Usually symmetrical.
- Stiff, stilted gait that usually progresses rapidly to lower motor neuron tetraparesis or tetraplegia; some dogs may remain ambulatory tetraparetic.
- Generalized hyporeflexia to areflexia, with the exception of a normal perineal reflex.
- Generalized hypotonia to atonia, severe neurogenic muscle atrophy.
- Affected dogs often show inability to hold the head up.
- Aphonia or dysphonia common; no megaesophagus.
- Facial paresis—bilateral incomplete palpebral closure in some patients.
- Respiration—labored in severely affected dogs; occasional progression to respiratory paralysis.
- Pain sensation intact; hyperesthesia common, may reflect variable dorsal nerve root inflammation.
- Motor dysfunction—always predominates; even tetraplegic patient can usually wag its tail.
- Mental status, urination and defecation—unaffected.

CAUSES

- CHP—contact with a raccoon; perhaps more important, contact with raccoon saliva.
- ACIP—none proven; possibly previous respiratory or gastrointestinal viral or bacterial infection.

- Post-vaccinal polyradiculoneuritis—recent vaccination (rare).

RISK FACTORS

- CHP—coonhounds tend to be predisposed primarily because of the nature of their activities; previous disease does not confer immunity and may increase risk of redevelopment; multiple bouts not uncommon.
- ACIP—unknown.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other acute polyneuropathy (i.e., paraneoplastic neuropathy)
- Distal denervating disease
- Botulism
- Tick bite paralysis
- Fulminant myasthenia gravis
- Black widow spider bite envenomation, coral snake envenomation
- Intoxications (lasalocid, blue-green algae)
- Generalized (diffuse) or multifocal myelopathy (involving both cervical and lumbosacral intumescences)

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal.

OTHER LABORATORY TESTS

- Serum immunoglobulins—high serum IgG but not IgM in some patients.
- Immunologic—serum reaction to raccoon saliva on ELISA; dogs with CHP have a strong positive reaction that decreases in intensity over time; dogs without disease but with raccoon contact have a strong positive reaction; dogs with ACIP but with no raccoon contact have a negative reaction.
- Immunologic—for dogs with ACIP, the identification of anti-GM2 ganglioside antibodies reached a diagnostic sensitivity of 60% and a specificity of 97%.

IMAGING

Thoracic radiographs and abdominal ultrasound—normal

DIAGNOSTIC PROCEDURES

CSF Analysis

- Lumbar—high protein without an increase in leukocytes at all stages of disease.
- Albumin leakage across the disrupted blood-nerve barrier of the affected ventral nerve roots is the primary cause of the protein increase.

Electrodiagnostics

- Electromyography (EMG)—generalized spontaneous activity (fibrillation potentials and positive sharp waves) consistent with denervation; EMG normal in the first 4–5 days.
- Markedly low compound muscle action potential amplitudes after motor nerve stimulation.

(CONTINUED)

COONHOUND PARALYSIS (ACUTE POLYRADICULONEURITIS)

C

- F waves (late waves that indicate proximal motor nerve and ventral nerve root function)—prolonged minimum latencies, increased F ratio, decreased amplitudes.
- Motor nerve conduction velocities—usually normal; severely affected patients may have mildly decreased values.
- Sensory nerve function—usually normal.
- Abnormalities provide evidence of severe peripheral motor axonopathy (more severe in proximal portions of the nerves and ventral nerve roots), along with demyelination in the proximal motor nerves and ventral nerve roots.

PATHOLOGIC FINDINGS

- Ventral nerve roots and the ventral root components of the spinal nerves—most severe lesions, various degrees of axonal degeneration, paranodal and segmental demyelination, and leukocyte infiltration (predominantly monocytes and macrophages).
- Peripheral nerves—affected to a lesser degree; might be normal.
- Dorsal nerve roots—much less severely affected.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Inpatient—closely monitor patients in the progressive phase of the disease (especially during first 5 days) for respiratory problems.
- Severe respiratory compromise—mechanical ventilation as required.
- Intravenous fluid therapy—administer if patient is dehydrated.
- Outpatient—once patient is stable and the progressive phase of the disease is over.

NURSING CARE

- Patients are usually able to eat and drink; hand feed in sternal position until able to reach food and water.
- Intensive physical therapy—important to decrease muscle atrophy; severe neurogenic muscle atrophy is inevitable.
- Frequent turning and excellent padding—essential to prevent pressure sores.

ACTIVITY

- Encourage as much movement as possible.

DIET

- No restrictions.
- Make sure patient is able to reach food and water.
- Cervical weakness—may need to hand feed patient in sternal position.

CLIENT EDUCATION

- Inform client that good nursing care is essential.
- Discuss importance of preventing pressure sores and urine scalding and of limiting the degree of muscle atrophy by frequent daily

physical therapy (passive limb movement, swimming as the patient's strength begins to improve).

- Patient needs soft bedding that must be kept free of urine and feces, frequent turning (every 3–4 hours), frequent bathing, and adequate nutrition.

SURGICAL CONSIDERATIONS

N/A

**MEDICATIONS****DRUG(S) OF CHOICE**

- None proven effective.
- Immunoglobulin—1 g/kg IV daily for 2 consecutive days, 0.5 g/kg IV daily for 3 consecutive days, or 0.4 g/kg IV daily for 5 consecutive days; given early may shorten recovery time in ACIP.

CONTRAINDICATIONS

Corticosteroids—do not improve clinical signs or shorten course of disease; may reduce survival in humans with Guillain-Barré syndrome.

PRECAUTIONS

Monitor for possible adverse reactions (anaphylaxis, hematuria) after IV immunoglobulin administration.

**FOLLOW-UP****PATIENT MONITORING**

- Outpatient—keep in close contact with client regarding complications or changes in the patient's condition.
- Urinalysis—perform periodically to check for cystitis in tetraplegic or severely tetraparetic patients.
- Ideally, reevaluate at least every 2 weeks.

PREVENTION/AVOIDANCE

- CHP—if possible, avoid contact with raccoons.
- Post-vaccinal polyradiculoneuritis—if strong association with a specific vaccination, avoid that particular vaccine in the future.

POSSIBLE COMPLICATIONS

- Respiratory paralysis—in progressive phase of the disease.
- Pressure sores, urine scalding, cystitis—common in chronically recumbent dogs.

EXPECTED COURSE AND PROGNOSIS

- Signs stabilize once the progressive phase of the disease is over.
- Most affected dogs recover fully over 3–6 weeks; severely affected cases may take up to 3–4 months to recover; incomplete recoveries can happen.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Unknown effect on the fetuses of an affected bitch.

SYNONYMS

Coondog paralysis

SEE ALSO

- Botulism
- Myasthenia Gravis
- Polyneuropathies (Peripheral Neuropathies)
- Tick Bite Paralysis

ABBREVIATIONS

- ACIP = acute canine idiopathic polyradiculoneuritis
- CHP = coonhound paralysis
- CSF = cerebrospinal fluid
- ELISA = enzyme-linked immunosorbent assay
- EMG = electromyography

Suggested Reading

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Client Education Handout
available online

COPPER ASSOCIATED HEPATOPATHY



BASICS

DEFINITION

- Severe hepatic accumulation of copper (Cu) causes acute or chronic hepatitis leading to cirrhosis or death from liver failure.
- Mild to moderate hepatic Cu accumulation augments oxidative injury and increases risk for liver disease by other hepatobiliary insults, notably, hepatotoxicity from NSAIDs.
- *Primary Copper Associated Hepatopathy* (Cu-AH) depicts copper accumulation in the absence of other liver disorders or as the major cause of liver injury.
- *Secondary Cu-AH* depicts Cu accumulation caused by severe chronic cholestasis in cats (not dogs) or fulminant hepatic failure (rare).
- *Genetic-Primary Cu-AH*: only proven in the Bedlington terrier.
- *Acquired-Primary Cu-AH*: Most common canine cause of Cu-AH, reflects dietary Cu availability in commercial dog food that exceeds an individual's ability to maintain a neutral Cu balance.
- *Congenital Primary Cu-AH*: (no gene mutation characterized) is comparatively rare in cats.
- Some animals with primary Cu-AH accumulate Cu without histologic evidence of liver damage despite vacillating liver enzyme activity (ALT most common).

PATOPHYSIOLOGY

- Hepatic Cu homeostasis depends on a complex regulatory system that includes: protein transporters, chaperones, membrane receptors, intracellular binding-proteins, and canalicular egress pumps. Cu is absorbed from the small intestine, stored in the liver, with excess excreted in bile.
- A single gene mutation in dogs (*COMMD1*) is proven to cause genetic-primary Cu-AH in Bedlington terriers.
- More commonly, canine hepatic Cu accumulation reflects Cu intake exceeding capacity to maintain neutral Cu balance; this likely reflects complex transporter differences between individual dogs and may reflect genetic drift associated with development of breed standards.
- Secondary Cu-AH reflects reduced canalicular Cu egress secondary to severe cholestasis (cats only) or severe panlobular liver injury (fulminant hepatic failure, rare).
- In primary Cu-AH: cytosolic hepatocellular Cu first accumulates in zone 3 (centrilobular region).
- In secondary Cu-AH (cats): cytosolic hepatocellular Cu accumulates in zone 1 (periportal) or adjacent to injured regions.
- Hepatic Cu concentrations are widely variable. Primary Cu-AH may range from 500 to > 10,000 µg/g dry weight liver (DWL) whereas secondary Cu-AH rarely exceeds 1,000 µg/g DWL.
- Cu accumulation causes hepatocellular injury due to oxidative membrane and mitochondrial injury.
- Focal

hepatitis progresses to chronic hepatitis and eventually cirrhosis and may initiate an immune-mediated process.

- Rarely, acute severe hepatic necrosis releases Cu into the systemic circulation causing hemolysis and/or an acute-onset acquired Fanconi syndrome (proximal renal tubular injury causing euglycemic glucosuria).

SYSTEMS AFFECTED

- Hepatobiliary—focal hepatitis, chronic hepatitis, eventual cirrhosis.
- Hemic/Lymphatic—hemolytic anemia a rare sequel to acute hepatic necrosis in dogs with high hepatic Cu concentrations (e.g., Bedlington terrier) in which large amounts of Cu are suddenly released into the systemic circulation.
- Renal—rare reversible Fanconi syndrome causing euglycemic glucosuria, granular casts, with or without clinicopathologic evidence of reduced renal function.

GENETICS

- Autosomal recessive *COMMD1* mutation in Bedlington terriers reduces biliary Cu excretion.
- Gene mutations remain unproven in other breeds and in cats.
- Predisposition to Cu-AH is recognized in Labrador retrievers, West Highland white terriers, Doberman pinschers, and other breeds likely reflecting pharmacogenetic differences in Cu regulatory proteins or processes selected during breed development.

INCIDENCE/PREVALENCE

- Bedlington terrier—at one time up to 2/3 of dogs carried the *COMMD1* mutation; incidence significantly declined with genetic testing.
- Prevalence of excess hepatic Cu remains high in West Highland white terriers, Labrador retrievers, Doberman pinschers and other breeds; historical account in Skye terriers.
- Cu-AH is currently the most common cause of chronically increased ALT activity in dogs (since the mid 1990s), likely linked with altered Cu supplements in dog foods.
- Cu-AH currently comprises ≥ 20% of liver biopsy submissions for abnormal enzyme activity in dogs. High hepatic Cu concentration (> 400 µg/g DWB) is not always associated with histologic evidence of liver injury.
- Primary-congenital Cu-AH occurs in cats but is comparatively rare.

GEOGRAPHIC DISTRIBUTION

Reported worldwide

SIGNALMENT

Species

Dog and cat; more common in dogs

Breed Predilections

Bedlington terrier, West Highland white terrier, Labrador retriever, Doberman pinscher, Dalmatian, Welsh Corgi, Keeshond, Staffordshire terrier observed to

have increased incidence of high hepatic Cu concentrations. No canine breed is exempt.

Mean Age and Range

- Bedlington terrier—Cu slowly accumulates to a maximum at ~ 6 years of age; dogs can be clinically affected at any age, most present as middle-aged to older dogs with chronic hepatitis.
- West Highland white terrier—maximum Cu accumulation observed by 12 months of age; clinical disease may occur at any time; some dogs with high hepatic Cu live to old age (15 y) without evidence of liver injury.
- Labrador retrievers, Dalmatians, other breeds with apparent increased risk—young adult to middle-aged at diagnosis for chronic hepatitis.
- Doberman pinschers—may begin to develop hepatitis with ALT increases and Cu accumulation at 1–3 years of age; clinical signs of liver disease often occur after 7 years of age.
- Skye terrier—all ages can be affected.

Predominant Sex

None

SIGNS

Historical Findings

- Primary Cu-AH: 4 categories (1) no clinical signs, (2) subclinical disease, (3) acute disease (uncommon) associated with severe acute hepatic necrosis, or (4) chronic progressive hepatitis (middle-aged to older dogs), progressive to cirrhosis.
- Secondary Cu-AH accompanies feline necroinflammatory cholestatic liver disease (cholangiohepatitis) or rarely, in dogs with fulminant liver necrosis.
- Acute signs—sudden onset lethargy, anorexia, vomiting; may have a rapid course, with dogs succumbing despite intensive supportive care.
- Chronic signs—variable, intermittent lethargy, hyporexia, weight loss, vomiting, diarrhea, polydipsia and polyuria. Later signs may include: abdominal distention (ascites), jaundice, bleeding tendencies, and HE.

Physical Examination Findings

- Acute signs—lethargy, weakness, jaundice, pallor (anemia), vomiting, diarrhea, and dark urine (bilirubinuria; rare hemoglobinuria).
- Chronic signs—weight loss, ascites, jaundice, and nodular microhepatia. Melena and petechial hemorrhage in animals with diffuse panlobular injury.

CAUSES

- Genetic Cu-AH—single gene mutation in Bedlington terriers.
- Primary Cu-AH: either Bedlington mutation or suspected pharmacogenetic differences in other dog breeds involving regulatory pathways influencing Cu homeostasis making them intolerant to current levels of dietary Cu supplementation.
- Secondary Cu-AH—necroinflammatory chronic cholestatic liver disease in cats or diffuse severe panlobular injury in dogs or cats (rare) impairing Cu regulatory pathways.

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COPPER ASSOCIATED HEPATOPATHY

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RISK FACTORS

- Primary—feeding diets or providing water with Cu concentrations exceeding an individual dog's ability to maintain a neutral Cu balance.
- Stress may precipitate acute disease.
- Asymptomatic dogs with primary Cu-AH may become symptomatic when additional disease processes or toxicities (e.g., NSAID administration; CCNU chemotherapy) impose oxidative challenge or another primary liver abnormality develops (e.g., immune-mediated hepatitis, severe glycogen-type vacuolar hepatopathy, cholangiohepatitis).

**DIAGNOSIS****DIFFERENTIAL DIAGNOSES**

- Acute diseases—*infectious diseases* (e.g., infectious canine hepatitis, leptospirosis, septicemia), acute hepatic necrosis, hepatic abscess, drug- or toxin-induced hepatic injury, acute pancreatitis, hepatic lymphoma, autoimmune hemolytic anemia, or zinc toxicity.
- Chronic diseases—chronic hepatitis; cholangiohepatitis of inflammatory or immune-mediated origin, drug- or toxin-induced liver injury, severe diffuse glycogen-type vacuolar hepatopathy (dogs), infectious hepatitis, chronic obstructive biliary disease, chronic fibrosing pancreatitis, congenital portosystemic shunt, hepatic neoplasia, or metastatic neoplasia.

CBC/BIOCHEMISTRY/URINALYSIS

- *CBC*—may be normal. Regenerative anemia, leukocytosis, neutrophilia in some animals with acute Cu-associated hemolysis. Microcytic or normocytic, normochromic non-regenerative anemia in some dogs with chronic progressive disease. RBC microcytosis may reflect acquired portosystemic shunting (APSS).
- *Biochemistry*—increased liver enzymes (ALT, AST, GGT and ALP; transaminase increases prominent with fold increase in ALT > ALP; hyperbilirubinemia notable in dogs with severe liver injury. Increased ALT without clinical signs increases suspicion for early or cyclic Cu-AH necrosis.
- As hepatic function deteriorates, hypoalbuminemia, \pm hyperglobulinemia, low BUN, rare hypoglycemia, and hypocholesterolemia develop.
- *Urinalysis*—usually normal or positive for bilirubinuria; later dilute urine, ammonium biurate crystalluria may appear in dogs with APSS which reflect sinusoidal hypertension (remodeling and fibrosis). Rarely, acquired Fanconi syndrome reflects proximal renal tubule Cu toxicity.

OTHER LABORATORY TESTS

- High fasting or postprandial TSBA values.
- Prolonged PT, APTT, ACT, and mucosal

bleeding time in advanced cases. • Rare increase in serum Cu concentrations in dogs with acute severe Cu-AH liver necrosis; otherwise serum Cu does not reflect liver Cu concentrations; a low yield screening test.

- Hepatic Cu measurements must be reconciled with histopathologic findings.
- Genetic marker testing in Bedlington terriers: microsatellite markers or specific *COMMD1* mutation. However, kindreds of Bedlington terriers with Cu-AH have had negative PCR-based gene tests (suspected additional gene mutation).

IMAGING

- Radiography—unremarkable in most dogs; small liver in chronic hepatic injury, poor abdominal detail if ascites.
- Ultrasonography—early: normal hepatic echogenicity; later: hyperechoic to mixed nodular echogenicity; abdominal effusion if ascites.

DIAGNOSTIC PROCEDURES

- *Liver biopsy*—confirms and characterizes liver injury. • Routine H&E staining—can overlook pathologic Cu accumulation.
- Cu-specific staining—rhodanine (preferred) or rubanic acid stains needed to identify and confirm Cu-protein aggregates and detail zonal distribution and association with liver injury.
- Semiquantitative scoring system—estimates severity of Cu accumulation.
- Cu measurements—can be completed on: fresh, frozen, formalin fixed liver, or liver tissue extracted from paraffin blocks.
- Distribution of hepatocytes with cytosolic Cu granules and quantification of Cu should be reconciled—areas of dense fibrosis, parenchymal extinction, regenerative nodules contain lower Cu concentrations than unremodeled liver tissue. This phenomenon causes discordance between measured and assessed Cu accumulation.

Cu Measurement

- *Atomic absorption spectroscopy*—gold standard method of Cu determination. • Cu must be expressed per DWL.
- Hepatic Cu determination (atomic absorption spectroscopy)—requires at least a full needle biopsy (≥ 16 g) sample.
- *Digital scanning of rhodanine-stained biopsy sections*—validated against atomic absorption spectroscopy; accurately measures liver Cu (Cornell University) on biopsy reconciling histologic change with Cu; routine diagnostic assessment (Cornell University).

Hepatic Cu Concentrations (DWL)

- Normal hepatic Cu: $\leq 400 \mu\text{g/g}$.
- Hepatic Cu concentration in dogs with primary Cu-AH ($\mu\text{g/g}$ DWL):
 - Bedlington terriers: 850–12,000
 - West Highland white terriers: up to 3,500
 - Labrador retrievers: 400–9,000
 - Doberman pinschers: 1,000–10,000
 - Dalmatians: 750–8,400
 - Cats: 700–8,000

- Avoid analytic methods “estimating” sample hydration or reporting Cu on a wet weight basis.

PATHOLOGIC FINDINGS

- Cu accumulates in lysosomes in Zone 3 (centrilobular) hepatocytes in dogs.
- Histochemical Cu staining (e.g., rhodanine) confirms affiliation of Cu with histologic injury.
- Histologic features commonly include formation of “copper granulomas” in areas of hepatocellular necrosis.
- Oxidative injury—mechanism of hepatocellular injury.
- In some cases, an apparent immune-mediated hepatitis accompanies the Cu-AH lesions, reflecting response to neopeptope formation.
- Chronic untreated necroinflammatory injury progresses to chronic hepatitis, parenchymal extinction, liver fibrosis, and eventually to cirrhosis with splanchnic hypertension, and formation of APSS.
- Cu-AH causing necroinflammatory liver injury leads to development of microhepatia with nodules reflecting regenerative nodules, and a fibrotic “firm” texture.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Outpatient for most dogs.
- Inpatient evaluation and treatment for dogs with signs of hepatic failure.
- See Hepatitis, Chronic Active and Cirrhosis and Fibrosis of the Liver for detailed management of liver disease.

NURSING CARE

- Animals in liver failure require fluid and electrolyte correction; treatment for HE; may require treatment for coagulopathy; and should be treated with IV N-acetylcysteine (NAC) for oxidative injury, with d-penicillamine chelation started as soon as oral treatment is possible.
- Dogs demonstrating hemolytic anemia may require whole or packed RBC transfusion and IV NAC.
- Dogs demonstrating acquired Fanconi syndrome require IV fluid therapy to protect against acute renal failure and IV NAC.

ACTIVITY

Normal; rest if signs of severe necrosis.

DIET

- Feed Cu-restricted diets to all affected dogs *for their lifetime*.
- Prescription liver diets deliver 2.2–2.5 g protein/kg body weight when fed for maintenance energy requirements.
- Dietary protein content should only be reduced for dogs exhibiting signs of nitrogen intolerance, e.g., HE or developing ammonium biurate crystalluria (reflects hyperammonemia and APSS formation).
- Supplemental protein is added to the base “liver” diet to increase protein

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intake by 0.5 g up to 1.5 g protein/kg body weight using low Cu-containing foods.

- Select supplemental low Cu-containing protein sources using the USDA food tables (available on internet).
- Determine the amount for selected foods to feed using the Nutritional Analysis Tool-2 (free web software, site maintained by the Illinois School of Human Nutrition).
- Balanced homemade diets avoiding Cu-rich foods (e.g., organ meats, nuts, certain grains) may also be formulated, but these should be recommended by a Veterinary Clinical Nutritionist. Such diets are frequently not feasible for large-breed dogs where commercial diets are often the better option as a baseline meal, as described above.
- Prescription type liver diets contain the lowest Cu content (approximately 4 mg/kg of diet) formulated originally to maintain neutral Cu balance in Cu-AH affected Bedlington terriers.
- Chelation therapy in conjunction with commercial diets can successfully manage affected dogs.
- All affected dogs *must* have lifetime dietary/water Cu restriction.
- Measure waterborne Cu and restrict access to water with Cu > 0.2 ppm.
- Avoid mineral supplements containing Cu.
- Supplement water-soluble vitamins but avoid ascorbate (vitamin C supplements during Cu hepatotoxicity: may augment oxidative injury).

CLIENT EDUCATION

- Educate all Bedlington terrier owners about the genetic basis of Cu-AH in this breed and appropriate genetic testing.
- Other breeds should be monitored for increased ALT activity and Cu should be specifically stained for in liver biopsies.
- Dogs receiving NSAIDs with associated increase in ALT activity should be investigated for potential "silent" hepatic Cu accumulation.
- Dietary management and chronic intermittent chelation or zinc administration are needed for life in most dogs.

SURGICAL CONSIDERATIONS

- Animals with hepatic failure are surgical and anesthetic risks.
- Hypoxia encountered during anesthesia or surgery can provoke Cu-driven oxidative injury.



MEDICATIONS

DRUG(S)

See other liver topics for other specific treatments of chronic hepatitis and cirrhosis.

CHELATION

d-penicillamine

- 10–15 mg/kg PO q12h.
- Chelates Cu, promotes urinary excretion of Cu, and suspected to have other Cu-protective effects.
- Initiate treatment in dogs with increased

ALT activity and biopsy confirmed centrilobular Cu accumulation affecting > 25% centrilobular hepatocytes or reconciling with lobular injury/remodeling (reticulin and Masson's trichrome staining assessment).

- Hepatic Cu as low as 600 µg/g DWL may require chelation and chronic management.
- Dogs with hepatic Cu < 1,500 µg/g DWL are usually easily cleared with 6 months of d-penicillamine chelation (biopsy proven).
- Dogs with hepatic Cu > 3,000 µg/g may require > 9–12 months of chelation.
- Administer drug 1 h before feeding.
- Drug-associated vomiting or hyporexia may be abated with low dose prednisone.
- Following a course of therapy (6 months–1 year) re-biopsy to monitor treatment efficacy is optimal, but following ALT is an alternative method of monitoring.
- Expect substantial decline in ALT by 8 weeks of chelation.
- Successful chelation results in remarkable histologic improvement and resolution of ALT activity.

Trentine hydrochloride

- 5–15 mg/kg PO q12h; alternative Cu chelator; as effective as d-penicillamine with similar guidelines.
- Administer 1 h before meals.
- Acute renal failure has been observed in some dogs given higher dosing of trentine.
- Trentine is currently restrictively expensive.
- Trentine is not more effective than d-penicillamine in humans with Wilson's disease; results are interchangeable.

Zinc—Blocking Enteric Cu Uptake

- Zinc therapy may assist in chronic control of Cu-AH. Use of zinc is predicated on study of 6 dogs (see Suggested Reading).
- Zinc reduced intestinal absorption of Cu; study demonstrated reduced hepatic Cu concentrations with 2 years of therapy in a few Bedlington (n=3) and West Highland white terriers (n=3).
- 100 mg of elemental zinc PO q12h as loading dose for 2 months, then 25–50 mg PO q12h for Bedlington-terrier-sized dog; zinc acetate is best tolerated.
- In humans with Wilson's disease, zinc dosing is optimized with Cu-isotope uptake studies.
- In humans, zinc therapy is less effective than chelation for chronic management (see Suggested Reading).
- Administer zinc 1 h before feeding.
- May be beneficial in earlier stages or dogs with lower hepatic Cu concentrations (generally < 1,000 µg/g DW).
- Zinc may lack efficacy in dogs with high Cu concentrations and hepatitis where chelation therapy is preferred.
- Coadministration of zinc and Cu chelators requires careful staggered dosing; direct physical interaction makes treatment ineffective.
- Vomiting, inappetence, gastritis—frequent side effects.
- Low concentrations of zinc given in a low Cu diet in previously chelated Labrador retrievers was found to be no better than feeding a Cu-restricted diet (see Suggested Reading).

ANTIOXIDANTS

- d- α -tocopherol (vitamin E)—10 U/kg q24h PO may protect the liver from oxidative damage imposed by Cu.
- S-Adenosylmethionine (SAMe), use product with proven bioavailability that increases hepatic GSH—20 mg/kg q24h, enteric-coated tablets given on an empty stomach.

HEPATOPROTECTANTS

- Silibinin (milk thistle extract, use form bound to PPC for best bioavailability)—5 mg/kg PO q24h; utility in Cu storage hepatopathy undetermined.
- Ursodeoxycholic acid—10–15 mg/kg PO divided BID given with food for best bioavailability; recommended if chronic hepatitis (see Hepatitis, Chronic Active) and high serum bile acid concentrations.

CONTRAINdications

- Ascorbic acid (vitamin C) may augment Cu hepatotoxicity.
- Avoid treatment with NSAID in affected dogs as these may cause centrilobular toxic adduct-related liver injury.

POSSIBLE INTERACTIONS

Penicillamine or trentine may not be effective if given concurrently zinc therapy.

PRECAUTIONS

- Remain aware of altered drug metabolism related to reduced first-pass extraction if APSS develop or altered hepatic metabolism/biotransformation in dogs with severe centrilobular necrosis and remodeling.
- Avoid NSAID administration—metabolized by p450 cytochromes in centrilobular region where toxin adducts with oxidative injury augmented by Cu accumulation.



FOLLOW-UP

PATIENT MONITORING

- Liver enzymes q3–6 months; evaluate body weight and condition.
- Examine hepatic biopsy and measure hepatic Cu concentration within 1 year of initiated treatment as optimal follow-up assessment.
- If using zinc therapy—assess serum zinc concentrations initially, then during first 2–3 weeks and until stable to assure values increase but remain within the non-toxic range (200–500 µg/dL), then q6 months.

POSSIBLE COMPLICATIONS

- d-Penicillamine can cause anorexia and vomiting. Start at the low end of the dose range for the first week; give 1 h before meals; small amount of food may reduce nausea but may reduce treatment efficacy when given with meals.
- d-Penicillamine side effects: glomerulonephritis, polyarthritis, drug-associated hepatopathy, or an autoimmune-like vesicular disease of the mucocutaneous junctions that resolves on

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drug withdrawal. • Excess zinc (oral dose of > 200 mg/day or blood concentration of > 800 µg/dL) can cause hemolytic anemia.

PREVENTION/AVOIDANCE

Breed only Bedlington terriers that do not carry the *COMMD1* mutation. A liver registry is available for Bedlington terriers proven unaffected on the basis of hepatic Cu concentration < 400 µg/g DW at 1 year of age or gene testing. Other breeds have unknown kindred predispositions.

EXPECTED COURSE AND PROGNOSIS

- Prognosis is poor in acutely affected young dogs with fulminant hepatic failure or older dogs with cirrhosis; however, some of these respond to acute supportive care and chelation, as described.
- Dogs with mild to moderate acute hepatic injury usually respond to chelation therapy (prognosis is good).
- Even dogs with nodular hepatopathy and microhepatia and ascites can respond remarkably well to the described treatment protocol with resolution of many histologic lesions (including fibrosis).
- A good prognosis is warranted if Cu-AH is detected before liver remodeling or development of hepatitis (liver biopsy pursued based on high ALT activity and high index of suspicion for Cu hepatotoxicity) in dogs treated as described above.

**MISCELLANEOUS****ASSOCIATED CONDITIONS*****Age-Related Factors***

- Health evaluations that include ALT measurement helps identify at-risk dogs.

- Important to evaluate ALT in any dog placed on chronic NSAIDs where Cu retention appears to augment centrilobular hepatotoxicity; measure ALT before and 2–4 weeks after NSAID initiation or sooner if patient demonstrates inappetence, vomiting, lethargy.

PREGNANCY/FERTILITY/BREEDING

Do not breed affected Bedlington terriers or carriers; genetics of other suspected breeds has not been determined.

SYNONYMS

- Bedlington hepatitis • Chronic active hepatitis • Chronic Cu toxicity • Cu toxicosis

SEE ALSO

- Hepatitis, Chronic Active • Cirrhosis and Fibrosis of the Liver

ABBREVIATIONS

- APSS = acquired portosystemic shunt
- Cu = Copper • Cu-AH = copper associated hepatopathy • DWL = dry weight liver
- GSH = glutathione • HE = hepatic encephalopathy • NAC = N-acetylcysteine
- TSBA = total serum bile acids

INTERNET RESOURCES

www.vetgen.com for genetic screening in Bedlington terriers

Suggested Reading

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Consulting Editor Sharon A. Center



**Client Education Handout
available online**

COPROPHAGIA AND PICA



BASICS

DEFINITION

Pica is an abnormal ingestive behavior in which non-food items are consumed. Coprophagia is a form of pica in which feces is consumed.

PATHOPHYSIOLOGY

- The pathophysiology of pica is unclear.
- Coprophagia is not usually a pathologic condition.
- Pica is a sign that may be associated with a variety of different conditions. Any medical condition leading to nutritional deficiencies, electrolyte imbalances, gastrointestinal disturbances, polyphagia, or CNS disturbances may lead to pica and/or coprophagia.
- Severely calorie-restricted diets or imbalanced diets leading to insufficiencies may also lead to pica and/or coprophagia.

SYSTEMS AFFECTED

Gastrointestinal—foreign body obstruction, GI upset leading to vomiting and diarrhea. Increased chance of GI parasitism with coprophagia.

GENETICS

None known

INCIDENCE/PREVALENCE

Unknown

SIGNALMENT

Species

Coprophagia is common in dogs but rare in cats. Pica is seen in both dogs and cats.

Breed Predilections

Oriental cat breeds such as Siamese may be at greater risk of pica.

Mean Age and Range

Pica occurs more often in puppies than in adult dogs. Pica in cats is most likely to begin during the first year of life.

SIGNS

Historical Findings

- In dogs, ingestion of inappropriate items such as rocks, clothing, and/or feces.
- In cats, ingestion of fabrics, plastic, or other inappropriate items.

Physical Examination Findings

- Halitosis if coprophagia is the presenting problem.
- Dental trauma if the dog targets hard objects.
- Pallor or weakness if anemia is a contributing condition.
- Poor body condition if malabsorption or maldigestion is a contributing condition.
- Neurologic signs if caused by neurologic disease.

CAUSES

Behavioral Causes

- Coprophagia is considered normal maternal behavior. The dam or queen licks the

anogenital region of the neonate to stimulate elimination and then consumes the excreta.

- Coprophagia may be considered a normal exploratory behavior in puppies. It has been postulated that the high levels of deoxycholic acid in feces may contribute to neurologic development.
- It is normal for dogs to seek out cat feces because it is high in protein—its odor and taste may also be appealing.
- Ungulate feces is also appealing to dogs, apparently due to the partially digested vegetable matter.
- Dogs on highly restricted diets may have a voracious appetite, leading to coprophagia and pica.
- Feces may be appetizing to some dogs, so that the behavior might be self-rewarding.
- Dogs that have been punished for eliminating in the house could learn to eat their own feces in an apparent attempt to avoid punishment.
- Dogs may also eat their own feces as a form of “nest cleaning.”
- Coprophagia may occur as a form of attention-seeking behavior if a dog learns that the behavior reliably leads to immediate owner attention.
- Coprophagia may also develop as a response to anxiety.
- Pica may occur secondarily to stealing behavior when the dog is highly motivated to prevent the owner from retrieving the stolen object or when the object has ingestive appeal.
- Pica may develop as a result of anxiety that leads to destruction and then consumption of an item.

Medical Causes

- Anemia
- Malnutrition leading to polyphagia
- Endocrinopathies—hyperthyroidism, diabetes mellitus, hyperadrenocorticism
- Maldigestion/malabsorption (e.g., exocrine pancreatic insufficiency)
- Inflammatory bowel disease
- Small intestinal bacterial overgrowth
- Central nervous system disease
- Portosystemic shunt
- Intestinal parasitism

Drug-Induced Causes

Administration of drugs such as corticosteroids, progestins, phenobarbital, or benzodiazepines can lead to polyphagia.

RISK FACTORS

- Early weaning of kittens has been postulated to lead to sucking and ingestion of fabrics.
- Cats fed low-roughage diets and/or not allowed access to roughage sources such as grass.
- Dogs lacking an appropriately stimulating environment, adequate activity, or social interactions may be at risk for pica and/or coprophagia.
- Long periods of confinement, especially in a barren environment, may predispose to coprophagia.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- The diagnosis is based on the history and description of the behavior.
- The history

should include

- Description of the problem—when and where does it happen

- Age of onset
- Owner's usual response, any corrections attempted so far, and their results
- Changes in household, schedule, diet, or health associated with onset of the problem
- Feeding routine of pets—when, where fed, and by whom
- Any other unusual oral behaviors
- Other behavioral problems
- House training status—when and where does the pet eliminate
- How the pet was house trained
- Relationships with other pets
- Environment, including daily schedule for play, exercise, attention, or training.
- Medical health should be evaluated, including appetite and weight, any signs of nausea or GI upset such as excessive lip licking or surface licking, and color and consistency of feces.
- Pica must be differentiated from destructive chewing, where items may be torn apart but not consumed.
- Pica must also be differentiated from those instances where an animal consumes a non-food item because the item smells and/or tastes like food.

CBC/BIOCHEMISTRY/URINALYSIS

- Results suggesting diabetes mellitus, hyperadrenocorticism, hyperthyroidism, or drug-induced causes of polyphagia.
- Anemia or hypoproteinemia.
- Results suggesting the presence of a portosystemic shunt—microcytosis, target cells, hypoalbuminemia, low BUN, ammonium biurate crystalluria.
- Peripheral eosinophilia may occur due to gastrointestinal parasitism or eosinophilic inflammatory bowel disease.

OTHER LABORATORY TESTS

- TLI—may be low if exocrine pancreatic insufficiency exists.
- Serum folate and cobalamin to evaluate for small intestinal bacterial overgrowth and small intestinal mucosal disease.
- Fecal fat and fecal trypsin may help to evaluate for exocrine pancreatic insufficiency and other malabsorption-/maldigestion-related conditions.
- Thyroid panel to determine if hyperthyroid.
- Fecal examinations to screen for intestinal parasites.
- Bile acids to evaluate for the presence of a portosystemic shunt.
- ACTH stimulation test to evaluate for hyperadrenocorticism.

IMAGING

Survey abdominal radiographs and/or abdominal ultrasonography may be necessary to rule out foreign body obstruction. May also demonstrate microhepatitis if a portosystemic shunt is present.

DIAGNOSTIC PROCEDURES

Small intestinal biopsy samples may be needed to evaluate for infiltrative small bowel disease. Cultures of the small intestine to evaluate for small intestinal bacterial overgrowth.

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

Treatment of Pica

- Prevent access to non-food items that are likely targets. ◦ Confine the animal away from targeted non-food items. ◦ Muzzle dogs; watch for overheating in warm climates and when worn for prolonged periods of time.
- Booby traps may be used to keep the pet away from certain areas and items.
- Change to a diet higher in fiber. • Provide feeding toys and acceptable foraging opportunities (e.g., green plants such as grass or catnip for cats). • Teach dogs a “Drop it” or “Leave it” command so the owner can prevent consumption of inappropriate items. • If diagnosis consistent with compulsive disorder see appropriate section in text for treatment.

Treatment of Coprophagia

- Prevent access to feces. • Walk dog on leash and pick up feces immediately.
- Muzzle; observe precautions to avoid overheating in warmer climates. ◦ Head collar for increased ability to guide pet away from feces and reward “turning away” after defecation. Use a remote-activated citronella collar to distract the animal every time it tries to sniff or ingest feces. ◦ This must be used every time the animal has access to feces in order for it to be effective. ◦ Dogs should then be rewarded with a tasty treat for returning to the owner on command.
- There is no evidence that changing the taste or texture of the stool helps to decrease coprophagia. • Taste aversion can be taught by treating the feces with a powerfully aversive substance (e.g., hot sauce, cayenne pepper, etc.). • All feces that the dog can come in contact with must be treated in order for this to be effective. However, even if effective, dogs can learn to recognize the smell of the treated feces, avoid it, and ingest untreated feces.

ACTIVITY

- Increased mental and physical stimulation may help in the treatment and prevention of pica and coprophagia. • More regular, predictable schedules of interaction and exercise can decrease anxiety and may aid in the treatment of pica and coprophagia.

DIET

Dietary changes may be helpful in some cases of coprophagia. A more highly digestible diet or the addition of plant-based enzyme supplements or meat tenderizers may rarely be successful in decreasing coprophagia.

CLIENT EDUCATION

- Owners should be counseled that coprophagia is, in most cases, normal canine behavior and not harmful unless the dog consumes feces containing pathogens or

parasites. • Owners should avoid the use of any form of direct or confrontational punishment for pica or coprophagia due to the risk of increasing anxiety, possibly worsening the behavior, and/or leading to other problem behaviors. Close supervision and preventing access are the best approach.



MEDICATIONS

DRUG(S) OF CHOICE

If the behavior is determined to be secondary to anxiety, psychoactive drugs including an SSRI such as fluoxetine or a TCA such as clomipramine may be indicated. (See Compulsive Disorders—Cats and Compulsive Disorders—Dogs).

CONTRAINdications

The use of any drugs that might contribute to polyphagia should be avoided when possible.

PRECAUTIONS

- Avoid the use of TCA in animals with aggression, a history of seizures, cardiac problems, glaucoma, or urine or stool retention. • Anticholinergic side effects are not uncommon. • Clomipramine and fluoxetine may potentiate the side effects of some CNS depressants, such as benzodiazepines, barbiturates, and general anesthetics.

POSSIBLE INTERACTIONS

Fluoxetine and clomipramine should not be given in conjunction with inhibitors or within 2 weeks of discontinuation of MAOIs. Clomipramine should not be combined with an SSRI.



FOLLOW-UP

PATIENT MONITORING

- Client should be contacted in 1–2 weeks to verify compliance and determine if there is improvement. • If no or minimal improvement, further diagnostics should be recommended.

PREVENTION/AVOIDANCE

- Prevent access to the items likely to be consumed. • Careful supervision during house training may help to prevent puppy exploration of feces and reinforcement of coprophagia. • Administration of monthly parasiticide to control GI parasites.

POSSIBLE COMPLICATIONS

Foreign body obstruction is the most common sequelae to pica in both dogs and cats.

EXPECTED COURSE AND PROGNOSIS

- Prognosis is guarded if: ◦ The condition has been present for a long period of time.

COPROPHAGIA AND PICA

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- The owner is not willing to closely supervise the dog when it eliminates.
- If owner is willing to supervise the dog and comply with treatment recommendations, the prognosis improves.



MISCELLANEOUS

AGE-RELATED FACTORS

In adult or geriatric onset of pica or coprophagia, primary underlying medical conditions should be strongly suspected.

PREGNANCY/FERTILITY/BREEDING

- The use of TCA's should be avoided in pregnant and nursing females. • Owners of wool-sucking cats should be cautioned that the behavior appears to have a breed disposition, so avoiding breeding of this individual may be the prudent and responsible action. • If this behavior is believed to be associated with a compulsive disorder, the animal should not be bred, as compulsive disorders appear to have a hereditary basis.

SYNOMYS

- Depraved appetite • Wool sucking or wool chewing in cats

SEE ALSO

- Compulsive Disorders—Cats • Compulsive Disorders—Dogs

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- CNS = central nervous system • GI = gastrointestinal • MAOI = monoamine oxidase inhibitor • SSRI = selective serotonin reuptake inhibitor • TCA = tricyclic antidepressant • TLI = trypsin-like immunoreactivity

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Client Education Handout
available online

CORNEAL AND SCLERAL LACERATIONS



BASICS

DEFINITION

- Penetrating—a wound or foreign body enters but does not completely pass through the cornea or sclera.
- Perforating—a wound or foreign body completely passes through the cornea or sclera; greater risk of vision loss than penetrating.
- Simple—involves only the cornea or sclera; may be penetrating or perforating; other ocular structures intact.
- Complicated—perforating; involves other structures besides the cornea or sclera; uveal, vitreal, or retinal incarceration or prolapse through the wound; traumatic cataract; hyphema; lid lacerations.

PATOPHYSIOLOGY

- Sharp trauma—wounds by an outside-in mechanism.
- Blunt trauma—wounds by an inside-out mechanism; eye undergoes sudden changes in its equatorial and axial dimensions and IOP; actual wound may be at a site other than the point of impact; often more damaging than sharp trauma.
- All or a portion of the foreign object initiating the injury may be retained in the wound or eye.

SYSTEMS AFFECTED

- Musculoskeletal—surrounding skull or orbital tissue
- Nervous—unconsciousness or brain injury
- Ophthalmic

INCIDENCE/PREVALENCE

Common

SIGNALMENT

Species

Dog and cat

SIGNS

Historical Findings

- Usually acute onset.
- Often a history of running through heavy vegetation, being hit by gunshot pellets or other projectiles, or being scratched by a cat.
- Trauma may not be observed.

Physical Examination Findings

- Varies with tissues affected.
- Common—corneal, scleral, or eyelid deformity; edema; hemorrhage.
- May see a retained foreign body.
- Often rapidly seals; may appear only as a subconjunctival hematoma.
- May also see iris defects, pupil distortion, hyphema, cataract, vitreal hemorrhage, retinal detachment, and exophthalmia.

CAUSES

Blunt or sharp trauma

RISK FACTORS

- Preexisting visual impairment
- Young, naive, or highly excitable animals
- Hunting or running through heavy vegetation
- Fighting



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- History or a retained foreign body usually diagnostic.
- Traumatic event not observed and no foreign body found—consider non-traumatic causes of corneal ulceration, hyphema, etc.
- Traumatic hyphema—almost invariably accompanied by corneal or scleral lesions and subconjunctival or periocular hemorrhage.
- Traumatic cataracts—disrupted lens capsule common.
- Traumatic retinal detachment—almost invariably accompanied by intraocular hemorrhage.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually noncontributory.
- Consider as a preanesthesia screen or when non-traumatic cause is possible.

OTHER LABORATORY TESTS

- Cytologic examination and aerobic culture and sensitivity testing of the wound and foreign body—recommended even if infection is not apparent; may need to collect specimen under general anesthesia at the time of surgery.
- Consider other tests (platelet count, coagulation profile, etc.) if non-traumatic causes are possible.

IMAGING

- Ocular ultrasonography—if the ocular media are opaque; may clarify the extent and nature of intraocular disease; may detect foreign body.
- Orbital radiographs, CT or MRI (if non-metallic)—may help determine projectile's course; may detect foreign body.

DIAGNOSTIC PROCEDURES

- Determine the nature, force, and direction of impact of the object—help identify which tissues may be involved.
- Do not put pressure on the eye until rupture or laceration of the globe has been ruled out.
- Assess vision—menace response; aversion to bright light.
- Periocular skin and orbit—examine for lacerations or deformities; suspect globe involvement if a lid laceration crosses the eyelid margin or penetrates the orbital septum; entry sites are often small and quickly seal.
- Abnormal ocular motility—suggests extraocular muscle trauma, orbital hemorrhage or edema, retained foreign bodies or peripheral nerve or CNS damage.
- Scleral rupture—consider this possibility with subconjunctival hemorrhage, especially if the anterior chamber is abnormally deep or shallow, there is vitreal hemorrhage, or the eye is abnormally soft.
- Pupils—size; shape; symmetry; direct and consensual light reflexes.
- Detailed ophthalmoscopy—assess clarity of ocular media and fundus integrity; rule out intraocular foreign body.
- Seidel test—if any question of corneal or scleral leaking; use a dry to slightly moist fluorescein strip to paint a thin coat of fluorescein over the surface of

the defect; leaking aqueous combines with the orange fluorescein, forming a bright green rivulet (seen best with cobalt illumination).

PATHOLOGIC FINDINGS

- Depends on wound and affected tissues.
- Usually correlates closely with clinical examination findings.
- Vitreal hemorrhage—may organize into a fibrous band that applies traction to the retina, causing it to detach.
- Post-traumatic sarcoma (cats)—may occur months to years after severe ocular trauma.



TREATMENT

APPROPRIATE HEALTH CARE

- Depends on severity.
- Outpatient—if integrity of the globe is ensured.

NURSING CARE

- Sedation—consider for excited or fractious patients.
- When walking—apply an Elizabethan collar and use a harness or put ipsilateral foreleg through the leash to avoid increasing intraocular pressure in affected eye.
- Avoid third eyelid flaps in patients with perforations or deep/long penetrating wounds until the wound is stable.

Injuries Considered for Medical Treatment

- Non-perforating wounds with no wound edge override or gape—apply an Elizabethan collar; give topical antibiotic or atropine ophthalmic solutions.
- Non-perforating wounds with mild wound gape or shelfed edges—apply a therapeutic soft contact lens and an Elizabethan collar; give topical antibiotic or atropine ophthalmic solutions.
- Simple full-thickness, pinpoint corneal perforation with a negative Seidel test that has a formed anterior chamber and no uveal prolapse—sedentary patients; use a therapeutic soft contact lens and an Elizabethan collar; give topical antibiotic or atropine ophthalmic solutions; reexamine a few hours after applying the lens and at 24 and 48 hours.

ACTIVITY

Usually confined indoors (cats) or limited to leash walks until healing is complete. A harness is preferred to a collar to reduce pressure on the neck and the risk of increased intraocular pressure and wound leaks.

CLIENT EDUCATION

Warn client that the full extent of the injury (cataracts, retinal detachment, infection) may not be apparent until several days or weeks after the injury and that long-term follow-up is necessary.

SURGICAL CONSIDERATIONS

Injuries Requiring Surgical Exploration or Repair

- Full-thickness corneal lacerations with a

(CONTINUED)

CORNEAL AND SCLERAL LACERATIONS

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positive Seidel test. • Full-thickness wounds with iris incarceration or prolapse. • Full-thickness scleral or corneoscleral lacerations. • Suspected retained foreign body or a posterior scleral rupture. • Simple non-perforating wound with edges that are moderately or overtly gaping and that are long or more than two-thirds the corneal thickness.

Injuries Considered for Surgical Exploration or Repair

- Small full-thickness corneal lacerations with a negative Seidel test and no uveal incarceration or prolapse. • Large conjunctival lacerations. • Partial-thickness corneal or scleral lacerations in an active patient.



MEDICATIONS

DRUG(S) OF CHOICE

Antibiotics

• Complicated wounds, those with retained plant material, and those caused by blunt trauma with tissue devitalization—*infection common*. • Bacterial endophthalmitis—5–7% of perforations; very rare in wounds that only penetrate but do not perforate the cornea. • Penetrating—topical antibiotics alone (e.g., neomycin, polymyxin B, and bacitracin) or gentamicin solution q6–8h; usually sufficient. • Perforating wounds with negative Seidel test—systemic ciprofloxacin (dogs, 10–20 mg/kg PO q24h); topical cefazolin (33 mg/mL by adding injectable cefazolin to artificial tears) and fortified gentamicin or tobramycin (add injectable aminoglycoside to the commercial ophthalmic solution to achieve a final concentration of 14 mg/mL), both drugs q4–6h. • Perforating wounds with positive Seidel test—systemic ciprofloxacin (dogs, 10–20 mg/kg PO q24h); topical cefazolin and fortified gentamicin or tobramycin as noted above, only after defect has been made watertight.

Anti-Inflammatories

• Topical 1% prednisolone acetate or 0.1% dexamethasone solution q6–12h; as soon as the wound is sutured or has epithelialized (becomes fluorescein stain negative), as long as infection is not present. • Systemic prednisone 0.5–1 mg/kg q12h–q24h; for sutured or epithelialized wounds when inflammation is severe; when the lens or more posterior structures are involved; when the wound is infected or not epithelialized and control of inflammation is mandatory to preserve the eye. • Topical NSAIDs—flurbiprofen or one of several others; may be used if topical corticosteroids are contraindicated and control of inflammation is mandatory to preserve the eye.

Mydriatics

- 1% atropine ophthalmic solution q6–12h; when there is significant miosis or anterior chamber reaction.

Analgesics

- Topical atropine or oral aspirin (dogs, 10–15 mg/kg PO q12h to q8h)—may provide sufficient pain relief. • Carprofen 2.2 mg/kg PO q12h or 4.4 mg/kg PO once daily. • Tramadol—start at 1–2 mg/kg q12h and can increase up to 5 mg/kg q6h or as needed. • Butorphanol: dogs, 0.2–0.4 mg/kg; cats, 0.1–0.2 mg/kg IV, SC, or IM q2–4h or as needed; acute mild pain; sedation not required. • Oxymorphone: dogs, 0.05–0.1 mg/kg; cats, 0.05 mg/kg IV, SC, or IM q4–6h or as needed; acute severe pain; sedation required. • Naloxone 0.04 mg/kg IV, SC, or IM; to reverse narcotics.

CONTRAINDICATIONS

- Topical ophthalmic ointments—avoid in perforations with positive Seidel test until wound closed. • Systemic ciprofloxacin—avoid in small and medium dog breeds aged 2–8 months; avoid in large dog breeds aged 2–12 months; avoid in giant dog breeds aged 2–18 months; potential for damaging rapidly growing articular cartilage.

PRECAUTIONS

- Aminoglycosides—topical application may be irritating and may impede reepithelialization if used frequently or at high concentrations; possibility of toxicity when given to very small patients or when giving by more than one route. • Topical solutions may be preferable to ointments if corneal integrity is questionable. • Atropine—may exacerbate KCS and glaucoma. • Topical or systemic NSAIDs—use cautiously with hyphema; safety of topical NSAIDs in cats unknown.

POSSIBLE INTERACTIONS

Systemic NSAIDs—may potentiate the nephrotoxicity of aminoglycosides; ensure good hydration and adequate renal function, especially in small dogs.

ALTERNATIVE DRUG(S)

Topical ciprofloxacin ophthalmic solution—may be used instead of the combination of topical cefazolin and a fortified aminoglycoside; some streptococcus are resistant.



FOLLOW-UP

PATIENT MONITORING

- Deep or long penetrating wounds that have not been sutured and perforating wounds—recheck q24–48h for the first several days to ensure integrity of the globe, to monitor for infection, and to check control of ocular inflammation. • Superficial penetrating wounds—usually recheck at 3- to 5-day

intervals until healed. • Antibiotic therapy—alter according to culture and sensitivity results.

PREVENTION/AVOIDANCE

- Take care when introducing new puppies to households with cats that have front claws. • Minimize running through dense vegetation or the owner should consider having a bottle of saline eyewash to irrigate foreign debris from the eye. • Minimize visually impaired or blind dog's exposure to dense vegetation.

POSSIBLE COMPLICATIONS

- Loss of the eye or vision. • Chronic ocular inflammation or pain. • Post-traumatic sarcoma—may develop in blind cat eyes that have been severely traumatized.

EXPECTED COURSE AND PROGNOSIS

- Most eyes with corneal lacerations or a retained corneal foreign body are salvageable. • The more posterior the injury, the poorer the prognosis for retention of vision. • Poor prognosis—scleral or uveal involvement; no light perception; perforating injuries involving the lens or with significant vitreal hemorrhage or retinal detachment.
- Penetrating injuries usually better prognosis than perforating injuries. • Blunt trauma carries a poorer prognosis than sharp trauma.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Depends on nature and extent of injury.

PREGNANCY / FERTILITY/ BREEDING

- Systemic corticosteroids—may complicate pregnancy. • Systemic ciprofloxacin—probably should be avoided during pregnancy.

SEE ALSO

- Cataracts • Hyphema • Keratitis, Ulcerative • Proptosis • Retinal Detachment

ABBREVIATIONS

- CNS = central nervous system • CT = computed tomography • IOP = intraocular pressure • KCS = keratoconjunctivitis sicca • NSAID = nonsteroidal anti-inflammatory drug

INTERNET RESOURCES

<http://dro.hs.columbia.edu/rptglobe.htm>

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Author Paul E. Miller

Consulting Editor Paul E. Miller



**Client Education Handout
available online**

CORNEAL OPACITIES—DEGENERATIONS AND INFILTRATES



BASICS

OVERVIEW

Corneal degeneration—an acquired corneal disorder characterized by lipid or calcium deposition. May be unilateral or bilateral, have distinct margins, and occur secondary to other ocular or systemic disorders.

SIGNALMENT

Corneal degeneration occurs primarily in dogs, uncommon in cats. Lipid deposition most commonly in geriatric dogs. May be associated with systemic hyperlipoproteinemia.

SIGNS

- Clinical signs vary based on type of deposit and associated ocular or systemic disorders.
- Lipid—gray-white or crystalline; can be band-shaped, irregular, or circular.
- Calcium—dense white to crystalline; irregular, punctate to band-shaped lesions in the superficial stroma. • Frequently associated with inflammatory disorders such as keratitis or uveitis. • Corneal vascularization, edema, and pigmentation often present. • With progression the cornea may develop a roughened appearance; the epithelium may become disrupted, leading to ulceration.
- Associated ocular conditions that may lead to corneal degeneration—corneal scars, KCS, exposure keratitis, chronic uveitis, episcleritis, phthisis bulbi, chronic topical steroid therapy, limbal neoplasia. • When lipid deposition occurs secondary to systemic hyperlipoproteinemia, a perlimbal annular ring (arcus lipoides cornea) may form with a clear zone between affected cornea and limbus; often bilateral but may be asymmetrical; vascularization is variable.

CAUSES & RISK FACTORS

- Lipid—hyperlipoproteinemia: may increase risk, may worsen preexisting deposits; can be secondary to hypothyroidism, diabetes mellitus, hyperadrenocorticism, dietary indiscretion, pancreatitis, nephrotic syndrome, liver disease, primary hyperlipidemia of miniature schnauzers.
- Calcium—hypercalcemia, hyperphosphatemia, hypervitaminosis D, hyperadrenocorticism, uremia, geriatric patients. • Both—lipid and calcium are frequently seen together.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of corneal opacities. • Corneal scar—non-painful lesion, gray to white depending on severity; fluorescein negative; relatively smooth corneal surface; distinct margins. • Corneal stromal

dystrophies—bilateral, often symmetrical foci of deposition, gray to white in appearance, distinct margins; heritable, not associated with ocular inflammation; do not retain fluorescein stain; often occur away from the limbus. • Edema—bluish to gray; usually more homogeneous; can vary in size depending on severity; indistinct margins; can retain fluorescein stain if corneal erosion/ulceration also present. • Corneal ulcer—results in ocular pain, retains fluorescein stain, varying degrees of edema may surround the lesion. • Inflammatory cell infiltrates—results in ocular pain, gray to tan to yellow with indistinct margins; cytologic examination of cornea reveals white blood cells, microorganisms.

CBC/BIOCHEMISTRY/URINALYSIS

- *Systemic tests only necessary if hyperlipidemia is suspected; no systemic tests necessary for most cases.*
- Lipid—evaluate fasting cholesterol, triglyceride, blood glucose levels.
- Calcium—evaluate serum calcium levels.
- Other laboratory tests
- Lipid—hypothyroidism: low thyroid hormone concentrations and depressed response to TSH. • Cushing's—ACTH stimulation test. • If suspect pancreatitis—PLI test.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

May retain fluorescein around margins of deposit if raised.



TREATMENT

- Treat primary ocular disease if present.
- Usually benefit from low-fat diet if hyperlipoproteinemia; treat primary systemic disease if present; both may help slow or stop progression of the disease. • Corneal deposits that are causing patient discomfort or are impairing vision may benefit from corneal debridement or superficial keratectomy, followed by medical treatment; deposits are likely to recur following treatment if underlying cause not corrected beforehand.



MEDICATIONS

DRUG(S)

- Topical broad-spectrum antibiotics (i.e., triple antibiotic) for ulcerated cornea; frequency depends on severity; usually uncomplicated ulcers treated q8–12h.
- Topical nonsteroidal anti-inflammatory q8–12h—indicated if uveitis noted.
- Topical 0.2% cyclosporine—to improve tear film quality, reduce inflammation.
- Topical 1% atropine q8–24h—indicated to

reduce pain if uveitis or ulceration is present.

- Topical EDTA solution 0.4%–1.38% q6h; may help minimize calcium deposits; usually used following debulking procedure to improve efficacy.
- Artificial tear ointment q6–12h; may prevent or reduce frequency of secondary corneal ulceration; provides lubrication and improves comfort when corneal surface is irregular.

CONTRAINdications/POSSIBLE COMPLICATIONS

- Topical corticosteroids—not recommended, may worsen severity; contraindicated with corneal ulceration.
- Topical atropine—contraindicated with KCS, glaucoma, lens luxations.



FOLLOW-UP

PATIENT MONITORING

Monitor serum cholesterol and triglycerides to assess efficacy of dietary management in hyperlipidemic patients; monitor treatment of primary disease if present.

EXPECTED COURSE AND PROGNOSIS

- Corneal ulceration—may be associated with worsening of disease. • Vision—may be affected in advanced disease; may be severe if primary ocular disease present (e.g., uveitis).
- Deposits may recur in patients following superficial keratectomy.



MISCELLANEOUS

SEE ALSO

- Corneal Opacities—Dystrophies
- Keratitis, Ulcerative

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone
- EDTA = ethylene diamine tetra-acetate
- KCS = keratoconjunctivitis sicca • PLI = pancreatic lipase immunoreactivity • TSH = thyroid stimulating hormone

INTERNET RESOURCES

<http://dro.hs.columbia.edu/ced1.htm>

Suggested Reading

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Client Education Handout
available online

CORNEAL OPACITIES—DYSTROPHIES



BASICS

OVERVIEW

- Primary, inherited (or familial), bilateral, and often symmetrical condition of the cornea that is not associated with other ocular or systemic diseases.
- Three types based on anatomic location—epithelial: associated with dyskeratotic and necrotic epithelial cells, focal absence of epithelial basement membrane, and increased cells in anterior corneal stroma; stromal: lipid deposition within the corneal stroma; and endothelial: characterized by abnormal, dystrophic endothelial cells.

SIGNALMENT

Usually dogs; rare in cats.

Epithelial

Shetland sheepdogs—age of onset 6 months–6 years; slow progression.

Stromal

- Usually young adult dogs at age of onset.
- Affected breeds—Afghan hound, Airedale terrier, Alaskan malamute, American cocker spaniel, beagle, bearded collie, bichon frise, Cavalier King Charles spaniel, German shepherd, Lhasa apso, mastiff, miniature pinscher, rough collie, Samoyed, Siberian husky, Weimaraner, whippet, and others; inheritance pattern identified in only a few breeds.

Endothelial

- Dogs—primarily affects Boston terriers, Chihuahuas, and dachshunds; may affect other breeds; typically middle-aged or older at onset of clinical signs; female predilection suggested.
- Cats—affects young animals; described most often in domestic shorthairs; a similar condition that occurs without endothelial disease is inherited in Manx as an autosomal recessive disorder.

SIGNS

All cause some degree of opacity in the cornea.

Epithelial

- Can be asymptomatic or have blepharospasm; multifocal white or gray circular to irregular opacities or rings; sometimes associated with multifocal corneal erosions.
- Vision—usually not affected.

Stromal

- Usually asymptomatic with no associated inflammation.
- Central—most common; gray, white, or silver oval to circular opacity of the central or paracentral cornea; with magnification may note multiple fibrillar to coalescing opacities that have a crystalline or ground-glass appearance (crystalline corneal dystrophy).
- Diffuse—affects Airedales; more

diffuse, dense opacity than with central dystrophy.

- Annular—affects Siberian huskies most commonly; doughnut-shaped opacity of the paracentral or peripheral cornea.
- Vision—usually not affected; visual deficit possible with advanced or diffuse disease.

Endothelial

- Asymptomatic in early stages.
- Edema of temporal or inferio-temporal cornea that usually progresses to involve the entire cornea after months to years.
- Corneal epithelial bullae (bullos keratopathy) and subsequent corneal erosion ulceration may develop; erosions or ulceration may cause blepharospasm due to pain.
- Vision—may be impaired with advanced disease.

CAUSES & RISK FACTORS

- Epithelial—result of degenerative or innate abnormalities of the corneal epithelium and/or basement membrane.
- Stromal—innate abnormality or localized error in corneal lipid metabolism; may be affected by hyperlipoproteinemia (may increase opacity).
- Endothelium—degeneration of the endothelial cell layer; subsequent loss of endothelial cell pump function results in corneal edema.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Epithelial, stromal—other causes of corneal opacity: corneal degenerations, ulcers, scars, inflammatory cell infiltrates.
- Endothelial—other causes of diffuse corneal edema: uveitis and glaucoma.

CBC/BIOCHEMISTRY/URINALYSIS

Epithelial, stromal—high concentrations of cholesterol and triglyceride levels may modify the course of the disease but are not the cause.

DIAGNOSTIC PROCEDURES

- Stromal—usually does not retain fluorescein stain.
- Epithelial or endothelial—may retain fluorescein stain, often in multifocal punctate areas, particularly with advanced disease.
- Tonometry—to eliminate glaucoma as cause of corneal edema.



TREATMENT

- Advanced epithelial or endothelial disease with ulceration—may require treatment for ulcerative keratitis.
- Stromal—usually none required; may perform superficial keratectomy to remove lipid deposits if severe

but usually unnecessary and deposits may recur.

- Inform client that some corneal dystrophies are inherited.
- Advanced endothelial dystrophy—may use therapeutic soft contact lens with or without debridement of redundant corneal epithelial tags; conjunctival flap surgery; thermal cautery of the cornea; penetrating keratoplasty (corneal transplant) may be of benefit but success rates vary (fair to good for cats, poor for dogs).



MEDICATIONS

DRUG(S)

- Corneal ulceration—topical antibiotics and possibly atropine (see Keratitis, Ulcerative).
- Epithelial—1–2% cyclosporine in oil or 0.2% ointment q8–24h as needed to relieve clinical signs.
- Endothelial—topical 5% sodium chloride ointment; palliative treatment; does not markedly clear cornea but may prevent progression and rupture of corneal epithelial bullae.

CONTRAINdications/POSSIBLE INTERACTIONS

Topical corticosteroids—no benefit to lipid (stromal) dystrophy; of questionable benefit to other forms of dystrophy.



FOLLOW-UP

- Reexamination—necessary only if ocular pain or corneal ulceration develops.
- Corneal opacity—may wax and wane with lipid dystrophy; unlikely to resolve.
- Corneal ulceration—may accompany progression of epithelial or endothelial dystrophy.
- Vision—not substantially affected except in advanced cases.



MISCELLANEOUS

SEE ALSO

- Corneal Opacities—Degenerations and Infiltrations • Keratitis, Ulcerative

Suggested Reading

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CORNEAL SEQUESTRUM—CATS



BASICS

OVERVIEW

- Corneal sequestrum is a focal, light brown to black, plaque-like area of stromal coagulation necrosis usually located axially or paraxially.
- Usually caused by chronic corneal ulceration, trauma or exposure.
- Synonyms—keratitis nigrum.

SIGNALMENT

- Cats—any breed, age.
- Brachycephalic (Persian, Himalayan) breeds, Siamese predisposed.
- Colorpoints may be genetically predisposed.

SIGNS

- Unilateral or bilateral, focal round to oval, variably sized areas of corneal discoloration ranging from a translucent golden-brown (early) to opaque black (chronic).
- Often has a chronic non-healing corneal ulcer.
- Corneal vascularization and edema.
- Often had previous episodes of feline herpesvirus-1 (FHV-1) keratoconjunctivitis.
- Blepharospasm and/or ocular discharge.
- Conjunctival hyperemia and chemosis.
- Miotic pupil.
- May be static for long periods or may rapidly progress.
- With chronicity, corneal vascularization may result in extrusion of the plaque.

CAUSES & RISK FACTORS

- Exact cause unknown but thought to involve chronic mechanical corneal irritation or ulceration with subsequent corneal necrosis and desiccation.
- Proposed risk factors include chronic corneal ulceration, chronic trichiasis or entropion, brachycephalic conformation, lagophthalmia (incomplete blink), keratoconjunctivitis sicca (KCS), qualitative tear film disorders (lipid or mucin deficiency), FHV-1 infection, topical drug use (corticosteroids), and iatrogenic trauma (multiple grid keratotomy).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Corneal perforation/iris prolapse—protruding iris is fleshy and is yellow to light brown.
- Corneal foreign body—usually obvious.
- Corneal pigmentation—rare in cats.
- Corneal neoplasia—melanocytoma occurs at the limbus and is typically non-painful.

CBC/BIOCHEMISTRY/URINALYSIS

No specific abnormalities

OTHER LABORATORY TESTS

- Schirmer tear test—very low values suggest KCS but some normal cats can have low

values.

- Corneal culture and cytology to rule out secondary corneal infection if corneal ulceration or inflammatory cellular infiltrate is present.
- Fluorescein stain to determine if ulcerated.
- Tear film breakup time (TBUT)—normal time to breakup of the fluorescein-stained tear film is 21 seconds. TBUT may be decreased in cats with sequestra or FHV-1 due to mucin tear film deficiency or secondary to the corneal disease.
- Corneal histopathology to confirm diagnosis and evaluate completeness of excision.
- The acellular necrotic cornea is undermined by inflammatory cells.
- Nested PCR for FHV-1 DNA—of limited value since normal healthy cats may carry FHV-1 and have positive PCR results.
- Conjunctival biopsy for goblet cell density—goblet cell numbers may be decreased secondary to conjunctival inflammation and/or FHV-1.



TREATMENT

- Lesion depth, degree of ocular pain, and financial status of the client are important factors in development of a treatment plan.
- Medical—supportive care while waiting for sequestrum to spontaneously slough; ocular pain may persist for months and sloughing of sequestrum may lead to deep corneal ulceration or perforation.

SURGICAL CONSIDERATIONS

- Lamellar keratectomy is surgical procedure of choice. If performed early, it can rapidly relieve ocular pain, promote faster corneal healing, and may prevent the lesion from involving the deeper corneal stroma.
- Adjunctive corneal grafting procedures should be performed if $\geq 50\%$ of the corneal stroma has been excised. Options include conjunctival pedicle grafting; grafting with synthetic, autogenous, or heterologous biomaterials; and corneoscleral transposition.
- Postoperative corneal ulcer management with a broad-spectrum topical antibiotic, atropine ointment, and a tear supplement.



MEDICATIONS

DRUG(S)

- Topical oxytetracycline HCl with polymyxin B (Terramycin) or bacitracin-neomycin-polymyxin B q6–8h as prophylaxis.
- Topical 1% atropine sulfate ointment q12–24h to improve ocular comfort..
- Topical lubricants (e.g., carboxymethylcellulose gel) q6–8h to reduce mechanical irritation and prevent corneal desiccation; may also prevent progression of early non-ulcerated sequestra.

- Adjunctive topical and/or systemic antiviral therapy in cases with history or clinical signs compatible with FHV-1 infection.

- Topical interferon-a-2b (1,000–3,000 units/mL) q6–8h. Anecdotal reports of clinical improvement in sequestra, particularly those related to FHV-1 infection.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Topical antibiotics (neomycin) may be irritating and cause chemical conjunctivitis.



FOLLOW-UP

PATIENT MONITORING

- If managing medically, examine weekly to monitor progression and for complications associated with sloughing of the sequestrum.
- If managed by keratectomy, examine every 5–7 days until the corneal defect has reepithelialized (usually occurs within 7–14 days).
- Sequestra may recur or occur in the contralateral eye. Recurrence is more likely in cats with low Schirmer tear tests, with full-thickness lesions, or in cases in which keratectomy did not result in complete excision of the pigmented corneal tissue or the predisposing cause was not addressed.

POSSIBLE COMPLICATIONS

Corneal perforation may occur if a sequestrum sloughs, leaving a full-thickness defect, and/or if sloughing results in a deep stromal corneal ulcer that becomes malacic or infected.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Corneal ulceration—cats
- Eyelid conformational abnormalities (trichiasis, entropion, etc.)

ABBREVIATIONS

- FHV-1 = feline herpesvirus-1
- KCS = keratoconjunctivitis sicca
- PCR = polymerase chain reaction
- TBUT = tear film breakup time

Suggested Reading

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BASICS

DEFINITION

• A sudden and often repetitively occurring defense reflex that helps clear large airways of excess secretions, irritants, foreign particles, and microbes, or clear foreign material from upper airways. • The cough reflex consists of three phases: inhalation, forced exhalation against a closed glottis, and violent expulsion of air from the lungs following opening of the glottis, usually accompanied by a sudden noise. Coughing can happen voluntarily as well as involuntarily, although in dogs and cats it is presumed to be essentially involuntary.

PATOPHYSIOLOGY

• A physiologic reflex in healthy animals that protects the lower airways from inhalation of foreign particles and helps clear particles that have been entrapped in the mucus; acts in conjunction with the mucociliary clearance mechanism. • The cough pathway includes cough receptors, (sensory nerves in the airways), the vagus nerve, the central cough center, and effector muscles. • The cough pathway can be stimulated by mechanical or chemical factors. Endogenous triggers include airway secretions and inflammation. Exogenous triggers include smoke and aspirated foreign material. • Cough receptors include rapidly adapting stretch receptors (sensitive to mechanical stimuli) that are located within the mucosa of the tracheobronchial tree (especially larynx and trachea), and pulmonary/bronchial C-fibers, which are more sensitive to chemical stimulation. Coughing mechanisms and pathways are very complex and are not fully understood, even in humans.

SYSTEMS AFFECTED

• Respiratory—cough of any origin can be an inciting factor for inflammation that aggravates and perpetuates further cough. • Cardiovascular—enlargement or impaired function of the right ventricle can result from a respiratory disorder (cor pulmonale); cough syncope can occur from a vasovagal response.

SIGNALMENT

• Dogs and cats of all ages and breeds. • Much more common clinical sign in dogs than in cats. • Cough of tracheal origin is less common in cats than in dogs. • Age, breed, and sex predispositions vary with inciting cause.

SIGNS

• Cough must be differentiated from similar signs such as reverse sneezing, gagging, retching, and vomiting. • Description of the cough can be helpful in identification of the anatomic structures involved in dogs (i.e., honking cough is typical of tracheal or airway

collapse, harsh sonorous cough followed by terminal retch characterizes cough of tracheal or bronchial origin, faint moist cough is heard in moderate to severe pneumonia). • Cough can be described as dry or moist, productive, honking, short or harsh, faint or sonorous, followed by gagging or retching. • Cough can be elicited by traction on the collar (laryngeal or tracheal origin), aggravated by exercise or excitement (tracheal collapse), or can occur after a period of rest (cough due to heart failure). • Can be accompanied by stertor or stridor (laryngeal, tracheal origin) or labored breathing (many areas).

CAUSES

Upper Respiratory Tract Diseases

• A variety of sinonasal conditions cause extension of inflammation and/or secretions into the pharynx and/or larynx and can lead to the “upper airway cough syndrome” (UACS), previously referred to as “post-nasal drip syndrome.” • Laryngeal disease (inflammation, paralysis, tumor, granuloma, collapse). • Tracheal disease (inflammation, infection, foreign body, collapse, stenosis, tumor).

Lower Respiratory Tract Diseases (Tracheobronchial or Bronchopulmonary Disease)

• Inflammatory (feline bronchitis syndrome; dogs: chronic bronchitis, eosinophilic bronchopneumopathy). • Infectious—bacterial, viral (distemper, kennel cough [dog]; calicivirus, herpesvirus [cat]), parasitic (*Filaroides* spp. [dog], *Aelurostrongylus abstrusus* [cat], *Paragonimus kellicotti* [dog, cat], *Dirofilaria immitis* [dog, cat], *Capillaria aerophilia* [dog], *Crenosoma vulpis* [dog]), protozoal (toxoplasmosis [cat]; pneumocystosis [dog]), fungal (blastomycosis, histoplasmosis, coccidiomycosis, cryptococcosis, aspergillosis). • Neoplastic (primary, metastatic, compression due to enlarged lymph nodes). • Chemical or traumatic (aspiration, near drowning, noxious fumes, foreign body, trauma, hemorrhage).

Other Diseases

• Cardiovascular diseases (pulmonary edema, heart-base tumor, embolism). • Gastroesophageal reflux. • Compression of the respiratory structures by adjacent organs (cardiomegaly, megaeosophagus, hilar lymph node enlargement) or by pleural effusion. • Non-cardiogenic pulmonary edema (multiple causes). • Passive smoking inhalation. • Adverse drug reaction—potassium bromide in cats.

RISK FACTORS

Breed

• Toy and miniature breeds at risk for tracheal collapse. • Terrier breeds at risk for pulmonary fibrosis. • Husky, rottweiler, Labrador, and Jack Russell terrier, at risk for eosinophilic bronchopneumopathy. • Giant

breeds at risk for dilated cardiomyopathy.

- Labrador retriever, large breeds at risk for laryngeal paralysis. • Siamese cats at risk for feline bronchitis syndrome.

Environmental Factors

- Longhaired cats that are infrequently groomed will periodically retch, cough, and then vomit up mats of hair.

Drugs

- Potassium bromide in cats

Geographic Area (or Travel History)

- Certain diseases are common in specific areas (e.g., dirofilariasis, angiostrongylosis).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Many conditions result in similar signs.
- Coughing can be confused with other signs such as sneezing, reverse sneezing, gagging, panting, retching, and vomiting. The presence of terminal retch is often misinterpreted as vomiting.

CBC/BIOCHEMISTRY/URINALYSIS

Minimum database may suggest acute bacterial infection (leukocytosis with left shift) or eosinophilic airway disease (peripheral eosinophilia).

OTHER LABORATORY TESTS

- Filter test for microfilaria and/or heartworm antigen serology—for heartworm disease.
- Serum antibody titer—toxoplasmosis, *Angiostrongylus vasorum*. • Coagulation profile—for any patient that presents with cough associated with either epistaxis or hemoptysis. • Fecal examination (Baermann test: identification of *Angiostrongylus* (dogs), *Aelurostrongylus* (cat) or other parasites (*Filaroides*, *Crenosoma*). • PCR diagnosis available for several micro-organisms. • Tests for evaluation of systemic diseases (e.g., hyperadrenocorticism, potentially predisposing to pneumonia or causing pulmonary thromboembolism).

IMAGING

- Thoracic radiographs are the first step prior to any additional testing; provide essential information about intrathoracic airways, lung parenchyma, pleural space, mediastinum and cardiovascular system. • Fluoroscopy—helpful to investigate diseases in which dynamic obstruction is suspected (tracheal collapse, bronchial collapse, bronchomalacia).
- Echocardiography—helpful when heart failure or dysfunction is suspected. • Thoracic ultrasonography—in case of pleural effusion or when a pulmonary or mediastinal mass is suspected.

DIAGNOSTIC PROCEDURES

- Endoscopy allows visualization of both static (tumor, granuloma, abnormal mucosa,

COUGH

(CONTINUED)

C

excessive secretions) and dynamic (laryngeal paralysis, dynamic airway collapse) airway abnormalities. • When bronchial and/or alveolar infiltrates are present—samples from lower airways can be obtained for diagnostic purpose (cytology, bacterial/mycologic cultures) by broncho-alveolar lavage or tracheal wash. • Transthoracic (fine-needle aspiration) biopsy or thoracoscopy—allow biopsy sample when interstitial infiltration is prominent. • Thoracocentesis—allows sampling of pleural fluid, can be performed under ultrasonographic guidance. • Pulse oximetry and blood gas determination. • Pulmonary function tests—require sophisticated material and/or experienced technicians, not readily available in private practice.



TREATMENT

• Usually treated as outpatient. • The most successful management of cough involves treatment and resolution of the underlying cause rather than use of medications that suppress signs. • If chronic cough is related to acute or chronic inflammation, anti-inflammatory therapy is preferred to cough suppressant therapy. • The use of cough suppressant therapy must be limited to cases in which the cause of the cough can neither be treated medically nor resolved, and in which excessive coughing leads to exhaustion of the patient or insomnia of the owners, as well as aggravation of the disease.



MEDICATIONS

DRUG(S) OF CHOICE

Antimicrobial Therapy

- Indicated for infectious tracheobronchitis or bronchopneumonia.

Anti-inflammatory Therapy

- Indicated in feline bronchitis syndrome, canine chronic bronchitis, or canine eosinophilic bronchopneumopathy.
- Oral prednisolone 0.5 mg/kg q12h in dogs and cats, then taper the dose progressively to q48h.
- Nebulized fluticasone with a metered dose inhaler including a spacer with face mask and inspiratory valve (variable concentrations exist, the most appropriate dose is not well established).

Antihistamines

- H1-receptor antagonists.
- May be helpful in suspected allergic tracheitis or bronchitis, or when light sedation is a positive side effect.

Antitussives

- Hydrocodone (dog only): 0.22 mg/kg PO q12h.

- Butorphanol (dog only): 0.5 mg/kg PO q12h.
- No antitussive available for cats. In humans, gabapentin (a neuromodulator) was recently described to treat refractory chronic cough. Not evaluated in dogs.

Bronchodilators

Theophylline (for Dogs and Cats)

- Pharmacokinetics are form- and species-dependent. Slow-release formulations exist. Dosage: dog, 5–10 mg/kg PO q12h; cats, 15–20 mg/kg/day PO in the evening.
- Beneficial effects of theophylline include relaxation of bronchial smooth muscle, improved diaphragmatic contraction, and probably some anti-inflammatory effects.
- Side effects are related to inotropic and chronotropic effects, as well as to an increase in blood pressure; can also cause nausea, diarrhea, arrhythmias, and CNS excitation.

β -2 Agonists (Essentially for Cats)

- Can be delivered via an injection, as a tablet, in syrup form, by nebulization, or via an inhaler; administered IV or SQ in emergency situations. Short-acting (salbutamol, terbutaline, fenoterol) or long-acting (salmeterol, formoterol) drugs.
- Can be administered temporarily to cause immediate and temporary relief but not as a long-term management; have a limited effect.
- Side effects include dry mouth, tachycardia, nausea. Regular inhalation of racemic and S-albuterol (but not R-albuterol) induces airway inflammation in both healthy and asthmatic cats.

Expectorants

- Guafenesin—included in some preparations but benefit not extensively studied or proven.

CONTRAINDICATIONS

Antitussive agents are strictly contraindicated when cough is needed to clean the airways, i.e., in infectious or inflammatory airway disease, bronchiectasis.

POSSIBLE INTERACTIONS

Theophylline—clearance is inhibited by other drugs such as fluoroquinolones, increasing the risk of theophylline toxicity.



FOLLOW-UP

PATIENT MONITORING

- Acute cough must be adequately treated in order to avoid chronic cough, which can lead to possibly irreversible lesions.
- Conditions leading to chronic cough sometimes can only be alleviated but not cured; communicate with client to ensure successful management of cough.

POSSIBLE COMPLICATIONS

- Aggravation of tracheal collapse.
- Progression toward chronic bronchitis,

chronic obstructive pulmonary disease, lung emphysema, irreversible bronchial and parenchymal remodeling, bronchiectasis.

- Acute severe cough might lead to syncope, rib fracture, or pneumothorax.
- Right heart dysfunction.



MISCELLANEOUS

AGE-RELATED FACTORS

• In dogs with anatomic disorders of inherited (e.g., primary ciliary dyskinesia) or congenital origin, signs might start early in life. • Puppies and kittens are more likely to suffer from infectious disease. • Inflammatory disorders affect middle-aged adults. • Heart failure and tumors are more common in older animals.

PREGNANCY/FERTILITY/BREEDING

- Dogs affected with primary ciliary dyskinesia more than cats. • Possible decreased fertility (in male and female dogs) as cilia from the urogenital tract and flagellated cells can be affected.
- Proven hereditary in some breeds (Old English sheepdog, carrier test detection exists).

SEE ALSO

- Asthma, Bronchitis—Cats
- Bronchitis, Chronic
- Canine Infectious Respiratory Disease
- Congestive Heart Failure, Left-Sided
- Hypoxemia
- Nasal Discharge
- Pneumonia, Bacterial
- Pneumonia, Eosinophilic
- Respiratory Parasites
- Tracheal and Airway Collapse

ABBREVIATION

- CNS = central nervous system

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Consulting Editor Lynelle R. Johnson



**Client Education Handout
available online**

CRANIOMANDIBULAR OSTEOPATHY



BASICS

OVERVIEW

- A non-neoplastic, non-inflammatory proliferative disease of the bones of the head.
- Primary bones affected—mandibular rami; occipital and parietal; tympanic bullae; zygomatic portion of the temporal. • Bilateral symmetric involvement most common.
- Affects musculoskeletal system.

SIGNALMENT

- Scottish, cairn, and West Highland white terrier breeds—most common. • Labrador retrievers, Great Danes, Boston terriers, Doberman pinschers, Irish setters, English bulldogs, bullmastiffs, Shetland sheepdogs, and boxers—may be affected. • Usually growing puppies 4–8 months of age. • No gender predilection. • Neutering may increase incidence.

SIGNS

Historical Findings

- Usually relate to pain around the mouth and difficulty opening the mouth progressively worsening. • Difficulty in prehension and mastication—may lead to starvation.

Physical Examination Findings

- Temporal and masseter muscle atrophy—common. • Palpable irregular thickening of the mandibular rami and/or TMJ region. • Inability to fully open jaw, even under general anesthesia. • Intermittent pyrexia. • Bilateral exophthalmos.

CAUSES & RISK FACTORS

- Believed to be hereditary—occurs in certain breeds and families. • West Highland white terriers—autosomal recessive trait. • Scottish terriers—possible predisposition. • Young terrier with periosteal long bone disease—monitor for disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Osteomyelitis—bones not symmetrically affected; generally not as extensive; lysis; lack of breed predilection; history of penetrating wound. • Traumatic periostitis—bones not symmetrically affected; generally not as extensive; history of trauma. • Neoplasia—mature patient; not symmetrically affected; more lytic bone reaction; metastatic disease.
- Calvarial hyperostosis—young patient—frontal, parietal, and occipital bones; does not involve mandible; may have long bone involvement.

CBC/BIOCHEMISTRY/URINALYSIS

- Serum ALP and inorganic phosphate—may be high • May note hypogammaglobulinemia or α_2 -hyperglobulinemia.

OTHER LABORATORY TESTS

Serology—rule out fungal agents; indicated in atypical cases.

IMAGING

- Skull radiography—reveals uneven, bead-like osseous proliferation of the mandible or tympanic bullae (bilateral); extensive, periosteal new bone formation (exostoses) affecting one or more bones around the TMJ; may show fusion of the tympanic bullae and angular process of the mandible. • CT—may help evaluate osseous involvement of the TMJ.

DIAGNOSTIC PROCEDURES

Bone biopsy and culture (bacterial and fungal)—necessary only in atypical cases; rule out neoplasia and osteomyelitis.

PATHOLOGIC FINDINGS

- Bone biopsy—reveals normal lamellar bone being replaced by an enlarged coarse-fiber bone and osteoclastic osteolysis of the periosteal or subperiosteal region. • Bone marrow—replaced by a vascular fibrous-type stroma. • Inflammatory cells—occasionally seen at the periphery of the bony lesion.



TREATMENT

- Palliative only. • Surgical excision of exostoses—results in regrowth within weeks.
- High-calorie, protein-rich gruel diet—helps maintain nutritional balance. • Surgical placement of a pharyngostomy, esophagostomy, or gastrostomy tube—considered to help maintain nutritional balance.



MEDICATIONS

DRUG(S)

- Analgesics and anti-inflammatory drugs—palliative use warranted.
- NSAIDs—inhibit cyclooxygenase enzymes.
- Deracoxib (1–2 mg/kg PO q24h, chewable).
- Carprofen (2.2 mg/kg PO q12h or 4.4 mg/kg q24h).
- Etodolac (10–15 mg/kg PO q24h).
- Meloxicam (load 0.2 mg/kg PO, then 0.1 mg/kg PO q24h—liquid).
- Tepoxalin (load 20 mg/kg, then 10 mg/kg PO q24h).
- Firocoxib (5 mg/kg PO q24h).



FOLLOW-UP

PATIENT MONITORING

Frequent reexaminations—mandatory to ensure adequate nutritional balance and pain control.

PREVENTION/AVOIDANCE

- Do not repeat dam-sire breedings that resulted in affected offspring. • Discourage breeding of affected animals.

EXPECTED COURSE AND PROGNOSIS

- Pain and discomfort may diminish at skeletal maturity (10–12 months of age); the exostoses may regress. • Prognosis—depends on involvement of bones surrounding the TMJ. • Elective euthanasia may be necessary.



MISCELLANEOUS

SYNONYMS

- Lion jaw • Craniomandibular osteoarthropathy • Craniomandibular osteodystrophy • Mandibular periostitis • Westie jaw • Scotty jaw

ABBREVIATIONS

- ALP = alkaline phosphatase • CT = computed tomography • NSAID = nonsteroidal anti-inflammatory drug • TMJ = temporomandibular joint

Suggested Reading

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CRUCIATE LIGAMENT DISEASE, CRANIAL



BASICS

DEFINITION

The acute or progressive failure of the cranial cruciate ligament, which results in partial to complete instability of the stifle joint.

PATHOPHYSIOLOGY

- Function of the CrCL includes passive constraint of the stifle joint by limiting internal rotation and cranial displacement of the tibia relative to the femur; it also limits stifle hyperextension.
- Two distinct bands—craniomedial band is taut on both flexion and extension of the joint (primary check) and caudolateral band is taut in extension and lax in flexion (secondary check).
- Without the CrCL, the active constraints (muscles) around the stifle are the main limits to slippage of the tibia cranially.
- Protective mechanism of hamstring activation during stifle loading decreases strain on CrCL.
- Avulsion—occurs in skeletally immature animals in which an acute load results in avulsion of the ligament for the femoral or more commonly tibial attachment site.
- Acute rupture—caused by traumatic actions exceeding the strength of the ligament; usually hyperextension, excessive limb loading, or internal rotation; generally, results in a midsubstance tear of the CrCL and osteophytosis are absent; most common cause in cats.
- Progressive (chronic) degeneration pathogenesis remains elusive; biomechanical and histologic changes occur in the CrCL with age and body weight > 15 kg. Changes include decreases in elasticity, stress/strain energy, failure to maintain collagen fiber organization, and chondroid metaplasia.
- Repetitive subclinical injury may be due to neuromuscular incoordination, aging, conformational abnormalities (excessive TPA, medial luxating patella, narrow intercondylar notch), breed variations, poor muscle tone related to sedentary habits or limb immobilization, and possibly immune-mediated damage.
- Microruptures of individual ligament fiber bundles leave the main structure intact but functionally compromised; cumulative weakening leads to ultimate disruption of CrCL even if from a minor insult; complete and partial tears exist in varying degrees.
- Untreated instability leads to degenerative osteoarthritic changes within a few weeks; severe within a few months.
- Medial meniscal (caudal horn) damage occurs in 33.2–77% of cases. Likely due to shearing force on caudal horn of medial meniscus.

SYSTEMS AFFECTED

Musculoskeletal, ± neurologic

GENETICS

Suspected

INCIDENCE/PREVALENCE

The most common cause of hind limb lameness in dogs; major cause of DJD in the stifle joint.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog; uncommon in cat

Breed Predilections

- All susceptible—especially large to giant breeds
- Rottweiler and Labrador retriever—increased incidence when < 4 years of age
- West Highland white terrier—overrepresented affected small breed

Mean Age and Range

- Incidence increases with age > 5 years.
- Large- to giant-breed dogs may present earlier in life; approx. 2 years of age.

Predominant Sex

Female—neutered

SIGNS

General Comments

Severity of lameness—related to the degree of rupture (partial vs. complete), the mode of rupture (acute vs. chronic), the occurrence of meniscal injury, and the severity of inflammation and DJD. The condition and therefore the lameness may be bilateral.

Historical Findings

- Athletic or traumatic events—generally precede acute injuries.
- Normal activity resulting in acute lameness—suggests degenerative rupture.
- Subtle to marked intermittent lameness (for weeks to months)—consistent with partial tears that are progressing to complete rupture.

Physical Examination Findings

- Varying degrees of lameness and joint effusion, pain, and/or crepitus; the affected limb generally held in partial flexion while standing.
- Cranial drawer test—diagnostic for rupture; test in flexion, normal standing angle, and extension.
- Tibial compression test—cranial movement of tibia relative to the femur when tightening the gastrocnemius by flexing the hock.
- Palpable thickening on the medial aspect of the stifle (medial buttress).
- Presence of click or pop within the joint is 63% accurate in detecting meniscal injury.
- Hind limb muscle atrophy—especially the quadriceps muscle group.
- False-negative drawer or compression tests with chronic or partial tears and in painful or anxious patients that are not sedated or anesthetized.

CAUSES

- Trauma
- Repetitive microinjury; excessive stifle loading
- Progressive degeneration

RISK FACTORS

- Obesity
- Patella luxation
- Conformational abnormalities
- Excessive caudal slope of tibial plateau
- Narrowed intercondylar notch



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Puppy laxity—positive drawer motion that stops abruptly as the CrCL is stretched taut.
- Patella luxation (medial or lateral)—alone or with CrCL rupture.
- Collateral ligament injury, long digital extensor tendon injury.
- Osteochondritis dissecans of the femoral condyle.
- Neoplasia (e.g., synovial sarcoma, osteosarcoma, chondrosarcoma).
- Traumatic fractures or avulsions.
- Caudal cruciate ligament rupture—uncommon.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

Radiography

- Warranted to verify secondary intra-articular changes such as DJD and rule out other differentials.
- Common findings—joint effusion with capsular distention and effacement of the infrapatellar fat pad; periarticular osteophytes; CrCL avulsion fractures; calcification of the CrCL and/or menisci.
- Cats commonly have mineralized menisci present (incidental finding).
- Necessary for pre-operative planning with some surgeries.

Alternative Diagnostic Imaging

- Ultrasound and MRI—facility and operator dependent.

DIAGNOSTIC PROCEDURES

- Arthrocentesis—joint cytology to classify synovial changes and rule out sepsis or immune-mediated disease.
- Arthroscopy—gold standard; allows direct visualization and magnification of the cruciate ligaments, menisci, and other intra-articular structures; allows for description and repair of meniscal pathology.

PATHOLOGIC FINDINGS

- Varying degrees of synovitis, cartilage fibrillation and erosion.
- Periarticular osteophyte formation.
- Meniscal damage.
- Ruptured fibers of the CrCL—hyalinization; fibrous tissue invasion; necrosis; loss of the parallel orientation of ligament bundles.



TREATMENT

APPROPRIATE HEALTH CARE

- Stabilization surgery—recommended; speeds rate of recovery; reduces degenerative changes; enhances function.
- Conservative management—NSAIDs, physical rehabilitation, and 10% weight loss; approx. 66% of patients have normal function over

(CONTINUED)

CRUCIATE LIGAMENT DISEASE, CRANIAL

C

the course of > 1 year; DJD is progressive; not generally recommended.

NURSING CARE

Post-surgery—restricted activity with physical rehabilitation (e.g., ice packing, range-of-motion exercises, massage, and muscle electrical stimulation); important for improving mobility and strength.

ACTIVITY

Restricted—duration depends on method of treatment and progress of patient.

DIET

- Weight control—important for decreasing the load and thus stress on the stifle joint.
- Joint health diets rich in omega-3 fatty acids and chondroprotectants may support overall joint health.

CLIENT EDUCATION

- Regardless of the method of treatment, DJD is common and progressive.
- Return to full athletic function is possible but requires early surgical intervention and rehabilitation.
- Rupture of contralateral CrCL can occur in 37–48% of patients.

SURGICAL CONSIDERATIONS

- No one technique has proven consistently superior to the others clinically or radiographically.
- Recent force plate studies show slight differences between common techniques; dogs with TPLO procedure achieve normal limb loading faster than extracapsular repair patients.
- In patients with concurrent meniscal injury, partial meniscectomy aims to alleviate pain associated with injury; however, has been shown to reduce and alter meniscal function and cause osteoarthritis.

Extra-articular Methods

- Wide variety of techniques that use a heavy-gauge implant to laterally tether the tibia to the femur to mimic the CrCL and restore stability; these techniques rely on periarticular fibrosis for long-term stability.
- Implant material—should be placed in the most isometric points of the CrCL origin and insertion.
- Alternative method includes fibular head transposition to realign and tension the lateral collateral ligament in order to restrict internal rotation and cranial drawer.

Intra-articular Methods

- Designed to replace the CrCL anatomically with autografts (patellar ligament, fascia), allografts, xenografts, and synthetic materials.
- Femoral intercondylar notchplasty—recommended to minimize graft injury.

Osteotomy Procedures**Cranial Tibial Closing Wedge Osteotomy**

- Involves leveling the TPA by removing a cranially based wedge of bone from the proximal tibia and eliminates cranial thrust.
- Held in place with a bone plate and screws.
- Can potentially shorten the tibia and alter stifle biomechanics.

Tibial Plateau Leveling Osteotomy

- Rotational osteotomy of the proximal tibia to level TPA and neutralize cranial tibial thrust.
- Held in place with a bone plate and screws.
- Can accomplish correction for angular and torsional deformities.

Tibial Tuberosity Advancement

- Tibial crest osteotomy; crest is held in an advanced position with a cage and plate; bone graft fills the defect.
- Active control of cranial tibial displacement is improved, which helps stabilize the stifle.
- Can combine technique with lateral transposition of tibial tuberosity to correct concurrent medial luxating patella.

**MEDICATIONS****DRUG(S) OF CHOICE**

- NSAIDs—minimize pain; decrease inflammation.
- Meloxicam (load 0.2 mg/kg PO, then 0.1 mg/kg daily PO).
- Carprofen (2.2 mg/kg PO q12h).

CONTRAINdications

Avoid concurrent use of corticosteroids with NSAIDs.

PRECAUTIONS

NSAIDs may cause gastrointestinal irritation/ulceration, liver toxicity, and renal damage; may preclude use in some patients.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Chondroprotective drugs (polysulfated glycosaminoglycans, glucosamine, and chondroitin sulfate) may help reduce cartilage damage and improve regeneration.

**FOLLOW-UP****PATIENT MONITORING**

- Most techniques require 2–4 months of rehabilitation.

PREVENTION/AVOIDANCE

Avoid breeding animals with conformational abnormalities.

POSSIBLE COMPLICATIONS

- Subsequent meniscal injury can occur in 6–22% of patients.
- Incisional and/or implant related infection.
- Tibial tuberosity avulsion and/or fractures.
- Patellar luxation.
- Delayed bone healing (osteotomy procedures).
- Pivot shift—unknown clinical significance < 2%.

EXPECTED COURSE AND PROGNOSIS

Regardless of surgical technique, the success rate is better than 85%.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Meniscal damage

AGE-RELATED FACTORS

See “Pathophysiology”

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Arthritis (Osteoarthritis)
- Patellar Luxation

ABBREVIATIONS

- CrCL = cranial cruciate ligament
- DJD = degenerative joint disease
- NSAID = nonsteroidal anti-inflammatory drug
- TPA = tibial plateau angle
- TPLO = tibial plateau leveling osteotomy

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Client Education Handout
available online

Cryptococcosis



BASICS

DEFINITION

A localized or systemic fungal infection caused by the environmental yeast *Cryptococcus* spp, most commonly *C. neoformans* and *C. gattii*.

PATHOPHYSIOLOGY

- *C. neoformans*—grows in bird droppings and decaying vegetation; soil disturbance increases risk of infection.
- Dogs and cats inhale the yeast and a focus of infection is established, usually in the nasal passages; smaller dried, shrunken organisms may reach the terminal airways (uncommon). There may be colonization or subclinical infection of the nasal passages that spontaneously resolves.
- Stomach and intestinal infections suggest that primary GI entry can occur.
- Dissemination—hematogenously spread via macrophages from the nasal passages to the brain, eyes, lungs, and other tissues; by extension to the skin of the nose, eyes, retro-orbital tissues, and draining lymph nodes.

SYSTEMS AFFECTED

- Cats—mainly upper respiratory signs affecting the nose and sinuses; skin; nasal planum; nasopharynx; CNS; eyes.
- Dogs—mainly the head and brain, nasal passages, and sinuses; skin over the nose and sinuses; mucous membranes; draining lymph nodes; eyes; periorbital areas; occasionally lungs and abdominal organs.

INCIDENCE/PREVALENCE

- Dogs—rare in United States; prevalence 0.00013%.
- Cats—7–10 times more common than in dogs; most common systemic mycoses of cats.

GEOGRAPHIC DISTRIBUTION

- Worldwide.
- Some areas of southern California and Australia have an increased incidence and an outbreak has occurred on Vancouver Island in British Columbia, Canada.
- *C. gattii* grows well on eucalyptus trees.

SIGNALMENT

Species

Cat and dog

Breed Predilections

- Dogs—American cocker spaniels, Great Danes, Doberman pinschers, and boxers appear overrepresented.
- Cats—Siamese breed may be at increased risk.

Mean Age and Range

- Most commonly young cats and dogs <4 years of age.
- May occur at any age but has been seen often in dogs <6 months of age.

Predominant Sex

- Dogs—none.
- Cats—males may be overrepresented.

SIGNS

Historical Findings

- Lethargy.
- Varies depending on organ systems involved.
- May have a history of problems for weeks to months.

Dogs

- Neurologic—seizures, ataxia, paresis
- Ocular signs—periorbital swelling, blindness
- Skin ulceration
- Lymphadenopathy
- Vomiting and diarrhea

Cats

- Nasal discharge and ocular signs
- Neurologic signs—seizures, disorientation, vestibular signs
- Granulomatous tissue seen at the nares
- Firm swellings over the bridge of the nose
- Lymphadenopathy
- Respiratory abnormalities less commonly noted

Physical Examination Findings

- Mild fever—<50% of patients.
- Dogs—anorexia; nasal discharge; multifocal CNS signs; ataxia; anterior uveitis.
- Cats—increased respiratory noise; ulcerated crusty skin lesions on the head; lymphadenopathy; neurologic (behavior change, circling, vestibular signs, ataxia); ocular (blindness, optic neuritis, retinal detachment).

CAUSES

Exposure to cryptococcal organisms and inability of the immune system to prevent colonization and invasion into tissues.

RISK FACTORS

- Exposure to disrupted soil
- Prior infection with FeLV or FIV



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Dogs

- Other causes of focal or diffuse neurologic disease—distemper; inflammatory meningoencephalomyelitis; bacterial meningoencephalitis; CNS neoplasia; rickettsial diseases; other fungal diseases.
- Nasal lesions, especially at the mucocutaneous junction—considered immune-mediated.
- Lymphoma—possible cause of the lymphadenopathy.
- With chorioretinitis and optic neuritis—consider other fungal infections, distemper, and neoplasia.

Cats

- Nasal lesions—similar to nasal tumors, chronic rhinitis, and chronic sinusitis.
- Ulcerative skin changes—may be the result of bacterial infection, fights, or neoplasia (especially squamous cell carcinoma of the nasal planum).
- Ocular and brain signs—consider lymphoma, FIP, and toxoplasmosis.

CBC/BIOCHEMISTRY/URINALYSIS

- Mild anemia in some cats
- Eosinophilia occasionally seen
- Chemistries usually normal

OTHER LABORATORY TESTS

- Latex agglutination or ELISA—detect cryptococcal capsular antigen in serum or CSF; highly sensitive assay; most infected animals have measurable capsular antigen titers; magnitude of titer correlates with extent of infection.
- Antigen assay may be less sensitive in dogs.
- May be positive when only colonization but antigen titers of 1:32 or greater are seen with fungal invasion.

IMAGING

- Nasal radiographs (cats)—soft tissue density material filling the nasal passage; occasional bone destruction of the nasal dorsum.
- Contrast-enhanced CT or MRI best for identifying brain and nasal lesions.
- Thoracic radiographs—not indicated, unless signs of lower respiratory tract disease.

DIAGNOSTIC PROCEDURES

Dogs

Neurologic disease—additional procedures: CNS imaging, cytologic examination and culture of CSF, measurement of CSF capsular antigen.

Cats

- Aspirates of the mucoid material in the nasal passages or biopsy of the granulomatous tissue protruding from the nares.
- Aspirates of lymph nodes or subcutaneous swellings often yield organisms.
- Patients with upper respiratory obstruction or severe respiratory noise—may identify a granuloma in the nasopharynx (pulling the soft palate forward with a spay hook to expose the mass or retroflexion of endoscope in nasopharynx to allow biopsy).
- Biopsy—skin lesions.
- Cultures—confirm the diagnosis; determine drug susceptibility if poorly responsive infection.

PATHOLOGIC FINDINGS

- Gross lesions—gray, gelatinous mass produced by the polysaccharide capsule; usually found in the nose, sinuses, and nasopharynx of cats; skin lesions are usually ulcerative.
- Neurologic lesions—usually seen in dogs; diffuse or fungal CNS granulomas.

(CONTINUED)

- Chorioretinitis with or without retinal detachment or optic neuritis—dogs and cats.
- Histologic response—usually pyogranulomatous; inflammatory cell infiltrate may be mild because the polysaccharide capsule interferes with neutrophil migration; organism characterized by capsulate yeast with narrow-neck budding.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient if stable.
- Neurologic signs—may initially require inpatient supportive care.

NURSING CARE

Cats—nasal obstruction influences appetite; encourage patients to eat by offering palatable food.

ACTIVITY

No restrictions in most cases.

DIET

- No special diet.
- Patients treated with itraconazole—give medication in fatty food (e.g., canned food) to improve absorption.

CLIENT EDUCATION

- Inform client that this is a chronic disease that requires months of treatment.
- Reassure client that the infection is not zoonotic.

SURGICAL CONSIDERATIONS

Remove granulomatous masses in the nasopharynx to reduce respiratory difficulties.



MEDICATIONS

DRUG(S) OF CHOICE

- Fluconazole—preferred for ocular or CNS involvement because it is water-soluble and better penetrates the CNS; cats, 50 mg PO q12–24h; dogs, 5 mg/kg PO q12h, most economical drug choice.
- Itraconazole capsules—give with a high-fat meal to maximize absorption; cats, 10 mg/kg PO daily; dogs, 5 mg/kg PO q12h; pellets in the capsule can be mixed with food; no apparent adverse taste. Itraconazole liquid: better absorption on empty stomach; compounded itraconazole: variable absorption and not recommended.
- Amphotericin B may have some advantage in severe disease at an intravenous dose of 0.5 mg/kg every 48 hours given over 3–4 hours. Monitor renal function closely.
- Terbinafine at a dose of 5 mg/kg q12h has been effective in treatment of cats with resistant infections.

CONTRAINDICATIONS

Caution with steroid use.

PRECAUTIONS

- Triazoles—hepatotoxicity; anorexia signals problems; monitor liver enzymes after first 3–4 weeks of treatment.
- Terbinafine—monitor for hepatic toxicity and anorexia.
- Amphotericin B—nephrotoxicity; caution if patient is azotemic but not an absolute contraindication if the infection is life-threatening.
- Itraconazole—ulcerative dermatitis (differentiate from the skin lesions of cryptococcosis); new skin lesions after the disease is much improved should be considered a drug reaction.

ALTERNATIVE DRUG(S)

- Cryptococcal organisms are prone to becoming resistant to antifungal treatment.
- Amphotericin B (intravenous)—dogs and cats that do not respond to a triazole; monitor creatinine closely for evidence of renal damage.



FOLLOW-UP

PATIENT MONITORING

- Monitor liver enzymes monthly (especially early in treatment) in patients receiving a triazole antifungal agent.
- Improvement in clinical signs, resolution of lesions, improvement in well-being, and return of appetite measure the response to treatment.
- Capsular antigen titers—after 2 months of treatment, the titers should decrease substantially if treatment is effective; if ineffective, try the terbinafine, because the organism can become resistant.
- Continue monitoring antigen titers every 1–2 months during treatment and after discontinuing treatment to identify recurrence of disease.
- Ideally treat until the cryptococcal antigen titers reach zero (can be > 2 years of treatment).

PREVENTION/AVOIDANCE

The organism is ubiquitous and cannot be avoided.

POSSIBLE COMPLICATIONS

Patients with neurologic disease may have seizures and permanent neurologic changes.

EXPECTED COURSE AND PROGNOSIS

Treatment—anticipated duration 4 months–1 year plus; patients with CNS disease may require life-long maintenance; median time of successful treatment with fluconazole was 4 months; median time for itraconazole treatment was 8 months.

CRYPTOCOCCOSIS



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

- Not considered zoonotic, but possibility of transmission through bite wounds.
- Inform client that the organism was acquired from the environment and that he or she could be at increased risk, especially if immunosuppressed.

PREGNANCY/FERTILITY/BREEDING

N/A

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- ELISA = enzyme-linked immunosorbent assay
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- FIP = feline infectious peritonitis
- GI = gastrointestinal
- MRI = magnetic resonance imaging

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Client Education Handout
available online

C

Cryptorchidism



BASICS

OVERVIEW

- The incomplete descent of one or both testes into the scrotum is the most common congenital anomaly of the testes.
- Inguinal—retained testis often palpable.
- Abdominal—testis difficult to palpate or identify by radiology; ultrasonography is the best available option to determine size and location of testis.
- Descent to final scrotal position—expected to be complete by 2 months postpartum; may occur later in some breeds, but rarely after 6 months in any individual; presume the diagnosis if no palpable testes at 2 months.
- Beagles—testes at the exterior inguinal ring by day 5 postpartum, between the inguinal ring and scrotum by day 15, and in the scrotum by day 40.

SIGNALMENT

- Dog—reported in almost all breeds; Chihuahua, toy poodle, Pomeranian, Yorkshire terrier; toy and miniature breeds are 2.7 times at greater risk to be cryptorchid than larger breeds; in certain populations German shepherd dog, boxer, and Staffordshire bull terrier also have greatly increased risk; unilateral more common than bilateral (75:25); right testis retained twice as often as left in dogs; right and left testis retained at equal frequency in cats.
- Incidence—dogs, ranges of 0.8–10% have been reported, incidence increases with the proportion of purebred dogs in the population; cats, 1–1.7%; 50% incidence in miniature schnauzer affected with persistent Müllerian duct syndrome.
- Genetics (dogs)—exact mode of inheritance unknown; complex genetic basis; likely polygenic recessive trait; likely heritable.
- Genetics (cats)—may be inherited, but no data documents hereditary defect; Persians overrepresented in surveys.

SIGNS

- Bilaterally cryptorchid animals are infertile; unilaterally cryptorchid animals are typically fertile.
- Rarely associated with pain or other signs of disease.
- Acute onset of abdominal pain—spermatic cord of retained testes at increased risk for torsion; 36% of retained testes with torsion of the spermatic cord were neoplastic.
- Feminizing paraneoplastic syndrome—estrogen-secreting Sertoli cell tumors in retained testes produce feminizing signs: gynecomastia, symmetrical alopecia of trunk and flanks, hyperpigmentation of inguinal skin, pendulous preputial sheath, prostatic squamous metaplasia.

CAUSES & RISK FACTORS

- Removal of affected males from breeding lines—believed to cause a reduction in

frequency; heritability thought to involve more than one gene.

- Non-hereditary predisposing factors (e.g., birth weight)—identified in humans; not reported in dogs.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Castration—differentiate bilateral condition from previous castration, previous castration of single scrotal testis with retained abdominal testis, or anorchidism (rare).
- Bilaterally cryptorchid cats may have urine odor and behavior of intact cats.

OTHER LABORATORY TESTS

hCG stimulation test—doubles blood testosterone with bilateral condition; doubles blood testosterone with unilateral condition in which only the scrotal testis has been removed; differentiates between cryptorchidism and castration; administration of 750 IU hCG IV or 50 µg GnRH IM with blood sample collection pre- and 2–3 hours post-injection; castrated dogs have testosterone concentrations < 0.1 ng/mL and do not stimulate with hCG or GnRH administration. Determination of blood canine anti-Müllerian hormone (produced by Sertoli cells; Spaycheck®) has also become commercially available for the diagnosis of cryptorchidism (uni- or bilateral conditions).

IMAGING

Transabdominal ultrasonography—useful to locate testes in the inguinal or abdominal regions. Recommended before laparotomy or laparoscopy to remove cryptorchid testes.



TREATMENT

- None except castration of both retained and scrotal testes generally recommended.
- Orchiopexy—surgical placement of a retained testis into the scrotum; considered unethical.
- hCG or GnRH—anecdotal evidence of causing descent when given to dogs < 4 months of age.
- Warn client of the increased risk of testicular neoplasia in dogs with retained testes; 53% of Sertoli cell tumors and 36% of seminomas occur in retained testes.



MEDICATIONS

DRUG(S)

- hCG (dogs)—100–1,000 IU IM four times in a 2-week period before 16 weeks of age (dogs); after 16 weeks, generally unsuccessful.
- GnRH (dogs)—50–750 µg one to six times between 2 and 4 months of age.



FOLLOW-UP

- Migration of testes into the scrotum after 4 months is unlikely; after 6 months, rare.
- Risk of testicular neoplasia thought to be approximately 13.6 times greater in affected dogs than in normal dogs; undescended testes at increased risk of torsion of the spermatic cord.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Inguinal hernia, umbilical hernia
- Hip dysplasia
- Patellar luxation
- Penile and preputial defects (e.g., hypospadias)

SEE ALSO

- Seminoma
- Sertoli Cell Tumor
- Sexual Development Disorders

ABBREVIATIONS

- GnRH = gonadotropin-releasing hormone
- hCG = human chorionic gonadotropin

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CRYPTOSPORIDIOSIS



BASICS

OVERVIEW

- *Cryptosporidium* spp.—apicomplexan protozoan; causes gastrointestinal disease in dogs, cats, humans, calves, and rodents; ubiquitous in nature; worldwide distribution; enteric life cycle.
- Infection—when sporulated oocysts are ingested, sporozoites are released and penetrate intestinal epithelial cells; after asexual reproduction, merozoites are released to infect other cells.
- Prepatent period—cats, 5–10 days.
- Immunocompetent animals—intestinal disease.
- Immunocompromised animals—intestinal, liver, gallbladder, pancreatic, and respiratory infection.
- Cats—serology suggests approximately 15% exposure rate in US cats.

SIGNALMENT

- Dogs and cats. • No sex or breed predilection.
- Dogs—virtually all clinical cases have occurred in animals ≤ 6 months of age; old dogs can excrete oocysts without clinical signs.
- More common in young and newborn kittens < 6 months of age.

SIGNS

- Most infections subclinical
- Principally small bowel diarrhea
- Large bowel diarrhea reported

CAUSES & RISK FACTORS

- *C. canis* (dogs) and *C. felis* (cats)—acquired by ingestion of contaminated water or feces.
- Morphologically, species very similar.
- Some species are host-specific (*C. canis* and *C. felis*); others (*C. parvum*) infect multiple species.
- Virtually all clinical cases reported in immunocompromized cats.
- Immunosuppression—major risk factor; common causes are FeLV (cats), canine distemper virus (dogs), canine parvovirus, and intestinal lymphoma (cats and dogs).
- Immunocompetent—usually asymptomatic intestinal infection with fecal oocyst shedding for 2 weeks.
- Immunocompromised—enteritis and possibly respiratory, liver, biliary, and pancreatic infections.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Dietary indiscretion or intolerance.
- Drugs—antibiotics.
- Toxins—lead.
- Parasites—giardiasis, trichuriasis.
- Infectious agents—parvovirus, coronavirus, FIP, *Salmonella*, *Campylobacter*, *Rickettsia*, *Histoplasma*.
- Organ disease—cardiac, renal, hepatic, and pancreatic exocrine insufficiency.

- Metabolic—hypoadrenocorticism, hyperthyroidism (cats).
- Neoplasia—intestinal lymphoma.
- Infiltrative diseases—e.g., inflammatory bowel disease.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal, unless an underlying immunosuppressive disease.

DIAGNOSTIC PROCEDURES

Sugar and zinc sulfate flotation—specific gravity = 1.18; concentrates fecal oocysts (oocysts are 5 µm, so routine salt flotation often fails); oocysts best visualized after staining with modified acid-fast stain.

- Oocysts often appear to have a slight pink color
- Fecal antigen detection test (ProSpecT *Cryptosporidium* Microtiter Assay; Color-Vue *Cryptosporidium*) available.
- Fluorescent antibody techniques—available in some laboratories (Meridian Diagnostics).
- Submitting feces to a laboratory—mix 1 part 100% formalin with 9 parts feces to inactivate oocysts and decrease health risk to laboratory personnel.
- PCR techniques—available from Michigan State Animal Disease Diagnostic laboratory; approximately 10–100 times more sensitive for the diagnosis of cryptosporidiosis in cats than other techniques.

PATHOLOGIC FINDINGS

- Gross lesions—enlarged mesenteric lymph nodes; hyperemic intestinal (particular ileum) mucosa; fix specimens in Bouin's or formalin solution within hours of death because autolysis causes rapid loss of the intestinal surface containing the organisms.
- Microscopic lesions—villous atrophy; reactive lymphoid tissue; inflammatory infiltrates in the lamina propria; parasites may be found throughout the intestines but most numerous in the distal small intestine.



TREATMENT

- Outpatient.
- In immunocompetent animals—diarrhea is usually mild and self-limiting; withhold food for 24–48 hours to control diarrhea; oral glucose-electrolyte solution in mild diarrhea; parenteral fluids (isotonic with potassium added) in severe diarrhea.



MEDICATIONS

DRUG(S)

- Paromomycin (Humatin), 125–165 mg/kg PO q12h for 5 days, is an aminoglycoside antibiotic effective in treating acute intestinal patients. It may cause nephropathy in young animals with a damaged gastrointestinal

barrier. Toxicity responds to diuresis; monitor renal toxicity by monitoring urine for casts.

- Tylosin 11 mg/kg PO q12h for 28 days; effective in treating an affected cat that also had lymphocytic duodenitis.

- Nitazoxanide (Alinia, 25 mg/kg PO q24h for 7–28 days); stops oocyst shedding in cats; dosing usually associated with vomiting, which can be ameliorated by antiemetics (e.g., chlorpromazine). Has only been used in a limited number of cats with cryptosporidiosis and needs further evaluation. Few side effects other than vomiting.



FOLLOW-UP

- Monitor clinical improvement for treatment efficacy.
- Monitor oocyst shedding in the feces 2 weeks after completion of treatment or if signs persist.
- Prognosis excellent if cause of immunosuppression can be overcome.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Warn clients of potential zoonotic transmission from organisms in feces and that immune-compromised people are at great risk. However, genetic sequencing has revealed that dog and cat isolates of the parasite are host-specific and transmission of *Cryptosporidium* from dogs and cats to people is extremely rare.

Disinfection

- Resistant to commercial bleach (5.25% sodium hypochlorite) and chlorination of drinking water.
- A 10% formaldehyde solution and 5% ammonia solution will kill oocysts but requires 18 hours of exposure.
- Higher concentrations of ammonia (50%) will kill oocysts in 30 minutes; moist heat (steam or pasteurization, > 55°C), freezing and thawing, or thorough drying effective.

ABBREVIATIONS

- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- HIV = human immunodeficiency virus
- PCR = polymerase chain reaction

Suggested Reading

Palmer CS, Traub RJ, Robertson ID, et al. Determining the zoonotic significance of *Giardia* and *Cryptosporidium* in Australian dogs and cats. Vet Parasitol 2008; 154:142–147.

Author Matt Brewer

Consulting Editor Stephen C. Barr

CRYSTALLURIA



BASICS

DEFINITION

Appearance of crystals in urine

PATHOPHYSIOLOGY

- Crystals form only in urine that is, or recently has been, supersaturated with crystalloidal substances; thus crystalluria represents a risk factor for urolithiasis.
- However, detection of urine crystals is not synonymous with uroliths and clinical signs associated with them, nor is detection of urine crystals irrefutable evidence of a stone-forming tendency.
- Certain crystal types such as cystine, urate, or 2,8-dihydroxyadenine may indicate an underlying disease. Proper identification and interpretation of urine crystals is important in formulation of medical protocols to dissolve uroliths. Evaluation of urine crystals may aid in (1) detection of disorders predisposing animals to urolith formation, (2) estimation of the mineral composition of uroliths, and (3) evaluation of the effectiveness of medical protocols initiated to dissolve or prevent uroliths.
- Crystalluria in individuals with anatomically and functionally normal urinary tracts is usually harmless because the crystals are eliminated before they grow large enough to interfere with normal urinary function.
- However, they represent a risk factor for urolithiasis.
- Crystals that form following elimination or removal of urine from the patient often are of little clinical importance. Identification of crystals that have formed in vitro does not justify therapy. In recent studies following time and temperature changes, crystals formed in 28% of dog and cat samples that were initially free of crystals.
- Detection of some types of crystals (e.g., cystine and ammonium urate) in clinically asymptomatic patients, frequent detection of large aggregates of crystals (e.g., calcium oxalate or magnesium ammonium phosphate) in apparently normal individuals, or detection of any form of crystals in fresh urine collected from patients with confirmed urolithiasis may have diagnostic, prognostic, or therapeutic importance.
- Drug crystals detected in patients being administered high doses of medications such as allopurinol, sulfadiazines, or fluoroquinolones may prompt a change in therapy as they are a risk factor for formation of drug-containing uroliths.

SYSTEMS AFFECTED

Renal/Urologic

SIGNALMENT

- Calcium oxalate in miniature schnauzer, Yorkshire terrier, Lhasa apso, and miniature poodle dogs, and Burmese, Himalayan, and Persian cats.
- Cystine in dachshunds, English bulldogs, Newfoundlands, and others.

- Ammonium urate in Dalmatians and English bulldogs.
- Struvite in any breed of dog with a concomitant urinary tract infection.
- Struvite in cats and ferrets is not typically associated with urinary tract infections.
- Xanthine in Cavalier King Charles spaniels.
- 2,8-dihydroxyadenine in Native American Indian dogs and wolves.

SIGNS

None, or those caused by concomitant urolithiasis.

CAUSES

In Vivo Variables

- Concentration of crystalloidal substances in urine (which in turn is influenced by their rate of excretion and urine concentration of water).
- Urine pH (struvite and calcium phosphate are most common in neutral-to-alkaline urine; ammonium urate, sodium urate, calcium oxalate, cystine, and xanthine crystals are most common in acid-to-neutral urine).
- Solubility of crystalloidal substances in urine.
- Excretion of diagnostic agents (e.g., radiopaque contrast agents) and medications (e.g., sulfonamides).
- Dietary influence—hospital diet may differ from home diet; timing of sample collection (fasting vs. post-prandial) may influence evidence of crystalluria.

In Vitro Variables

- Temperature.
- Evaporation.
- pH changes following sample collection.
- Technique of specimen preparation—centrifugation versus non-centrifugation, volume of urine examined.
- Important in vitro changes that occur following urine collection may enhance formation or dissolution of crystals. When knowledge of in vivo urine crystal type and quantity is especially important, examine fresh specimens, ideally at body temperature. If this is not possible, they should be at room temperature, not refrigeration temperature.
- Collection container—spurious crystals may be contaminants from unclean collection containers.

RISK FACTORS

See preceding discussion about in vivo and in vitro variables in crystalluria.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Ammonium Urate, Sodium Urate, and Amorphous Urate Crystalluria

- Uncommonly observed in apparently healthy dogs and cats.
- Frequently observed in dogs and occasionally observed in cats with portal vascular anomalies, with or without concomitant ammonium urate uroliths.
- Observed in some dogs and cats with urate uroliths caused by disorders other than portal vascular anomalies such as canine breeds

identified as carriers of the hyperuricosuria gene.

Bilirubin Crystalluria

- Observed in highly concentrated urine from some healthy dogs.
- Large numbers in serial samples should arouse suspicion of an abnormality in bilirubin metabolism.
- Usually associated with underlying diseases in cats.

Calcium Oxalate Monohydrate and Calcium Oxalate Dihydrate Crystalluria

- May be observed in apparently healthy dogs and cats and in dogs and cats with uroliths primarily composed of calcium oxalate.
- Calcium oxalate monohydrate crystals are most commonly associated with ethylene glycol toxicity, but calcium oxalate dihydrate may be observed, or ethylene glycol toxicity may also occur without crystalluria.

Calcium Phosphate Crystalluria

- Large numbers of crystals presumed to be composed of calcium phosphate have been observed in apparently healthy dogs, dogs with persistently alkaline urine, dogs with calcium phosphate uroliths, and dogs with uroliths composed of a mixture of calcium phosphate and calcium oxalate.
- Small numbers of calcium phosphate crystals may occur in association with infection-induced struvite crystalluria.
- May be observed in dogs and cats with primary hyperparathyroidism, and renal tubular acidosis.

Cystine Crystalluria

Observed in dogs and cats with inborn errors of metabolism characterized by abnormal transport of cystine and other dibasic aminoacids.

Struvite Crystalluria

- Observed in dogs and cats that are apparently healthy.
- Observed in dogs and cats with infection-induced struvite uroliths, sterile struvite uroliths, non-struvite uroliths, and uroliths of mixed composition (e.g., a nucleus composed of calcium oxalate and a shell composed of struvite).
- Observed in dogs and cats with urinary tract disease without uroliths.

Uric Acid Crystalluria

- Uncommon in dogs and cats.
- Importance as described for ammonium and amorphous urates.

Xanthine Crystalluria

- Suggests administration of excessive dosages of allopurinol in conjunction with consumption of relatively high amounts of dietary purine precursors.
- Primary xanthinuria has been observed in Cavalier King Charles spaniels.
- Primary xanthinuria and xanthine uroliths occur in cats.

Miscellaneous Crystalluria

- Cholesterol crystals—observed in humans with excessive tissue destruction, nephrotic

(CONTINUED)

CRYSTALLURIA

C

- syndrome, and chyluria; observed in apparently healthy dogs. • Hippuric acid crystals—apparently rare in dogs and cats; importance unknown. • Leucine crystals in dogs—importance not determined; may occur in association with cystinuria. • Tyrosine crystals—occur in association with severe liver disease in humans; uncommonly observed in dogs and cats with liver disorders. Sodium urate needle-like appearance commonly misinterpreted as tyrosine needles. • 2,8-dihydroxyadenine- is a genetic disorder, the result of a metabolic abnormality due to the deficiency of the enzyme, adenine phosphoribosyl transferase (APRT).

Drug-Induced Crystalluria

- May be observed following administration of radiopaque contrast agents. • May be observed following treatment with sulfadiazine, fluoroquinolones, primidone, xanthine oxidase inhibitors, and tetracycline.

LABORATORY FINDINGS**Drugs That May Alter Laboratory Results**

- Urinary acidifiers (e.g., *d,l*-methionine and ammonium chloride). • Urinary alkalinizers (e.g., sodium bicarbonate and potassium citrate). • Phenothiazines and phenazopyridine may cause red or orange urine.

Disorders That May Alter Laboratory Results

N/A

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Bilirubin crystals may be associated with bilirubinemia and other laboratory abnormalities of hepatic disorders. • Most dogs and cats with calcium oxalate and calcium phosphate crystalluria are normocalcemic; some are hypercalcemic.
- Some dogs and cats with calcium oxalate crystalluria may be acidemic. • Serially examine fresh specimens when knowledge of in vivo urine crystal type is especially important; evaluate the number, size, and structure of crystals and their tendency to aggregate. • Microscopic evaluation of the appearance of urine crystals gives only a tentative indication of their composition; variable conditions associated with their formation, growth, and dissolution may alter their appearance. Definitive identification of crystal composition depends on one or more of these techniques: optical crystallography, infrared spectroscopy, X-ray diffraction, and electron microprobe analysis.

OTHER LABORATORY TESTS

- Cystine crystalluria is usually associated with a positive urine cyanide-nitroprusside reaction. • Sulfonamide crystalluria may be associated with a positive lignin test.
- Ammonium urate and amorphous urate crystals are insoluble in acetic acid; addition of 10% acetic acid to urine sediment containing these crystals often yields uric acid and sometimes sodium urate crystals. • Most dogs and a few cats with struvite crystalluria have urinary tract infections caused by urease-producing bacteria (especially staphylococci and sometimes *Proteus* spp.).
- Dogs and cats with ammonium urate crystalluria and portosystemic shunts often have high serum bile acid levels and hyperammonemia. • Dogs and cats with calcium oxalate crystalluria secondary to ethylene glycol poisoning have detectable levels of ethylene glycol in serum and urine up to 48 hours after ingestion. • Cystine crystals may be confused with struvite crystals. Cystine crystals are insoluble in acetic acid while struvite crystals are soluble. A urine nitroprusside test is positive for cystine.

IMAGING

Crystalluria may be associated with radiographically or ultrasonographically detectable uroliths.

DIAGNOSTIC PROCEDURES

Voiding urohydropropulsion or aspiration through a transurethral catheter to retrieve small urocystoliths.

**TREATMENT**

- Manage clinically important in vivo crystalluria by eliminating or controlling the underlying cause(s) or associated risk factors.
- Minimize clinically important crystalluria by increasing urine volume, encouraging complete and frequent voiding, modifying the diet, by appropriate drug therapy, and in some instances by modifying pH.

**MEDICATIONS****DRUG(S) OF CHOICE**

N/A

PRECAUTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

- Recheck urinalysis to determine if crystalluria is persistent. • See chapters on specific urolith types for monitoring urolithiasis.

POSSIBLE COMPLICATIONS

- Persistent crystalluria may contribute to formation and growth of uroliths.
- Crystalluria may solidify crystalline-matrix plugs, resulting in urethral obstruction.

**MISCELLANEOUS****AGE-RELATED FACTORS**

N/A

SEE ALSO

- Nephrolithiasis • Urolithiasis, Calcium Phosphate • Urolithiasis, Cystine
- Urolithiasis, Struvite—Cats and Ferrets
- Urolithiasis, Struvite—Dogs • Urolithiasis, Urate • Urolithiasis, Xanthine

ABBREVIATION

APRT = adenine phosphoribosyl transferase

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Authors Carl A. Osborne and Lisa K. Ulrich

Consulting Editor Carl A. Osborne

CUTANEOUS DRUG ERUPTIONS



BASICS

OVERVIEW

- A wide spectrum of diseases and clinical signs that vary markedly in clinical appearance.
- Many mild drug eruptions may go unnoticed or unreported; incidence rates for specific drugs are unknown.

SIGNALMENT

- Dogs and cats.
- Age, breed, and sex predispositions—largely unknown.
- Some types of drug eruptions appear to have a familial basis (e.g., rabies vaccine reactions in canine littermates).

SIGNS

- Pruritus—can be activated by a wide variety of compounds.
- Macular and papular rashes—commonly accompany pruritus as a non-specific sign of inflammation.
- Exfoliative erythroderma—a diffuse erythematous response caused by vasodilation; often leads to exfoliation (diffuse scaling).
- Urticaria/angioedema—results from an immediate (type I) hypersensitivity; requires prior sensitization; increased vascular permeability leads to fluid leakage into the interstitium.
- Hypersensitivity vasculitis— inflammation of cutaneous vasculature; results in poor blood flow and anoxic injury to recipient tissue; in most cases, thought to represent a type III hypersensitivity response.
- Eosinophilic dermatitis with edema (Wells'-like syndrome) of dogs—deeply erythematous plaques or macules (may be targetoid) that may be accompanied by marked edema; localized, regional, or generalized distribution; clinical appearance of lesions may be indistinguishable from vasculitis and erythema multiforme.
- Erythema multiforme—erythematous macules or plaques expand peripherally and may clear in the center (targetoid); multiple shapes/forms noted.
- Stevens-Johnson syndrome—similar to toxic epidermal necrolysis with less extensive epidermal detachment (< 30%) and often involvement of the oral mucosa.
- TEN—extensive (> 30%) necrosis and sloughing of the epidermis in sheets; results in a moist and intensely inflamed skin surface.
- Drug-induced pemphigus/pemphigoid—least common drug reaction in animals; can closely mimic the auto-immune (spontaneous) forms of these diseases; symptoms may persist after drug withdrawal.

CAUSES & RISK FACTORS

- Drugs of any type.
- Can occur after the first dose or after weeks to months of administration of the same drug.
- Exfoliative erythroderma—most often associated with shampoos and dips; also commonly seen with reactions to topical ear medications (in ear

canals and on concave pinnae).

- Eosinophilic dermatitis with edema—strong association with concurrent acute gastrointestinal disease and use of antidiarrheal and/or antiemetic drugs.
- Temporal association in dogs between application of metaflumizone (Promeris) and onset of pemphigus foliaceus.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pruritus, macular/papular rashes, and urticaria/angioedema—allergic and parasitic diseases (e.g., atopy, adverse reactions to foods, contact hypersensitivity, flea bite hypersensitivity, scabies, stinging insects).
- Exfoliative erythroderma—epitheliotropic lymphoma in old dogs and cats.
- Vasculitis—once confirmed by biopsy: rule out infectious, neoplastic, and auto-immune diseases for cause; many cases of vasculitis are idiopathic.
- EM/SJS/TEN—rule out respiratory infections, herpes virus, parvovirus, bacterial infection (non-cutaneous) and internal neoplasia; an idiopathic/chronic form of EM occurs in older adult dogs.
- Pemphigus/pemphigoid—consider drug reaction whenever these diseases are diagnosed; however, spontaneously occurring auto-immune disease is much more common.

CBC/BIOCHEMISTRY/URINALYSIS

Potential for concurrent hepatic, renal, and gastrointestinal disease with concurrent vasculitis.

OTHER LABORATORY TESTS

- Dogs with vasculitis—rickettsial serology.
- Cats with vasculitis—FIV and FeLV serology, and tests to rule out FIP.
- Both dogs and cats—bacterial and fungal cultures when vasculitis with pyogranulomatous inflammation is diagnosed.

DIAGNOSTIC PROCEDURES

Skin biopsy for histopathology—mandatory for diagnosis of most drug-induced diseases (vasculitis, EM, TEN, eosinophilic dermatitis, pemphigus/pemphigoid).

PATHOLOGIC FINDINGS

Determined by specific disease process



TREATMENT

- Discontinue use of the offending or suspect drug.
- SJS/TEN—intensive supportive care and fluid/nutritional support because of fluid and protein exudation and risk of sepsis.
- Pain relief when indicated; however, minimal drug use recommended when drug eruption is suspected.
- For chronic/persistent idiopathic EM, azathioprine or cyclosporine may be effective.



MEDICATIONS

DRUG(S)

Most conditions respond to immunosuppressive therapy if withdrawal of the offending drug alone is insufficient (controversial in the case of SJS/TEN due to risk for sepsis).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Avoid the offending drug or any other drug in the same class or family.



FOLLOW-UP

PATIENT MONITORING

- Inpatient—if debilitated.
- Outpatient—regular rechecks, depending on physical condition.

PREVENTION/AVOIDANCE

See "Contraindications/Possible Interactions"

POSSIBLE COMPLICATIONS

- Secondary infections
- Electrolyte and plasma protein depletion (SJS/TEN)

EXPECTED COURSE AND PROGNOSIS

- Some reactions appear to activate self-perpetuating immune responses.
- Some drug metabolites may persist for days to weeks and provoke a continued response.
- TEN—prognosis poor.
- Vasculitis—prognosis guarded when there are systemic complications.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Cutaneous vasculitis—arthropathy, hepatitis, glomerulonephritis, and neuromuscular disorders, among others.

SEE ALSO

- Pemphigus
- Vasculitis, Cutaneous

ABBREVIATIONS

- ANA = antinuclear antibody
- EM = erythema multiforme
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- SJS = Stevens-Johnson syndrome
- TEN = toxic epidermal necrolysis

Suggested Reading

Miller WH, Griffin CE, Campbell KL eds. Cutaneous adverse drug reaction. In: Muller & Kirk's Small Animal Dermatology, 7th ed. St. Louis, MO: Elsevier, 2013, pp. 466–488.

Author Daniel O. Morris

Consulting Editor Alexander H. Werner



BASICS

OVERVIEW

- Flies of the genus *Cuterebra* are found in the Americas, where they are obligatory parasites of rodents and lagomorphs. Adult flies lay eggs on blades of grass or in nests, and they hatch and crawl onto the skin of the passing host. The small maggots enter a body orifice, migrate through various internal tissues, and, ultimately, make their way to the skin, where they establish a warble. The mature maggots, which may be an inch long, then drop out of the rodent or rabbit host and then pupate in the soil.
- Dogs and cats become infected when they walk past a blade of grass with an egg containing an infective maggot that is stimulated to hatch and to jump onto the passing animal. The maggots then crawl around on the cat or dog until they find an orifice in which to enter.
- Dogs and cats can develop maggots in warbles or can develop signs associated with the larvae migrating within their tissues.
- Dogs and cats can present with respiratory signs, neurologic signs, ophthalmic lesions, or maggots in their skin.

SIGNALMENT

- Dogs and cats—all ages.
- In northern United States, most cases occur in late summer and early autumn based on the time of emergence of the adult egg-laying females in spring and early summer.

SIGNS

- Dermatologic—warble containing bot with protruding spiracles.
- Neurologic—ataxia, circling, paralysis, blindness, recumbency.
- Ophthalmic lesions—larva in conjunctiva.
- Respiratory—eosinophilic respiratory disease.

CAUSES & RISK FACTORS

- Dogs and cats with access to outdoors, where they contact the eggs and larvae.
- Neonatal cats have been infected, presumably with larvae being brought home on the queen's fur.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Respiratory—allergies, lungworms, migrating ascarids, or hookworms.
- Neurologic—rabies, distemper, angiostrongylosis.
- Ophthalmic lesions—larval *Hypoderma* or *Oestrus*.
- Dermatologic—mature warble unmistakable, young warble may present as a pustule or papule.

CBC/BIOCHEMISTRY/URINALYSIS

May have elevated eosinophils

OTHER LABORATORY TESTS

N/A

IMAGING

CT scan has shown lesions in cranial images of cats

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Can remove maggots from subcutaneous lesions, eyes, or nares.
- Manifestations of lung migration may be alleviated by corticosteroids.
- Neurologic disease may have a poor prognosis; euthanasia is an option.



MEDICATIONS

DRUG(S)

Ivermectin 0.2 mg/kg SC should kill migrating maggots; may want to begin corticosteroid treatment before administering the ivermectin. The ivermectin can be administered either to alleviate the signs caused by maggots suspected of migrating in the lungs or to kill larvae in other tissues, including the CNS.



FOLLOW-UP

Good return of function following ivermectin treatment possible



MISCELLANEOUS

- In northern United States, disease is very seasonal, with most cases occurring in late summer and early fall when the adult flies are active. Seasonality is less demarcated in areas where warmer temperatures and active flies occur through longer periods of the year.
- Does not seem to be any prolonged immunity; the same cat can develop skin lesions several years in a row.
- Application of monthly heartworm preventatives (ivermectin-containing products), flea development control products (lufenuron-containing products), or topical flea and tick treatments may prevent the maggots from either developing in the dog or cat, or may kill them before they have time to gain access to an orifice for entry. However, based on anecdotal information, some cats and dogs on these products still develop warbles with maggots.

ZOONOTIC POTENTIAL

The maggots in the dog or cat pose no zoonotic threat.

ABBREVIATIONS

- CNS = central nervous system
- CT = computed tomography

Suggested Reading

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CYANOSIS



BASICS

DEFINITION

A bluish discoloration of the skin and mucous membranes owing to an increase in the amount of reduced, or deoxygenated, hemoglobin within the blood.

PATHOPHYSIOLOGY

- Concentration of deoxygenated hemoglobin—must be > 5 g/dL to detect condition; thus anemia (PCV < 15%) may obscure recognition of cyanosis.
- Central—associated with systemic arterial hypoxemia or hemoglobin abnormalities.
- Peripheral—limited to one or more extremities of the body; associated with diminished peripheral blood flow; arterial oxygen tension and saturation typically normal.

Arterial Hypoxemia

- Decreased fraction of inspired oxygen—high altitude. • Hypoventilation—upper airway obstructive disorders; restrictive or obstructive lung diseases; pleural space disorders; neuromuscular failure.
- Ventilation-perfusion mismatching—pulmonary parenchymal or thromboembolic diseases. • Diffusion impairment—thickening of the alveolar barrier through which oxygen must pass to reach the RBCs. • Addition of venous blood to the arterial circulation—congenital right-to-left shunting cardiac defects (e.g., tetralogy of Fallot, transposition of the great vessels); reversed shunting cardiac defects caused by high pulmonary vascular resistance (e.g., right-to-left shunting PDA, ASD, VSD). • Anatomic shunts—distinguished from other causes of hypoxemia by the failure to respond to supplemental oxygen.

Abnormal Hemoglobin

- Methemoglobin—most common abnormal heme pigment; unable to bind oxygen; normally formed at a low rate in erythrocytes.
- NADH-MR—intracellular reductive enzyme; maintains the methemoglobin: hemoglobin ratio at $< 2\%$; deficiency and/or exposure to oxidizing agents causes methemoglobinemia. • Hypoxia—when $> 20\text{--}40\%$ of hemoglobin has been oxidized to methemoglobin.

Other

- Peripheral cyanosis—results from increased oxygen extraction from the arterial supply to an area (e.g., a limb); caused by severe vasoconstriction, poor peripheral blood flow, obstruction to flow associated with arterial thromboembolism, or stagnation or obstruction of venous blood flow.
- Differential cyanosis—with reverse shunting PDA, the head and neck receive oxygenated blood via the brachiocephalic trunk and left subclavian artery, which arise from the aortic

arch; the rest of the body receives desaturated blood through the ductus located in the descending aorta.

SYSTEMS AFFECTED

- Central—all systems affected.
- Peripheral—may diminish or abolish neuromuscular function of the affected limb(s).

SIGNALMENT

- Right-to-left cardiac shunts in association with high pulmonary vascular resistance and pulmonary hypertension (Eisenmenger physiology)—dogs: Keeshonden, English bulldogs, and beagles; some cats; generally young animals. • Tracheal collapse—usually young or middle-aged small-breed dogs (e.g., Pomeranians, Yorkshire terriers, poodles).
- Congenital laryngeal paralysis—young animals; reported in Dalmatians, Bouvier des Flandres, and Siberian huskies. • Acquired laryngeal paralysis—most common in old large-breed dogs (e.g., retrievers).
- Hypoplastic trachea—identified in young English bulldogs; occasionally other breeds.
- Brachycephalic airway syndrome—dogs: English and French bulldogs, Pekinese, Pugs; cats: Himalayan, Persian. • Asthma (cats)—higher incidence reported in Siamese.

SIGNS

Historical Findings

- Central—stridor; respiratory distress; cough; voice change; episodic weakness; syncope; exposure to oxidizing substances or drugs causing methemoglobinemia.
- Peripheral—limb paresis or paralysis.

Physical Examination Findings

- Heart murmur or splitting of the second heart sound—with cardiac disease or pulmonary hypertension. • Pulmonary crackles or wheezes—with pulmonary edema or respiratory disease. • Muffled heart sounds—owing to pleural space or pericardial disease. • Upper airway stridor with laryngeal paralysis. • Honking cough—typical of tracheal collapse; often induced by tracheal palpation. • Dyspnea—may be inspiratory, expiratory, or a combination (see “Differential Diagnosis”). • Limbs—may be cyanotic, cool, pale, painful, and edematous; can lack a pulse in conditions causing peripheral cyanosis.
- Weakness—can be generalized and persistent with severe cardiac diseases; can be episodic and especially noticeable with exercise or excitement. • Posterior paresis or paralysis—can be seen with distal aorta arterial thromboembolism; differentiated from primary neuromuscular disease by absence (or near absence) of pulses.

CAUSES

Respiratory System

- Larynx—paralysis (acquired or congenital); collapse; spasm; edema; trauma; neoplasia; granulomatous disease. • Trachea—collapse; neoplasia; foreign body; trauma; hypoplasia.

- Lower airway and parenchyma—pneumonia (viral, bacterial, fungal, eosinophilic, mycobacteria, aspiration); chronic bronchitis; hypersensitivity bronchial disease or asthma; bronchiectasis; neoplasia; foreign body; parasites (*Filaroides*, *Paragonimus*, *Pneumocystis jiroveci*, toxoplasmosis, *Aelurostrongylus* spp.); pulmonary contusion or hemorrhage; non-cardiogenic edema (inhalation, snake bite, electric shock); near drowning. • Pleural space—pneumothorax; infectious (bacterial, fungal, FIP); chylothorax; hemothorax; neoplasia; trauma.
- Thoracic wall or diaphragm—congenital (pericardial, diaphragmatic hernia); trauma (diaphragmatic hernia, fractured ribs, flail chest); neuromuscular disease (tick bite paralysis, coonhound paralysis).

Cardiovascular System

- Congenital defects—Eisenmenger physiology (right-to-left shunting PDA, VSD, ASD); tetralogy of Fallot; truncus arteriosus; double outlet right ventricle; anomalous pulmonary venous return; atresia of aortic or tricuspid or pulmonary valves. • Acquired disease—mitral valve disease; cardiomyopathy.
- Pericardial effusion—idiopathic disease; neoplasia. • Pulmonary thromboembolic disease—hyperadrenocorticism; immune-mediated hemolytic anemia; protein-losing nephropathy; dirofilariasis.
- Pulmonary hypertension—idiopathic; right-to-left cardiac shunts. • Peripheral vascular disease—arterial thromboembolism (feline cardiomyopathies); venous obstruction; reduced cardiac output; shock, arteriolar constriction.

Neuromusculoskeletal System

- Brainstem dysfunction—encephalitis; trauma; hemorrhage; neoplasia; drug-induced depression of respiratory center (morphine, barbiturates). • Spinal cord dysfunction—edema; trauma; vertebral fractures; disk prolapse. • Neuromuscular dysfunction—overdose of paralytic agents (succinylcholine, pancuronium); tick bite paralysis; botulism; acute polyradiculoneuritis (coonhound paralysis); dysautonomia; myasthenia gravis.

Methemoglobinemia

- Congenital—NADH-MR deficiency (dogs). • Ingestion of oxidant chemicals—acetaminophen; nitrates; nitrites; phenacetin; sulfonamides; benzocaine; aniline dyes; dapsone.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Generalized—systemic hypoxemia or heme abnormality. • Peripheral only—reduced blood flow to extremities. • Caudal

(CONTINUED)

CYANOSIS

C

- body—right-to-left shunting PDA. • Cardiac versus respiratory causes—differentiation can be difficult; cardiac murmur may suggest cardiac disease but murmurs are often heard in older patients with primary respiratory disease; thoracic radiography and echocardiography useful for differentiation.
- Central or peripheral neurologic signs—should prompt concern of arterial hypoxemia owing to primary neuromuscular disease.

Breathing Pattern

- May help define cause. • Inspiratory effort—often associated with obstructive upper airway or pleural space disease; stridor frequently localizes problem to the larynx or cervical trachea. • Expiratory effort—generally seen with obstructive lower airway disease. • Rapid shallow (restrictive)—may be associated with pleural space disease or neuromuscular abnormalities of the thoracic wall.

CBC/BIOCHEMISTRY/URINALYSIS

- Color of blood—may be darkened; chocolate brown with methemoglobinemia.
- Polycythemia—often accompanies congenital heart disease; may occur with chronic hypoxemia owing to severe respiratory disease. • Proteinuria—accompanies protein-losing nephropathies, which may result in secondary pulmonary thromboembolism. • Panhypoproteinemia—accompanies protein-losing enteropathies, which may lead to pulmonary thromboembolism.

OTHER LABORATORY TESTS

- Methemoglobin concentrations—measure through a laboratory; alternatively, shake a blood sample in air 15 minutes: red, reduced hemoglobin with cardiac or respiratory disease; chocolate brown, methemoglobin.
- Arterial blood gas analysis. • Urine protein:creatinine ratio—with suspected pulmonary thromboembolism secondary to a protein-losing nephropathy.

IMAGING

- Radiography—essential for determining cause. • Echocardiography with Doppler—aids in diagnosis of congenital or acquired cardiac disease, pulmonary hypertension, and pulmonary thromboembolism. • Computed tomography—can further define obstructive nasal, pulmonary or pleural space disease.

DIAGNOSTIC PROCEDURES

- Pulse oximetry—determine oxygen saturation. • Laryngoscopic examination—evaluate laryngeal structure and arytenoid function. • Bronchoscopy—often useful in the diagnosis of airway and pulmonary diseases. • Transtracheal wash, bronchoalveolar lavage, or fine-needle lung aspirate—often required to characterize bronchopulmonary diseases.

- Thoracocentesis—required for diagnosis and treatment of pleural space disorders.
- Electrocardiography—may reveal heart enlargement changes; unreliable; echocardiography better. • Lung biopsy—can be necessary for diagnosis of interstitial lung disease.

**TREATMENT**

- Inpatient—immediate diagnostic testing and treatment. • Stabilization therapy (e.g., oxygen, thoracocentesis, tracheostomy)—usually instituted before aggressive diagnostics. • Specific therapy—depends on the ultimate diagnosis; usually exercise restriction and dietary modification required.
- Surgical treatment—depends on primary disease process and the extent of cardiac or respiratory involvement. • Warn client when admitting the patient that diseases associated with cyanosis can have dire outcomes.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Oxygen therapy—provide as soon as possible.
- Additional drug therapy depends on final diagnosis.
- Furosemide—aggressive use indicated with suspected cardiogenic pulmonary edema.
- Methemoglobinemia as a result of ingestion of oxidizing substances (acetaminophen)—give acetylcysteine as soon as possible (140 mg/kg PO or IV; then 70 mg/kg q4h for five treatments); cimetidine (10 mg/kg PO; then 5 mg/kg PO q6h for 48 hours) is a useful adjunct to acetylcysteine; ascorbic acid (30 mg/kg PO q6h for seven treatments) may be of some value but do not use as the sole agent.
- Sildenafil citrate—phosphodiesterase type 5 inhibitor used to treat pulmonary arterial hypertension at 1–3 mg/kg PO q8–12h.

CONTRAINDICATIONS

Avoid using paralytic agents (succinylcholine, pancuronium) and agents that cause profound depression of the respiratory center (morphine, barbiturates).

**FOLLOW-UP****PATIENT MONITORING**

- Patients in an oxygen cage should be disturbed as infrequently as possible for monitoring. • Assess efficacy of therapy—changes in depth and rate of respiration; color of mucous membranes (should return to a

normal pink color if the cause is not an anatomic shunt and patient has adequate reserves); pulse oximetry or arterial blood analysis. • Instruct client to monitor mucous membrane color and respiratory effort and advise immediate veterinary care if cyanotic condition returns.

POSSIBLE COMPLICATIONS

Advanced pulmonary or airway disease and severe cardiac disease—poor long-term prognosis.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Obesity—can complicate or exacerbate underlying respiratory or cardiac diseases.
- Ascites—can complicate or exacerbate respiratory effort and reduce lung capacity due to cranial displacement of diaphragm.

AGE-RELATED FACTORS

Congenital cardiac abnormalities—usually the cause in young patients.

PREGNANCY/FERTILITY/BREEDING

- Advanced pregnancy may exacerbate signs because of pressure on the diaphragm and reduced lung expansion. • Fetuses are likely to be harmed or aborted by hypoxemia associated with cyanosis.

SEE ALSO

- Dyspnea and Respiratory Distress • Panting and Tachypnea • Stertor and Stridor

ABBREVIATIONS

- ASD = atrial septal defect • FIP = feline infectious peritonitis • MR = methemoglobin reductase • NADH-MR = nicotinamide adenine dinucleotide dependent-methemoglobin reductase • PCV = packed cell volume • PDA = patent ductus arteriosus • RBC = red blood cell • VSD = ventricular septal defect

Suggested Reading

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Author Ned F. Kuehn

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Client Education Handout
available online

CYCIC HEMATOPOIESIS



BASICS

OVERVIEW

- Cyclic hematopoiesis in color-dilute gray collie pups is characterized by frequent episodes of infection with failure to thrive and early death. Systems affected are hematopoietic, respiratory, gastrointestinal, and skin. Clinically, the pups may appear normal for the first 4–6 weeks and then develop diarrhea, conjunctivitis, gingivitis, pneumonia, skin infections, carpal joint pain, and fever. A frequent cause of death is intussusception of the small intestine.
- Episodes of illness, varying from inactivity accompanied by fever to life-threatening infection, repeat at 11- to 14-day intervals.
- The gray pups are usually smaller than their litter mates at birth, weak, and often pushed aside by the bitch.
- Cyclic hematopoiesis has been observed in many collie bloodlines in the United States and in other countries.
- Cyclic hematopoiesis has also been reported in two cats with FeLV infection.

SIGNALMENT

- Cyclic hematopoiesis in the collie breed is present only in the color-dilute pups. The color dilution and bone marrow disorder are inherited as an autosomal recessive trait (presumably the same gene). The bone marrow disorder and color dilution have been present in crossbred collie/beagle pups.
- Clinical signs occur as early as 1–2 weeks of age and are always apparent by 4–6 weeks of age.
- An apparently similar disease was reported in normal-colored pups in two border collie litters in the UK. Single cases of cyclic hematopoiesis have been reported in Pomeranians and cocker spaniels; the disease is not well characterized in these breeds.
- Cyclic hematopoiesis observed in the two cats appears to be another possible non-neoplastic manifestation of FeLV infection.

SIGNS

Historical Findings

- Weakness
- Failure to thrive
- Conjunctivitis
- Gingivitis
- Diarrhea
- Pneumonia
- Skin infections
- Carpal joint pain

Physical Examination Findings

- Dilute coat color with color dilution of nasal epithelium.
- Smaller and weaker than normal-colored littermates.
- Fever.
- Watery eyes, reddened gums, tonsillitis, and diarrhea nearly always present during the phase of the hematopoietic cycle when clinical signs are evident; other signs vary depending on the site of sepsis.
- Painful carpal joints observed during the initial recovery phase of the disease cycle.
- Signs and symptoms of FeLV in cats.

CAUSES & RISK FACTORS

- Inherited disease in purebred or crossbred collie dogs.
- FeLV infection, cats.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Coat color dilution pathognomonic for the disease in collies or collie mixed breeds.
- Color dilution not associated with cyclic hematopoiesis also observed in collie pups. However, the pups are normal size, do not develop frequent episodes of infection, may attain normal coat color intensity by 6 months of age, normal color intensity on the nose.
- Collie pups with cyclic hematopoiesis always have nasal epithelial color dilution.
- Cats will present with signs and symptoms consistent with FeLV infection.

CBC/BIOCHEMISTRY/URINALYSIS

- Severe neutropenia, lasting 2–5 days and occurring at 11- to 14-day intervals with marginal normocytic to microcytic anemia in dogs; slight to moderate normocytic or macrocytic anemia in cats.
- Important to recognize that signs of infection are often minimal during the neutropenic episodes.
- Local swelling, redness, and systemic signs of infection usually occur during the first days of the neutrophilic phase of the disease cycle; therefore, on initial CBC examination, neutrophilia with moderate monocytosis is observed.
- CBC should be repeated at 1- to 2-day intervals to confirm the diagnosis.



TREATMENT

- Advise clients not to attempt to raise the pup(s).
- Antibiotics and supportive therapy may extend the life of the pups for several years but at considerable cost.



MEDICATIONS

DRUG(S)

Antibiotics and fluids as required for infections.



FOLLOW-UP

PATIENT MONITORING

Owner advised to watch for signs of infection.

PREVENTION/AVOIDANCE

Dogs should not be boarded.

POSSIBLE COMPLICATIONS

Respiratory infection can be life threatening if untreated.

EXPECTED COURSE AND PROGNOSIS

Intermittent infections are expected. Prognosis is guarded.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Carriers or affected collies should not be bred.

SEE ALSO

Neutropenia

ABBREVIATION

FeLV = feline leukemia virus

Suggested Reading

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CYLINDRURIA



BASICS

OVERVIEW

- Abnormally high number of casts ($> 2-3$ casts/lpf) in urine sediment. May develop in dogs or cats with primary kidney disease or systemic disorders that secondarily affect the kidneys.
- High numbers of casts indicate accelerated renal cellular degeneration, glomerular leakage of protein, hemorrhage, or exudation into renal tubular lumens.

SYSTEMS AFFECTED

Renal/Urologic

SIGNALMENT

Dog and cat

CAUSES & RISK FACTORS

Nephrotoxicosis

- Toxins—ethylene glycol, grape/raisin ingestion (dogs), lily ingestion (cats), hypercalcemia
- Nephrotoxic drugs—aminoglycosides, intravenously administered tetracycline, amphotericin B, cisplatin, nonsteroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors
- Diagnostic agents—intravenously administered radiocontrast agents

Renal Ischemia (Anoxia)

- Dehydration
- Low cardiac output—congestive heart failure, cardiac arrhythmia, or pericardial disease
- Renal vessel thrombosis—emboli from bacterial endocarditis or DIC
- Hemoglobinuria—intravascular hemolysis
- Myoglobinuria—rhabdomyolysis

Renal Inflammation

Infectious diseases (e.g., pyelonephritis, leptospirosis, feline infectious peritonitis, Rocky Mountain spotted fever, or ehrlichiosis)

Glomerular Disease

- Glomerulonephritis
- Amyloidosis



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- History of potential exposure to toxins or nephrotoxic drugs—rule out acute tubular necrosis.
- Recent onset of vomiting or diarrhea—rule out renal ischemia caused by dehydration.
- Recent inhalational anesthesia—rule out tubular necrosis caused by ischemia.
- Potential for exposure to infectious diseases—rule out nephritis.
- Fever—rule out infectious, inflammatory, and neoplastic disease.
- Cardiac murmur, especially if diastolic and of recent onset—rule out bacterial endocarditis.
- Petechiae and ecchymoses—rule out systemic thrombosis.
- Cylindruria plus azotemia and adequately concentrated urine (specific gravity 1.030 in dogs and 1.040 in

cats)—consider prerenal disorders such as dehydration.

- Cylindruria plus azotemia and inadequately concentrated urine (specific gravity < 1.030 in dogs and < 1.040 in cats)—consider kidney failure.
- Cylindruria plus leukocytosis—consider infectious and inflammatory disorders.
- Cylindruria plus thrombocytopenia—consider DIC.
- Cylindruria plus glucosuria and proteinuria—consider renal tubular necrosis.

LABORATORY FINDINGS

Disorders That May Alter Laboratory Results

- Waiting longer than 2 hours to perform urinalysis may result in disappearance of casts.
- Alkaline urine causes dissolution of casts.
- Dilute urine (specific gravity < 1.003) causes dissolution of casts; interpret numbers of casts in light of urine specific gravity.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Epithelial, granular, and/or waxy casts indicate diseases that cause degeneration and necrosis of renal tubular epithelial cells.
- RBC casts indicate severe glomerular disease or hemorrhage into renal tubules.
- WBC casts indicate renal inflammation, most often caused by pyelonephritis; however, most patients with pyelonephritis do not have WBC casts.
- Hyaline casts—associated with disorders that cause proteinuria; also may be observed during diuresis and after dehydration.
- Anemia, hemoconcentration, leukocytosis, or thrombocytopenia in some patients.
- High serum concentrations of urea nitrogen, creatinine, and phosphorus in patients with dehydration or kidney disease.

OTHER LABORATORY TESTS

- If the patient has thrombocytopenia or RBC casts, perform coagulation studies (e.g., PTT, PT, FDP, D-dimers) to rule out consumptive coagulopathy such as DIC.
- If the patient has proteinuria, determine urine protein:creatinine ratio to evaluate magnitude of proteinuria.
- If the patient has pyuria or WBC casts, perform urine culture to rule out urinary tract infection.
- If systemic infectious diseases are suspected, submit serum for appropriate titers.

DIAGNOSTIC PROCEDURES

Consider renal biopsy if kidney disease persists or progresses and the cause cannot be determined from routine diagnostic tests.



TREATMENT

- Manage as an outpatient unless the patient is dehydrated or has decompensated kidney failure.
- If the patient is healthy otherwise, feed normal food and allow normal exercise.
- If there is chronic kidney disease and creatinine remains > 2 mg/dL, recommend a

therapeutic renal diet to improve survival time and quality of life.

- If the patient cannot maintain hydration, administer lactated Ringer's solution or a maintenance fluid either intravenously or subcutaneously.
- If the patient has dehydration or continuing fluid losses such as vomiting or diarrhea, administer fluids intravenously to correct hydration deficits, maintain daily fluid requirements, and replace ongoing losses.



MEDICATIONS

CONTRAINDICATIONS

Avoid nephrotoxic drugs.



FOLLOW-UP

PATIENT MONITORING

Physical examination including patient's weight to assess hydration status.

PREVENTION/AVOIDANCE

Avoid or correct risk factors that predispose to development of exposure of kidneys to toxins and/or renal anoxia.

POSSIBLE COMPLICATIONS

Permanent kidney disease depending on underlying cause of cylindruria.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Possible in patients with leptospirosis. Avoid direct contact with infected urine in these

SEE ALSO

Nephrotoxicity, Drug-Induced

ABBREVIATIONS

- DIC = disseminated intravascular coagulation
- FDP = fibrin degradation products
- lpf = low power field
- PT = prothrombin time
- PTT = partial thromboplastin time
- RBC = red blood cell
- WBC = white blood cell

Suggested Reading

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CYSTICERCOSIS



BASICS

OVERVIEW

- Rare disease of dogs caused by the larvae of *Taenia crassiceps*, the adults of which are found in foxes, coyotes, and sometimes domestic dogs, and *Taenia solium*, the adults of which are found in humans.
- In the case of *T. crassiceps*, eggs shed by foxes are consumed by rabbits or other rodents, where they develop into a cysticercal stage in the abdominal and subcutaneous tissues. The cysticercus of *T. crassiceps* is capable of undergoing asexual multiplication, so very large numbers of cysticerci can develop in the tissues of the intermediate hosts. Dogs have been infected with the cysticercal stage and have developed large masses of cysticerci in the abdominal cavity, lungs, muscles, and subcutaneous tissues. Rare cases reported from Europe and the United States.
- In the case of *T. solium*, eggs shed by people are consumed by pigs, where they develop into a solitary cysticercal stage in muscles and neural tissues. Most common in countries where the infection is endemic, but rare cases of neurologic disease have been reported in the United States, most often in dogs that have traveled to endemic areas such as parts of Latin America.

SIGNALMENT

Dogs, older dogs, and young immunocompromised animals

SIGNS

- T. crassiceps*: Subcutaneous masses. Signs associated with masses in other organs—respiratory insufficiency (lungs), pericardial effusion and circulatory collapse (pericardium), icterus (abdominal cavity) pale mucous membranes (anemia) and anorexia.
- T. solium*: Neurologic signs.

CAUSES & RISK FACTORS

- T. crassiceps*: Mode of infection not clear, but three hypothesized: (1) Ingestion of parasite eggs (probably in feces of infected fox); (2) Autoinfection with eggs from an intestinal infection with the adult stages; (3) Ingestion of cysticercal stage.
- T. solium*: Ingestion of eggs (from feces of infected human).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Larval *Mesocestoides* spp. infection
- Neoplasia, especially in older animals

CBC/BIOCHEMISTRY/URINALYSIS

Anemia of chronic disease

OTHER LABORATORY TESTS

N/A

IMAGING

- Radiographs—determine degree of spread to internal organs; *T. solium* typically diagnosed as cyst-like lesions in the brain seen on radiographs.
- Ultrasound—delineates cystic nature of mass (in cutaneous or abdominal cavity) as opposed to solid mass of a neoplasm.
- Ultrasound and computed tomography have identified cysticerci of *T. solium* in dogs.

DIAGNOSTIC PROCEDURES

- Aspirate cytology
- Surgical biopsy



TREATMENT

- Inpatient if debilitated.
- Treat signs as needed.
- Surgically remove, through biopsy or laparotomy, as many organisms as possible.



MEDICATIONS

DRUG(S)

- Praziquantel 5 mg/kg PO, initially, then progressively increase dose over several weeks to 50 mg/kg if appears tolerated. Concern is that dog may react to dying cysticerci.
- Albendazole 50 mg/kg PO q24h for 10–20 days after the termination of praziquantel therapy may aid in preventing recurrence. NOTE: Albendazole may be myelosuppressive at this dose—monitor CBC.
- Fenbendazole 50 mg/kg PO q24h for 30 days may be used also with some hope of success for long-term prevention of recurrence.



FOLLOW-UP

- Lesions of *T. crassiceps* very often recur. Thus, necessary to carefully monitor the dog with abdominal ultrasound for the potential spread of lesions and the development of new lesions in different sites.
- Removal of *T. solium* cysticerci will be curative.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Stages causing clinical signs in dogs pose no zoonotic threat.

Suggested Reading

- Buback JL, Schulz KS, Walker MA, et al. Magnetic resonance imaging of the brain for diagnosis of neurocysticercosis in a dog. J Am Vet Med Assoc 1996, 208:1846–1848.
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Author Dwight D. Bowman

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BASICS

OVERVIEW

- Infection with the protozoan *Cytauxzoon felis*.
- Affects vascular system of lungs, liver, spleen, kidneys, and brain; bone marrow; developmental stages of RBCs.
- Uncommon in most regions, but common during the spring and summer in endemic regions.
- Affects feral and domestic cats in south-central, southeastern, and mid-Atlantic United States. Range appears to be expanding towards the eastern and northeastern United States.

SIGNALMENT

- Feral and domestic cats of all ages
- No breed or sex predilection

SIGNS

- Most cats have severe illness at presentation.
- Pale mucous membranes.
- Depression.
- Anorexia.
- Dehydration.
- High fever.
- Icterus.
- Splenomegaly.
- Hepatomegaly.
- Some cats may be infected but asymptomatic.

CAUSES & RISK FACTORS

- Bite of infected tick (*Amblyomma americanum* or *Dermacentor variabilis*).
- Roaming in areas shared by reservoir hosts (bobcat, Florida panther).
- Living in the same household as a cat diagnosed with cytauxzoonosis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of pancytopenia such as sepsis and panleukopenia.
- Other causes of fever and jaundice such as pancreatitis, hepatitis, and cholangitis.

CBC/BIOCHEMISTRY/URINALYSIS

- Bi-cytopenia or pancytopenia are the most common findings. Thrombocytopenia is almost always present.
- Moderate hyperbilirubinemia and bilirubinuria.

- Normal to mildly increased ALT.
- Mild hyperglycemia.
- Reflect changes associated with the severe anemia, caused by combination of hemolysis and hemorrhage.

OTHER LABORATORY TESTS

- Fresh blood smear—*Cytauxzoon* erythrocytic form; 1–3 µm in diameter; shape of a signet ring or safety pin.
- Splenic, lymph node, liver, or bone marrow aspirate—best suited to demonstrate extra-erythrocytic form.
- A PCR assay is commercially available.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

Organisms inside myeloid cells in bone marrow aspirate and in dramatically enlarged myeloid cells in vessels of multiple organs including lung, liver, spleen, kidney, and brain.



TREATMENT

- Inpatient with aggressive supportive therapy
- Blood transfusion
- Feeding tube for medication and nutritional support



MEDICATIONS

DRUG(S)

- Combination of atovaquone (15 mg/kg PO q8h with a fatty meal) and azithromycin (10 mg/kg PO q24h) and supportive care is associated with survival rates of 60%.
- Imidocarb dipropionate 5 mg IM two injections 14 days apart has been recommended but is associated with survival rates of approximately 27%.
- Heparin (100–300 U/kg SC q8h or 300–900 U/kg/day as a CRI) until time of discharge (longer if develop significant coagulation problems such as pulmonary thromboembolism).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS

- With aggressive supportive care and treatment expect 3–7 days of hospitalization with severe illness.
- Some cats develop pleural effusion (presumably secondary to pulmonary hypertension) and require thoracocentesis.
- However, cats that survive will return to normal within 2–4 weeks of discharge and appear immune to re-infection.
- Some cats remain persistently infected with the intra-erythrocytic form without overt signs.
- Without treatment, most infected cats have died within 5 days of presentation.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- No known risk to humans.
- Cannot be directly transmitted to another cat except by blood or tissue inoculation

ABBREVIATIONS

- PCR = polymerase chain reaction
- RBC = red blood cell

INTERNET RESOURCES

<http://www.vet.uga.edu/vpp/clerk/Dailey/index.htm>.

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DEAFNESS



BASICS

DEFINITION

- Partial or complete hearing loss.
- Two forms:
 - Sensorineural deafness—caused by damage to receptors in cochlea, cochlear nerve, or auditory pathways in central nervous system.
 - Conduction deafness—caused by inability to conduct sound vibration through external-to-inner-ear structures.

PATHOPHYSIOLOGY

Sensorineural Deafness

- Hereditary—breed-related cochlear degeneration of neonatal dogs and cats; closely associated with merle and piebald pigmentation genes. Recessive alleles of these genes alter the ability of neural crest melanocytes to populate regions of the body including skin, hair, iris, ocular tapetum, and portions of the cochlea. The absence of melanocytes in the stria vascularis of cochlea is associated with early post-natal degeneration of this structure. Can also be non-pigment associated such as in Doberman pinchers.
- Acquired—cochlear degeneration due to chronic infection, ototoxicity, neoplasia, chronic exposure to loud noises, anesthesia-associated or age-related loss of hair cells and ganglion nerves (presbycusis).

Conduction Deafness

- Congenital defects in external ear canal, tympanic membrane, or ossicles that transmit vibration in middle ear are rare. Hereditary predisposition in primary secretory otitis media in the CKCS.
- Acquired defects resulting in stenosis/obstruction of external ear canal, rupture of tympanic membrane or fusion of bony ossicles; most commonly associated with chronic otitis or middle ear polyps.

SYSTEMS AFFECTED

Nervous—inner ear

GENETICS

Genetics of congenital deafness unknown although strong association with the piebald and the merle genes (pigment-associated genes related to coat color).

INCIDENCE/PREVALENCE

- Dogs with a single merle allele—3.5%.
- Dogs with double merle allele—25%; no genetic test for the piebald gene.
- Prevalence of congenital deafness in one or both ears available for the following breeds—Catahoula leopard dog—63%, dappled dachshund—55%, Dalmatian—30% in USA, 18% in UK, Jack Russell terrier—4.07%, Australian cattle dog—15%, bull terrier—11% (20% if

white), English setter—8%, English cocker spaniel—7% border collie—2.4%, whippet—1.3%, purebred white cats—20.2%.

GEOGRAPHIC DISTRIBUTION

Prevalence for different breeds varies between countries.

SIGNALMENT

- Breed-related congenital cochlear degeneration described in > 90 breeds of dogs. Most breeds have a large amount of white pigmentation associated with merle or piebald genes except for Doberman pinscher, Puli, Shropshire terrier. Congenital sensorineural deafness present by 6 weeks of age.
- No association with gender or coat pigmentation genes unrelated to merle or piebald. Dogs with blue iris color have a higher incidence of congenital deafness.
- Mixed-breed cats with white hair coat and blue irises—high incidence of deafness. Purebred white cats that carry the Siamese gene for blue eyes have a lower incidence of congenital deafness.
- Acquired deafness may occur in any breed or age dog.

SIGNS

- Unilateral deafness often goes unnoticed. Rarely dogs have difficulty localizing sound.
- With bilateral disease, animals do not respond to auditory cues such as calling its name or rattling food dish. Often they are easily startled. Commonly have heightened response to vibration and visual cues.

CAUSES

Sensorineural Deafness

- Genetic etiology likely in neonates.
- Acquired cochlea and cochlear nerve damage—*infectious, neoplasia of bony labyrinth or nerve, trauma, systemic, or topically applied drugs or toxins (antibiotics—aminoglycosides, polymyxin, erythromycin, vancomycin, chloramphenicol; antiseptics—ethanol, chlorhexidine, cetrimide; antineoplastics—cisplatin; diuretics—furosemide; heavy metals—arsenic, lead, mercury; miscellaneous—ceruminolytic agents, propylene glycol, salicylates); middle-ear polyps.*

Conduction Deafness

- Otitis externa and other external ear canal disease (e.g., stenosis of canal, neoplasia, or ruptured tympanum).
- Otitis media.

RISK FACTORS

- Merle, piebald gene, or white coat color
- Chronic otitis externa, media, or interna
- Use of ototoxic drugs.
- General anesthesia



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Early age onset—suggests congenital causes in predisposed breeds.
- Use of ototoxic drugs, recent anesthesia or chronic ear disease—suggests acquired causes.
- Evaluate for brain disease.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

- Bacterial culture and sensitivity of ear canal if otitis externa.
- Myringotomy with culture of aspirates if otitis media.

IMAGING

- Tympanic bullae and skull radiographs—not sensitive for otitis media or otitis interna.
- CT/MRI—sensitive for middle-inner-ear disease.

DIAGNOSTIC PROCEDURES

- Brainstem auditory evoked response (BAER)—measure electrical response of cochlea and auditory pathways in the brain to an auditory stimulus; reliable to identify dogs with unilateral disease or partial hearing loss. Bone conduction stimulation can be useful to distinguish sensorineural from conduction deafness. Can be used to determine the hearing threshold.
- Otoacoustic emissions (OAEs)—low-level sounds produced by inner ear as part of the normal hearing process that can be measured by placing a probe containing a microphone in the external ear canal. Two forms have been used in dogs for assessment of sensorineural deafness: transient-evoked OAEs (TEOAEs) and distortion-product OAEs (DPOAEs). OAE is best suited for cases with congenital deafness as it tests outer hair cell function and is not affected by inner hair cell, synapse or cochlear nerve deficiencies.

PATHOLOGIC FINDINGS

- Congenital deafness—degeneration of the stria vascularis with subsequent collapse of membranous labyrinth structures. Bony labyrinth remains intact.
- Acquired deafness—related to primary disease such as otitis or neoplasia.
- Ototoxicity—degeneration of otic hair cells, ganglion cell loss, and loss of stria vascularis.



TREATMENT

CLIENT EDUCATION

Deaf animals may be functional pets but require patience, specialized training, and extra protection from traffic.

(CONTINUED)

DEAFNESS

D

SURGICAL CONSIDERATIONS

- Directed toward acquired causes; congenital deafness irreversible.
- Otitis externa, media, or interna—medical or surgical approaches depend on culture and sensitivity test results, response to antibiotics, and imaging findings.
- Conduction—may improve as otitis externa or media resolve.
- Cochlear implants can be used in dogs with moderate to profound deafness but only preliminary data available and very expensive.

**MEDICATIONS****DRUG(S) OF CHOICE**

- None for congenital deafness.
- Treat otitis based on culture and sensitivity results.

PRECAUTIONS

- Aminoglycosides or other ototoxic drugs—use with caution.

- Topical treatment of external ear canal—avoid if tympanic membrane is ruptured.

**FOLLOW-UP****PATIENT MONITORING**

As needed for management of otitis

POSSIBLE COMPLICATIONS

Deaf dogs need protected environments and training to be functional pets.

**MISCELLANEOUS****PREGNANCY/FERTILITY/BREEDING**

Dogs homozygous for recessive merle gene can be blind and sterile.

ABBREVIATIONS

- BAER = brainstem auditory evoked responses
- CKCS = Cavalier King Charles spaniel
- CT = computed tomography
- DPOAE = distortion product OAE
- MRI = magnetic resonance imaging
- OAE = otoacoustic emission
- TEOAE = transient evoked OAE

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Client Education Handout
available online

DECIDUOUS TEETH, PERSISTENT



BASICS

OVERVIEW

- A persistent (retained) deciduous tooth is one that is still present when the permanent tooth begins to erupt or has erupted.
- Numerous factors influence the exfoliation of deciduous teeth: lack of a permanent successor; ankylosis of the deciduous crown or root to the alveolus; and failure of the developing permanent crown to contact the deciduous root preventing resorption of the deciduous root.

SIGNALMENT

- More common in dogs than cats. • More common in small-breed dogs (e.g., Maltese, poodle, Yorkshire terrier, etc). • Occurs during permanent tooth eruption phase—beginning at 3 months of age for the incisors and 6–7 months of age for the canine teeth and molars. • Persistent deciduous teeth may go undetected and therefore undiagnosed until adulthood. • No sex predilection.

SIGNS

General Comments

- Persistent deciduous teeth can cause the permanent teeth to erupt in an abnormal positions resulting in a malocclusion. Early recognition and intervention is essential.
- Maxillary canine teeth erupt mesial (rostral) to the persistent deciduous canine teeth. This can narrow the space (diastema) between the maxillary canine tooth and the third incisor, leaving no room for the mandibular canine tooth to occupy. • Mandibular canine teeth erupt lingual (medial) to the persistent deciduous teeth. This can result in a narrow space between the lower canines (base narrow), resulting in impingement on the soft tissue of the hard palate. • All permanent incisors erupt lingual to the persistent deciduous incisors. This can result in a rostral (anterior) crossbite.

Physical Examination Findings

- Presence of a deciduous tooth with the permanent tooth either partially or fully erupted. • Abnormal position of the permanent tooth due to persistence of the deciduous tooth. • Oral malodor from accumulation of debris and plaque due to crowding of the permanent tooth and the persistent deciduous teeth. • Local gingivitis and early-onset periodontal disease due to plaque accumulation from crowding.
- Oronasal fistula from base-narrow mandibular permanent canine teeth (linguoversion). • Deciduous tooth present with no permanent successor. • Deciduous tooth is usually smaller than the permanent tooth. • Without underlying permanent tooth, deciduous tooth will often remain intact and viable, though can eventually exfoliate.

CAUSES & RISK FACTORS

- Cause is unknown but is suspected to have a genetic basis. • Small-breed dogs are predisposed.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Supernumerary teeth • Gemination of the crown

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

Intraoral Radiography

- Distinguish between permanent teeth and deciduous teeth. • Provide evidence or extent of root resorption of the deciduous tooth.
- Identify dental abnormalities prior to extraction, including persistent deciduous tooth with no permanent successor, retained root with crown missing, and unerupted permanent tooth. • Identify relationship of deciduous root and permanent crown prior to extraction.

DIAGNOSTIC PROCEDURES

- Complete oral examination—charting of oral cavity to indicate presence of deciduous teeth, malpositioned teeth, missing teeth, soft tissue trauma, and other abnormalities.
- Appropriate preoperative diagnostics when indicated prior to procedure.

PATHOLOGIC FINDINGS

N/A



TREATMENT

CLIENT EDUCATION

- Persistent deciduous teeth may be prevalent in certain breeds. • Start looking at teeth from the first puppy or kitten visit. • Inform owners that you will be evaluating for exfoliation of deciduous teeth as well as proper eruption of permanent teeth.

SURGICAL CONSIDERATIONS

- Ideally, extract the deciduous tooth as soon as the permanent tooth has erupted through the gingiva. • General anesthesia with endotracheal tube in place and cuff inflated. • Intraoral radiographs.

Extraction

- Careful, gentle elevation is critical. Excessive force or pressure can damage the developing permanent tooth. • If a permanent tooth has erupted in an abnormal position, full root extraction of the deciduous tooth is essential.
- A fractured or retained root may need to be removed with a gingival flap. • In some cases, the root may have already undergone

resorption and the remaining crown needs to be extracted.



MEDICATIONS

DRUG(S)

- Topical oral antimicrobial rinse prior to extraction.
- Pain management prior to, during and following extraction.

CONTRAINdications/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING AND HOMECARE

- After surgery, restrict activity for the rest of the day. • Soft diet for 24 hours—canned food or moistened dry kibble. • Analgesia (NSAIDs) for 24–36 hours post-op. • No chew toys for 24 hours. • Oral rinse (chlorhexidine) for 3–5 days if indicated.
- Continue daily tooth brushing after 24 hours.

PREVENTION/AVOIDANCE

May be prevalent in certain breeds and lines—avoid similar breeding.

POSSIBLE COMPLICATIONS

- Malocclusion of permanent teeth may need to be treated. • Base narrow (linguoversion) of the mandibular canine teeth. • Rostral crossbite. • Rostrally deviated maxillary canine teeth.

EXPECTED COURSE AND PROGNOSIS

- Once extracted, there should be no further problems. • Gingiva generally heals uneventfully. • Prognosis depends on occlusion after eruption of permanent teeth is complete.



MISCELLANEOUS

SEE ALSO

Malocclusion—Skeletal and Dental

ABBREVIATION

NSAID = nonsteroidal anti-inflammatory drug

INTERNET RESOURCES

<http://www.avdc.org/nomenclature.html>

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DEGENERATIVE MYELOPATHY



BASICS

DEFINITION

Canine progressive adult-onset fatal neurodegenerative disease that has recently been shown in many breeds to be a result of a mutation in the superoxide dismutase 1 gene (*SOD1*). Mutations in *SOD1* are known to cause some forms of amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease. Initial signs of progressive upper motor neuron spastic paresis and general proprioceptive ataxia in the pelvic limbs occur in older dogs. If euthanasia is delayed, clinical signs progress to flaccid tetraparesis/plegia and other lower motor neuron signs.

PATHOPHYSIOLOGY

- A *c.118 G > A* transition in Exon 2 of *SOD1* that predicts an E40K missense mutation underlies most DM. A second *SOD1* missense mutation (*c.52 A > T*) has been seen only in Bernese mountain dogs.
- Lesions may represent a multisystem central-peripheral axonopathy.
- Predilection for lesion severity in mid-thoracic spinal cord may be a result of lower percentages of radicular artery contributions and small diameter vessels when compared to other spinal cord regions.
- Paucity of vascular supply in thoracic spinal cord may predispose it to damage from oxidative and metabolic disturbances.

SYSTEMS AFFECTED

- Central and peripheral nervous systems.
- Thoracolumbar spinal cord in early stage.
- Progresses to involve the cervical and lumbar spinal cord and the peripheral nervous system later in the course of the disease.
- Neurons in brainstem also may be affected.
- Disease also involves the sensory nerve roots and dorsal root ganglia.

GENETICS

- Most commonly autosomal recessive inheritance.
- Due to preponderance of purebred dogs affected, a familial inheritance is currently suspected.
- Mutations in *SOD1* are causative for degenerative myelopathy but are incompletely penetrant.
- Dogs that are homozygous for the mutant allele are at highest risk for developing degenerative myelopathy. Not all dogs that test homozygous for the mutation will develop DM. Dogs that test normal (clear) are highly unlikely to develop DM. Dogs that test carrier are less likely to develop DM.

INCIDENCE/PREVALENCE

Prevalence rate of DM reported for all dogs collected from the Veterinary Medical Database (1990–1999) was 0.19%.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Breed Predilections

So far the DM-associated *SOD1:c.118A* allele in 124 different dog breeds or varieties; a second *SOD1* mutation (*c.52 A > T*) was found only in Bernese mountain dogs. DM has been histopathologically confirmed in over 25 purebred and mixed-breed dogs.

Mean Age and Range

- Mean—9 years of age in large dogs. Mean age at onset is 11 years in Pembroke Welsh Corgi.
- Range—between 8 and 14 years.

Predominant Sex

No known sex predilection

SIGNS

- Early:
 - Upper motor neuron paraparesis.
 - Insidious, progressive, asymmetric general proprioceptive ataxia. Gait shows long-strided spastic paraparesis.
 - Paw replacement deficits.
 - Spinal reflexes usually present or exaggerated (patellar reflex may be reduced).
 - Presence of crossed-extensor reflex is variable.
 - Lack of paraspinal hyperesthesia is a key clinical feature.
- Later:
 - Pelvic limb paresis leading to plegia, eventually progressing to tetraparesis/plegia.
 - Mild to moderate loss of muscle mass in pelvic limbs due to neurogenic atrophy.
 - Reduced spinal reflexes in pelvic limbs.
 - ± urinary and fecal incontinence.
- End stage:
 - Flaccid tetraplegia.
 - Difficulty with swallowing and tongue movements.
 - Absence of spinal reflexes in all limbs.
 - Reduced to absent cutaneous trunci reflex.
 - Profound generalized muscle wasting.
 - Urinary and fecal incontinence.
 - Nociception remains unaffected.

CAUSES

- Hereditary disease and genetic predisposition.
- Other hypothesized causes include: immune-mediated, metabolic deficiencies, toxic and oxidative stress.

RISK FACTORS

- Dogs homozygous for the mutant allele(s) are at highest risk.
- There may be other environmental factors and modifying genes; studies underway.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Type II intervertebral disc herniation
- Intramedullary spinal cord neoplasia
- Degenerative lumbosacral stenosis
- Hip dysplasia
- Other coexisting orthopedic disease

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal
- Performed to rule out other underlying metabolic disease
- Urinalysis may identify secondary urinary tract infection

OTHER LABORATORY TESTS

- Urine culture and sensitivity testing
- Thyroid function testing
- Electrodiagnostic testing results are normal in the early diagnosis of DM
- Genetic testing—test result of at-risk can support a presumptive diagnosis of DM in light of typical clinical signs and normal findings on neuroimaging and CSF analysis.

IMAGING

- Survey spinal radiography.
- Myelography evaluates for compressive spinal cord disease.
- Myelography combined with CT—more sensitive technique to evaluate suspicious lesions.
- MRI—preferred technique to evaluate for extramedullary compressive and intramedullary lesions.

DIAGNOSTIC PROCEDURES

- Cerebrospinal fluid analysis evaluates for inflammatory disease.
- Definitive diagnosis is determined by post-mortem histopathology of the spinal cord.

PATHOLOGIC FINDINGS

- Spinal cord axons and myelin affected most severely in the dorsal, and dorsal portion of the lateral funiculi.
- Vacuolated axon cylinders/myelin sheaths most extensive in the mid-thoracic spinal cord.
- Astroglial proliferation is prominent in severely affected areas of lesion distribution.
- Usually, lesion distribution is described as asymmetric and discontinuous. However, more recent evidence describes lesion distribution as symmetric and continuous in dogs that survive for long periods with DM.
- Neuronal cell body loss in the ventral horn is evident at terminal or end-stage disease.
- Nerve specimens show nerve fiber loss resulting from axonal degeneration and secondary demyelination.
- Muscle specimens show large and small groups of atrophic fibers typical of denervation.

DEGENERATIVE MYELOPATHY

(CONTINUED)

D



TREATMENT

APPROPRIATE HEALTH CARE

- Supportive care.
- Breeds of small size may survive longer with DM because the pet owner is able to more easily give the appropriate care.

NURSING CARE

- When dog becomes non-ambulatory, keep on a well-padded surface to prevent decubitus ulceration over bony prominences.
- Keep hair trimmed, and skin clean and dry to prevent urine scald secondary to incontinence.
- The urine should be monitored for odor and color change, which may indicate a urinary tract infection.
- Physical therapy using range-of-motion and active exercises may help maintaining limb mobility and muscle strength.

ACTIVITY

- Exercise is encouraged to slow disuse atrophy of pelvic limbs but fatigue should be monitored and exercise intensity adjusted.
- Hydrotherapy can involve use of an underwater treadmill setup.
- A wheel cart may assist with patient mobility.

DIET

- Maintain balanced diet.
- Prevent weight gain.

CLIENT EDUCATION

- Long-term prognosis is poor.
- Meticulous nursing care is crucial to preventing secondary complications in a recumbent patient.

SURGICAL CONSIDERATIONS

None



MEDICATIONS

DRUG(S) OF CHOICE

No drug has been proven to be effective in slowing or halting disease progression.

CONTRAINdicATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Repeat neurologic examinations
- Urinary retention
- Urinalysis and urine culture to monitor for urinary tract infection

PREVENTION/AVOIDANCE

- Decubitus ulceration
- Urine retention
- Dermatitis from urine scald
- Weight gain

POSSIBLE COMPLICATIONS

- Urine retention may predispose to urinary tract infections.
- Local skin infections from decubitus ulceration.

EXPECTED COURSE AND PROGNOSIS

- Paraplegia occurs within 9–12 months from time of onset of signs.
- Tetraparesis may be evident within 3 years from time of onset of signs.
- Long-term prognosis is poor.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Other neurologic diseases associated with old-age onset
- Spinal cord neoplasia
- Intervertebral disc disease
- Orthopedic disease

AGE-RELATED FACTORS

Older-aged dogs commonly affected

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYS

- Canine ALS
- Canine degenerative myelopathy
- Degenerative radiculomyelopathy
- German Shepherd dog myelopathy

SEE ALSO

- Intervertebral Disc Disease—Cervical
- Intervertebral Disc Disease—Thoracolumbar
- Lumbosacral Stenosis and Cauda Equina Syndrome

ABBREVIATIONS

- ALS = amyotrophic lateral sclerosis
- CT = computed tomography
- DM = degenerative myelopathy
- MRI = magnetic resonance imaging
- SOD1 = superoxide dismutase 1

INTERNET RESOURCES

www.caninegeneticdiseases.net/dm

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Client Education Handout
available online

DEMODICOSIS



BASICS

DEFINITION

- An inflammatory parasitic disease of dogs and rarely cats that is characterized by an increased number of mites in the hair follicles and on the epidermis. • Often leads to furunculosis and secondary bacterial infection. • May be localized or generalized.

PATOPHYSIOLOGY

Dogs

- Three species of mites identified in the dog:
 - *Demodex canis*—follicular mite; part of the normal fauna of the skin; typically present in small numbers; resides in the hair follicles and sebaceous glands of the skin, transmitted from the mother to the neonate in 2–3 days of nursing.
 - *Demodex injai*—large, long-bodied mite found in the pilosebaceous unit, mode of transmission unknown; only associated with adult-onset disease with highest incidence noted in the terrier breeds often along the dorsal midline (West Highland white terrier and wirehaired fox terrier).
 - *Demodex cornei*—lives in the stratum corneum of the epidermis; mode of transmission unknown; most likely a morphologic variant of *D. canis*.
- Pathology develops when numbers exceed those tolerated by the immune system, causing immunologic exhaustion. • The initial proliferation of mites may be the result of a genetic or immunologic disorder.

Cats

- Poorly understood disorder. • Mites have been identified on the skin and within the external ear canal.
- Two species of mites identified in the cat (a third, unnamed mite has been reported):
 - *Demodex gatoi* is considered to be potentially contagious and associated with pruritic dermatitis.
 - *Demodex cati* infections are often associated with immunosuppressive and metabolic disease.

SYSTEMS AFFECTED

Skin/Exocrine

GENETICS

Initial proliferation of mites may be the result of a genetic disorder

INCIDENCE/PREVALENCE

- Dogs—common
- Cats—rare

SIGNALMENT

Species

Dogs and cats

Breed Predilections

- *D. canis*: American Staffordshire terrier, Shar-Pei, Boston terrier, English bulldog, and West Highland white terrier.
- *D. injai*: West Highland white and wirehaired fox terriers, Shih Tzu.
- Potential increased incidence in Siamese and Burmese cat.

Mean Age and Range

- Localized—usually in dogs < 1 year of age; median 3–6 months.
- Generalized—both young and old animals.
- No data collected for the cat.

SIGNS

Dogs

Localized, Juvenile-Onset

- Lesions—usually mild; consist of erythema and a light scale.
- Patches—several may be noted; most common site is the face, especially around the perioral and periocular areas and forelegs; may also be seen on the trunk and rear legs.

Generalized, Juvenile-Onset or Adult-Onset

- Can be widespread from the onset, with multiple poorly circumscribed patches of erythema, alopecia, and scale. • As hair follicles become distended with large numbers of mites, secondary bacterial infections are common, often with resultant rupturing of the follicle (furunculosis). • With progression, the skin can become severely inflamed, exudative, and granulomatous.
- *D. injai* may be associated with a greasy seborrheic dermatitis of the dorsal trunk, comedones, erythema, alopecia, and hyperpigmentation.

Pododemodicosis

- Can present without generalized lesions
- Secondary and deep pyoderma common
- Lesions often painful and edematous

Cats

- Often characterized by partial to complete multifocal alopecia of the eyelids, periocular region, head, neck, flank, and ventrum.
- Lesions—variably pruritic with erythema, scale, and crust; those caused by *D. gatoi* are often quite pruritic and may be contagious.
- Ceruminous otitis externa has been reported.
- *D. cati* often associated with immunosuppressive disease.

CAUSES

- Dog—*Demodex canis*, *Demodex injai*, and *Demodex cornei*.
- Cat—*Demodex cati* and *Demodex gatoi*.

RISK FACTORS

Dogs

- Exact immunopathologic mechanism unknown.
- Studies indicate that dogs with generalized demodicosis may have abnormal numbers of IL-2 receptors on lymphocytes and subnormal IL-2 production by lymphocytes, abnormal T_H1 versus T_H2 responses, and depressed T-cell function.
- Genetic factors (especially localized, juvenile-onset), immunosuppression, and/or metabolic diseases may predispose animal.

Cats

- *D. cati*—often associated with metabolic diseases (e.g., FIV, systemic lupus erythematosus, diabetes mellitus).
- *D. gatoi*—short and blunted; rarely a marker for metabolic disease; may be transferable from cat to cat within the same household.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Dogs

- Bacterial folliculitis/furunculosis
- Dermatophytosis
- Contact dermatitis
- Pemphigus complex
- Dermatomyositis
- Systemic lupus erythematosus

Cats

- Allergic dermatitis
- Notoedres
- Dermatophytosis
- Psychogenic dermatitis

CBC/BIOCHEMISTRY/URINALYSIS

Normal unless there is an underlying process

OTHER LABORATORY TESTS

- FeLV and FIV serology, toxoplasmosis titers
- Fecal samples: rare finding of mites in feces

DIAGNOSTIC PROCEDURES

- Skin scrapings—diagnostic for finding mites in the majority of cases.
- Trichograms may be an effective technique for mite identification.
- Skin biopsy—may be needed when lesions are chronic, granulomatous, and fibrotic (especially on the foot).



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient.
- Localized—conservative; most cases (90%) resolve spontaneously with no treatment.
- Evaluate the general health status of dogs with either the localized or the generalized form.

CLIENT EDUCATION

- Localized—most cases resolve spontaneously.
- Generalized—frequent management problem; expense and frustration with the chronicity of the problem; juvenile-onset cases may resolve with treatment; adult-onset cases are usually medically controlled but not cured; juvenile-onset considered an inheritable predisposition therefore breeding of affected animals is not recommended.



MEDICATIONS

DRUG(S) OF CHOICE

Amitraz

- A formamidine, which inhibits monoamine oxidase and prostaglandin synthesis; an α₂-adrenergic agonist: use weekly to every other week until resolution of clinical signs and negative skin scrapings; do not rinse off; let air-dry.
- Treat for 1 month following negative skin scrape.
- Clipping the hair coat and applying a benzoyl peroxide shampoo before application

DEMODICOSIS

(CONTINUED)

of the rinse as bactericidal therapy and to increase exposure of the mites by removal of debris from the skin and follicles.

- Efficacy is proportional to the frequency of administration and the concentration of the rinse.
- Rarely used in cats—0.015%–0.025% applied to the entire body every 1–2 weeks (do not use on diabetic cats).
- Dogs—0.03–0.05% applied weekly to every other week; total body/additional topical treatments for focal areas (pododermatitis) may be used every 1–3 days with 0.125% solution.
- Preventic collar—anecdotal reports of success; change collar every 2–4 weeks; non-FDA-approved usage.
- Between 11% and 30% of cases will not be cured; may need to try an alternative therapy or control with maintenance rinse every 2–8 weeks.

Ivermectin

- A macrocyclic lactone with GABA agonist activity.
- Dog: daily oral administration of 0.3–0.6 mg/kg very effective, even when amitraz fails; initiate therapy with a test dose of 0.12 mg/kg q24h for the first week to observe for any signs of toxicity/side effects.
- Treat for 30–60 days beyond negative skin scrapings (average 3–8 months).
- Reported as a treatment option in the cat; exact dose is unknown (often dosed at 300 µg/kg).
- Non-FDA-approved usage.

Milbemycin

- A macrocyclic lactone with GABA agonist activity.
- Dosage of 1–2 mg/kg PO q24h cures 50% of cases; 2 mg/kg PO q24h cures 85% of cases.
- Treat for 30–60 days beyond multiple negative skin scrapings.
- Very expensive/not commercially available in the US.
- Non-FDA-approved usage.

Moxidectin and Doramectin

- Anecdotal reports in the dog when used topically once weekly or orally (0.2–0.3 mg/kg q24h moxidectin; 0.2–0.6 mg/kg weekly doramectin).
- Do not use orally in ivermectin sensitive breeds.
- Non-FDA-approved usage.

Cats

- Exact protocols are not defined.
- Topical lime-sulfur dips every 3–7 days for four to eight treatments often lead to good resolution of clinical signs; recommended therapy in cats.
- Studies with milbemycin and ivermectin are lacking, although there are numerous anecdotal reports of efficacy.
- Doramectin has also been reported to be effective at 0.6 mg/kg SC once weekly.

CONTRAINDICATIONS

- Ivermectin—contraindicated in collies, Shetland sheepdogs, Old English sheepdogs, Australian shepherds, other herding breeds, and crosses with these breeds; sensitive breeds appear to tolerate the acaricidal dosages of milbemycin (see above).
- Sensitive breeds may lack a gene (*MDR1/ABCB1* mutation) that codes for a p-glycoprotein (drug-efflux pump) that predisposes to toxicity.

PRECAUTIONS

Amitraz

- Side effects—somnolence, lethargy, depression, anorexia seen in 30% of patients for 12–36 hours after treatment.
- Rare side effects—vomiting, diarrhea, pruritus, polyuria, mydriasis, bradycardia, hypoventilation, hypotension, hypothermia, ataxia, ileus, bloat, hyperglycemia, convulsions, death.
- Incidence and severity of side effects do not appear to be proportional to the dose or frequency of use.
- Human beings can develop dermatitis, headaches, and respiratory difficulty after exposure.
- Yohimbine at 0.11 mg/kg IV is an antidote.

Ivermectin and Milbemycin

- Signs of toxicity—salivation, vomiting, mydriasis, confusion, ataxia, hypersensitivity to sound, weakness, recumbency, coma, and death.
- Ivermectin—contraindicated in collies, Shetland sheepdogs, Old English sheepdogs, Australian shepherds, other herding breeds, and crosses with these breeds; sensitive breeds appear to tolerate the acaricidal dosages of milbemycin (see above).
- Sensitive breeds may lack a gene (*MDR1/ABCB1* mutation) that codes for a p-glycoprotein (drug-efflux pump) that predisposes to toxicity.

POSSIBLE INTERACTIONS

- Amitraz—may interact with heterocyclic antidepressants, xylazine, benzodiazepines, and macrocyclic lactones.
- Ivermectin and milbemycin—cause elevated levels of monoamine neurotransmitter metabolites, which could result in adverse drug interactions with amitraz and benzodiazepines.
- Spinosad (flea control) usage contraindicated with ivermectin therapy.



FOLLOW-UP

PATIENT MONITORING

Repeat skin scrapings (trichograms) and evidence of clinical resolution are used to monitor progress.

PREVENTION/AVOIDANCE

Do not breed animals with generalized form.

POSSIBLE COMPLICATIONS

Secondary bacterial folliculitis and furunculosis

EXPECTED COURSE AND PROGNOSIS

- Prognosis (dogs)—depends heavily on genetic, immunologic, and underlying diseases.
- Localized—most cases (90%) resolve spontaneously with no treatment; < 10% progress to the generalized form.
- Adult-onset (dogs)—often severe and refractory to treatment.
- Feline cases with *D. cati* may have a poor prognosis associated with underlying disease.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Adult-onset—sudden occurrence is associated with internal disease, malignant neoplasia, and/or immunosuppressive disease; approximately 25% of cases are idiopathic over a follow-up period of 1–2 years.
- *D. cati* associated with FeLV, FIV, toxoplasmosis, and SLE.

AGE-RELATED FACTORS

Young dogs are often predisposed to a localized form.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Do not breed animals with the generalized form.

SYNONYMS

- Mange • Red Mange

SEE ALSO

- Amitraz Toxicosis • Ivermectin and Other Macrocylic Lactones Toxicosis

ABBREVIATIONS

- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- GABA = gamma-aminobutyric acid
- IL = interleukin
- SLE = systemic lupus erythematosus

Suggested Reading

Miller WH, Griffin CE, Campbell KL, eds. Demodicosis. In: Muller & Kirk's Small Animal Dermatology, 7th ed. St. Louis, MO: Elsevier, 2013, pp. 304–315.

Sastre N, Rovira I, Villanueva S, et al.

Phylogenetic relationships in three species of canine *Demodex* mite based on partial sequences of mitochondrial 16S rDNA. Vet Derm 2012, 23(6):509–e101.

Author Karen Helton Rhodes

Consulting Editor Alexander H. Werner



Client Education Handout
available online



BASICS

OVERVIEW

- Caries is the decay of the dental hard tissues (enamel, cementum, and dentin) due to the effects of oral bacteria on fermentable carbohydrates on the tooth surface.
- The word "caries" is Latin for rottenness and is both the singular and plural form.
- Oral bacteria ferment carbohydrates on the tooth surface, resulting in the production of acids leading to demineralization of the hard tissues, thus allowing bacterial and leukocytic digestion of the organic matrix of the tooth.
- Caries has been very common in humans in "westernized" society, where diets rich in highly refined carbohydrates are the norm. Aggressive public education and preventive measures have resulted in a decline in the incidence over the past several decades.
- In humans, *Streptococcus mutans* is particularly implicated in the development of caries.
- For various reasons (e.g., diet lower in refined carbohydrates, higher salivary pH, lower salivary amylase, conical crown shape, wider interdental spacing, different indigenous oral flora), caries is not common in the domestic dog, but it does occur and should be looked for.
- A study published in the *Journal of Veterinary Dentistry* in 1998 (see "Suggested Reading") reported that 5.3% of dogs 1 year of age or older had one or more caries lesions, with 52% having bilaterally symmetrical lesions.
- Caries can affect the crown or roots of the teeth and is classified as pit-and-fissure, smooth-surface, or root caries.

SIGNALMENT

- Caries occurs in dogs.
- Reported in cats; tooth resorption (feline odontoclastic resorptive lesions) have sometimes been misnamed feline caries. To the author's knowledge, there are no published reports of true dental caries occurring in the domestic cat, though it is theoretically possible.
- There is no reported breed, age, or gender predilection.

- Anecdotally, the author has observed a higher incidence of pit-and-fissure lesions in the occlusal tables of the maxillary first molar teeth in large-breed dogs such as Labrador retrievers and German shepherds.

SIGNS

- Incipient smooth-surface caries—appears as an area of dull, frosty-white enamel.
- Clinical caries—appears as a structural defect on the surface of the crown or root.
- The defect is frequently filled with or lined by dark, soft necrotic dentin. The defect may also trap and hold food debris.
- Affected dentin will yield to a dental explorer and can be removed with a dental excavator or curette.

CAUSES & RISK FACTORS

- Caries is caused by oral bacteria fermenting carbohydrates on the tooth surface, leading to the production of acids (acetic, lactic, propionic) that demineralize the enamel, cementum, and dentin, followed by digestion of the organic matrix of the tooth by oral bacteria and/or leukocytes.
- There is a constant exchange of minerals between the tooth surfaces (enamel, any exposed dentin or root cementum) and the oral fluids; if there is a net loss of mineral, caries develops.
- Early (incipient) caries may be reversible through remineralization.
- Once the protein matrix collapses, the lesion is irreversible.
- Any factors that allow prolonged retention of fermentable carbohydrates and bacterial plaque on the tooth surface predispose to the development of caries.
- A deep occlusal pit on the maxillary first molar is the most common place for caries to develop.
- Dental surfaces in close contact with an established caries are at risk of developing a lesion by extension.
- Deep occlusal pits and developmental grooves on the crown surface predispose to pit-and-fissure caries.
- Tight interdental contacts predispose to smooth-surface caries.
- Deep periodontal pockets predispose to root caries.
- Animals with poorly mineralized enamel, lower salivary pH, diets high in fermentable

carbohydrates, and poor oral hygiene are at risk of developing caries.

- Loss of enamel through any means (hypocalcification at the developmental stage, abrasive wear or attrition, traumatic fracture) that exposes the softer, underlying dentin may increase the risk for the development of caries.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Crown fracture, abrasive wear or attrition with exposed tertiary dentin, or extrinsic staining.
- Enamel hypocalcification with exposed and stained dentin.
- Tooth resorption (TR; feline odontoclastic resorptive lesions [FORL]) has been misnamed feline caries in the past.
- Tooth resorption can also occur in dogs and may be mistaken for caries.
- Sound dentin is hard and will not yield to a dental explorer, whereas carious dentin is soft and will yield to a sharp instrument.
- Root caries may be confused with external root resorption, though the distinction would often be academic, as either usually indicates the need for extraction.
- The lesion should be staged as to the depth of the pathology.
- Table 1 below is adapted from the American Veterinary Dental College approved nomenclature for tooth resorption as published on their website.

CBC/BIOCHEMISTRY/URINALYSIS N/A

OTHER LABORATORY TESTS N/A

IMAGING

Intraoral dental radiography:

- Areas of demineralization and tissue loss will appear as lucent areas contrasted against radiodense normal dental tissues.
- If the lesion has penetrated into the pulp chamber, there will be endodontic disease and there may be periapical disease evident if the lesion is sufficiently long-standing.
- Small lesions may be difficult to demonstrate due to superimposition of normal, radiodense tissues (dental and skeletal).

Table 1

Stage	Description
Stage 1	Defect involves enamel or cementum only.
Stage 2	Defect extends into dentin but not into pulp chamber.
Stage 3	Deep dental hard tissue loss (cementum and/or enamel with loss of dentin that extends to the pulp cavity); most of the tooth retains its integrity.
Stage 4	Extensive dental hard tissue loss (cementum and/or enamel with loss of dentin that extends to the pulp cavity); most of the tooth has lost its integrity.
Stage 5	Majority of crown lost; root remnants remaining.

DENTAL CARIES

(CONTINUED)

DIAGNOSTIC PROCEDURES

- Visual examination of the clean, dry tooth surface under good light and with the aid of magnification.
- Exploration with a sharp dental explorer—the explorer will sink into carious dentin and stick, providing the sensation of “tug-back” upon withdrawal.
- Subgingival exploration—reveals irregularities in the root surface.
- Caries detection dyes have been used by human and veterinary dentists to aid in the differentiation between sound and carious dentinal tissue. However, their use may lead to false-positive results and overtreatment through the removal of excess tissue. Reliance on visual, tactile, and radiographic findings is preferable.



TREATMENT

- Focus on prevention—examine the adult dentition of adolescent dogs (6–8 months of age) to identify anatomically compromised areas at risk for the development of caries. Deep pits in the occlusal surface of the maxillary first molar (for example) can be filled with a pit-and-fissure sealant or fluoride-releasing dental bonding agent to prevent caries development if identified prior to the development of any decay.
- Incipient caries—can be arrested and possibly reversed by application of a fluoride varnish or fluoride-releasing dental bonding agent and modification of the risk factors.
- Lesions that result in mild to moderate coronal tissue loss (stage 1 or 2)—remove carious dentin and unsupported enamel using hand instruments and power rotary dental instruments, then restore the coronal anatomy with a bonded, composite restoration or prosthetic restoration.
- Lesions that extend into pulp tissue (stage 3)—endodontic treatment must precede restorative treatment. Alternatively, extraction may be indicated. As the pulp tissue in the roots will be contaminated, complete removal of all root remnants is essential if extraction is performed.
- Lesions that result in extensive coronal tissue loss (stage 4 or 5)—extraction is typically the only treatment option. As the pulp tissue in the roots will be contaminated, complete removal of all root remnants is essential.

- Root caries—if the periodontal disease can be managed and the restoration placed supragingivally, restoration may be possible; however, for most teeth with root caries, extraction will be the treatment of choice.
- If only one root of a multirooted tooth is carious—extraction of the affected root with endodontic treatment of the remaining root(s) is also an option.
- For high-risk patients—application of a pit-and-fissure sealant and/or fluoride-releasing dental bonding agent on remaining teeth with occlusal surfaces may be considered.



MEDICATIONS

DRUG(S)

- Postoperative broad-spectrum antibiotics—may be indicated if there is pulp involvement necessitating endodontic treatment or extraction.
- Postoperative analgesia with non-steroidal anti-inflammatory drugs and/or narcotics is indicated following endodontic or exodontic treatment or extensive restorative work of vital teeth.

CONTRAINdications/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Examine and radiograph treated teeth 6 months postoperatively, then annually or as the opportunity presents.
- Evaluate the integrity of the restorations, assess for further decay at the margins or under the restorations, assess for the development of endodontic disease.
- As affected individuals frequently have more than one caries, examine all teeth carefully (clinically and radiographically) at any opportunity to monitor for the development of new lesions.

PREVENTION/AVOIDANCE

Avoidance of diet and treats high in refined carbohydrates may reduce the risk of the development of further caries.

EXPECTED COURSE AND PROGNOSIS

If a lesion has been properly debrided and restored it should have an excellent prognosis. Appropriate staging and case selection, thorough removal of all carious tissues, and adherence to restorative principles are essential.



MISCELLANEOUS

SYNONYMS

- Cavities
- Dental decay

ABBREVIATIONS

- FORL = feline odontoclastic resorptive lesions
- TR = tooth resorption

INTERNET RESOURCES

- Regarding dental caries in dogs: <http://www.toothvet.ca/PDFfiles/DentalCaries.pdf>
- Regarding staging of tooth resorption: <http://www.avdc.org/Nomenclature.html#resorption>.
- Regarding tooth resorption in cats: http://www.toothvet.ca/PDFfiles/Tooth_resorption_in_cats.pdf Regarding tooth resorption in dogs: http://www.toothvet.ca/PDFfiles/RLs_inDogs.pdf

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Consulting Editor Heidi B. Lobprise



BASICS

OVERVIEW

Cyst formation originating from tissue surrounding the crown of an unerupted tooth.

SIGNALMENT

- Any breed that is at an increased risk for impaired eruption.
- Boxers, bulldogs—mandibular first premolars, often bilateral.
- Unerupted teeth at 6–7 months of age, but cystic development may not occur until much later, if at all.

SIGNS

- Cystic changes may be initially unapparent without diagnostic imaging.
- “Missing” tooth.
- Formation of a soft swelling at the site of a missing tooth, often fluctuant with fluid.
- Patient may present, with no previous indication of a problem, for a pathologic fracture of the mandible due to cystic destruction of the surrounding bone.

CAUSES & RISK FACTORS

Unerupted teeth



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Odontogenic keratocyst—cysts of the jaw demonstrating aggressive expansion that may, or may not, be associated with unerupted teeth.
- Primordial cyst—cystic degeneration of a tooth bud before enamel/dentin formation (cyst without a tooth).
- Oral mass—odontoma. Tooth structures (complex or compound) sometimes contained within cystic structure, but with different levels of organization.
- Transformation to ameloblastomas has been reported in humans; histologic evaluation of the cyst lining is highly recommended.

CBC/BIOCHEMISTRY/URINALYSIS

- No abnormalities typically found.
- Preoperative diagnostics where appropriate.

OTHER LABORATORY TESTS

N/A

IMAGING

- Definitive diagnosis from radiography.
- Radiographs are essential in any instance of missing or unerupted teeth.
- Radiographically—radiolucent cyst originating from the remnant enamel organ at the neck of the tooth and encompassing the crown (a halo).

DIAGNOSTIC PROCEDURES

Histopathologic assessment if atypical.



TREATMENT

- Appropriate preoperative antimicrobial and pain management therapy when indicated.
- Appropriate patient monitoring and support during anesthetic procedure.
- If cystic formation is present—surgical extraction, complete debridement of cyst lining, and histologic evaluation.
- If an embedded tooth has been present in a mature animal—assess for any cystic structure or other pathologic changes involving the tooth; continued monitoring may be reasonable if surgical extraction would damage large amounts of bone.
- If a non-strategic tooth can be easily extracted, it would be best to do so, even if cystic changes are not present.



MEDICATIONS

DRUG(S)

Postoperative analgesics, as necessary.

CONTRAINdications/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

POSSIBLE COMPLICATIONS

- Pathologic fracture may occur if dentigerous cyst is not diagnosed and treated.
- Fracture of mandible at time of extraction, if compromised.

EXPECTED COURSE AND PROGNOSIS

- Good with early detection and extraction.
- Fair to guarded with extensive bone destruction or pathologic fracture.



MISCELLANEOUS

INTERNET RESOURCES

<http://www.avdc.org/Nomenclature.html>.

Suggested Reading

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DERMATOMYOSITIS



BASICS

DEFINITION

An inheritable inflammatory disease of the skin, muscles, and vasculature that develops in young collies, Shetland sheepdogs, and their crossbreeds.

PATHOPHYSIOLOGY

- The exact pathogenesis of dermatomyositis is unknown.
- A familial predisposition has been reported in collies and Shetland sheepdogs; however, possible triggers for the disease include infectious agents (especially viral), vaccines, drugs, malignancy, toxins, infection—as seen with ischemic dermatopathy in other breeds.
- Based on the clinical and histopathologic evidence, an immune-mediated or auto-immune process may be involved.

SYSTEMS AFFECTED

- Skin/Exocrine
- Musculoskeletal

GENETICS

Autosomal dominant inheritance, with variable expression in collies and Shetland sheepdogs.

INCIDENCE/PREVALENCE

Exact prevalence is unknown

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dogs

Breed Predilections

- Inheritable disease of collies, Shetland sheepdogs, and their crossbreeds, Beauceron shepherds, Belgian Tervurens, and Portuguese water dog.
- Similar symptoms reported in the mongrel, Welsh corgi, Lakeland terrier, chow chow, German shepherd dog, schipperke, and Kuvasz.
- Some animals in other breeds with similar signs are now classified as ischemic dermatopathy (dermatomyositis-like), and not dermatomyositis as previously reported.

Mean Age and Range

- Cutaneous lesions typically develop before 6 months, and may develop as early as 7 weeks of age.
- The full extent of lesions is usually present by 1 year of age, and may lessen thereafter.
- Adult-onset dermatomyositis can occur, but is rare, and is usually less severe.

Predominant Sex

None reported

SIGNS

General Comments

- The clinical signs vary from subtle skin lesions and subclinical myositis to severe skin

lesions with generalized muscle atrophy, abnormal gait and megaesophagus.

- Several littermates may be affected, but the severity of the disease often varies significantly among affected dogs.

Physical Examination Findings

- Waxing and waning lesions around the eyes, lips, face, inner ear pinnae, tip of the tail, and bony prominences—usually seen in affected dogs before they are 6 months old.
- Scarring—often a sequela to the initial skin lesions.
- Atrophy of the masseter and temporal muscles.
- Severe cases may have difficulty eating, drinking, and swallowing.
- Stiff or high-stepping gait.
- Skin lesions—characterized by variable degrees of crusted erosions, ulcers, and alopecia, with erythema, scaling, and scarring on the face, around the lips and eyes, in the inner ear pinnae, on the tip of the tail; the entire face may be involved.
- Pressure points over bony prominences, especially the carpal and tarsal regions.
- Foot pad and oral ulcers, as well as nail abnormality or loss may occur.
- Myositis—signs may be absent or vary from subtle decrease in the mass of the temporalis muscles to generalized symmetric muscle atrophy and stiff high-stepping gait.
- Dogs with megaesophagus may present with aspiration pneumonia.

CAUSES

- Hereditary in collies, Shetland sheepdogs, and their crosses.
- Infectious agents, toxins, malignancy, vaccines or drugs may be a triggering event.
- Immune-mediated disease in other breeds.

RISK FACTORS

Mechanical pressure and trauma, and ultraviolet light exposure may worsen cutaneous lesions.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Demodicosis
- Dermatophytosis
- Bacterial folliculitis
- Juvenile cellulitis
- Discoid lupus erythematosus
- Systemic lupus erythematosus
- Polymyositis
- Ischemic dermatopathy
- Epidermolysis bullosa simplex

CBC/BIOCHEMISTRY/URINALYSIS

Serum creatine kinase may be elevated due to muscle damage.

OTHER LABORATORY TESTS

- Antinuclear antibody titers—rule out systemic lupus erythematosus.

- Elevated levels of immunoglobulin G and circulating immune complex correlated with disease severity.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Skin biopsy—may be diagnostic for dermatomyositis, although this disease can be difficult to definitively diagnose; avoid infected and scarred lesions.
- Muscle biopsy—proper muscle selection can be difficult because pathologic changes may be mild consisting of muscle necrosis and atrophy.
- EMG—ideally, is used to select affected muscles for biopsy; if EMG is not available, atrophied muscles should be biopsied.

PATHOLOGIC FINDINGS

Skin Biopsy

- Scattered apoptosis or vacuolation of individual and follicular basal cells; may lead to intrabasal or subepidermal clefting.
- Mild pigmentary incontinence.
- Superficial, mild, diffuse dermal and perivascular cellular infiltrates—composed of lymphocytes, plasma cells, and histiocytes.
- Follicular atrophy and perifollicular fibrosis in chronic cases.
- Secondary epidermal ulceration and dermal scarring—may be present.
- Histopathologic features may be subtle and consist mostly of atrophic changes; however, the combination of epidermal and follicular basal cell degeneration, perivascular inflammation, and follicular atrophy with fibrosis is highly suggestive of dermatomyositis.

Muscle Biopsy

- Variable multifocal accumulations of inflammatory cells, including lymphocytes, plasma cells, macrophages, and neutrophils.
- Myofibril degeneration—characterized by fragmentation, vacuolation, atrophy, fibrosis, and regeneration.

Electromyography

EMG abnormalities are present especially in the muscles of the head and distal limbs; findings include fibrillation potentials (rapid, irregular, and unsynchronized contraction of muscle fibers), and positive sharp waves.



TREATMENT

APPROPRIATE HEALTH CARE

- Most dogs can be treated as outpatients.
- Dogs with severe myositis and megaesophagus may need to be hospitalized for supportive care.
- Severe cases may warrant euthanasia.
- Assist to eat if muscles of mastication are affected; feed at an elevated position if megasophagus develops.

(CONTINUED)

- Nonspecific supportive therapy includes gentle bathing and soaking to remove crusts, and treatment of secondary bacterial folliculitis (if present).

ACTIVITY

- Avoid activities that may traumatize the skin.
- Keep indoors during the day to avoid solar radiation.

DIET

N/A

CLIENT EDUCATION

- Discuss the hereditary nature of the disease.
- Note that affected dogs should not be bred.
- Inform the owner that the disease is not curable, although spontaneous resolution or waxing and waning of symptoms may occur.
- Discuss prognosis and possible complications, especially in severely affected dogs.
- Therapeutic efficacy of medical treatment can be difficult to assess because the disease tends to be cyclic in nature and is often self-limiting.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Vitamin E 200–800 IU PO q12–24h.
- Essential fatty acid supplements.
- Prednisone 1–2 mg/kg PO q12–24h until remission, then alternate day to twice weekly administration using the lowest dosage possible for long-term control.
- Nonsteroidal anti-inflammatory medication.
- Pentoxifylline 10–25 mg/kg q12h.
- Tetracycline (250 mg > 10 kg, 500 mg < 10 kg q8–12h), doxycycline (10 mg/kg q24h), minocycline (5 mg/kg q12h), with niacinamide (250 mg > 10 kg, 500 mg < 10 kg q8–12h).
- Tacrolimus 0.1% applied q12h.

CONTRAINDICATIONS

Pentoxifylline should not be used in dogs that are sensitive to methylxanthine derivatives.

PRECAUTIONS

- Pentoxifylline—rarely causes gastric irritation; can affect clotting times (PT/PTT prolongation and thrombocytopenia) and dogs receiving anticoagulant therapy should be monitored carefully when treated with this drug; possible rare seizure or reduction of seizure threshold in epileptics.

- Glucocorticoids—discuss possible side effects with the owner.
- Tacrolimus can cause local irritation.

POSSIBLE INTERACTIONS

Glucocorticoids and nonsteroidal anti-inflammatory medications can cause GI bleeding if used concurrently.

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

N/A

PREVENTION/AVOIDANCE

- Do not breed affected animals.
- Neuter intact animals to reduce hormonal influence on symptoms.
- Minimize trauma and exposure to sunlight.

POSSIBLE COMPLICATIONS

- Secondary bacterial folliculitis.
- Mildly to moderately affected dogs may have residual scarring.
- Severely affected dogs may have trouble chewing, drinking, and swallowing due to scarring of the masticatory and esophageal muscles.
- Megaesophagus may develop, predisposing the dog to aspiration pneumonia.
- Dogs may be lame due to damage of the muscles of the extremities.

EXPECTED COURSE AND PROGNOSIS

- Long-term prognosis—variable, depending on severity of disease.
- Minimal disease—prognosis good; tends to spontaneously resolve with no evidence of scarring.
- Mild-to-moderate disease—tends to resolve spontaneously, but residual scarring is common.
- Severe disease—prognosis for long-term survival is poor as damage to the skin and muscle may be life-long.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

None

DERMATOMYOSITIS**AGE-RELATED FACTORS**

- Initial clinical signs usually occur in dogs younger than 6 months.
- Adult-onset—rare; more commonly seen in dogs that had subtle lesions as puppies.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

- Do not breed affected dogs.
- Pregnancy may exacerbate clinical symptoms.
- Oestrus may exacerbate clinical symptoms.

SYNONYMS

- Familial canine dermatomyositis
- Canine familial dermatomyositis
- Ischemic dermatopathy in collies and Shetland sheepdogs

SEE ALSO

- Lupus Erythematosus, Cutaneous (Discoid)
- Lupus Erythematosus, Systemic

ABBREVIATIONS

- EMG = electromyography, electromyographic
- GI = gastrointestinal
- PT = prothrombin time
- PTT = partial thromboplastin time

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Client Education Handout
available online

D

DERMATOPHILOSIS



BASICS

OVERVIEW

- “Mud rash” or “mud fever” a rare crusting dermatitis of dogs and cats.
- A rare nodular subcutaneous and oral disease in cats.
- *Dermatophilus congolensis*—causative agent; Gram-positive, branching filamentous bacterium classified as an actinomycete; very common cause of crusting dermatoses in hoofed animals; persists in the environment within crusts.
- Dogs, cats, humans, and other animals can rarely be secondarily infected.

D

SYSTEMS AFFECTED

Skin/Exocrine

SIGNALMENT

- Dogs and cats
- No age, breed, or sex predilection

SIGNS

Historical Findings

- Association with cattle, sheep, or horses.
- Occasionally free-roaming dogs.
- Cats with subcutaneous disease—episode of trauma; existence of a foreign body; lesions generally chronic; no systemic clinical signs, except when internal organs or large oral lesions develop.

Physical Examination Findings

- Dogs—circular to coalescing, papular, crusted lesions on the head and/or trunk; lesions resemble superficial bacterial pyoderma caused by *Staphylococcus pseudintermedius*; lesions may resemble dermatophilosis in horses (adherent thick, gray-yellow crusts that incorporate hair and leave a circular, glistening, shallow erosion when removed); variable pruritus.
- Cats—subcutaneous, oral, or internal ulcerated and fistulated nodules or abscesses similar to lesions caused by other actinomycetes; superficial pyogenic crusting disease of the face has been reported.

CAUSES & RISK FACTORS

- Dogs, cats, and humans can be exposed directly from lesions on large animals or from environmental exposure.
- Infectious stage—requires wetting for activation; cannot penetrate intact epithelium; minor trauma or mechanical transmission by biting ectoparasites (*Amblyomma variegatum*) may help in establishing infection.
- Deeper infection—require traumatic inoculation of infectious materials.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Dogs

- Staphylococcal folliculitis
- Acute moist dermatitis
- Dermatophytosis
- Pemphigus foliaceus
- Keratinization disorder

Cats

- Actinomycosis and nocardiosis
- Opportunistic mycobacterial granuloma
- Sporotrichosis
- Cryptococcosis
- Foreign body
- Chronic bite/wound abscess
- Bacterial L-form infection
- *Rhodococcus equi* infection
- Cutaneous or mucosal neoplasm, especially squamous cell carcinoma

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal; possible neutrophilic leukocytosis in cats.

DIAGNOSTIC PROCEDURES

Dogs

- Cytologic examination of crusts—most important procedure; differentiates from more typical bacterial pyoderma.
- Organism—distinctive morphology in cytologic and histopathologic preparations; resembles “railroad tracks” as the bacterium forms branching chains of small diplococci.
- Cytologic diagnosis—impression smears of exudate from under crusts or by preparation of macerated crusts; mince crusts finely in a drop of water and allow to macerate several minutes; dry the preparation and stain with Wright-Giemsa.
- Histopathologic specimens—crusts contain organisms; submit with tissue samples.

Cats

- Histopathologic examination—biopsy of nodules; procedure of choice.
- Cytologic examination—exudate obtained from aspiration of nodule or swabbing of a draining tract.
- Culture of biopsy specimens—may yield the organism; facilitated if the laboratory is alerted to the differential diagnosis of *Dermatophilus* (aerobic, relatively slow growing, and easily obscured by contamination).
- Culture from crusts—requires the use of special selective medium; isolation is possible but usually very difficult.

PATHOLOGIC FINDINGS

- Dogs—crusting and superficial pustular dermatitis; palisading of the crusts with orthokeratotic and parakeratotic hyperkeratosis; organism visualized within the crusts.
- Cats—pyogranulomatous inflammation; central necrosis; fistulous tract formation; organism visualized near the necrotic center of granulomas, especially with Gram stain.



TREATMENT

- Dogs—antibacterial shampoo and gentle removal (and disposal) of crusts; shampoo containing benzoyl peroxide, ethyl lactate, chlorhexidine, or selenium disulfide; one or two applications suffice in most cases. Iodine or lime-sulfur may also be used.
- Cats—for pyogranulomas and abscesses: surgical debridement; exploration for foreign body; establishment of drainage for exudate.



MEDICATIONS

DRUG(S)

- Penicillin V 10 mg/kg PO q12h for 10–20 days; drug of choice.
- Tetracycline 22–30 mg/kg, q8h, PO; doxycycline 5–10mg/kg, q12h, PO; or minocycline 5–12 mg/kg, q12h, PO.
- Ampicillin 10–20 mg/kg PO q12h for 10–20 days; some isolates resistant in vitro.
- Amoxicillin 10–20 mg/kg PO q12h for 10–20 days; some isolates resistant in vitro.

CONTRAINdications/POSSIBLE INTERACTIONS

Penicillin and ampicillin hypersensitivity



FOLLOW-UP

PATIENT MONITORING

- Dogs—reexamine after 2 weeks of treatment to ensure complete resolution; give an additional 7 days of systemic therapy if indicated.
- Cats—monitor biweekly for 1 month after apparent resolution of lesions, depending on location.

EXPECTED COURSE AND PROGNOSIS

- Dogs—excellent.
- Cats—varies with the location of lesions; recurrence possible due to persistence of organism in crusts and extent of surgical debridement; complete resolution can be achieved with early diagnosis and medical/surgical therapy.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Veterinarians and animal care workers—seldom infected, even after traumatic exposure when working with infected farm animals.
- Dogs and cats—unlikely but possible to serve as a source for human infection; caution is warranted for exposure of immunocompromised individuals.

INTERNET RESOURCES

<http://www.grjournals.com/portals/grjournals/JASA/Vol3%20Issue7/JASA-2013-37-337-344.pdf>

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Consulting Editor Alexander H. Werner

DERMATOPHYTOSIS

D



BASICS

DEFINITION

- A cutaneous fungal infection affecting the cornified regions of hair, nails, and occasionally the superficial layers of the skin.
- *Microsporum* and *Trichophyton* dermatophytes are most commonly isolated: the majority of cases caused by *Microsporum canis*; infection with *Trichophyton mentagrophytes*, *M. gypseum*, or *M. persicolor* also occurs.

PATHOPHYSIOLOGY

- Dermatophytes—grow in the keratinized layers of hair, nail, and skin; do not thrive in living tissue or persist in the presence of severe inflammation.
- Exposure to or contact with a dermatophyte does not necessarily result in an infection.
- Infection may not result in clinical signs.
- Incubation period from exposure to clinical lesions: approximately 2–4 weeks.
- Infective spores must contact the skin surface and defeat host protective mechanisms (innate immunity, normal flora, sebum, grooming), in order for infection to occur.
- Factors that favor the development of disease: stress, trauma, ectoparasite infestations, and immunosuppression.
- An infected animal may remain as an asymptomatic (inapparent) carrier for a prolonged period of time; some animals never become symptomatic.

SYSTEMS AFFECTED

Skin/Exocrine

INCIDENCE/PREVALENCE

- Lesions may mimic many dermatologic conditions; over-diagnosis is likely common.
- Infection rates (inapparent and clinical) vary widely, depending on the population studied.

GEOGRAPHIC DISTRIBUTION

- More common in hot, humid climates.
- Incidence of dermatophyte species may vary seasonally and geographically (e.g., northern vs. southern hemisphere, rural vs. urban environment, indoor vs. outdoor housing).

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Cat—more common in longhaired breeds (i.e., Persian and Himalayan)
- Dog: Yorkshire terrier and Manchester terrier

Mean Age and Range

- *M. canis* is more common in younger animals; other species (associated with rodents or wildlife) seen more often in adults.
- Generalized dermatophytosis in older dogs associated with immunosuppression.

SIGNS

Historical Findings

Previously confirmed infection or exposure to an infected animal or environment (e.g., a cattery) is a useful but not consistent finding.

Physical Examination Findings

- Inapparent carrier state—cats.
- Only consistent finding is extreme variability of clinical signs.
- Classical lesion: slowly expanding circular patch of alopecia with scale.
- Seborrheic or greasy hair coat.
- Papular or pustular eruptions.

CAUSES

Multiple species identified; majority of cases caused by *Microsporum canis*, *Microsporum gypseum*, *Trichophyton mentagrophytes*, and *Microsporum persicolor* (non-follicular).

RISK FACTORS

- Immunocompromise caused by disease (FeLV, FIV) or by medications (glucocorticoids).
- High population density.
- Poor management practices.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Staphylococcal folliculitis
- Demodexis
- Allergic dermatitis
- Pemphigus (especially foliaceus)
- Keratinization defects

DIAGNOSTIC PROCEDURES

Wood's Lamp Examination

- Can be misleading: only 50% of *M. canis* isolates fluoresce; most other pathogenic dermatophytes do not fluoresce.
- True positive reaction consists of apple-green fluorescence of the hair shaft.

Microscopic Examination of Hair

- Choose hairs that fluoresce under Wood's lamp illumination to increase success.
- Hyphae and arthrospores seen invading hair shafts.

Fungal Culture with Identification

- "Gold standard" for diagnosis.
- Choose hairs that fluoresce under Wood's lamp if possible.
- Sampling methods: Pluck hairs from the periphery of an alopecic area. Brush haircoat with a sterile toothbrush or carpet square (especially inapparent or treated patient).
- Dermatophyte test media—dermatophytes change media color to red during the early growing phase of the culture; saprophytes cause color change after significant colony growth; examine inoculated media daily.
- Fungal colonies are non-pigmented.
- Microscopic examination of the growth for microconidia and macroconidia—necessary to confirm pathogenic dermatophyte and to identify

genus and species; helps identify source of infection.

- Positive culture—indicates presence of a dermatophyte; however, organisms may be transient (i.e., geophilic dermatophytes on the feet).

Skin Biopsy

- Not usually required for diagnosis.
- Can be helpful in confirming true invasion and infection, or to diagnose suspicious cases with negative fungal culture.

PATHOLOGIC FINDINGS

- Folliculitis, perifolliculitis, or furunculosis.
- Hyperkeratosis, intraepidermal pustules, and pyogranulomatous reaction pattern may occur.
- Fungal hyphae seen in H&E-stained sections; special stains allow easier visualization of the organism.



TREATMENT

APPROPRIATE HEALTH CARE

- Most animals are treated as outpatients.
- Consider quarantine owing to the infective and zoonotic nature of the disease.

CLIENT EDUCATION

- Many shorthaired cats in a single-cat environment and many dogs will undergo spontaneous remission within 3 months.
- Longhaired animals should be clipped to reduce environmental contamination.
- Decontamination of the environment reduces the risk of false positive fungal cultures which can lead to prolonged treatment and confinement.
- Infective spores are shed into the environment, but do not multiply in the environment; transmission of the disease strictly from a contaminated environment (i.e., no direct contact with an infected animal) is extremely rare.
- Effective disinfectants
 - Sodium hypochlorite (0.5%): potential to react with other chemicals to create toxic gases; can be irritating and result in "bleaching" of colors.
 - Enilconazole: available as a concentrated spray or fogger; 10-minute contact time is recommended.
 - Accelerated hydrogen peroxide: should not be mixed with concentrated sodium hypochlorite products; 10-minute contact time recommended.
 - Potassium peroxyomonosulfate (2% solution): recent studies report antifungal properties against *M. canis* and *Trichophyton* spp.
- Advise that treatment can be both frustrating and expensive, especially in multi-animal households or with recurrent cases; consider referral to a veterinarian with expertise in treatment of dermatophytosis.

DERMATOPHYTOSIS

(CONTINUED)



MEDICATIONS

DRUG(S) OF CHOICE

- Topical therapy and clipping—recommended concurrently with systemic therapy; may help prevent environmental contamination; may be associated with an initial exacerbation of signs
- Rinses: lime sulfur (1:16 dilution or 8 oz. per gallon of water), miconazole/ chlorhexidine (0.2%), or enilconazole (0.2%) applied once to twice weekly; lime sulfur is odoriferous and can stain; enilconazole is not currently approved for use in companion animals in the US. Shampoos containing 1–2% ketoconazole, miconazole, or 0.5% climbazole; a minimum of a 3-minute contact time is recommended; have little to no residual effect.
- Use of an Elizabethan collar, particularly in cats, is recommended to prevent ingestion of these products.
- Griseofulvin—effective but use is declining due to relatively high costs and side effects.
- Ketoconazole—true efficacy unknown; some studies have shown *in vitro* resistance of *M. canis*: dogs, 10 mg/kg PO q24h or divided q12h for 4–8 weeks; anorexia and vomiting are the most common side effects; not recommended in cats.
- Itraconazole—similar to ketoconazole, but more effective; fewer side effects, expensive: dogs, 5–10 mg/kg PO q24h for 4–8 weeks; cats, 10 mg/kg PO q24h for 4–8 weeks or until cured. Alternate dosing—20 mg/kg q48h cats and dogs. In some cats, dosage regimen is altered after 4 weeks of therapy to every other week schedule for a total of 8–10 weeks of therapy; alternative schedule—one-week-on, one-week-off with apparent efficacy to reduce drug cost; manufactured drug preferred over compounded formulations due to absorption/concentration variability.
- Terbinafine—may be helpful in cases resistant to azole drugs; dogs, 20–30 mg/kg q12–24h for 4–8 weeks; cats, 20–40 mg/kg q24–48h for 4–8 weeks; dermatophyte carriers, 8.25 mg/kg q24h for 4–8 weeks; side effects may include gastrointestinal upset, hepatotoxicity, neutropenia, and pancytopenia.

CONTRAINdications

- Corticosteroids: can modulate inflammation and prolong the infection. • Griseofulvin: cats with FeLV or FIV; teratogen.

PRECAUTIONS

Ketoconazole

- Hepatopathy has been reported and can be severe in cats. • Inhibits endogenous production of steroid hormones in dogs.

Itraconazole

- Rare vasculitis and ulcerative skin lesions at doses of 5 mg/kg q12h; not noted in patients receiving 5 mg/kg q24h. • Hepatotoxicity reported infrequently in dogs.

Terbinafine

- Gastrointestinal upset, hepatotoxicity, and bone marrow suppression (pancytopenia, neutropenia). Decrease dosage with renal and/or hepatic insufficiency. Cimetidine increases blood concentration; rifampin decreases blood concentration.

Lime-Sulfur Solution

- Ingestion of lime sulfur may lead to oral erosions.

ALTERNATIVE DRUG(S)

- Lufenuron—a chitin synthesis inhibitor used in flea control; not effective in controlled studies. • Fluconazole—effectiveness not well documented in studies; less expensive than itraconazole.



FOLLOW-UP

PATIENT MONITORING

- Dermatophyte culture is the only appropriate method for monitoring response to therapy; many animals clinically improve but remain culture-positive. • Repeat fungal cultures toward the end of the treatment regimen and continue treatment until at least two subsequent cultures are negative. • In resistant cases, cultures should be repeated weekly using the toothbrush technique.
- Weekly or biweekly CBC if treating with griseofulvin; periodic evaluation of liver enzymes if treating with ketoconazole, itraconazole, or terbinafine.

PREVENTION/AVOIDANCE

- Initiate a quarantine period and obtain dermatophyte cultures of all animals entering the household to prevent reinfection from inapparent carriers. • Consider the possibility of rodents aiding in the spread of the disease.
- Decontaminate the environment. • Avoid infective soil if a geophilic dermatophyte is cultured. • Consider prophylactic treatment of exposed animals.

POSSIBLE COMPLICATIONS

False-negative dermatophyte culture

EXPECTED COURSE AND PROGNOSIS

- Many animals will “self-clear” infection over a period of a few months. • Treatment hastens clinical cure and helps reduce environmental contamination. • Some infections, particularly in longhaired cats or multi animal situations, can be persistent.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Dermatophytosis is a significant zoonosis. • Considered a low level pathogen; disease is not life-threatening, can be easily treated, but may cause scarring.

PREGNANCY/FERTILITY/BREEDING

- Griseofulvin is teratogenic. • Ketoconazole can affect steroid hormone synthesis, especially testosterone.

SYNONYMS

Ringworm

ABBREVIATIONS

- FeLV = feline leukemia virus • FIV = feline immunodeficiency virus • H&E = hematoxylin and eosin

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Client Education Handout
available online

DERMATOSES, DEPIGMENTING DISORDERS



BASICS

DEFINITION

- Pathologic or cosmetic condition involving loss of pigmentation of the skin and/or hair coat either by lack of pigmentation or by melanocyte damage.
- Leukotrichia—whitening of the hair (nonspecific location).
- Poliosis—whitening of hair on the head/face.
- Leukoderma—whitening of the skin.

PATHOPHYSIOLOGY

- Dependent on cause.
- Melanocytes may be damaged or destroyed by toxins (including toxic melanin precursors), inflammatory mediators, auto-antibodies, and/or inhibitors of melanogenesis.
- Some diseases may be distinguished clinically by depigmentation as the initial symptom versus depigmentation occurring secondary to inflammation.

SYSTEMS AFFECTED

- Skin/Exocrine
- Ophthalmic

GEOGRAPHIC DISTRIBUTION

Discoid lupus erythematosus and pemphigus erythematosus more common in locations with higher exposure to ultraviolet light.

SIGNALMENT

- Mucocutaneous pyoderma—German shepherd dog
- Systemic lupus erythematosus—German shepherd dog
- DLE—collie, Shetland sheepdog, German shepherd dog, Siberian husky; may occur more often in females
- Pemphigus foliaceus—chow chow, Akita, cocker spaniels, dachshunds, Labrador retriever
- Uveodermatologic syndrome—Akita, Samoyed, Siberian husky
- Vitiligo—Dogs: Belgian Tervuren, German shepherd dog, Doberman pinscher, rottweiler, German shorthaired pointer, Old English sheepdog, dachshund; usually less than 3 years of age: Cats: Siamese
- Seasonal nasal hypopigmentation—Siberian husky, Alaskan malamute, yellow Labrador retriever, golden retriever
- Epitheliotropic lymphoma (mycosis fungoïdes)—typically dogs > 10 years old
- Proliferative arteritis of the nasal philtrum—Saint Bernard, giant schnauzer
- Periocular leukotrichia—Siamese cat
- Chediak-Higashi syndrome—Persian cat

SIGNS

- Leukotrichia
- Leukoderma
- Lightening of the pigmentation in the skin (seen as a “graying” or “browning” of previously pigmented areas)

- Erythema
- Erosion and ulcerations

CAUSES

- Mucocutaneous pyoderma
- Discoid lupus erythematosus
- Systemic lupus erythematosus
- Pemphigus foliaceus
- Pemphigus erythematosus
- Uveodermatologic syndrome
- Contact hypersensitivity
- Vitiligo
- Seasonal nasal depigmentation
- Albinism
- Schnauzer gilding syndrome
- Endocrinopathy
- Drug reaction
- Erythema multiforme
- Proliferative arteritis of the nasal philtrum
- Post-inflammatory depigmentation
- Immune-mediated pigmentary incontinence

RISK FACTORS

Sun exposure—DLE, SLE, and PE

Drug triggered—PF, EM



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Mucocutaneous Pyoderma

- Depigmentation is secondary and develops with chronicity.
- Skin lesions—affects the lips, perioral area, and nasal/alar folds.
- Clinically similar to intertrigo (skin-fold bacterial folliculitis).
- Swelling and fissuring leads to erosions and crusts.
- Biopsy—epidermal hyperplasia with superficial pustulation.
- Very antibiotic-responsive.
- Frequent recurrence if due to an underlying cause.

Nasal Solar Dermatitis

- Depigmentation is secondary and develops with chronicity.
- Lesions confined primarily to dorsal muzzle and precipitated by actinic radiation.
- Begins in poorly pigmented skin at the junction of the nasal planum and dorsal muzzle.
- Negative for direct immunofluorescence.
- Solar vasculopathy may appear similar.

Discoid Lupus Erythematosus

- Depigmentation is a primary symptom.
- Primarily affects nasal area, eyelid margins, and lip margins.
- Exacerbated by actinic radiation.
- Positive direct immunofluorescence at basement membrane zone.
- Biopsy—interface dermatitis.

Systemic Lupus Erythematosus

- Depigmentation is a primary symptom.
- Multisystemic disease.

- Skin lesions—often involve nose, face, and mucocutaneous junctions; multifocal or generalized.
- ANA—positive.
- Positive direct immunofluorescence at basement membrane zone.

Pemphigus Foliaceus

- Depigmentation is secondary and develops with chronicity.
- Lesions—usually start on face and ears; commonly involve footpads; eventually generalized.
- Biopsy—subcorneal pustules with acantholysis.
- Positive direct immunofluorescence in intercellular spaces of epidermis.

Pemphigus Erythematosus

- Depigmentation is a primary symptom.
- Lesions—primarily confined to face and ears, nasal planum, and lip margins.
- Depigmentation is more striking than in PF and often precedes significant lesions.
- Exacerbated by actinic radiation.
- Biopsy— intraepidermal pustules with acantholysis and interface dermatitis.
- Positive direct immunofluorescence at basement membrane zone and intercellular spaces.
- ANA—occasionally positive.

Uveodermatologic Syndrome

- Depigmentation is a primary symptom.
- Uveitis—usually (but not always) precedes dermatologic disease.
- Cutaneous macular depigmentation with inflammation on nose, lips, and eyelids.
- Striking poliosis and leukotrichia.
- Biopsy of early lesions—interface dermatitis, pigmentary incontinence.

Others

- Plastic or rubber dish/toy dermatitis (very uncommon)—depigmentation is secondary and develops with chronicity; erythema of the rostral nasal planum and lips; no ulceration and minimal crusting; history of exposure.
- Vitiligo—depigmentation is a primary symptom; cutaneous macular depigmentation without inflammation on nose, lips, eyelids, footpads, and nails; leukotrichia may be present with leukoderma.
- Seasonal nasal hypopigmentation—depigmentation is a primary symptom; normal black coloration of nasal planum fades to light tan or pink; usually seasonal or slowly progressive with age.
- Albinism—hereditary lack of pigment of the skin, hair coat, and irises (not a depigmenting process).
- Schnauzer gilding syndrome—young miniature gray schnauzers may develop idiopathic golden hair coat coloration, primarily of the trunk.
- Endocrinopathy can cause coat color change, mainly from black to reddish-brown.
- Drug reaction—depigmentation is often secondary; resembles many cutaneous

DERMATOSSES, DEPIGMENTING DISORDERS

(CONTINUED)

- disorders such as DLE, SLE, PF, and PE; pruritus is variable; onset of symptoms is usually within 2 weeks of administration.
- Proliferative arteritis of the nasal philtrum—depigmentation is secondary and develops with chronicity; marked focal ulceration of the nasal planum often resulting in acute, severe hemorrhage. No additional skin lesions noted. This may be an idiopathic syndrome associated with allergy.
 - Dermatophytosis—depigmentation is secondary and develops with chronicity; especially develops on the dorsal muzzle and face. Hyperpigmentation may also occur, especially with *Trichophyton mentagrophytes* infection.
 - Epitheliotropic lymphoma—depigmentation is secondary and develops with chronicity; occurs in mucocutaneous areas, nose, and skin.
 - Erythema multiforme in dogs—classic annular lesions with a clear center; depigmentation is secondary and develops with chronicity.
 - Zinc deficiency—depigmentation may be a primary or secondary symptom; zinc is required for normal melanin synthesis.
 - Chediak-Higashi syndrome—depigmentation is a primary symptom; young Persian cats (blue smoke color); ophthalmologic signs, prolonged bleeding.
 - Cyclic neutropenia in young silver-gray collie dogs with light-colored nose.
 - Post-inflammatory depigmentation is a benign loss of pigment and should resolve when the cause of inflammation is treated.
- CBC/BIOCHEMISTRY/URINALYSIS**
- Usually normal.
 - SLE—may see hemolytic anemia, thrombocytopenia, or evidence of glomerulonephritis.
 - Hematologic abnormalities in Persian cats with Chediak-Higashi syndrome.
 - Cyclic neutropenia in collie dogs (cyclic hematopoiesis anomalies).
- OTHER LABORATORY TESTS**
- Fungal culture—dermatophytosis
 - ANA—positive in most cases of SLE
- DIAGNOSTIC PROCEDURES**
- Cytology—acantholytic cells (pemphigus), neoplastic lymphocytes (epitheliotropic lymphoma).
 - Joint tap—evidence of polyarthritis in SLE.
 - Ocular examination—uveitis in uveodermatologic syndrome.
 - Direct immunofluorescence—deposition of immunoglobulin at the basement membrane zone with DLE, SLE, and PE, and in the intercellular spaces of the epidermis with PF and PE.
 - Skin biopsy.

PATHOLOGIC FINDINGS

Histopathologic examination of the skin

- Interface dermatitis—DLE, SLE, uveodermatologic syndrome.
- Pigmentary incontinence—DLE, PE.
- Intraepidermal pustules with acantholysis—PF and PE.
- Hypomelanosis—vitiligo, uveodermatologic syndrome, seasonal nasal hypopigmentation, and schnauzer gilding syndrome.
- Apoptosis (individual cell necrosis of keratinocytes)—drug reaction and erythema multiforme.
- Proliferation of spindle cells of dermal arteries and arterioles—proliferative arteritis.
- Infiltration of neoplastic lymphocytes—epitheliotropic lymphoma.



TREATMENT

- Outpatient, except for SLE, EM, and cutaneous lymphoma with systemic involvement.
- Reduce exposure to sunlight—DLE, SLE, and PE.
- Immunosuppressive therapy—SLE, PF, PE.
- Avoid contact with topical drugs.
- Replace plastic or rubber dishes—particularly if roughened edges cause abrasions.
- Application of water-resistant sunblock ointments or gels with an SPF/UVA and UVB > 30 to depigmented and sun-exposed areas of skin.
- Uveodermatologic syndrome—management by veterinary ophthalmologist recommended.
- Appropriate antibiotics—pyoderma.
- Appropriate antifungals—dermatophytosis.



MEDICATIONS

DRUG(S) OF CHOICE

- SLE—immunosuppressive therapy with prednisolone or dexamethasone and azathioprine (dogs) or chlorambucil (cats).
- Tetracycline and niacinamide (dogs, < 10 kg 250 mg each q8h; > 10 kg, 500 mg each q8h): PE, DLE.
- Topical corticosteroids—PE, DLE.
- Vitiligo and nasal depigmentation—no treatment.
- Epitheliotropic lymphoma—multiple treatment protocols.

CONTRAINDICATIONS

Azathioprine therapy—not recommended in cats; may cause fatal leukopenia or thrombocytopenia.

PRECAUTIONS

Ketoconazole may cause lightening of the hair coat, elevated alkaline phosphatase, and gastrointestinal distress.

ALTERNATIVE DRUG(S)

- Cyclosporine, modified—5 mg/kg/day for auto-immune disorders.
- Tacrolimus—0.1% gel applied daily to lesions in combination with or to replace corticosteroids. May sting. Avoid licking. Wear latex gloves to apply.
- Pimecrolimus—1% cream applied daily to lesions in combination with or to replace corticosteroids. May sting. Avoid licking. Wear latex gloves to apply.



FOLLOW-UP

PATIENT MONITORING

Varies with specific disease and treatment prescribed.

POSSIBLE COMPLICATIONS

- Sunburn in areas of depigmentation.
- Squamous cell carcinoma—in cases of solar damage and actinic keratosis of depigmented areas.
- SLE—associated scarring with ulcerative dermatitis.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Dermatophytosis—can cause infection in humans.

SEE ALSO

- Cutaneous Drug Eruptions
- Lupus Erythematosus, Cutaneous (Discoid)
- Lupus Erythematosus, Systemic
- Lymphoma, Cutaneous Epitheliotropic
- Pemphigus
- Uveodermatologic Syndrome

ABBREVIATIONS

- ANA = antinuclear antibody
- DLE = discoid lupus erythematosus
- EM = erythema multiforme
- PE = pemphigus erythematosus
- PF = pemphigus foliaceus
- SLE = systemic lupus erythematosus

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**Client Education Handout
available online**

DERMATOSSES, EROSIONS OR ULCERATIVE



BASICS

DEFINITION

A heterogenous group of skin disorders characterized by disruption of the epidermis (erosions) or, if the basement membrane is compromised, the epidermis and dermis (ulcers).

PATOPHYSIOLOGY

Varies widely, depending on the cause; may include congenital or developmental disorders that compromise tissue cohesion; cell-mediated (inflammatory or neoplastic) injury; anoxic injury; antigen-specific auto-immune disorders; and necrosis due to trauma, toxins, contactants (irritants), microbial organisms, or parasitic migration.

SYSTEMS AFFECTED

Skin/Exocrine

GENETICS

Some diseases are likely heritable due to breed predilections; however, there are no genetic screening tests available for any of the diseases listed.

INCIDENCE/PREVALENCE

- Rare to common, depending on the cause.

SIGNALMENT

Species

Dogs and cats

Breed Predilections

Some specific causes (see below) have strong breed predilections, e.g., lupoid disorders, familial dermatomyositis and zinc-responsive dermatosis.

Mean Age and Range

- Highly variable according to etiology.
- Canine juvenile cellulitis and several congenital diseases (see below) are diagnosed in very young animals.

Predominant Sex

Sex predispositions may vary according to the disease in question.

SIGNS

Historical Findings

- Pruritus may result in ulcers or erosions due to self-trauma; especially ectoparasitism, superficial pyoderma, and *Malassezia* dermatitis.
- Exposure to caustic chemicals, burns, cold stress, venomous reptiles and insects, etc.
- Some infectious diseases (e.g., pythiosis, coccidioidomycosis, feline cow pox) have very restricted ranges.
- Previous or concurrent systemic symptoms or illness.

Physical Examination Findings

- Lesions may be heterogenous in gross appearance. Some diseases result in erythematous erosions with minimal crust or scale, while others cause scale or crusting that (when removed) results in erosion.
- Ulcers may be shallow/superficial or deep; deep

ulceration can present as sinuses with draining tracts, cavitated lesions with well-demarcated borders, or exudative crusted lesions.

- Some specific diseases are typically accompanied by fever and malaise; especially auto-immune disorders and infectious etiologies.
- May be associated with extra-cutaneous disease (e.g., superficial necrolytic dermatitis and hypereosinophilic syndrome of cats).

CAUSES

Auto-immune

- Pemphigus foliaceus*: crusting with erosion.
- Pemphigus vulgaris*: superficial ulcerative.
- Bullous pemphigoid* and *epidermolysis bullosa acquisita*: superficial ulcerative.
- Discoid lupus erythematosus*: erosive or superficial ulcerative.
- Exfoliative lupus* (German shorthaired pointers): scaling with erosion.
- Vesicular lupus* (rough collies and Shetland sheepdogs): superficial ulcerative.
- Cold agglutinin disease*: deep ulcerative.

Immune-Mediated

- Erythema multiforme* and toxic epidermal necrolysis (usually drug-induced): erosive to superficial ulcerative.
- Vasculitis*: superficial to deep ulcerative (may be cavitated).
- Idiopathic panniculitis*: deep ulcerative (usually exudative with crusting).
- Canine eosinophilic furunculosis* of the face (may be insect-related): ulcerative and crusting.
- Canine juvenile cellulitis* (puppy strangles): erosive to superficial or deep ulcerative.
- Feline indolent ulcer* (rodent ulcer): erosive to superficial or deep ulcerative.

Infectious

- Surface pyoderma*: acute moist pyotraumatic dermatitis ("hot spots"): erosive.
- Superficial staphylococcal folliculitis*: erosive to superficial ulcerative.
- Bacterial folliculitis/furunculosis*: deep ulcerative (usually crusted, with or without sinuses and draining tracts).
- Superficial fungal* (*Malassezia* dermatitis, dermatophytosis): erosive to superficial ulcerative.
- Deep fungal* (e.g., sporotrichosis, cryptococcosis, histoplasmosis, blastomycosis, coccidioidomycosis): deep ulcerative with or without sinuses and draining tracts.
- Opportunistic mycobacteriosis*: deep ulcerative nodules with sinuses and draining tracts.
- Actinomycetic bacteria* (e.g., *Nocardia* spp., *Actinomyces* spp., *Streptomyces* spp.): deep ulcerative nodules with sinuses and draining tracts.
- Pythiosis/laegenidiosis* and *protothecosis*: ulcerative, proliferative with or without draining tracts.
- Leishmaniasis*: erosive to superficial or deep ulcerative.
- Feline cow pox*: deep ulcerative.
- FIV/FeLV-related*: erosive to superficial ulcerative.
- Feline herpesvirus-associated dermatosis*: ulcerative with crusting.

Parasitic

- Demodicosis*: ulcerative with crusting (especially with secondary bacterial

folliculitis).

- Sarcoptic/notoedric mange*: erosive with crusting.
- Flea bite allergy*: erosive to ulcerative (if secondary infection is present).
- Feline mosquito bite hypersensitivity*: erosive to superficial or deep ulcerative.
- Pelodera* and hookworm migration: deep ulcerative.

Congenital/Hereditary

- Canine familial dermatomyositis* (predominantly in collies and Shetland sheepdogs): erosive.
- Epidermolysis bullosa*: superficial ulcerative.
- Cutaneous asthenia* (Ehlers-Danlos syndrome): skin tears.

Metabolic

- Superficial necrolytic dermatitis* (usually associated with hepatic disease or pancreatic glucagonoma): crusting with erosion.
- Hyperadrenocorticism*: erosive to ulcerative when complicated by secondary infections or calcinosis cutis.
- Uremia* (mucous membranes): superficial ulcerative.

Neoplastic

- Squamous cell carcinoma*: erosive to ulcerative with scale or crust.
- Feline squamous cell carcinoma in situ* (Bowenoid *in situ* carcinoma): erosive with scale or crust.
- Mast cell tumors*: superficial to deep ulcerative.
- Epitheliotropic lymphoma* (mycosis fungoides): erosive to superficial ulcerative.
- Feline thymoma-associated exfoliative dermatosis*: scaling with erosion.
- Feline paraneoplastic alopecia*: erosive.

Nutritional

- Zinc-responsive dermatosis*: crusting with erosion.
- Generic dog food dermatosis*: crusting with erosion.

Physical/Conformational Dermatoses

- Pressure point ulcers*: deep ulcerative.
- Intertrigo* (skin fold pyoderma): erosive.
- Self-trauma* as a result of pruritic dermatoses: highly variable.

Idiopathic

- Feline dorsal neck ulcer*: deep ulcerative with crusting.
- Canine and feline acne*: erosive to ulcerative with crusting (especially with secondary bacterial infection).
- Feline plasma cell pododermatitis*: superficial to deep ulcerative.

Miscellaneous

- Thermal, electrical, solar, or chemical burns*: depth of lesions depends on severity of insult.
- Frost bite*: depth of lesions depends on severity of insult.
- Chemical irritants*: depth of lesions depends on severity of insult.
- Venomous snake and insect bites*: deep ulcerative (usually with necrosis).

RISK FACTORS

Highly variable according to disease (e.g., underlying immunosuppression associated with secondary infectious diseases).

DERMATOSSES, EROSIONS OR ULCERATIONS

(CONTINUED)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

History and physical examination are especially important due to the extensive differential list. Many of these diseases exhibit subtle differences in appearance and distribution of lesions. Careful attention to the character and progression of lesions, and the distribution pattern on the patient, can yield valuable clues.

CBC/BIOCHEMISTRY/URINALYSIS

Most helpful when metabolic disease is suspected or in any patient with signs of systemic disease.

OTHER LABORATORY TESTS

See "Diagnostic Procedures" for routine tests.

IMAGING

- Rarely indicated.
- Thoracic radiographs—for deep/systemic fungal diseases, feline thymoma-associated exfoliative dermatitis, and systemic neoplasia.
- Abdominal ultrasound—superficial necrolytic dermatitis (dogs) or paraneoplastic alopecia (cats) suspected or confirmed by skin biopsy.

DIAGNOSTIC PROCEDURES

- Skin scraping—suspected parasitism.
- Direct impression cytology—identify bacteria, yeast, or acantholytic keratinocytes in pemphigus.
- Fine-needle aspirate with cytology—indurated or nodular lesions.
- Culture: bacterial (aerobic and anaerobic), mycobacterial, and/or fungal—suspected infectious disease (especially in cats with ulcers or draining tracts).
- Fungal serology and serology for pythiosis and lagendiosis may be indicated on a case-by-case basis and depending upon geographic location.
- PCR and immunohistochemistry are adjuncts to the histologic diagnosis of feline herpesvirus-associated dermatitis.

PATHOLOGIC FINDINGS

- Skin biopsy for histopathology—most informative test.
- For cavitated lesions, the leading edge should be harvested with a scalpel blade if the defect is too large to be excised in total.
- Punch biopsy sufficient for diffuse erosive lesions; should take normal skin near a lesion and lesions that are both early and late in their development.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient for most diseases
- Varies widely according to the cause

NURSING CARE

- Supportive therapy.
- Pain control may be an important consideration for some animals.

ACTIVITY

No restrictions necessary for most conditions (except zoonotic infections and infestations).

DIET

- Nutritional support may be necessary in debilitated animals, especially those with superficial necrolytic dermatitis.
- Correcting dietary deficiencies is the only treatment for generic dog-food dermatosis.
- Supplementation of zinc is necessary for zinc-responsive dermatosis.

CLIENT EDUCATION

Variable by diagnosis; most important with suspected or diagnosed zoonotic disease.

SURGICAL CONSIDERATIONS

- Indicated as curative treatment for feline thymoma-associated exfoliative dermatitis.
- May be curative for non-metastatic pancreatic or hepatobiliary tumors causing paraneoplastic alopecia.
- Radical surgical excision of nodules and draining tracts may be an adjunct to antimicrobial therapy of infections caused by rapid-growing *Mycobacterium* spp. and *Nocardia* spp. in cats and pythiosis or lagendiosis in dogs.



MEDICATIONS

DRUG(S) OF CHOICE

Vary widely according to cause

CONTRAINDICATIONS

Definitive diagnosis is imperative because some immune-mediated cases that require immunosuppression may mimic infectious diseases that require specific antimicrobial chemotherapy (and for which immunosuppression could prove fatal).

PRECAUTIONS

Side effects—associated with many antimicrobial, immunosuppressive, and antineoplastic drugs.

POSSIBLE INTERACTIONS

Dependent on medications administered



FOLLOW-UP

PATIENT MONITORING

Dependent on the disease process, concurrent systemic disease(s), drugs used, and potential side effects expected.

PREVENTION/AVOIDANCE

- The incidence of many feline infectious diseases can be minimized by restricting outdoor activity.
- Some auto-immune diseases (e.g., discoid lupus erythematosus and pemphigus erythematosus) are aggravated by ultraviolet light exposure; patients should be restricted from sun exposure during peak hours of the day.

POSSIBLE COMPLICATIONS

- Determined by cause.
- Some diseases are potentially life-threatening.
- Some diseases have zoonotic potential.
- Infections and drug side effects are possible in cases requiring immunosuppression.

EXPECTED COURSE AND PROGNOSIS

- Some infectious diseases (nocardiosis, atypical mycobacteriosis) may be controlled with chronic antimicrobial therapy, but are generally not curable if lesion progression is extensive by the time of diagnosis.
- Pythiosis/lagendiosis: prognosis is extremely poor for response to therapy and survival when lesions are extensive.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Sarcoptic acariasis.
- Dermatophytosis.
- Sporotrichosis.
- Mycelial phase of some fungi (e.g., *Coccidioides immitis*, *Blastomyces dermatitidis*), when grown on culture media, can be infectious to humans through inhalation. In-clinic fungal culturing (other than for dermatophytes) is not advised.

PREGNANCY/FERTILITY/BREEDING

- Due to the potential severity of clinical signs and syndromes, any patient diagnosed with an erosive/ulcerative disease that occurs with moderate to strong breed predilections should not be used for breeding.
- Many drugs used to treat the auto-immune, immune-mediated, and infectious diseases listed may be teratogens.

SYNOMYS

Superficial necrolytic dermatitis = necrolytic migratory erythema, metabolic epidermal necrosis, hepatocutaneous syndrome

SEE ALSO

Specific chapters devoted to diseases listed under "Causes"

ABBREVIATIONS

- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- PCR = polymerase chain reaction

Suggested Reading

Mason IS. Erosions and ulcerations. In: Ettinger SH, Feldman EC, eds., Textbook of Veterinary Internal Medicine, 6th ed. St. Louis, MO: Elsevier, 2005, pp. 46–50.
Miller WH, Griffin CE, Campbell KL, eds. Muller & Kirk's Small Animal Dermatology (various chapters), 7th ed. St. Louis, MO: Elsevier, 2013.

Author Daniel O. Morris

Consulting Editor Alexander H. Werner



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DERMATOSSES, EXFOLIATIVE

D



BASICS

DEFINITION

Excessive or abnormal shedding of epidermal cells resulting in the clinical presentation of cutaneous scaling.

PATHOPHYSIOLOGY

- An increase in the production, an increase in the desquamation, or a decrease in the cohesion of keratinocytes results in abnormal shedding of epidermal cells individually (fine scale) or in sheets (coarse scale).
- Primary exfoliative disorders—keratinization defects, in which the genetic control of epidermal cell proliferation and maturation is abnormal.
- Secondary exfoliative disorders—the effects of a disease alter the normal maturation and proliferation of epidermal cells.
- Anomalies in sebaceous or apocrine gland function may be present.

SYSTEMS AFFECTED

Skin/Exocrine

SIGNALMENT

- Dog and cat.
- Primary—apparent by 2 years of age; characteristic in affected breeds (see “Causes”).
- Secondary—any age; any breed of dog or cat.

SIGNS

Historical Findings

- Excessive scaling
- Malodorous skin
- Pruritus
- Oily skin and hair

Physical Examination Findings

- Dry or greasy collections of fine or coarse scale located diffusely throughout the hair coat or focally in keratinaceous plaques
- “Rancid fat” odor
- Comedones
- Follicular casts (collection of adherent debris around the hair shaft)
- Candle wax–like deposits on hair
- Alopecia
- Pruritus
- Secondary bacterial folliculitis and/or *Malassezia* dermatitis.

CAUSES

Primary

• Primary idiopathic seborrhea (primary keratinization disorder)—primary cellular defect; accelerated epidermopoiesis and hyperproliferation of the epidermis, follicular infundibulum, and sebaceous gland. Breeds at risk: cocker and springer spaniel, West Highland white terrier, basset hound, Doberman pinscher, Irish setter, and Labrador retriever.

• Vitamin A-responsive dermatosis—nutritionally responsive seen mainly in young cocker spaniels; clinically similar to severe idiopathic seborrhea; identified by response to oral vitamin A supplementation.

• Zinc-responsive dermatosis—nutritionally responsive; results in alopecia, dry scaling, crusting, and erythema around the eyes, ears, feet, lips, and external orifices; two syndromes: young adult dogs (mainly Siberian husky and Alaskan

malamute) and rapidly growing large-breed puppies

- Ectodermal defects—follicular dysplasias; seen as color mutant or dilution alopecia; represent anomalies in melanization of the hair shaft and structural hair growth; keratinization defects theorized as causative for several syndromes; breeds commonly affected: blue and fawn Doberman pinscher, Irish setter, dachshund, chow chow, Yorkshire terrier, poodle, Great Dane, whippet, saluki, and Italian greyhound; signs include the failure to regrow blue or fawn hair with normal “point” hair growth, excessive scaliness, comedone formation, and secondary pyoderma
- Idiopathic nasodigital hyperkeratosis—excessive build-up of scale and crusts on the nasal planum and footpad margins; possibly a senile change; generally asymptomatic: seen in spaniels and retrievers. Cracking and secondary bacterial infection can cause pain
- Sebaceous adenitis—*inflammatory disease targeting sebaceous glands and ducts*. Three specific syndromes: (1) middle-aged standard poodle and Samoyed: patchy or diffuse hair loss and excessive scaling; tightly adherent follicular casts; most dogs are healthy and asymptomatic; (2) Akita: similar appearance but frequently develop severe secondary bacterial pyoderma; (3) vizsla: disease appears distinctly different and granulomatous. Other breeds show lower incidence
- Ichthyosis—rare and severe congenital disorder of keratinization; reported in West Highland white terrier, golden retriever, Cavalier King Charles spaniel, and Norfolk terrier; generalized accumulations of scale and crusts at an early age; secondary infections (bacterial and yeast) common
- Primary seborrhea in newborn Persian kittens.

Secondary

- Cutaneous hypersensitivity—atopy, flea allergic dermatitis, food allergy, and contact dermatitis; pruritus, secondary skin trauma, and irritation
- Ectoparasitism—scabies, demodicosis, and cheyletiellosis; inflammation and exfoliation
- Bacterial folliculitis—bacterial enzymatic disadhesion and increased exfoliation of keratinocytes in the attempt to shed pathogenic organisms
- Dermatophytosis—usually exfoliative; increased shedding of affected keratinocytes is a primary skin mechanism in resolving fungal infection
- Endocrinopathy—hypothyroidism: abnormalities in keratinization, failure to regrow hair, and excessive sebum production; hyperadrenocorticism: abnormal keratinization and decreased follicular activity; excessive scaling and secondary pyoderma common in both syndromes; other hormonal abnormalities may also be associated with excessive scaling
- Age—geriatric animals may have a dull, brittle, and scaly hair coat; alterations may be caused by natural changes in epidermal metabolism associated with age;

no specific defect identified

- Nutritional disorders—malnutrition and generic dog food dermatosis; result in scaling from abnormalities in keratinization
- Auto-immune dermatoses—pemphigus complex: may appear exfoliative; vesicles become scaly and crusty; cutaneous and systemic lupus erythematosus: cutaneous signs often appear as areas of alopecia and scaling
- Neoplasia—primary epidermal neoplasia (*epitheliotropic lymphoma*): may produce alopecia and scaling as epidermal structures are damaged by infiltrating lymphocytes; preneoplastic conditions (*actinic keratosis*): initially appear exfoliative
- Miscellaneous—any disease process may result in excessive scale formation due to a metabolic disorder or to cutaneous inflammation
- Exfoliative disorders—rare in cats: tail gland hyperplasia, feline thymoma-associated exfoliative dermatitis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Signalment and history—capital in distinguishing the possible causes of exfoliation
- Presence of pruritus—helps in determining the possibility of a cutaneous hypersensitivity; primary keratinization defects are often non-pruritic, unless secondary bacterial folliculitis or *Malassezia* dermatitis develops
- Concurrent signs (e.g., lethargy, weight gain, polyuria/polydipsia, reproductive failure, change in body conformation, and lack of hair regrowth), with or without inflammation, can aid in differentiation.

CBC/BIOCHEMISTRY/URINALYSIS

- Normal with primary keratinization disorders.
- Mild, nonregenerative anemia and hypercholesterolemia are consistent with hypothyroidism.
- Neutrophilia, monocytosis, eosinopenia, lymphopenia, elevated serum alkaline phosphatase, hypercholesterolemia, and hyposthenuria suggest hyperadrenocorticism.

OTHER LABORATORY TESTS

Thyroid hormone levels and adrenal function tests if an endocrinopathy is suspected; see specific chapters for test recommendations.

IMAGING

Thoracic radiographs—feline thymoma-associated exfoliative dermatitis

DIAGNOSTIC PROCEDURES

- Skin scraping—diagnose ectoparasitism
- Skin biopsy—rule out particular differential diagnoses; strongly recommended for most cases
- Intradermal allergy test—identify allergens for immunotherapy
- Restricted-ingredient food trial—identify food hypersensitivity
- Cytology of skin surface—identify bacteria and/or yeast on the skin

DERMATOSSES, EXFOLIATIVE

(CONTINUED)

- Examination of plucked hairs—macromelanosomes and structural anomalies in follicular dysplasia and color dilution alopecia.

D



TREATMENT

- Frequent and adequate topical therapy—cornerstone of proper treatment.
- Underbathing, rather than overbathing, is a common error. • Diagnose and control all treatable primary and secondary diseases.
- Recurrence of secondary infections may require repeated therapy and further diagnostics. • Maintaining control is often life-long. • Recent emphasis on restoring epidermal barrier integrity and function.



MEDICATIONS

DRUG(S) OF CHOICE

Shampoos

- Contact time—5–15 minutes required; > 15 minutes discouraged, may result in epidermal maceration, loss of barrier function, and excessive epidermal drying and irritation
- Hypoallergenic—useful only in mild cases of dry scale and to maintain secondary exfoliation after the primary disease has been controlled
- Sulfur/salicylic acid—keratolytic, keratoplastic, and bacteriostatic; excellent first choice for the moderately scaly patient; not overly drying
- Benzoyl peroxide—strongly keratolytic, and antimicrobial; may cause irritation and severe dryness; good for recurrent bacterial infection and/or extreme greasiness
- Ethyl lactate—less effective than benzoyl peroxide for antimicrobial activity, but not as irritating or drying; most useful for moderate bacterial folliculitis and dry scale
- Chlorhexidine—antimicrobial; mildly drying; useful for moderate bacterial folliculitis and *Malassezia* dermatitis
- Tar—keratolytic, keratoplastic, and antipruritic; less degreasing than benzoyl peroxide; use for moderate scale associated with pruritus, can be irritating, might be carcinogenic.

Moisturizers

- Excellent for restoring skin hydration and increasing effectiveness of subsequent shampoos
- Humectants—enhance hydration of the stratum corneum by attracting water from the dermis; at high concentrations may be keratolytic

- Propylene glycol spray (50–75% dilution with water) applied frequently
- Microencapsulation—may improve the residual activity of moisturizers by allowing sustained release after bathing
- Emollients—coat the skin; smooth the roughened surfaces produced by excessive scaling; usually combined with occlusives to promote hydration of the epidermis.

Systemic Therapy

- Specific causes require specific treatments (e.g., thyroxine replacement for hypothyroidism; zinc supplements for zinc-responsive dermatosis)
- Systemic antibiotics—indicated for secondary pyoderma
- Retinoids—varied success for idiopathic or primary seborrhea; reports of individual response to retinoid in refractory cases: isotretinoin (1 mg/kg PO q12–24h); if response is seen, taper dosage (1 mg/kg q48h or 0.5 mg/kg q24h); difficult to dispense due to strict prescription procedures.
- Cyclosporine 5 mg/kg/day until controlled, then decreased to minimal effective maintenance dosage for individual cases of keratinization disorder associated with hypersensitivity, sebaceous adenitis, epidermal dysplasia, ichthyosis, and/or *Malassezia* dermatitis.

PRECAUTIONS

- Corticosteroids—may be used judiciously to control the inflammation resulting from many exfoliative disorders; will mask signs of pyoderma and prevent accurate diagnosis of primary disease • Vitamin A- and D-analogs—side effects can be severe; thus, patients should be referred to a dermatologist before being treated with these drugs; teratogenic.



FOLLOW-UP

PATIENT MONITORING

- Antibiotics and topical therapy—monitor response every 3 weeks; patients may respond differently to the various topical therapies
- Development of additional diseases (especially cutaneous hypersensitivity), and recurrence of pyoderma—may cause previously controlled patients to worsen; reevaluation critical to determine if new factors are involved and if changes in therapy are necessary • Endocrinopathy—routine thyroid monitoring or ACTH-stimulation tests should be used for proper management
- Selective autoimmune disorders—reevaluate frequently during the initial phase of

induction; less often after remission; clinical evaluation and laboratory data required

- Immunosuppressive therapy—frequent hemograms, serum chemistries, and urinalyses with culture to monitor for complications
- Retinoid drugs—serum chemistries, including triglycerides, and Schirmer tear tests
- Ketoconazole—serum chemistries.



MISCELLANEOUS

AGE-RELATED FACTORS

Skin aging might be related to increase in exfoliative disorders or relapses.

ZOONOTIC POTENTIAL

Dermatophytosis and several ectoparasites have zoonotic potential.

PREGNANCY/FERTILITY/BREEDING

Systemic retinoids and vitamin A in therapeutic dosages—extreme teratogen; do not use in intact females because of severe and predictable teratogenicity and extremely long withdrawal period; women of childbearing age should not handle these medications.

SYNONYMS

- Keratinization disorders = seborrhea, idiopathic seborrhea, keratinization defect, dyskeratinization, and incorrect human terms (eczema, psoriasis, dander, dandruff); sebopsoriasis: correct term to describe the similarities between some human and canine keratinization defects • Bacterial folliculitis = pyoderma.

SEE ALSO

- Atopic Dermatitis • Demodicosis
- Hyperadrenocorticism (Cushing's Syndrome)—Cats • Hyperadrenocorticism (Cushing's Syndrome)—Dogs
- Hypothyroidism • *Malassezia* Dermatitis
- Pyoderma • Sarcoptic Mange

ABBREVIATIONS

ACTH = adrenocorticotropic hormone

Suggested Reading

Gross TL, Ihrke PJ, Walder EJ, Affolter V. Skin Diseases of the Dog and Cat: Clinical and Histopathologic Diagnosis, 2nd ed. Oxford: Blackwell Science, 2005.

Muller and Kirk's Small Animal Dermatology, 7th ed., Elsevier Inc., 2013.

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Client Education Handout
available online



BASICS

DEFINITION

- Neoplastic proliferation of cells derived from the skin or migrating to the skin.
- Epidermal tumors include those arising from keratinocytes, melanocytes, Merkel cells, and Langerhans cells, and epitheliotrophic lymphoma.
- Adnexal tumors include those arising from hair follicles, sebaceous glands, and sweat glands.
- Dermal and subcutaneous skin tumors include those of mesenchymal origin and tumors of round cell origin.
- Secondary or metastatic skin tumors result from the proliferation of cells from primary neoplasms of other organs in the skin.

PATOPHYSIOLOGY

- Neoplasia develops as a result of changes in genes controlling cell proliferation and homeostasis.
- More than 100 cancer-related genes have been identified
- Oncogenes encode proteins that promote cell growth; tumor-suppressor genes encode proteins that restrict cell proliferation and differentiation.
- Mutations in p53, a tumor-suppressor gene, are found in approximately 50% of cancers in humans and have also been found in many tumors affecting dogs and cats.
- Ultraviolet light promotes tumor development by damaging DNA and suppressing the immune system.
- Many viruses promote tumor growth through stimulating cell proliferation and/or suppressing the immune system.
- Reports of specific cutaneous neoplasia associated with medications and/or vaccinations.

SYSTEMS AFFECTED

Skin/Exocrine

GENETICS

- Breed predispositions have been reported for specific tumors, but the mode of inheritance in these breeds has not been determined.
- Mutations in oncogenes and/or tumor-suppressor genes (e.g., p53) are present in many types of skin tumors

INCIDENCE/PREVALENCE

- The combined incidence rate for skin tumors has been reported as 728/100,000 (0.728%) for dogs and 84/100,000 (0.084%) for cats.
- The skin is the most common site of occurrence of neoplasia in the dog (30% of total tumors) and the second most common site in the cat (20% of total tumors).
- Canine skin tumors are approximately 55% mesenchymal, 40% epithelial, and 5% melanocytic.

- The most frequently reported cutaneous or subcutaneous tumors in dogs are lipoma, sebaceous gland tumor, mast cell tumor, histiocytoma, and papilloma.

- Feline skin tumors are approximately 50% epithelial, 48% mesenchymal, and 2% melanocytic.
- The most frequently reported cutaneous or subcutaneous tumors in cats are basal cell tumor, squamous cell carcinoma, mast cell tumor, and fibrosarcoma.
- Skin tumors in cats are more frequently malignant; skin tumors in dogs are more frequently benign.

GEOGRAPHIC DISTRIBUTION

Geographic regions near the equator, with high altitude, or with sand or other reflective surfaces, have a higher incidence of solar-induced neoplastic dermatoses.

SIGNALMENT

Species

Dogs and cats

Breed Predilections

- Canine breeds with the highest overall incidence of skin tumors include boxer, Scottish terrier, bullmastiff, basset hound, Weimaraner, Kerry blue terrier, and Norwegian elkhound.
- Feline breeds with the highest overall incidence of skin tumors include Siamese and Persian.
- Certain breeds are predisposed to specific types of tumors (see "Suggested Reading").
 - Dog—breeds associated with the most common cutaneous neoplasms:
 - Lipoma—cocker spaniel, dachshund, Doberman pinscher, Labrador retriever, miniature schnauzer, Weimaraner.
 - Sebaceous gland tumor—beagle, cocker spaniel, dachshund, Irish setter, Lhasa apso, malamute, miniature schnauzer, poodle, Shih Tzu, Siberian husky.
 - Mast cell tumor—American Staffordshire terrier, beagle, Boston terrier, boxer, bull terrier, dachshund, English bulldog, fox terrier, golden retriever, Labrador retriever, pug, Shar-Pei, Weimaraner.
 - Histiocytoma—American Staffordshire terrier, Boston terrier, boxer, cocker spaniel, dachshund, Doberman pinscher, English springer spaniel, Great Dane, Labrador retriever, miniature schnauzer, rottweiler, Scottish terrier, Shar-Pei, Shetland sheepdog, West Highland white terrier.
 - Papilloma—cocker spaniel, Kerry blue terrier.
 - Cat—breeds associated with the most common cutaneous neoplasms:
 - Basal cell tumor—Persian, Himalayan (basal cell carcinoma—Siamese).
 - Squamous cell carcinoma—no predisposed breed reported.
 - Mast cell tumor—Siamese.
 - Fibrosarcoma—no predisposed breed reported.

Mean Age and Range

- The median age for cutaneous neoplasia is 10.5 years in dogs and 12 years in cats.
- The peak age period for cutaneous neoplasia in dogs and cats is 6 to 14 years.

Predominant Sex

- Females have a higher incidence of tumors in dogs (56%).
- Males have a higher incidence of tumors in cats (56%).

SIGNS

General Comments

- Most common clinical sign is a cutaneous or subcutaneous nodule; some tumors have an ulcerated surface; others may result in excessive scaling or in the formation of cutaneous plaques.

Historical Findings

- Tumors are most often slow growing; the owner may find them during petting, bathing, or grooming of the pet.
- Tumors may be rapidly growing and appear (or increase in size) quickly (e.g., histiocytoma).

Physical Examination Findings

- Nodules—cutaneous or subcutaneous
- Cutaneous ulcers
- Excessive scaling
- Cutaneous papillomas
- Cutaneous plaques

CAUSES

- Genetic (gene mutations).
- Environmental (e.g., ultraviolet light, radiation exposure).
- Viruses (e.g., papillomaviruses, FeLV, FIV).
- Toxins (e.g., tars).
- Drugs (e.g., immunosuppressive agents, chemotherapeutic agents).
- Epidermal neoplasms:
 - Keratinocytes—papillomas, squamous cell carcinoma, basal cell carcinoma, basosquamous carcinoma
 - Melanocytes—melanoma
 - Merkel cells—Merkel cell carcinoma
 - Langerhans cells—histiocytoma and malignant histiocytosis
 - Epitheliotrophic lymphoma—T lymphocytes.
- Adnexal neoplasms:
 - Hair follicles—trichofolliculoma, trichoepithelioma, infundibular keratinizing acanthoma, tricholemmoma, pilomatricoma, trichoblastoma
 - Sebaceous glands—sebaceous adenoma, sebaceous epithelioma, sebaceous adenocarcinoma, perianal gland epithelioma, perianal gland carcinoma
 - Sweat glands—apocrine cystadenoma, apocrine secretory adenoma/adenocarcinoma, apocrine ductal adenoma/carcinoma, eccrine carcinoma.
- Dermal and subcutaneous neoplasm:
 - Mesenchymal origin—soft tissue sarcoma: fibroma/fibrosarcoma, myxoma/

DERMATOSSES, NEOPLASTIC

(CONTINUED)

D

- myxosarcoma, hemangiopericytoma, lymphangioma/lymphangiosarcoma, hemangioma/hemangiosarcoma, lipoma/liposarcoma, neurofibrosarcoma, leiomyoma/leiomyosarcoma, synovioma/synovial sarcoma, rhabdomyoma/rhabdomyosarcoma
 - Round cell origin—transmissible venereal tumor, mast cell tumor, plasmacytoma, lymphoma, histiocytoma and histiocytic tumors.
- Secondary or metastatic skin tumors result from the metastasis or primary neoplasms in other organs to the skin.

RISK FACTORS

- Hair coat color and length (e.g., hairless breeds, white hair coat, lightly pigmented skin—increased risk for squamous cell carcinoma).
- Age (e.g., young animals highest risk for viral infections, older animals at highest risk for environment-associated neoplasia).
- Sunlight exposure (e.g., dogs and cats that sunbathe or spend time outdoors on reflective surfaces have higher risk of ultraviolet light—induced skin tumors).
- Genetics—certain breeds have higher risk of developing specific types of tumors (see above and in “Suggested Reading”).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cyst
- Abscess
- Inflammatory nodule/granuloma/plaque—sterile granulomatous and pyogranulomatous disease, sterile panniculitis, fungal infection, mycobacterial infection, foreign body
- Trauma/self-induced skin ulceration
- Hamartoma/nevus

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

- Cytology (fine-needle aspirate or impression smear)
- Regional lymph node aspirate (for staging)

IMAGING

Thoracic radiographs and abdominal ultrasonography useful for staging (evaluate for metastatic disease or underlying primary neoplasia).

DIAGNOSTIC PROCEDURES

- Cytology
- Biopsy with histopathologic examination
- Immunohistochemistry (useful in confirming certain types of tumors)

PATHOLOGIC FINDINGS

Varies with tumor type; see specific tumors for additional information.



TREATMENT

APPROPRIATE HEALTH CARE

- Varies with tumor type.
 - Observation is appropriate for some benign tumors.
 - Surgical excision, cryosurgery, radiation therapy, and/or tumor specific chemotherapy or immunotherapy may be curative or palliative.

NURSING CARE

- Varies with tumor type and location.
- Traumatized tumors may become secondarily infected.

ACTIVITY

Varies with tumor type and location.

DIET

Diets high in omega-3 fatty acids, arginine, and protein may be beneficial in boosting the immune response and preventing cancer-associated cachexia.

CLIENT EDUCATION

Varies with tumor type and location.

SURGICAL CONSIDERATIONS

- Varies with tumor type and location—wide margins may be needed to prevent reoccurrence of infiltrative tumors.
- Pretreatment with antihistamines appropriate when excising mast cell tumors.



MEDICATIONS

DRUG(S) OF CHOICE

Varies with tumor type—chemotherapy protocols are useful in some cases.

CONTRAINDICATIONS

Varies with tumor type and presence of concurrent disease.

PRECAUTIONS

Varies with tumor type and location.

POSSIBLE INTERACTIONS

Varies with tumor type and location.

ALTERNATIVE DRUG(S)

Varies with tumor type and location.



FOLLOW-UP

PATIENT MONITORING

Varies with tumor type and location.

PREVENTION/AVOIDANCE

- Varies with tumor type and location.
- Minimize exposure to ultraviolet light to help prevent some types of tumors.

POSSIBLE COMPLICATIONS

Varies with tumor type and location.

EXPECTED COURSE AND PROGNOSIS

Varies with tumor type and location.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Varies with tumor type and location.

AGE-RELATED FACTORS

Varies with tumor type and location.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Varies with tumor type; some may have a genetic predisposition.

SYNONYMS

N/A

SEE ALSO

Specific tumor types

ABBREVIATIONS

- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus

INTERNET RESOURCES

- <http://www.oncolog.org/types/section.cfm?c=22&s=69> (Oncolog Vet)
- <http://www.vetcancersociety.org/>

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Client Education Handout
available online

DERMATOSSES, PAPULONODULAR

D



BASICS

DEFINITION

- Diseases whose primary lesions manifest as papules and nodules.
- Papule: solid, elevated lesions of the skin less than 1 cm in diameter.
- Nodule: solid, elevated lesion of the skin more than 1 cm in diameter that extends into deeper layers of the skin.

PATHOPHYSIOLOGY

- Papules—usually the result of tissue infiltration by inflammatory cells; accompanying intraepidermal edema or epidermal hyperplasia and dermal edema.
- Nodules—usually the result of a massive infiltration of inflammatory or neoplastic cells into the dermis or subcutis.

SYSTEMS AFFECTED

Skin/Exocrine

GENETICS

Determined by cause; specific diseases may be more commonly seen in certain breeds.

INCIDENCE/PREVALENCE

Determined by cause

GEOGRAPHIC DISTRIBUTION

Determined by cause

SIGNALMENT

Species

Dogs and cats

Breed Predilection

Determined by cause

Mean Age and Range

Determined by cause

Predominant Sex

Determined by cause

SIGNS

- Papules and/or nodules with distribution characteristic of the cause.
- Accompanying crusting, inflammation, pigmentation changes, and hair coat changes often noted; also characteristic of the cause.

CAUSES

- Superficial and deep bacterial folliculitis (e.g., *Staphylococcus*)
- Other bacterial (mycobacterial, actinomycetes, nocardiosis, abscess)
- Fungal (dermatophytosis, kerion, histoplasmosis, cryptococcosis, coccidiomycosis, sporotrichosis, phaeohyphomycosis)
- Sebaceous adenitis, granulomatous
- Canine and feline acne
- Parasitic (demodicosis, flea bite hypersensitivity, sarcoptic mange, *Pelodera* dermatitis)
- Sterile nodular (sterile granuloma/pyogranuloma syndrome, reactive histiocytosis)
- Neoplasia

RISK FACTORS

- Bacterial folliculitis, dermatophytosis, and demodicosis—any disease or medication that causes immune compromise or interferes with the barrier function of the skin.
- Pelodera* dermatitis—may be associated with contact with decaying organic debris (straw or hay) containing *Pelodera* *strongyloides*.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Determined by cause.
- These diseases can be differentiated by diagnostic tests (see below).

CBC/BIOCHEMISTRY/URINALYSIS

- Should be normal in most patients unless underlying disease is present.

OTHER LABORATORY TESTS

- Appropriate immunoassays if deep/systemic fungal disease is suspected.
- Determined by cause.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Skin scraping—identify mites or rhabditiform larvae.
- Dermatophyte cultures—identify dermatophytosis.
- Pustule (Tzanck) preparations (if present)—bacteria and degenerative neutrophils compatible with bacterial folliculitis; eosinophils can be compatible with rupturing folliculitis or furunculosis; acantholytic keratinocytes may indicate an inflammatory folliculitis or pemphigus disease.
- Fungal cultures—identify deep/systemic fungal disease.
- Bacterial culture and sensitivity—identify bacteria and appropriate antibiotic therapy.
- Aspirate and cytology from nodule—identify cellular infiltrate; presence of organisms.
- Skin biopsy—useful to determine a definitive diagnosis if baseline diagnostic procedures are normal and/or initial empiric treatment is ineffective.

PATHOLOGIC FINDINGS

Depends upon underlying disease process.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient for nearly all causes (except some cases of neoplasia).
- Generalized demodicosis with secondary sepsis requires hospitalization.

NURSING CARE

Depends upon underlying issue

ACTIVITY

No specific alteration of activity recommended.

DIET

No specific alteration of diet recommended.

CLIENT EDUCATION

- For fungal infections, treatment may be expensive and prognosis can be guarded for deep/systemic fungal infections.
- For immune-mediated processes, treatment may be for the duration of the patient's life.

SURGICAL CONSIDERATIONS

Rarely necessary unless neoplasia is diagnosed.



MEDICATIONS

DRUG(S) OF CHOICE

Bacterial Folliculitis

- Superficial pyoderma—appropriate antibiotics based on bacterial culture and sensitivity for at least 3–4 weeks or 1 week beyond resolution of clinical signs.
- Deep pyoderma—appropriate antibiotics based on bacterial culture and sensitivity for at least 6–8 weeks or 2 weeks beyond resolution of clinical signs.
- Identify and control underlying cause to prevent recurrence.
- See specific chapter for additional recommendations.

Sebaceous Adenitis

- Appropriate antibiotics if secondary bacterial infection present.
- Propylene glycol and water (50–75% dilution) once daily as a spray to affected areas helpful in mild cases.
- Essential fatty acid dietary supplements (omega 3 and omega 6 PO).
- Topical therapy: antiseborrheic shampoos, emollient rinses (baby oil) and humectants.
- Cyclosporine (5 mg/kg PO q24h).
- Vitamin A (10,000–30,000 IU Vit A PO daily or 1000 IU Vit A/kg PO daily).
- Refractory cases—isotretinoin (1 mg/kg PO q12–24h); if response is seen, taper dosage (1 mg/kg q48h or 0.5 mg/kg q24h). The synthetic retinoids have become difficult to dispense due to strict prescription procedures.
- Most cases are refractory to corticosteroids.
- See specific chapter for additional recommendations.

Canine and Feline Acne

- May resolve without therapy in mild cases.
- Warm water soaks or Epsom salt solution (2 T/quart or 30 ml/L of water) for 5–10 minutes
- Chlorhexidine-based pads, or acetic acid/boric acid pads/wipes, or benzoyl peroxide gels used daily or alternated daily; topical ceramide/EFA preparations may be helpful.

DERMATOSSES, PAPULONODULAR

(CONTINUED)

D

- Topical creams/ointments: Mupirocin 2% ointment—topical antibiotic; apply q24h; should not be used in cats with deep lesions; metronidazole, 0.05% Vitamin A acid cream, clindamycin are alternative options.
- Secondary bacterial infection: systemic antibiotics.
- Underlying cause(s) should be determined and treated accordingly.
- Refractory cases—isotretinoin (1–2 mg/kg PO q24h). The oral synthetic retinoids have become difficult to dispense due to strict prescription procedures; prednisolone PO (1–2 mg/kg/day for 10–14 days and taper) may reduce scar tissue formation.
- See specific chapter for additional recommendations.

Pelodera Dermatitis

- Remove and destroy bedding.
- Wash kennels, beds, and cages and treat with a premise insecticide or flea spray.
- Bathe affected animal and remove crusts.
- Parasiticidal dip or ivermectin as recommended for sarcoptic mange.
- Corticosteroids as needed for inflammation.
- Severe infection—may require use of antibiotics.

Sterile Nodular Dermatoses

- Attempt to identify underlying cause.
- Cyclosporine 5 mg/kg PO q24h.
- Tetracycline (250 mg < 10 kg, 500 mg > 10 kg q8–12h), doxycycline (10 mg/kg q24h), or minocycline (5 mg/kg q12h) with niacinamide (250 mg < 10 kg, 500 mg > 10 kg q8–12h).
- Corticosteroids at immunosuppressive doses and taper according to response.
- Chemotherapeutic drugs (chlorambucil or azathioprine).

Other

- Dermatophytosis—griseofulvin, itraconazole, ketoconazole, or terbinafine; see specific chapter.
- Kerion—see Dermatophytosis.
- Demodicosis/sarcoptic mange—see specific chapters.
- Other bacterial infection—antibiotics dependent upon culture and sensitivity results.
- Deep/systemic fungal infection—see specific chapter.
- Urticaria—remove triggering factor; may need epinephrine or glucocorticoids depending upon severity; antihistamines may be helpful in chronic cases.
- Feline miliary dermatitis/feline eosinophilic dermatitis—see specific chapters, look for underlying cause.
- Neoplasia—see specific chapter.

CONTRAINDICATIONS

Corticosteroids and immunosuppressive medications should be avoided with folliculitis, dermatophytosis, kerion, and demodicosis.

PRECAUTIONS

- Cats can be sensitive to the irritant effects of benzoyl peroxide.
- Fatty acids—use with caution in dogs with inflammatory bowel disease or recurrent pancreatitis.
- Isotretinoin—may cause keratoconjunctivitis sicca, hyperactivity, pinna pruritus, erythematous mucocutaneous junctions, swollen tongue, lethargy with anorexia or vomiting, abdominal distension, or collapse; CBC and chemistry screen abnormalities include high platelet count, hypertriglyceridemia, hypercholesterolemia, and high alanine transaminase; teratogen.
- Cyclosporine—may cause vomiting and diarrhea, gingival hyperplasia, B lymphocyte hyperplasia, hirsutism, papillomatous skin eruptions, and increased incidence of infection; decreased glucose homeostasis; potential toxic reactions rare and include nephrotoxicity and hepatotoxicity.
- Azathioprine and chlorambucil—potential for bone marrow suppression, gastrointestinal upset; azathioprine can cause hepatotoxicity and possibly pancreatitis.

POSSIBLE INTERACTIONS

- Cyclosporine and corticosteroids interact with several medications; an appropriate drug handbook should be consulted prior to usage.
- An appropriate drug handbook should be consulted when prescribing an unfamiliar medication.

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- CBC, chemistry screen, urinalysis, and urine cultures—monitor periodically in patients receiving immunosuppressive medications. Monitoring will depend upon medication and dosage.
- CBC, chemistry screen, and urinalysis—monitor monthly for 4–6 months in patients receiving synthetic retinoid therapy.
- Tear production—monitor monthly for 4–6 months, then every 6 months in patients receiving synthetic retinoid therapy.
- Skin scraping—monitor therapy in patients with demodicosis (see Demodicosis).
- Repeat fungal culture—monitor therapy in patients with dermatophytosis (see Dermatophytosis).
- Resolution of lesions—monitor progress of sebaceous adenitis, actinic conditions, and all other diseases.

POSSIBLE COMPLICATIONS

Dependent on specific disease



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

- Dermatophytosis—incidence in humans reported in 30–50% of cases of *Microsporum canis* cases, but possible with all dermatophytosis cases.
- Sarcoptic mange.

PREGNANCY/FERTILITY/BREEDING

- Synthetic retinoids—teratogens; do not use in pregnant animals, animals intended for reproduction, or intact female animals; should not be handled by women of childbearing age.
- Corticosteroids—avoid use in pregnant animals.
- Cyclosporine—avoid during pregnancy unless absolutely necessary; dosages two to five times normal have been fetotoxic and embryotoxic in rats and rabbits.
- Antifungal agents should be avoided in pregnant animals.
- All drugs should be used with caution in pregnant and breeding animals.

SEE ALSO

- Acne—Cats
- Acne—Dogs
- Demodicosis
- Dermatophytosis
- Pyoderma
- Sebaceous Adenitis, Granulomatous

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- Author** Karen A. Kuhl
Consulting Editor Alexander H. Werner



Client Education Handout
available online

DERMATOSSES, STERILE NODULAR/GANULOMATOUS



BASICS

DEFINITION

Diseases whose primary lesions are nodules and/or plaques that are solid, may be multiple, elevated, and > 1 cm in diameter.

PATHOPHYSIOLOGY

- Nodules/plaques—usually result from an infiltration of inflammatory cells into the dermis and subcutis; may be secondary to endogenous or exogenous stimuli.
- Inflammation is typically, but not always, granulomatous to pyogranulomatous.

SYSTEMS AFFECTED

Skin/Exocrine

GENETICS

Oligogenic transmission is proposed for histiocytic sarcoma for Bernese mountain dogs.

SIGNALMENT

- Can affect any age, breed, or sex.
- Collagenous nevi—German shepherd dogs 3–5 years old. • Calcinosis circumscripta—German shepherd dogs < 2 years old.
- Systemic histiocytosis and malignant histiocytosis—Bernese mountain dogs (primarily), rottweilers, and retriever (golden and Labrador). • Eosinophilic granuloma—Siberian huskies < 3 years, males.

SIGNS

- Characterized by single to multiple dermal to subcutaneous nodules and/or plaques.
- Firm to fluctuant. • Occasionally painful.
- Overlying epidermis may be normal to ulcerated.

CAUSES

- Amyloidosis • Foreign body reaction
- Spherulocytosis • Idiopathic sterile granuloma and pyogranuloma • Canine eosinophilic granuloma • Calcinosis cutis
- Calcinosis circumscripta • Malignant histiocytosis (disseminated histiocytic sarcoma) • Reactive histiocytosis (cutaneous and systemic) • Sterile nodular panniculitis
- Collagenous nevi (nodular dermatofibrosis)
- Cutaneous xanthoma

RISK FACTORS

- Foreign body reaction—induced by exposure to any irritating material (e.g., concrete dust or fiberglass). • Hair foreign bodies—increased risk for large dogs that rest on hard surfaces. • Calcinosis cutis—increased risk with exposure to high doses of exogenous or endogenous glucocorticosteroids.
- Panniculitis—increased risk with vitamin E-deficient diet. • Cutaneous xanthoma—high-fat treats or diet, diabetes mellitus, hyperlipidemia.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- See “Causes.” • Sterile nodular dermatoses must be differentiated from deep bacterial and fungal infections and dermal neoplasia.
- Diagnosed by histopathology and deep tissue cultures. • Immunohistochemistry is helpful in differentiating histiocytic conditions. • Immunohistochemical staining is best performed on fresh frozen tissue; PCR may be used to help rule out leishmaniasis and mycobacterial infections.

CBC/BIOCHEMISTRY/URINALYSIS

- Amyloidosis—possible changes in biochemistry and/or urinalysis if internal organs are affected. • Malignant histiocytosis—pancytopenia. • Calcinosis cutis—changes characteristic of hyperglucocorticoidism (e.g., stress leukogram, high ALP, hyperglycemia, low urine specific gravity). • Cutaneous xanthomas—may have glucosuria, hyperglycemia, and/or lipid profile abnormalities. • Sterile panniculitis—may have biochemistry changes associated with pancreatitis, hepatic disease or systemic lupus erythematosus if systemic diseases are present.

OTHER LABORATORY TESTS

Serum ferritin levels—may be high with malignant histiocytosis but not with reactive histiocytosis.

IMAGING

- Radiology and ultrasonography—delineate involvement of internal organs in amyloidosis and histiocytosis. • Radiology—identify other areas of dystrophic calcification in dogs with calcinosis cutis. • Ultrasonography—identifies renal or uterine tumors in German shepherd dogs with collagenous nevi; adrenal tumor or enlargement and liver changes may be seen in dogs with calcinosis cutis.

DIAGNOSTIC PROCEDURES

- Skin biopsy for histopathology and cultures (fungal, aerobic, anaerobic, and mycobacterial); essential for the appropriate diagnosis of nodular dermatoses. • Biopsies should be excisional and taken from an intact or early (non-draining) nodule if possible. • Cultures should be taken from the nodular tissue, not exudates; fungal and mycobacterial organisms can easily be missed. • Special histopathologic stains for bacteria, mycobacteria and fungi can be requested to help rule out any infectious agent.

PATHOLOGIC FINDINGS

- Amyloidosis—accumulation of amorphous eosinophilic deposits that may extend into the subcutis; deposits stain apple green with Congo red in polarized light. • Foreign body reaction—suppurative to pyogranulomatous inflammation that affects the dermis, subcutis, and occasionally the underlying

muscle. The inciting foreign body may or may not be present in the tissue sampled.

- Spherulocytosis—histiocytes surrounding thin-walled parent bodies filled with homogeneous eosinophilic spherules.
- Idiopathic sterile granuloma and pyogranuloma—granulomatous to pyogranulomatous inflammation that can extend from the dermis to the panniculus; the inflammation mimics that seen with nodular infectious diseases; differentiated by obtaining negative aerobic, anaerobic, mycobacterial and fungal tissue cultures. • Canine eosinophilic granuloma—accumulation of numerous eosinophils with edema and possible mucin. Collagen degeneration is common, especially in more acute lesions.
- Calcinosis cutis—diffuse calcium deposition of the dermal collagen and adnexa that may extend into the deeper tissue. • Calcinosis circumscripta—focal to multifocal deposits of mineral that efface the soft tissue. • Reactive histiocytosis (cutaneous and systemic)—markedly angiocentric infiltrate of histiocytes that do not form granulomas or pyogranulomas; cutaneous and systemic disease cannot be differentiated by biopsy.
- Malignant histiocytosis (disseminated histiocytic sarcoma)—dense pleomorphic cell proliferation of spindle or round cells that efface normal tissue architecture; tumors from other spindle and round cell tumors differentiated by immunohistochemistry; histiocytic sarcomas consistently express CD45, CD18, CDI, CD11c, and MHC II.
- Sterile nodular panniculitis—neutrophilic to pyogranulomatous inflammation that affects the deep dermis and panniculus predominately; adipocytes may be necrotic or may be infiltrated by foamy macrophages.
- Collagenous nevi—focal dermal thickening of normal collagen bundles; histopathologic changes are very subtle; it is important to provide the pathologist with signalment and clinical history. • Cutaneous xanthoma—diffuse granulomatous inflammation composed of large foamy macrophages; lakes of extracellular amorphous lipid deposits and cholesterol clefts are not present in all cases.



TREATMENT

APPROPRIATE HEALTH CARE

- Dogs with calcinosis cutis may require hospitalization for treatment of sepsis and intensive topical therapy. • Most of these disorders can be treated on an outpatient basis. • Neoplastic or metabolic disorders may require hospitalization and supportive care.

NURSING CARE

Dogs with any of these diseases in which the nodules have ulcerated or ruptured open will benefit from gentle bathing and soaking to clean the skin and remove debris.

DERMATOSSES, STERILE NODULAR/GANULOMATOUS

(CONTINUED)

ACTIVITY

No restriction in activity indicated.

DIET

Animals with xanthoma should be on low-fat diet.

D**CLIENT EDUCATION**

- Malignant histiocytosis, amyloidosis, collagenous nevi of German shepherd dogs and systemic reactive histiocytosis are almost always fatal.
- Prognoses for cutaneous reactive histiocytic disease, sterile panniculitis and sterile pyogranuloma are guarded since they may require long-term immunosuppressive therapy; a few of these cases will not respond to therapy at all.

**MEDICATIONS****DRUG(S)**

- Amyloidosis—no known therapy, unless the lesion is solitary and can be surgically removed.
- Spherulocytosis—only effective treatment is surgical removal.
- Idiopathic sterile granuloma and pyogranuloma:
 - Prednisolone (2.2–4.4 mg/kg divided PO q12h) is the first line of therapy; continue steroids for 7–14 days after complete remission, then taper dose.
 - Azathioprine (2.2 mg/kg q48h) can be added as a steroid sparing drug.
 - Cyclosporine (5–10 mg/kg q24h) may be effective in cases that are unresponsive to steroids.
- Foreign body reactions—best treated by removal of the offending substance; for hair foreign bodies, the dog should be placed on softer bedding and topical therapy with keratolytic agents should be initiated; many dogs with hair foreign bodies also have secondary deep bacterial infections that require treatment with both topical and systemic antibiotics.
- Canine eosinophilic granuloma—prednisolone (1.1–2.2 mg/kg PO q24h) usually effective.
- Malignant histiocytosis—no effective long-term therapy; lomustine has been used with some short-term success; disease is usually rapidly fatal (mean survival time is usually less than 3 months).
- Cutaneous/systemic histiocytosis—high-dose glucocorticosteroids, cyclosporine, leflunomide, and other cytotoxic drugs can result in remission but long-term therapy is usually necessary and recurrences are common.
- Calcinosis cutis—underlying disease must be controlled if possible; most cases require antibiotics to control secondary bacterial infections; hydrotherapy and frequent bathing in antibacterial shampoos minimize secondary infection; topical DMSO is useful (applied to

no more than one-third of the body once daily until lesions resolve); if lesions are extensive, serum calcium levels should be monitored closely while using DMSO.

- Calcinosis circumscripta—surgical excision is the therapy of choice.
- Sterile nodular panniculitis—single lesions can be removed surgically; prednisolone (2.2–4.4 mg/kg PO q24h or divided PO q12h) treatment of choice; administer until lesions regress, then taper; some dogs remain in long-term remission, others require prolonged alternate-day therapy; a few cases respond to oral vitamin E (400 IU q12h); refractive cases may respond to cyclosporine.
- Collagenous nevi—no therapy for most cases since the cystadenocarcinomas are usually bilateral; for rare unilateral case of cystadenocarcinoma or a cystadenoma, removal of the single affected kidney may be helpful; ovariohysterectomy should be performed in intact females to remove leiomyomas.
- Cutaneous xanthoma—correction of the underlying diabetes mellitus or hyperlipoproteinemia is usually curative.
- Azathioprine (2.2 mg/kg q48h) can be used together with prednisolone as a corticosteroid-sparing agent.
- Cyclosporine (5–10 mg/kg 24h) can be used as an alternative to glucocorticosteroid therapy if the patient is steroid intolerant or steroids are not sufficiently effective.
- Tetracycline (250 mg < 10 kg, 500 mg > 10 kg q8–12h), doxycycline (10 mg/kg q24h), or minocycline (5 mg/kg q12h) with niacinamide (250 mg < 10 kg, 500 mg > 10 kg q8–12h) can also be used as an alternative to glucocorticoid therapy; this is effective only in mild cases.

CONTRAINdications

Corticosteroids and other immunosuppressive drugs should be avoided, if possible, in any animal with secondary bacterial folliculitis.

PRECAUTIONS

DMSO—handle with care; monitor serum calcium levels if used to treat calcinosis cutis.

**FOLLOW-UP****PATIENT MONITORING**

Patients on long-term immunosuppressive therapy should have a CBC, chemistry screen, urinalysis, and urine culture performed at least every 6 months.

- Dogs treated with DMSO for calcinosis cutis should have calcium levels checked every 7–14 days for the first month of therapy if large areas are affected.

POSSIBLE COMPLICATIONS

Long-term use of immunosuppressive therapy (especially glucocorticosteroids) may make patients more susceptible to other dermatoses such as bacterial folliculitis, demodicosis and

dermatophytosis, as well as systemic side effects.

EXPECTED COURSE AND PROGNOSIS

- Systemic amyloidosis, malignant histiocytosis, systemic reactive histiocytosis and nodular dermatofibrosis—invariably fatal.
- Many of the other conditions have a guarded prognosis; many require life-long immunosuppressive therapy to remain in remission.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Calcinosis cutis—hyperglucocorticoidism, chronic renal failure, and diabetes mellitus.
- Calcinosis circumscripta—(occasionally) hypertrophic osteodystrophy and idiopathic polyarthritis.
- Collagenous nevi—renal cystadenoma/cystadenocarcinoma and uterine, leiomyoma/leiomyosarcoma.
- Cutaneous xanthoma—diabetes mellitus and hyperlipoproteinemia.

SEE ALSO

- Adenocarcinoma, Renal
- Amyloidosis
- Hyperadrenocorticism (Cushing's Syndrome)—Dogs

ABBREVIATIONS

- ALP = alkaline phosphatase
- DMSO = dimethyl sulfoxide
- PCR = polymerase chain reaction

INTERNET RESOURCES

<http://www.histiocytosis.ucdavis.edu/>

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Client Education Handout
available online

DERMATOSSES, SUN-INDUCED

D



BASICS

OVERVIEW

The hair coat and epidermal pigmentation protect the skin from damage caused by ultraviolet light (UV) radiation. Excessive UV exposure damages keratinocytes (producing mutation), causes inflammation, and decreases cutaneous immune system surveillance. UVA (320–400 nm) penetrates more deeply than UVB (290–320 nm). Prolonged and repeated damage leads to pre-neoplastic changes and eventual neoplasia. Prolonged sun exposure in darkly-pigmented individuals may cause thermal burn. UV exposure may also exacerbate symptoms of pemphigus erythematosus, discoid lupus erythematosus, systemic lupus erythematosus, and dermatomyositis.

SIGNALMENT

Dogs—Dalmatian, bull terrier, boxer, bulldog, basset hounds, beagle, whippet, American Staffordshire terrier, Australian shepherd (nasal solar dermatitis).

CAUSES & RISK FACTORS

- White- and lightly-haired individuals with poorly-pigmented skin.
- History of sun-bathing.
- Outdoor housing.
- Regions with greater sun exposure; can be seasonal.

SIGNS

- Dogs—glabrous areas especially axillae, flank folds, ventral abdomen, and lateral aspects of extremities; lesions often multiple.
- Cats—pinnal tips, nasal planum, dorsal muzzle, eyelids, lips (uncommon).
- Solar dermatitis—nasal: erythema and scaling at the junction of the nasal planum and dorsal muzzle; expands caudally followed by scarring; truncal: erythema, scaling, and lichenification; gradual palpable thickening; comedones; secondary deep pyoderma leading to bullae.
- Actinic keratosis—palpable plaques with crusting and hyperkeratosis; cutaneous horns; often multiple; less than 1 cm in diameter.
- Hemangioma—punctate, flat, red to purple discolorations that enlarge to well-circumscribed plaques or nodules.
- Hemangiosarcoma—discrete to poorly-circumscribed, dark red to purple, fluctuant nodules; may become large; commonly ulcerate and bleed.
- Squamous cell carcinoma—proliferative and ulcerated plaques; crateriform; easily traumatized; secondary pyoderma common.
- Radiant thermal burn—large patches of alopecia, erythema and thickening; necrosis when severe; dorsal orientation; affects dark-haired and pigmented skin especially.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pyoderma
- Dermatophytosis
- Demodicosis
- Discoid lupus erythematosus
- Pemphigus erythematosus
- Pemphigus foliaceus
- Drug eruption
- Contact dermatitis
- Chemical burn

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Biopsy—only method for definitive diagnosis.
- Solar dermatitis—epidermal hyperplasia, apoptotic keratinocytes, perivascular inflammation, vascular dilatation, dermal fibrosis, solar elastosis.
- Actinic keratosis—parakeratotic hyperkeratosis with epidermal atypia and solar elastosis.
- Hemangioma—well-defined dermal mass of proliferative, blood-filled vascular channels with minimal atypia or mitosis.
- Hemangiosarcoma—poorly-defined vascular channels lined by irregular endothelial cells; pleomorphic nuclei; atypical mitosis.
- Squamous cell carcinoma—invasion of dermis by neoplastic cells; irregular islands, nests, trabeculae; keratin pearls; enlarged nuclei with moderate mitotic activity.
- Radiant thermal burn—epidermal hyperplasia with keratinocyte atypia; hydropic degeneration; pigmentary incontinence; occasional apoptosis; eosinophilic elastin fibers.



TREATMENT

- Outpatient.
- Sun avoidance—keep indoors during the day; avoid reflected sunlight; apply waterproof (> 30 SPF) sunscreen; sun-protective clothing.
- Surgical excision of neoplastic lesions whenever possible.



MEDICATIONS

DRUG(S)

- Cyclooxygenase-2 inhibitors—overexpression by sun-damaged cells; inhibition demonstrated improvement: firocoxib 5 mg/kg/day PO.
- Retinoids—regulate differentiation and growth of epithelial cells; Isotretinoin 1–2 mg/kg q24–48h PO.
- Corticosteroids—reduce inflammation noted in acute cases; prednisolone 0.5 mg/kg PO tapering dosage; discontinue when possible.
- Imiquimod—induces local immune response; for individual lesions, especially actinic keratosis; apply q48h until resolution.
- Diclofenac gel—topical nonsteroidal anti-inflammatory: apply q12h until resolution.
- Antibiotics—control secondary pyoderma (see chapter, Pyoderma).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Retinoids—keratoconjunctivitis sicca; elevated serum triglycerides; teratogen; gastrointestinal upset
- Firocoxib—gastrointestinal upset; elevated liver chemistries



FOLLOW-UP

- Patients should be regularly screened for development of new lesions; when detected early, excision with local anesthesia is possible.
- Sun-induced dermatoses rarely metastasize; prognosis is fair to good with early detection.
- Long-term therapy necessary following extended periods of sun damage.



MISCELLANEOUS

Suggested Reading

Albanese F, Abramo F, Caporali C, Vichi G, Millant F. Clinical outcome and cyclo-oxygenase-2 expression in 5 dogs with solar dermatitis/actinic keratosis treated with firocoxib. *Vet Dermatol* 2013; 24(6):606–e147, 2013.

Burrows AK. Actinic dermatoses and sun protection. In: Kirk's Current Veterinary Therapy XV. St. Louis, MO: Elsevier, 2014, pp. 480–482.

Author Alexander H. Werner

Consulting Editor Alexander H. Werner

DERMATOSSES, VESICULOPUSTULAR



BASICS

DEFINITION

- Pustule—small (< 1 cm), circumscribed elevation of the epidermis filled with pus.
- Vesicle—small (< 1 cm), circumscribed elevation of the epidermis filled with clear fluid.

PATHOPHYSIOLOGY

Pustules and vesicles—produced by edema, acantholysis (pemphigus), ballooning degeneration (viral infections), proteolytic enzymes from neutrophils (pyoderma), degeneration of basal cells (lupus), or dermoepidermal separation (bullous pemphigoid).

SYSTEMS AFFECTED

Skin/Exocrine

SIGNALMENT

- Lupus—collies, Shetland sheepdogs, and German shepherd dogs may be predisposed.
- Pemphigus erythematosus—collies and German shepherd dogs may be predisposed.
- Pemphigus foliaceus—Akitas, chow chows, dachshunds, bearded collies, Labrador retrievers, Newfoundlands, Doberman pinschers, and schipperkes may be predisposed.
- Bullous pemphigoid—collies and Doberman pinschers may be predisposed.
- Dermatomyositis—young collies and Shetland sheepdogs.
- Subcorneal pustular dermatosis—schnauzers affected most frequently.
- Linear IgA dermatosis—dachshunds exclusively; very rare.
- Dermatophytosis—young animals.

SIGNS

N/A

CAUSES

Pustules/Vesicles

- Superficial pyoderma—impetigo, superficial spreading pyoderma, superficial bacterial folliculitis, canine or feline acne.
- Pemphigus complex—pemphigus foliaceus, pemphigus erythematosus, panepidermal pemphigus; pemphigus vulgaris produces deep clefts that rapidly erode into ulcers.
- Subcorneal pustular dermatosis.
- Dermatophytosis.
- Demodicosis.
- Sterile eosinophilic pustulosis.
- Linear IgA dermatosis.
- Systemic lupus erythematosus.
- Discoid lupus erythematosus.
- Bullous pemphigoid
- Dermatomyositis.
- Cutaneous drug eruption.
- Epidermolysis bullosa.

RISK FACTORS

- Drug exposure—SLE and bullous pemphigoid.
- Bacterial folliculitis usually secondary to a predisposing factor (e.g. demodicosis, hypothyroidism, allergy, or corticosteroid administration).
- Ultraviolet light—pemphigus erythematosus, bullous pemphigoid, SLE, DLE, and dermatomyositis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Superficial Pyoderma

- Most common cause.
- Readily responds to appropriate antibiotic therapy if the underlying cause is effectively managed.
- Intact pustule—direct smear reveals neutrophils engulfing bacteria; most often *Staphylococcus pseudintermedius*; biopsy demonstrates intraepidermal neutrophilic pustules or folliculitis with bacteria.

Pemphigus Complex

- Group of immune-mediated diseases characterized histologically by disadhesion of keratinocytes within the epidermis (acantholytic keratinocytes).
- Direct smears—many acantholytic keratinocytes, non-degenerate neutrophils, eosinophils, and few to no bacteria.
- Culture of an intact pustule negative.
- Direct immunofluorescence—deposits in the intercellular spaces of the epidermis in approximately 50% of the cases.
- Tends to wax and wane irrespective of antibiotic therapy; responds to immunosuppressive therapy.
- Pemphigus foliaceus and erythematosus: superficial acantholysis leading to erosions; face, pinnae, and footpads (foliaceus) commonly affected; mucous membranes not affected; biopsy—subcorneal acantholysis; interface and lichenoid inflammation with pemphigus erythematosus.
- Pemphigus vulgaris: severe and deep form of pemphigus; characterized by erosions rapidly leading to ulcerations of the oral cavity, mucocutaneous junctions, and skin; biopsy—suprabasal acantholysis and cleft formation.
- Direct immunofluorescence positive at the intercellular spaces of the deeper epidermis.

Subcorneal Pustular Dermatosis

- Rare idiopathic pustular dermatosis of dogs.
- Tends to wax and wane.
- Intact pustules—direct smears reveal numerous neutrophils, no bacteria, and occasional acantholytic keratinocytes; cultures negative.
- Direct immunofluorescence negative.

- Poor response to glucocorticosteroids and antibiotics.

Dermatophytosis

- Common disease of both dogs and cats.
- Dermatophyte culture positive.
- Secondary bacterial folliculitis common.
- Skin biopsy—folliculitis with fungal elements.

Sterile Eosinophilic Pustulosis

- Rare idiopathic dermatosis of dogs.
- Direct smears—numerous eosinophils, non-degenerate neutrophils, occasional acantholytic keratinocytes, and no bacteria.
- Biopsy—eosinophilic intraepidermal pustules, folliculitis, and furunculosis.
- Direct immunofluorescence negative.
- Rapid response to glucocorticosteroids.

Linear IgA Dermatosis

- Rare idiopathic dermatosis of dachshunds.
- Tends to wax and wane.
- Pustules—sterile and subcorneal.
- Direct immunofluorescence positive for IgA at the basement membrane zone.

Systemic Lupus Erythematosus

- Multisystemic disease with variable clinical signs and cutaneous manifestations, including mucocutaneous ulceration.
- Direct immunofluorescence positive at the basement membrane zone.
- ANA positive.

Discoid Lupus Erythematosus

- Affects only the skin; lesions usually confined to the face.
- Depigmentation, erythema, and ulceration of the nasal planum common.
- Skin biopsy—interface and lichenoid dermatitis.
- Direct immunofluorescence positive at the basement membrane zone.
- ANA negative.

Bullous Pemphigoid

- Ulcerative disorder of the skin and/or mucous membranes.
- Skin biopsy—subepidermal cleft formation.
- Direct immunofluorescence positive at the basement membrane zone.
- No acantholysis.

Dermatomyositis

- Idiopathic inflammatory disease of the skin and muscle of young collies and Shetland sheepdogs; seen rarely in adult animals.
- Lesions affect the face, ear tips, tail tip, and pressure points of the extremities.
- Characterized by alopecia, crusting, pigmentation disturbances, erosions/ulceration, and scarring.
- Skin biopsy—follicular atrophy, perifolliculitis, and hydropic degeneration of the basal cells.
- Direct immunofluorescence negative.
- Muscle biopsy and EMG—evidence of inflammation.

(CONTINUED)

DERMATOSSES, VESICULOPUSTULAR**CBC/BIOCHEMISTRY/URINALYSIS**

- Usually unremarkable.
- SLE—possible anemia, thrombocytopenia, or glomerulonephritis.
- Eosinophilic pustular dermatosis—most affected dogs have peripheral eosinophilia.

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Direct smear from intact pustule/vesicle.
- Culture of intact pustule/vesicle.
- Skin biopsy for histopathology.
- Direct immunofluorescence, including IgA.
- ANA titer: may be positive with SLE.
- EMG: fibrillation potentials (rapid, irregular, and unsynchronized contraction of muscle fibers) and positive sharp waves in dermatomyositis.
- Muscle biopsy—myofibril degeneration, characterized by fragmentation, vacuolation, atrophy, fibrosis, and regeneration in dermatomyositis.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Periodic bathing with an antimicrobial shampoo—helps remove surface debris and control secondary bacterial folliculitis.
- Usually treated as an outpatient.
- SLE, pemphigus vulgaris, and bullous pemphigoid may be life-threatening and require inpatient intensive care.

**MEDICATIONS****DRUG(S) OF CHOICE*****Bacterial Folliculitis***

- Empiric choices: cephalixin 22 mg/kg q12h; clindamycin 11 mg/kg q24h; amoxicillin-clavulanic acid 15 mg/kg q12h.
- Appropriate antibiotic choice based on cultures from intact pustules.

Pemphigus Complex/Bullous Pemphigoid

Azathioprine (2 mg/kg PO q48h to twice weekly).
 Chlorambucil 2 mg/m² PO q48h
 Tetracycline (250 mg < 10 kg, 500 mg > 10 kg PO q8-12h), doxycycline (10 mg/kg PO q24h), or minocycline (5 mg/kg PO q12h) with niacinamide (250 mg < 10 kg, 500 mg > 10 kg PO q8-12h).
 Cyclosporine (5 mg/kg PO q24h).

Subcorneal Pustular Dermatosis

- Dapsone 1 mg/kg PO q8h until remission (usually 1–4 weeks); tapered to 1 mg/kg q24h or twice weekly.
- Sulfasalazine 10–20 mg/kg PO q8h until remission; then as needed.

Linear IgA Dermatoses

- Prednisolone 2.2–4.4 mg/kg PO q24h until remission; taper to alternate-day therapy.
- Dapsone—1 mg/kg PO q8h until remission; taper and give as needed; individual patients may respond to one drug and not the other.

Sterile Eosinophilic Pustulosis

- Prednisolone 2.2–4.4 mg/kg PO q24h until remission (usually 5–10 days); then as needed to prevent relapses (usually long-term, alternate-day therapy required).
- See specific diseases.

CONTRAINdications

N/A

PRECAUTIONS***Prednisolone***

- Secondary infection
- Iatrogenic Cushing disease
- Muscle wasting
- Steroid hepatopathy
- Behavioral changes
- Polydipsia, polyuria
- Polyphagia

Dapsone

- Dogs—mild anemia, mild leukopenia, and mild elevation of ALT, not associated with clinical signs; usually return to normal when dosage is reduced for maintenance.
- Rare fatal thrombocytopenia or severe leukopenia.
- Occasional vomiting, diarrhea, or pruritic skin eruption.
- Cats—more susceptible to dapsone toxicity; hemolytic anemia and neurotoxicity reported.

Sulfasalazine

Keratoconjunctivitis sicca.

Azathioprine and Chlorambucil

Potential for bone marrow suppression, gastrointestinal upset; azathioprine can cause hepatotoxicity and possibly pancreatitis.

Cyclosporine

May cause vomiting and diarrhea, gingival hyperplasia, B-lymphocyte hyperplasia, hirsutism, papillomatous skin eruptions, and increased incidence of infection; decreased glucose homeostasis; potential toxic reactions rare and include nephrotoxicity and hepatotoxicity.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

- Dapsone—monitor hemogram, platelet count, and ALT every 2 weeks initially and if any clinical side effects develop.
- Long-term sulfasalazine therapy—monitor tear production.
- Immunosuppressive therapy—monitor every 1–2 weeks initially; then every 3–4 months during maintenance therapy.

POSSIBLE COMPLICATIONS

N/A

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

Dermatophytosis: may infect human beings in the household.

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Acne—Cats
- Acne—Dogs
- Dermatomyositis
- Dermatophytosis
- Lupus Erythematosus, Cutaneous (Discoid)
- Lupus Erythematosus, Systemic
- Pemphigus
- Pyoderma

ABBREVIATIONS

- ALT = alanine aminotransferase
- ANA = antinuclear antibody
- DLE = discoid lupus erythematosus
- EMG = electromyography
- SLE = systemic lupus erythematosus

Suggested Reading

Helton-Rhodes KA, Werner A. Blackwell's Five-Minute Veterinary Consult Clinical Companion: Small Animal Dermatology, 2nd ed. Chichester: Wiley-Blackwell, 2011.
 Miller WH, Griffin CE, Campbell KL. Muller & Kirk's Small Animal Dermatology, 7th ed. St. Louis, MO: Elsevier Mosby, 2013.

Author Karen Helton Rhodes

Consulting Editor Alexander H. Werner



Client Education Handout
available online

DERMATOSSES, VIRAL (NON-PAPILLOMATOSIS)



BASICS

OVERVIEW

- Dermatoses caused by viral infection within keratinized structures.
- Viral replication within keratinized structures may cause cytosuppressive effects or upregulate keratinization resulting in hyperplastic or crusted conditions.

SIGNALMENT

- Dogs and cats
- Uncommon dermatoses
- No breed, sex, or geographic predilections reported
- No genetic basis for these diseases
- Young to young adult dogs
- Cats of any age

SIGNS

- Facial involvement or involvement of the head is common.
 - Lesions are often asymmetrical in distribution.
 - Paws and/or paw pads may be affected as well as other mucocutaneous junctions.
 - Acute or gradual onset; lesions may be associated with the history of a bite wound or fight.
 - Variable pruritus; can progress to self-mutilation with some viral infections.
 - Crusts.
 - Associated superficial bacterial folliculitis.
 - Abscess.
 - Paronychia.
 - Poor wound healing.
 - Seborrhea.
 - Exfoliative dermatitis.
 - Cutaneous horns.
 - Gingivitis/stomatitis.
 - Cutaneous or oral ulceration.
 - Nasodigital hyperkeratosis.
 - Impetigo in young dogs, without expected inflammation.
 - Pigmented macules or plaques.
 - Progression to bowenoid *in situ* carcinoma (FIV, papillomavirus).
 - Multiple mast cell tumors (FIV).
 - Systemic signs of illness may be present.
 - Signs consistent with an upper respiratory infection may or may not be present prior to the development of skin lesions.

CAUSES & RISK FACTORS

- FeLV • FIV • Feline cowpox virus infection
- Feline infectious peritonitis • Feline papillomavirus • Canine papillomavirus
- Canine distemper • Contagious viral pustular dermatitis (orf [parapoxvirus])
- Pseudorabies (α -herpesvirus) • Feline rhinotracheitis infection (α -herpesvirus-1)
- Feline calicivirus infection • Fighting or hunting behavior, multiple animal households, exposure to infected animals, and/or ingestion of infected material increases risk of exposure.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Crusting diseases—if crust formation precedes other symptoms, consider drug eruption, actinic keratoses, pemphigus foliaceus, systemic lupus erythematosus, other causes for exfoliative dermatitis.
- Allergic disorders—usually pruritic: flea allergic

dermatitis, cutaneous adverse reaction to food, or atopic dermatitis. Feline herpesvirus dermatitis lesions can mimic lesions of the eosinophilic granuloma complex and are also pruritic. Skin biopsy may not distinguish the syndromes unless viral inclusion bodies are present.

- Parasitic diseases—canine and/or feline scabies, demodicosis, cheyletiellosis.
- Infectious diseases—superficial and deep bacterial and fungal infections, leishmaniasis.
- Dogs—zinc deficiency syndromes, hepatocutaneous syndrome, nasal hyperkeratosis.
- Neoplasia—with extensive crusting and ulceration; squamous cell carcinoma, mast cell tumor, and epitheliotrophic lymphoma.

CBC/BIOCHEMISTRY/URINALYSIS

Nonspecific

OTHER LABORATORY TESTS

- Skin biopsy—necessary to prove viral origin of skin lesions; not always conclusive. If considering herpesvirus dermatitis, inform pathologist of suspicion.
- Virus isolation.
- Serology—confirms FeLV, FIV, or other viral infection.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Skin scrapings, trichograms—parasitic infestations.
- Dermatophyte culture—fungal infections.
- Epidermal cytology—bacterial folliculitis.
- Skin biopsy is the definitive diagnostic test.
- Immunohistochemical staining for viral particles.
- Viral serology and/or PCR.

PATHOLOGIC FINDINGS

- Irregular hyperplasia.
- Ballooning degeneration.
- Hydropic interface dermatitis.
- Syncytial-type giant cell formation within the epidermis and/or outer root sheath of the hair follicle with associated apoptotic keratinocytes.
- Keratinocyte inclusion bodies.
- Epidermal ulceration with dermal necrosis, necrosis of epidermal sweat glands, neutrophilic and/or eosinophilic inflammation.



TREATMENT

- Usually outpatient, except for systemically ill patients.
- Prevent exposure to other animals that could become infected.



MEDICATIONS

DRUG(S)

- Supportive care and treatment of secondary infections.
- Cats—herpesvirus: L-lysine 200–500 mg/cat q12h; interferon- α 30 units/cat/day

orally, famcyclovir 125 mg q12h, use of topical acyclovir has been reported.

- Cats—bowenoid *in situ* carcinoma: imiquimod.
- Dogs—individual papillomas—surgical excision; imiquimod.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Immunosuppressive therapies.



FOLLOW-UP

PATIENT MONITORING

Varies based upon viral infection and presence or absence of systemic involvement.

PREVENTION/AVOIDANCE

Prevent hunting behavior and exposure to potentially infectious materials and infected animals.

POSSIBLE COMPLICATIONS

Bacteremia and septicemia

EXPECTED COURSE AND PROGNOSIS

- Skin lesions may not respond to therapy.
- Systemic signs may eventually develop as a result of viral infection.
- Dependent upon the causal virus, animals may self-cure.
- In cats, papillomavirus infection may progress to bowenoid *in situ* carcinoma.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

Dependent on viral cause.

ZOONOTIC POTENTIAL

Feline cowpox virus and contagious viral pustular dermatitis (parapoxvirus) can be transmitted to other dogs, humans, and cats.

SEE ALSO

- Canine Distemper • Feline Calicivirus Infection • Feline Herpesvirus Infection
- Feline Immunodeficiency Virus Infection (FIV) • Feline Leukemia Virus Infection (FeLV) • Papillomatosis

ABBREVIATIONS

- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus

Suggested Reading

Miller WH, Griffin CE, Campbell KL. Muller & Kirk's Small Animal Dermatology, 7th ed. St. Louis, MO: Saunders, 2013, pp. 343–351.

Author Elizabeth R. May

Consulting Editor Alexander H. Werner

DESTRUCTIVE AND SCRATCHING BEHAVIOR—CATS



BASICS

OVERVIEW

- Behavior that causes damage to an owner's home or belongings.
- Primary destructive behavior is a normal behavior that includes exploratory and play-based behavior as well as scratching of surfaces for marking and claw maintenance.
- Secondary destructive behavior is a clinical sign reflecting other behavioral conditions and disease states.

SYSTEMS AFFECTED

- Gastrointestinal—damage to teeth; vomiting and diarrhea, obstruction if target items are ingested.
- Musculoskeletal—traumatic damage caused by intense scratching or chewing.
- Ingestion of toxic material could affect any organ system.

SIGNALMENT

- Any breed or gender; probable genetic basis in Oriental breeds that present for sucking or chewing fabric.
- Primary destructive behavior seen in cats < 6 months of age.
- Secondary destructive behavior more often in mature animals.

SIGNS

Primary Destructive Behavior

- May occur in the presence or absence of the owner.
- No specific environmental trigger.
- Common targets for scratching are furniture, door frames and speakers.
- May chew houseplants.
- Items resembling string, including shoelaces, necklaces, and rubber bands are often chewed and ingested. Small items that are batted, may be accidentally swallowed.

Secondary Destructive Behavior

- Attention-seeking—destructive behavior in the presence of the owner, often when owners are preoccupied.
- Compulsive behavior—excessive licking, chewing, and/or ingesting non-food items; fabrics particularly wool are targeted; occurs in the presence or absence of the owner.
- Stress related scratching may occur secondary to household conflict or change or in response to outside triggers, such as non-household cats.

CAUSES & RISK FACTORS

- Primary destructive behavior represents normal behavior; inadequate supervision and insufficient access to appropriate scratching posts or toys are risk factors.
- Owners may reinforce or increase stress by scolding cats scratching inappropriate items.
- Compulsive chewing or wool sucking most common in Oriental breeds.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Rule out medical conditions.
- If pica accompanies destructive chewing rule out conditions affecting digestion, absorption, and appetite, including recent diet change.
- For sudden onset of chewing in a mature cat rule out oral, gastrointestinal and medical disease and medical conditions associated with pain or anxiety.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

As indicated to rule out medical condition (T_4).

IMAGING

As needed to rule out medical conditions.

DIAGNOSTIC PROCEDURES

Physical examination with attention to oral cavity.



TREATMENT

Treat any underlying disease.

PRIMARY DESTRUCTIVE BEHAVIOR

- Keep claws trimmed.
- Supervise/confine until appropriate behavior patterns have been established.
- Assure access to acceptable scratching substrate; place posts in prominent locations and in target area; select suitable substrate—sisal, cardboard and loosely woven carpet are preferred; avoid posts covered with tightly woven carpet; position vertical or horizontal based on cat's preference.
- Reward appropriate behavior.
- Interrupt inappropriate behavior—apply non-toxic bitter-tasting product to deter chewing or double-sided sticky tape to deter scratching.
- Provide regular interactive play.
- Provide access to appealing toys.
- Declawing should not be a first-line therapy for normal scratching; while behavior modification is being implemented, plastic claw covers may be applied to prevent further damage.

SECONDARY DESTRUCTIVE BEHAVIOR

- Attention-seeking behavior—provide owner-initiated interactions; clicker training; review principles of learning and reinforcement.
- Compulsive disorder—identify and reduce sources of anxiety; offer interactive play and appropriate chewable items; some cats will chew rawhide bones; prevent access to target items.
- Reduce household conflict, manage intercat aggression.
- Block view of outside cats.



MEDICATIONS

DRUGS

- Medication complements behavior modification when treating anxiety-based conditions.
- Compulsive behavior may require SSRI or clomipramine.
- Medication is not indicated for primary destructive behaviors or attention-seeking behavior.
- Obtain informed consent when prescribing medication not approved for use in cats.

Tricyclic Antidepressants

Clomipramine: 0.5 mg/kg q24h

Selective Serotonin Reuptake Inhibitors

Fluoxetine: 0.5 mg/kg q24h

Nutraceuticals

- Novifit (SAMe): anxiety related to cognitive decline
- Zylkene • Royal Canin Calm Feline
- Anxitane

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- TCAs and SSRIs should not be used with monamine oxidase inhibitors, e.g., selegiline.



FOLLOW-UP

PATIENT MONITORING

Weekly follow-up during initial treatment.

EXPECTED COURSE AND PROGNOSIS

- Resolution of normal exploratory behavior is usually rapid.
- Anxiety-based conditions often require long-term management, including long-term psychotropic medication.



MISCELLANEOUS

AGE-RELATED FACTORS

Rule out medical in adult or senior onset.

PREGNANCY/FERTILITY/BREEDING

Preparturient destructive behavior (nesting).

SEE ALSO

- Compulsive Disorders—Cats

ABBREVIATIONS

- SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant

Suggested Reading

Casey R. Management problems in cats. In: Horwitz DF, Mills DS, eds., BSAVA Manual of Canine and Feline Behavioural Medicine, 2nd ed. Gloucestershire, UK: BSAVA, 2009, pp. 98–110.

Landsberg G, Hunthausen W, Ackerman L. Handbook of Behavior Problems of the Dog and Cat, 2nd ed. Philadelphia: Elsevier Saunders, 2003, pp. 311–347.

Author Ellen M. Lindell

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DESTRUCTIVE BEHAVIOR—DOGS



BASICS

OVERVIEW

- Behavior that causes damage to an owner's home or belongings.
- Primary destructive behavior is a normal behavior that includes exploratory and play-based behavior.
- Secondary destructive behavior is a clinical sign of another behavior condition.

SYSTEMS AFFECTED

- Gastrointestinal—damage to teeth; vomiting and diarrhea, obstruction if ingested.
- Musculoskeletal—traumatic damage caused by scratching or chewing.
- Ingestion of toxic material could affect any organ system.

SIGNALMENT

- Any breed or gender.
- Primary destructive behavior seen in dogs < 1 year of age.
- Secondary destructive behavior can be seen at any age.

SIGNS

Primary Destructive Behavior

- Initially occurs in the presence or absence of the owner.
- Not preceded by a specific environmental trigger.
- Absence of anxiety or aggression.

Secondary Destructive Behavior

- Attention-seeking behavior—destructive behavior in the presence of the owner.
- Separation-related anxiety—destructive behavior consistently occurs in the absence of the owner, and rarely in the presence of the owner; target items may include personal belongings, furniture, or points of egress.
- Storm phobia, noise phobia—destructive behavior and/or anxiety-related behavior in response to stimuli whether or not owner is present. Intensity may be greater during owner absence.
- Territorial aggression—arousal is observed in presence of owner; destructive behavior is intermittent based on presence of triggers; window frames and doorways are damaged.

CAUSES & RISK FACTORS

- Primary destructive behavior represents normal behavior; inadequate supervision and insufficient access to appropriate outlets may affect destructive behavior.
- Owner scolding, leading to either fear or attention seeking.
- Risk factors for anxiety-based conditions not clearly identified.
- Territorial aggression may have genetic and learned components.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Identify pathologic conditions.
- If pica accompanies destructive chewing—rule out

conditions affecting digestion, absorption, polyphagia and appetite, including recent diet change.

- If licking surfaces, rule out upper GI disease.
- For sudden onset in a mature pet with no notable environmental changes—rule out medical conditions.
- For age-related onset, rule out cognitive dysfunction syndrome.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

As indicated to rule out medical condition.

IMAGING

May be indicated if sudden onset in mature pet.

DIAGNOSTIC PROCEDURES

Physical examination with attention to GI tract.



TREATMENT

Treat underlying disease.

PRIMARY DESTRUCTIVE BEHAVIOR

- Supervise, confine or dog proof until appropriate behavior has been established.
- Assure access to acceptable chew toys.
- Reward appropriate behavior—select toys that dispense food or can be stuffed with food.
- Interrupt inappropriate behavior, apply non-toxic bitter-tasting product, then offer appropriate activity.
- Provide adequate interactive play.
- Use caution in applying any form of punishment. Any correction must be applied humanely, without causing pain or fear that could trigger anxiety or aggression.

SECONDARY DESTRUCTIVE BEHAVIOR

- Attention-seeking—provide owner-initiated interactions; teach sit for all interactions.
- Compulsive disorder—reduce sources of anxiety; offer interactive play and appropriate chew items; prevent access to target items.
- Separation-related anxiety—behavior modification; punishment is contraindicated.
- Noise phobia—behavior modification; reduce access to triggers.
- Territorial aggression—behavior modification, prevent access to doors and windows.



MEDICATIONS

DRUGS

- Medication complements behavior modification and may provide more rapid resolution when treating anxiety-based conditions.
- Medication is not indicated for primary destructive behaviors or attention-seeking behavior.

Tricyclic Antidepressants

Clomipramine: 1–3 mg/kg PO q12h

Selective Serotonin Reuptake Inhibitors

Fluoxetine: 0.5–2 mg/kg PO q24h

For situational anxiety (alone or together with SSRI or TCA)

Alprazolam: 0.01–0.1 mg/kg PO prior to event. Trazodone: 3–10 mg/kg PO prior to event. Clonidine: 0.01–0.05 mg/kg PO prior to event.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Psychotropic medication is not indicated for primary destructive behavior.
- TCAs and SSRIs should not be used with monoamine oxidase inhibitors including amitraz and selegiline.
- Benzodiazepines may disinhibit aggression; use with caution in dogs with a history of aggressive behavior.



FOLLOW-UP

PATIENT MONITORING

Weekly follow-up during initial phase of treatment.

EXPECTED COURSE AND PROGNOSIS

- Resolution of normal exploratory behavior is usually rapid.
- Anxiety-based conditions often require long-term management, including medication.



MISCELLANEOUS

AGE-RELATED FACTORS

Age of onset may aid in diagnosis.

PREGNANCY/FERTILITY/BREEDING

Preparturient destructive behavior (nesting).

SEE ALSO

- Compulsive Disorders—Dogs
- Separation Distress Syndrome
- Thunderstorm and Noise Phobias

ABBREVIATIONS

- SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant

Suggested Reading

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Author Ellen M. Lindell

Consulting Editor Gary M. Landsberg

DIABETES INSIPIDUS



BASICS

DEFINITION

Diabetes insipidus (DI) is a disorder of water metabolism characterized by polyuria, urine of low specific gravity or osmolality (so-called insipid, or tasteless, urine), and polydipsia.

PATHOPHYSIOLOGY

- Central DI—deficiency in the secretion of ADH
- Nephrogenic DI—renal insensitivity to ADH

SYSTEMS AFFECTED

- Endocrine/Metabolic • Renal/Urologic

GENETICS

N/A

INCIDENCE/PREVALENCE

- Central DI—rare • Nephrogenic—rare

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat

Breed Predilections

None

Mean Age and Range

- Congenital forms < 1 year • Acquired forms (e.g., neoplastic, traumatic, and idiopathic), any age

Predominant Sex

None

SIGNS

- Polyuria • Polydipsia
- Incontinence—occasional

CAUSES

Inadequate Secretion of ADH

- Congenital defect • Idiopathic • Trauma
- Neoplasia

Renal Insensitivity to ADH

- Congenital • Secondary to drugs (e.g., lithium, demeclocycline, and methoxyflurane)
- Secondary to endocrine and metabolic disorders (e.g., hyperadrenocorticism, hypokalemia, pyometra, and hypercalcemia)
- Secondary to renal disease or infection (e.g., pyelonephritis, chronic renal failure, pyometra)

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Polyuric Disorders

- Hyperadrenocorticism • Diabetes mellitus
- Liver disease—portosystemic shunt
- Hyperadrenocorticism • Pyometra
- Pyelonephritis • Hyperthyroidism—cats

- Hypercalcemia • Psychogenic polydipsia
- Renal failure

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal, hypernatremia in some patients • Urinary specific gravity low (usually < 1.012, often < 1.008)

OTHER LABORATORY TESTS

Plasma ADH

IMAGING

MRI or CT scan if a pituitary tumor is suspected

DIAGNOSTIC PROCEDURES

- Modified water deprivation test (see Appendix II-A for protocol) • ADH supplementation trial—therapeutic trial with synthetic ADH (DDAVP); a positive response (water intake decreases by 50% in 3–5 days)
- Rule out all other causes of PU/PD before conducting an ADH trial.

PATHOLOGIC FINDINGS

Degeneration and death of neurosecretory neurons in the neurohypophysis (CDI)



TREATMENT

APPROPRIATE HEALTH CARE

Patients should be hospitalized for the modified water deprivation test; the ADH trial is often performed as an outpatient procedure.

ACTIVITY

Not restricted

DIET

Normal, with free access to water

CLIENT EDUCATION

- Review dosage of DDAVP and administration technique • Importance of having water available at all times

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

- CDI—DDAVP (1–2 drops of the intranasal preparation in the conjunctival sac q12–24h to control PU/PD); alternatively, the intranasal preparation may be given SC (2–5 µg q12–24h). An oral preparation of DDAVP is available in 0.1–0.2 mg tablets with each 0.1 mg comparable to 1 large drop of the intranasal preparation
- NDI—hydrochlorothiazide (2–4 mg/kg PO q12h)

CONTRAINdications

None

PRECAUTIONS

Overdose of DDAVP can cause water intoxication.



FOLLOW-UP

PATIENT MONITORING

- Adjust treatment according to the patient's signs; the ideal dosage and frequency of DDAVP administration is based on water intake.
- Laboratory tests such as PCV, total solids, and serum sodium concentration to detect dehydration (inadequate DDAVP replacement)—usually not necessary

PREVENTION/AVOIDANCE

Circumstances that might markedly increase water loss

POSSIBLE COMPLICATIONS

Anticipate complications of primary disease (pituitary tumor).

EXPECTED COURSE AND PROGNOSIS

- The condition is usually permanent, except in rare patients in which the condition was trauma induced.
- Prognosis is generally good, depending on the underlying disorder.
- Without treatment, dehydration can lead to stupor, coma, and death.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

- Congenital CDI and NDI usually manifest before 6 months of age • CDI related to pituitary tumors is usually seen in dogs > 5 years old

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Central diabetes insipidus • Cranial diabetes insipidus • ADH-responsive diabetes insipidus • Nephrogenic diabetes insipidus

SEE ALSO

Hyposthenuria

ABBREVIATIONS

- ADH = antidiuretic hormone • CDI = central diabetes insipidus • DDAVP = brand name of desmopressin • DI = diabetes insipidus • MRI = magnetic resonance imaging • NDI = nephrogenic diabetes insipidus • PCV = packed cell volume • PU/PD = polyuria/polydipsia

Suggested Reading

Feldman EC, Nelson RW. Canine and Feline Endocrinology and Reproduction, 3rd ed. Philadelphia: Saunders, 2006.

Author: Rhett Nichols

Consulting Editor: Deborah S. Greco



Client Education Handout
available online

DIABETES MELLITUS WITH HYPEROSMOLAR COMA



BASICS

DEFINITION

Disease characterized by severe hyperglycemia, hyperosmolarity, severe dehydration, lack of urine or serum ketones, lack of or mild-to-moderate metabolic acidosis, and CNS depression.

PATHOPHYSIOLOGY

- Insulin deficiency causes reduced use of glucose and excessive glucose production.
- The resultant high extracellular blood glucose concentration causes a hyperosmolar state with a reduced extracellular fluid volume.
- Intracellular dehydration, azotemia, and uremia develop, and intracellular dehydration becomes more pronounced as the glomerular filtration rate decreases; tissue hypoxia ensues.
- Azotemia, hyperglycemia, and hyperosmolarity worsen as a result of glucose retention and glucose-induced osmotic diuresis.
- Although ketonemia and ketonuria usually are not features of this syndrome, anorexia (especially when prolonged) may cause mild ketoacidosis in some patients, but increased lactic acid is a major contributor to the metabolic acidosis that may develop in these patients.

SYSTEMS AFFECTED

- Renal/Urologic—prerenal and primary renal azotemia develop because of reduced extracellular fluid volume, reduced tissue perfusion, or diabetic glomerulonephropathy; urinary specific gravity is low because of osmotic diuresis, diabetic glomerulonephropathy, or concurrent renal insufficiency.
- Cardiovascular—hypotension because of low extracellular fluid volume, vascular collapse, and depressed myocardial contractility.
- Nervous—depression, disorientation or mental confusion, seizures, and coma are caused by intracellular dehydration and hyperosmolarity; CNS dysfunction worsens as serum osmolarity rises.

GENETICS

N/A

INCIDENCE/PREVALENCE

Uncommon

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Mostly cat, rarely dog

Breed Predilections

N/A

Mean Age and Range

- Dogs—peak prevalence, 7–9 years of age
- Cats—any age; most > 6 years old

Predominant Sex

- Dogs—female
- Cats—neutered males

SIGNS

Historical Findings

- Polydipsia/polyuria, polyphagia, and weight loss.
- Late signs—weakness, vomiting, anorexia, depression, stupor, and coma.

Physical Examination Findings

- Dehydration (severe 10–15%)
- Hypothermia
- Prolonged capillary refill time
- Lethargy, depression
- Seizures (severe hyperosmolarity)
- Stupor or coma (severe hyperosmolarity)
- Cataracts (dogs)

CAUSES

Diabetes mellitus associated with severe hyperosmolarity, severe hyperglycemia, prerenal azotemia, and severe dehydration.

RISK FACTORS

- Concurrent problems such as heart disease, renal insufficiency, pneumonia, acute pancreatitis, neoplasia and other severe diseases.
- Drugs—anticonvulsants, glucocorticoids, and thiazide diuretics may precipitate or aggravate this syndrome.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Myxedema coma—similar clinical findings, low TT₄, high TSH.
- Uncomplicated diabetes mellitus—mentally alert with fasting hyperglycemia and glucosuria.
- Ketoacidotic diabetes mellitus—fasting hyperglycemia with glucosuria, ketonuria, and metabolic acidosis.
- Extreme lethargy and depression with severe hyperosmolarity, severe hyperglycemia, severe dehydration without ketonemia and ketonuria usually differentiate diabetes mellitus non-ketotic hyperosmolar syndrome from uncomplicated and ketoacidotic diabetes mellitus.

CBC/BIOCHEMISTRY/URINALYSIS

- Severe hyperglycemia—usually > 600 mg/dL.
- High BUN and creatinine concentration.
- Hypernatremia.
- Normokalemia (despite total body potassium depletion) or hypokalemia.
- Hyperkalemia is expected in patients with anuric or oliguric renal failure.
- Low TCO₂.
- High anion gap.

- Glucosuria.

- Low urinary specific gravity.

OTHER LABORATORY TESTS

- Severe hyperosmolarity—usually > 350 mOsm/L.
- Estimated serum osmolarity may be calculated from serum chemistries as follows: 1.86(Na + K) + BUN/2.8 + glucose/18.
- High plasma lactate concentration may help confirm metabolic lactic acidosis in the absence of ketonemia and ketonuria.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

- Pancreatic islet cell atrophy (dogs)
- Pancreatic amyloid (cats)
- Cerebral necrosis, thromboembolism



TREATMENT

APPROPRIATE HEALTH CARE

A life-threatening medical emergency requiring inpatient treatment.

NURSING CARE

- Fluid therapy is a major component of medical management. Nasogastric tube allows for slow replacement of water orally (caution in comatose patients).
- Replace one-half the fluid deficits in the first 12 hours and the remainder during the next 24 hours.
- Administer normal saline (0.9%) IV if the patient is hypotensive or hyponatremic; use 0.45% saline if hypernatremic (caution to lower Na by only 2.2 mEq/kg/day).
- Add potassium (20 mEq/L) to the initial fluids unless the patient has hyperkalemia.
- Switch to IV administration of 0.45% saline after restoration of normal blood pressure and urine output.
- Switch to 2.5%–5% dextrose plus 0.45% saline when blood glucose < 250 mg/dL, and continue until the patient is eating and drinking on its own.

ACTIVITY

N/A

DIET

- A low-fat, high-fiber, high-complex carbohydrate diet is recommended for dogs once the patient is stabilized.
- A low carbohydrate, high protein diet is recommended for cats once the patient is stabilized.

CLIENT EDUCATION

- Poor-to-guarded prognosis.
- Intensive care and frequent monitoring are required during hospitalization.

SURGICAL CONSIDERATIONS

N/A

(CONTINUED)

DIABETES MELLITUS WITH HYPEROSMOLAR COMA**MEDICATIONS****DRUG(S) OF CHOICE**

- Administer regular insulin 2–4 hours after initiating IV fluid therapy.
- IV constant-rate infusion of regular insulin may be used at a dosage of 1.1 U/kg/24h. Add 1.1 U/kg regular insulin to 250 mL 0.9% NaCl and administer at 10 mL/h (0.045 U/kg/h) in a separate line. Discard the first 50 mL of the solution to compensate for insulin binding to the plastic tubing.
- Reduce the dosage/rate of the constant-rate infusion when the blood glucose is < 250 mg/dL.
- Once the patient is stabilized (eating and drinking on its own without vomiting), discontinue fluids and regular insulin; glargine PZI, or Lente insulin can then be administered SC in a routine manner.
- Other concurrent diseases must be treated appropriately.

CONTRAINDICATIONS

N/A

PRECAUTIONS

Avoid rapid reduction of serum osmolarity and glucose because the brain will become hyperosmolar compared with serum; fluid may then shift from extracellular to intracellular spaces, resulting in cerebral edema and worsening of neurologic status.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Once stable, oral hypoglycemics (e.g., glipizide) may be used in cats.

**FOLLOW-UP****PATIENT MONITORING**

- Blood glucose concentrations, closely, to avoid hypoglycemia and abrupt, precipitous decreases.

- Ideally, the blood glucose should drop 50–100 mg/dL/h until a concentration of 250 mg/dL is reached.

- Blood glucose hourly before administering the next dose of regular insulin IM during initial stabilization.
- Urine output for early detection of acute renal failure.
- Hydration status, ECG, CVP, serum electrolytes, BUN, and urine glucose every 2 hours during the initial stabilization period.
- Long-term glucose control by determining serum glycosylated hemoglobin and serum fructosamine concentrations.
- Watch for return of clinical signs such as polydipsia, polyuria, and polyphagia.

PREVENTION/AVOIDANCE

- Avoid inappropriate, insufficient insulin therapy.
- Avoid hypoglycemia, hypokalemia, and hyponatremia.

POSSIBLE COMPLICATIONS

- Irreversible coma and death are possible, especially in patients with renal insufficiency.
- Acute renal failure.

EXPECTED COURSE AND PROGNOSIS

Clinical signs and laboratory values may improve within the initial 24 hours of treatment, but these patients have a guarded prognosis.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Congestive heart failure, renal disease, infection, gastrointestinal hemorrhage, and other serious illnesses.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYMS

- Diabetic coma
- Hyperosmolar coma

SEE ALSO

- Diabetes Mellitus with Ketoacidosis
- Diabetes Mellitus without Complication—Cats
- Diabetes Mellitus without Complication—Dogs
- Hyperglycemia
- Hyperosmolarity

ABBREVIATIONS

- CNS = central nervous system
- CVP = central venous pressure
- ECG = electrocardiogram
- PZI = protamine zinc insulin
- TCO₂ = total carbon dioxide
- TSH = thyroid stimulating hormone

Suggested Reading

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Consulting Editor Deborah S. Greco

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DIABETES MELLITUS WITH KETOACIDOSIS



BASICS

DEFINITION

A true medical emergency secondary to absolute or relative insulin deficiency, characterized by hyperglycemia, ketonemia, metabolic acidosis, dehydration, and electrolyte depletion.

PATHOPHYSIOLOGY

- Insulin deficiency causes an increase in lipolysis, which results in excessive ketone body production and acidosis; an inability to maintain fluid and electrolyte homeostasis causes dehydration, prerenal azotemia, electrolyte disorders, obtundation, and death.
- Many diabetic ketoacidosis patients have underlying conditions such as infection, inflammation, or heart disease that cause stress hormone (e.g., glucagon, cortisol, growth hormone, and epinephrine) secretion; this probably contributes to the development of insulin resistance and diabetic ketoacidosis by promoting lipolysis, ketogenesis, gluconeogenesis, and glycogenolysis.
- Dehydration and electrolyte abnormalities result from osmotic diuresis, promoting the loss of total body water and electrolytes.

SYSTEMS AFFECTED

- Endocrine/metabolic • Gastrointestinal
- Hematologic (cats)

GENETICS

None

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Dog—miniature poodle and dachshund
- Cat—none

Mean Age and Range

- Dog—mean age 8.4 years • Cat—median age 11 years (range 1–19 years)

Predominant Sex

- Dogs—females 1.5 times males
- Cats—males 2 times females

SIGNS

- Polyuria • Polydipsia or adipsia
- Diminished activity • Anorexia • Weakness
- Vomiting • Lethargy and depression
- Muscle wasting and weight loss • Unkempt haircoat • Tachypnea • Dehydration • Thin body condition • Hypothermia • Dandruff
- Thickened bowel loops • Hepatomegaly
- Ketone odor on breath • Icterus

CAUSES

- Insulin-dependent diabetes mellitus
- Infection (e.g., skin, respiratory, urinary

tract, prostate gland, pyelonephritis, pyometra, and pneumonia) • Concurrent disease (e.g., heart failure, pancreatitis, renal insufficiency or failure, asthma, neoplasia, acromegaly, and estrus) • Idiopathic

- Medication noncompliance • Stress
- Surgery

RISK FACTORS

- Any condition that leads to an absolute or relative insulin deficiency • History of corticosteroid or β -blocker administration



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hyperosmolar nonketotic coma • Acute hypoglycemic coma • Uremia • Lactic acidosis

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis with mature neutrophilia
- Hyperglycemia—blood glucose usually > 250 mg/dL • High liver enzyme activity
- Hypercholesterolemia and lipemia
- Azotemia • Hypochloremia • Hypokalemia
- Hyponatremia • Hypophosphatemia
- High anion gap—anion gap = (sodium + potassium) – (chloride + bicarbonate); normal is 16 ± 4 • Glucosuria and ketonuria
- Variable urinary specific gravity with active or inactive sediment • Hyperproteinuria
- Heinz body anemia (cats)

OTHER LABORATORY TESTS

- Metabolic acidosis—venous $\text{TCO}_2 < 15$ mEq/L caused by ketosis • Hyperosmolarity (> 330 mOsm/kg) • Bacterial culture of urine and blood

DIAGNOSTIC PROCEDURES

ECG may help evaluate potassium status; prolonged Q-T interval in some patients with hypokalemia; tall, tented T waves in some patients with hyperkalemia.

PATHOLOGIC FINDINGS

Pancreatic islet cell atrophy



TREATMENT

APPROPRIATE HEALTH CARE

- If the animal is bright, alert, and well hydrated, intensive care and intravenous fluid administration are not required; start subcutaneous administration of insulin (short- or intermediate-acting insulin), offer food, and supply constant access to water; monitor closely for signs of illness (e.g., anorexia, lethargy, vomiting). • Treatment of “sick” diabetic ketoacidotic dog or cat requires inpatient intensive care; this is a life-threatening emergency; goals are to correct the depletion of water and electrolytes, reverse ketonemia and acidosis, and increase
- the rate of glucose use by insulin-dependent tissues.

NURSING CARE

- Fluids—necessary to ensure adequate cardiac output and tissue perfusion and to maintain vascular volume; also reduce blood glucose concentration. • IV administration of 0.9% saline supplemented with potassium is the initial fluid of choice. Volume determined by dehydration deficit plus maintenance requirements; replace over 24–48h.

ACTIVITY

N/A

DIET

A low-fat, high-fiber, high-complex-carbohydrate diet recommended once the patient is stabilized.

CLIENT EDUCATION

Serious medical condition requiring life-long insulin administration in most patients.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

Insulin

- Necessary to inhibit lipolysis, inhibit hepatic gluconeogenesis, and promote peripheral glucose uptake.
- Regular insulin is the insulin of choice.
- Initial dosage—0.2 U/kg IM (or SC if hydration is normal).
- Subsequent dosage 0.1–0.2 U/kg given 3–6h later—may be given hourly if patient is closely monitored; response to previous insulin dosage should be considered when calculating subsequent dosages. Ideally, glucose concentration should drop to 50–100 mg/dL/h.
- Regular insulin can also be administered as a continuous-rate infusion via a designated catheter. For dogs, place 2.2 units/kg into 250 mL of 0.9% NaCl fluid. For cats, place 1.1 units/kg into 250 mL 0.9% NaCl fluid. Then, allow 50 mL of the dilute insulin to flow through the IV tubing and discard. If blood glucose is > 250 mg/dL, administer at 10 mL/hour. If blood glucose is 200–250 mg/dL, administer at 7 mL/hour. If blood glucose is 150–200 mg/dL, administer at 5 mL/hour. If blood glucose is 100–150 mg/dL, administer at 5 mL/hour and add 2.5% dextrose to the IV crystalloid fluids. If blood glucose is < 100 mg/dL, discontinue IV insulin infusion and continue 2.5–5% dextrose in IV crystalloid infusion.
- Check blood glucose every 1–3 hours with Chemstrip BG reagent strips and an automated test strip analyzer (Accu-Chek III, Boehringer Mannheim; Alpha Trak glucometer, Abbott Laboratories).

(CONTINUED)

DIABETES MELLITUS WITH KETOACIDOSIS

D

- Monitor urine glucose and ketones daily.
- Start administering longer-acting insulin when the patient is eating, drinking, and no longer receiving IV fluids and ketosis is resolved or greatly diminished; the dosage is based on that of short-acting insulin given in hospital.

Potassium Supplementation

- Total body potassium is depleted and treatment (e.g., fluids and insulin) will further lower serum potassium; potassium supplementation is always necessary.
- If possible, check potassium concentration before initiating insulin therapy to guide supplementation dosage; if it is extremely low, insulin therapy may need to be delayed (hours) until serum potassium concentration increases.
- Refractory hypokalemia may indicate magnesium depletion, requiring magnesium replacement at 0.75–1 mEq/kg/day as magnesium chloride or magnesium sulfate as a continuous-rate infusion.
- If potassium concentration is unknown, add potassium (40 mEq/L) to the IV fluids, obtain results of pretreatment biochemical analysis ASAP, and draw blood for follow-up biochemical analysis 24 hours after treatment is initiated.

Dextrose Supplementation

- Must give insulin, regardless of the blood glucose concentration, to correct the ketoacidotic state.
- Whenever blood glucose is < 200–250 mg/dL, 50% dextrose should be added to the fluids to produce a 2.5% dextrose solution (increase to 5% dextrose if needed). Discontinue dextrose once glucose is maintained above 250 mg/dL.
- Do not stop insulin therapy.

Bicarbonate Supplementation

- Controversial; consider if patient's venous blood pH is < 7.0 or total CO₂ is < 11 mEq/L; bicarbonate is of no benefit if the pH is > 7.0.
- Dosage—body weight (kg) × 0.3 × base deficit (base deficit =; normal serum bicarbonate – patient's serum bicarbonate); slowly administer one-quarter to one-half of the dose IV and give the remainder in fluids over 3–6 hours.
- Recheck blood gas or serum TCO₂ before further supplementation.

Phosphorus Supplementation

- Pretreatment serum phosphorus usually is normal; however, treatment of ketoacidosis reduces phosphorus, and serum concentrations should be checked every 12–24 hours once supplementation is initiated.
- Dosage—0.01–0.03 mmol/kg/h for 6–12 hours in IV fluids (may need to increase dose to 0.03–0.06 mmol/kg/h).

CONTRAINDICATIONS

If the patient is anuric or oliguric or if potassium is > 5 mEq/L, do not supplement potassium until urine flow is established or potassium concentration decreases.

PRECAUTIONS

Use bicarbonate with caution in patients without normal ventilation because of their inability to excrete carbon dioxide created during treatment.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

- Attitude, hydration, cardiopulmonary status, urine output, and body weight • Blood sugar q1–3h initially; q6h once stable
- Electrolytes q4–8h initially; q24h once stable • Acid–base status q8–12h initially; q24h once stable

PREVENTION/AVOIDANCE

Appropriate insulin administration

POSSIBLE COMPLICATIONS

- Hypokalemia • Hypoglycemia
- Hypophosphatemia • Cerebral edema
- Pulmonary edema • Renal failure • Heart failure

EXPECTED COURSE AND PROGNOSIS

Guarded



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Pancreatitis • Hyperadrenocorticism
- Diestrus • Bacterial infection • Electrolyte depletion

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

- Risk of fetal death may be relatively high.
- Glucose regulation is often difficult.

SYNOMYS

N/A

SEE ALSO

- Diabetes Mellitus without Complication—Cats • Diabetes Mellitus without Complication—Dogs

ABBREVIATIONS

TCO₂ = total carbon dioxide

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Consulting Editor Deborah S. Greco
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Client Education Handout available online

DIABETES MELLITUS WITHOUT COMPLICATION—CATS



BASICS

DEFINITION

- Disorder of carbohydrate, fat, and protein metabolism caused by an absolute or relative insulin deficiency, insulin resistance, and insulin amyloidosis.
- Type II (non-insulin-dependent DM) is characterized by inadequate or delayed insulin secretion relative to the needs of the patient; many of these patients live without exogenous insulin and are less prone to ketoacidosis; most common form in cats.

PATHOPHYSIOLOGY

- Insulin resistance impairs the ability of tissues (especially muscle, adipose tissue, and liver) to use carbohydrates, fats, and proteins.
- Impaired glucose utilization and ongoing hepatic gluconeogenesis cause hyperglycemia.
- Glucosuria develops, causing osmotic diuresis, polyuria, and compensatory weight loss; mobilization of free fatty acids to the liver causes both hepatic lipidosis and ketogenesis.

SYSTEMS AFFECTED

- Endocrine/Metabolic—electrolyte depletion and metabolic acidosis.
- Hepatobiliary—hepatic lipidosis; liver failure may develop.
- Nervous—peripheral neuropathy.
- Renal/Urologic—urinary tract infection and osmotic diuresis.

INCIDENCE/PREVALENCE

Prevalence in cats is 1:200

SIGNALMENT

Species

Cat

Mean Age and Range

75% are 8–13 years; range 1–19 years

Predominant Sex

Male

SIGNS

- Early signs—obesity is typical.
- Dorsal muscle wasting and an oily coat with dandruff—common.
- Hepatomegaly; jaundice—more prevalent in cats than dogs.
- Less common findings—a plantigrade stance (diabetic neuropathy).
- Later signs—polyuria and polydipsia, polyphagia, weight loss, anorexia, lethargy, depression, and vomiting.

CAUSES

- Genetic susceptibility
- Amyloid
- Pancreatitis
- Predisposing diseases (e.g., hyperadrenocorticism and acromegaly)
- Drugs (e.g., glucocorticoids and progestogens)

RISK FACTORS

- Obesity for type II DM
- See “Causes”



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Renal glucosuria—usually does not cause PU/PD, weight loss, or hyperglycemia.
- Stress hyperglycemia in cats—no PU/PD or weight loss; blood glucose concentration normal if sample taken when cat is not stressed. Fructosamine normal.

CBC/BIOCHEMISTRY/URINALYSIS

- Results of hemogram usually normal.
- Glucose > 150 mg/dL.
- High SAP, ALT, AST activities, and hypercholesterolemia and lipemia common.
- Electrolytes vary, but hypernatremia, hypokalemia, and hypophosphatemia indicate severe decompensation.
- Total CO₂ or HCO₃ is low if the patient has ketoacidosis or severe dehydration.
- Glucosuria is a consistent finding.
- Ketonuria is uncommon.
- Urinary specific gravity often is low.

OTHER LABORATORY TESTS

- Anion gap—high in patients with ketoacidosis
- Fructosamine > 350 μmol/L

IMAGING

- Radiography—useful to evaluate for concurrent or underlying disease (e.g., cystic or renal calculi, emphysematous cystitis or cholecystitis, and pancreatitis).
- Ultrasonography—indicated in selected patients, particularly those with jaundice, to evaluate for hepatic lipidosis, cholangiohepatitis, and pancreatitis.

DIAGNOSTIC PROCEDURES

Liver biopsy (percutaneous)—indicated in some jaundiced patients.

PATHOLOGIC FINDINGS

- Usually no gross necropsy changes.
- Histopathologic findings may be normal or reveal vacuolar degeneration of the islets of Langerhans or low numbers of islet cells; usually see amyloid deposits in the islets.



TREATMENT

APPROPRIATE HEALTH CARE

- Compensated cats can be managed as outpatients; they are alert, hydrated, and eating and drinking without vomiting.
- For management of decompensated patients, see Diabetes Mellitus with Ketoacidosis.

NURSING CARE

Fluid therapy—see Diabetes Mellitus with Ketoacidosis.

ACTIVITY

Strenuous activity may lower insulin requirement; a consistent amount of activity each day is helpful.

DIET

- Studies suggest that ultra-low-carbohydrate canned diets may induce diabetic remission in 70–95% of newly diagnosed diabetic cats; monitor closely for change in insulin requirement following any adjustment in diet.
- Avoid soft, moist foods because they cause severe post-prandial hyperglycemia.

CLIENT EDUCATION

- Discuss daily feeding and medication schedule, home monitoring, signs of hypoglycemia and what to do, and when to call or visit veterinarian.
- Clients are encouraged to keep a chart of pertinent information about the pet, such as urine dipstick results, daily insulin dose, and weekly body weight.

SURGICAL CONSIDERATIONS

Intact females should have an ovariohysterectomy when stable; progesterone secreted during diestrus makes management of DM difficult.



MEDICATIONS

DRUG(S) OF CHOICE

- Insulin—treatment of choice for most cats.
- Pork Lente insulin (Vetsulin)—intermediate duration; given SC; initial dosage 2 U q12h. Availability may be limited.
- Protamine zinc (PZI, U-40)—long-acting insulin; given SC, usually q24h; some cats require injections q12h, starting with a dose of 2 U q12h.
- Glargin (Lantus, U-100)—basal peakless human recombinant insulin gives best results when combined with a low-carbohydrate, high-protein diet. Remission rates of 70–100% reported with this combination. Dose: 2 U SC q12h.
- Oral administration of hypoglycemic agent—glipizide is useful with dietary therapy in cats with type II DM; the cat should have uncomplicated DM and no history of ketoacidosis; initial dosage, 2.5 mg PO q12h; monitoring is the same as for patients on insulin; if hyperglycemia is not controlled, 5 mg PO q12h may be tried; potential side effects are hypoglycemia, hepatic enzyme alterations, icterus, and vomiting.

PRECAUTIONS

- Glucocorticoids, megestrol acetate, and progesterone cause insulin resistance. If steroid therapy is necessary use oral medrol. Avoid injectable steroids.

(CONTINUED)

DIABETES MELLITUS WITHOUT COMPLICATION—CATS

D

- Hyperosmotic agents (e.g., mannitol and radiographic contrast agents) if the patient is already hyperosmolar from hyperglycemia.

POSSIBLE INTERACTIONS

Many drugs (e.g., NSAIDs, sulfonamides, miconazole, chloramphenicol, monoamine oxidase inhibitors, and β -blockers) potentiate the effect of hypoglycemic agents given orally; consult the product insert.

ALTERNATIVE DRUG(S)

Acarbose 12.5 mg PO q12h

**FOLLOW-UP****PATIENT MONITORING**

- Glucose curve—not helpful in cats.
- Urinary glucose monitoring—urine is tested for glucose and ketones before the meal and insulin injection; to use this as a regulatory method, the pet must be allowed to have trace to 1/4% glucosuria to avoid hypoglycemia.
- Fructosamine—maintain < 400 $\mu\text{mol/L}$. Recheck monthly during initial regulation, then every 3 months.
- Clinical signs—owner can assess degree of PU/PD, appetite, and body weight; if these are normal, the disease is well regulated.

PREVENTION/AVOIDANCE

Prevent or correct obesity; avoid unnecessary use of glucocorticoids or megestrol acetate.

POSSIBLE COMPLICATIONS

- Seizure, blindness, or coma with insulin overdose
- Diabetic nephropathy
- Diabetic neuropathy

EXPECTED COURSE AND PROGNOSIS

- Some cats recover but may relapse at a later time.
- Prognosis with treatment is good; most animals have a normal lifespan.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Urinary tract infection

AGE-RELATED FACTORS

Juvenile DM is rare and may be more difficult to manage.

ZOONOTIC POTENTIAL

None

SEE ALSO

- Diabetes Mellitus with Ketoacidosis
- Diabetes Mellitus with Hyperosmolar Coma

ABBREVIATIONS

- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- DM = diabetes mellitus
- NSAID = nonsteroidal anti-inflammatory drug
- PU/PD = polyuria and polydipsia
- SAP = serum alkaline phosphatase

Suggested Reading

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**Client Education Handout
available online**

DIABETES MELLITUS WITHOUT COMPLICATION—DOGS



BASICS

DEFINITION

- Fasted hyperglycemia of sufficient severity to result in concurrent glucosuria.
- Disorder of carbohydrate, fat, and protein metabolism caused by an absolute or relative insulin deficiency.
- Generally canine diabetes mellitus is characterized by loss of insulin-secreting ability through presumed immune-mediated destruction of pancreatic β cells resulting in a dependence on exogenous insulin (insulin-dependent diabetes mellitus or IDDM).
- Far less frequently, canine DM can develop as a result of the combination of a relative insulin deficiency with concurrent peripheral insulin resistance. This combination of events may result in IDDM, non-insulin dependent diabetes mellitus (NIDDM), or both.

PATHOPHYSIOLOGY

- Absolute or relative insulin deficiency results in accelerated tissue catabolism, an impaired ability to maintain carbohydrate, lipid, and protein homeostasis, as well as insulin resistance.
- Hypoinsulinemia, peripheral insulin resistance, and continued hepatic gluconeogenesis results in persistent hyperglycemia of sufficient severity to overload renal tubular glucose resorption leading to glucosuria, a resultant osmotic diuresis and polyuria and compensatory polydipsia.
- Loss of insulin-dependent glucose-mediated hypothalamic satiation signal results in polyphagia.
- Decreased insulin-dependent utilization of glucose results in catabolic protein breakdown with weight loss and increased lipid mobilization (hyperlipidemia, hepatic lipidosis, ketone production).
- Insulin is most efficient at inhibiting peripheral lipolysis so uncontrolled ketone body production only occurs in animals with IDDM.
- Accumulations of large amounts of ketone bodies leads to metabolic acidosis and depletion of total body potassium.

SYSTEMS AFFECTED

- Endocrine/Metabolic—electrolyte depletion and metabolic acidosis.
- Hepatobiliary—hepatocellular lipidosis.
- Ophthalmic—cataracts.
- Renal/Urologic—glucosuria resulting in osmotic diuresis and increased likelihood of bacterial urinary tract infection.

GENETICS

Certain breeds dramatically over- and under-represented, suggesting inherited susceptibility to immune-mediated "isletitis."

INCIDENCE/PREVALENCE

- Prevalence varies between 1:400 and 1:500.
- Onset has a seasonal incidence; more animals diagnosed in the autumn and winter.

SIGNALMENT

Species

Dog

Breed Predilections

- Breeds overrepresented include Samoyed, Tibetan terrier, cairn terrier, and golden retriever (United States only).
- Possibly higher risk than other breeds—Keeshond, poodle, dachshund, miniature schnauzer, and beagle.
- Breeds underrepresented include boxer, German shepherd, and golden retriever (UK only).

Mean Age and Range

Mean ~ 8 years; range 4–14 years (excluding rare juvenile form)

Predominant Sex

Female

SIGNS

- Polyuria and polydipsia, polyphagia with weight loss.
- Hepatomegaly.
- Cataracts are a common finding in chronic cases or in dogs that have had poor control of their disease.
- Lethargy, depression, inappetance, anorexia and vomiting may occur in animals with marked ketoacidosis.

CAUSES

- Primary immune-mediated isletitis.
- Disorders that predisposing to secondary immune-mediated isletitis such as pancreatitis, various viral illnesses.

RISK FACTORS

- Diestrus
- Genetic susceptibility to immune-mediated isletitis
- Drugs such as glucocorticoids and progestins



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Renal glucosuria—does not cause hyperglycemia and usually no signs of weight loss with polyphagia.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram usually normal.
- Glucose > 200 mg/dL.
- High SAP and ALT with generally a greater proportionate increase in SAP, consistent with an obstructive hepatopathy.
- Hypercholesterolemia, lipemia and ketonemia are common.
- Electrolyte alterations vary, although hypokalemia and hypophosphatemia indicate severe decompensation.
- Total CO₂ or HCO₃ will be low with ketoacidosis or severe dehydration.
- Glucosuria consistently present.
- Ketonuria is common.
- Urinary specific gravity can be variable depending upon the level of glucosuria.

OTHER LABORATORY TESTS

- Anion gap—high in patients with ketoacidosis.
- Plasma insulin concentrations are not particularly helpful. While a low insulin concentration suggests an absolute

insulin deficiency this may be a reflection of reversible islet exhaustion as persistent hyperglycemia can impair insulin secretory activity, even if functional β cells are present.

IMAGING

- Radiography—useful to evaluate for concurrent or underlying disease (e.g., cystic or renal calculi, emphysematous cystitis or cholecystitis, and pancreatitis).
- Ultrasonography—indicated in selected patients, particularly those with jaundice, to evaluate possible other causes for a significant obstructive hepatopathy or concurrent complicating pancreatitis.

DIAGNOSTIC PROCEDURES

Liver biopsy (percutaneous)—indicated in some jaundiced patients to evaluate possible other causes for an obstructive hepatopathy.

PATHOLOGIC FINDINGS

- Necropsy findings—hepatomegaly with significant hepatic lipid accumulation.
- Histopathologic findings generally reveal dramatic reduction in the size and numbers of pancreatic islets with relatively normal exocrine tissue architecture except in dogs with concurrent exocrine pancreatic disease.



TREATMENT

APPROPRIATE HEALTH CARE

- Compensated dogs are generally alert, well hydrated, eating and drinking without vomiting and should be managed as outpatients.
- For management of decompensated patients, see Diabetes Mellitus with Ketoacidosis.

DIET

- The diet must be consistent—the food should be calorically and constitutionally controlled and consistent and the animal should consume the same caloric intake every morning and night.
- Match the glucose lowering effects of the insulin with glucose raising effects of the meal. As most insulins act maximally two to four hours after SC administration, and normally most food is being absorbed within an hour of consumption; glycemic control is almost always improved if the dog is fed 60–90 minutes AFTER q12h insulin dosing.
- Animals that "graze" throughout the day can be fed dry food ad libitum and given two small meals of canned food as described. If insulin can only be administered once daily, feed the total daily caloric intake in two or three meals within the first 6–8 hours after insulin dosing.
- Feed a caloric quantity appropriate for the animal's ideal body weight (~ 50–70 kcal/kg). The food should be something that the dog will eat reliably and within a short period of time.
- Obese diabetic dogs—feed a restricted caloric intake to ensure their ideal body weight is achieved

(CONTINUED)

DIABETES MELLITUS WITHOUT COMPLICATION—DOGS

D

within 2–4 months using a high-fiber, low-calorie food. While a high-fiber diet may improve patient satiety and possibly owner satisfaction, it has no role in improving diabetic control. • No snacks should be provided unless they have virtually no calories.

CLIENT EDUCATION

- Discuss daily feeding and medication schedule, home monitoring, signs of hypoglycemia and what to do, and when to call or visit veterinarian.
- Clients are encouraged to keep a chart of pertinent information about the pet, such as daily water consumption, weekly body weight, current insulin dose and amount of food consumed.

SURGICAL CONSIDERATIONS

Intact females should have an ovariohysterectomy when stable; progesterone secreted during diestrus makes management of DM more unpredictable.



MEDICATIONS

DRUG(S) OF CHOICE

- Insulin—required for IDDM; frequently utilized as part of management of NIDDM.
- Vetsulin (porcine-origin Lente) 0.75 units/kg SC q12h initial dose. **Note:** U-40 insulin; must use with U-40 insulin syringe. Availability may be limited.
- Humulin N—intermediate-acting, human insulin; 0.75 units/kg SC q12h initial dose.
- Novolin N—intermediate-acting, human insulin; 0.75 units/kg SC q12h initial dose.
- PZI Vet (Idexx) rarely used in dogs; intermediate- to longer-acting protamine/zinc, human insulin. NOTE: U-40 insulin, must use with U-40 syringe.
- Glargine and detemir insulins: intermediate- to longer-acting synthetic insulins that have a “peakless” level of activity and delayed release from subcutaneous injection sites. These are rarely used in dogs.
- Species of origin of the insulin may affect pharmacokinetics; canine and porcine insulin have identical amino acid sequence, hence Vetsulin does not produce a significant insulin antibody response, whereas most other commercially available insulins do. However, there is no evidence that the development of insulin antibodies has any clinical significance.

PRECAUTIONS

- Glucocorticoids, megestrol acetate, and progesterone cause insulin resistance.
- Hyperosmotic agents (e.g., mannitol and radiographic contrast agents) if the patient is already hyperosmolar from hyperglycemia.

ALTERNATIVE DRUG(S)

Oral hypoglycemic agents are generally not recommended. The rare dog with NIDDM may be amenable to treatment with oral hypoglycemic agents but must be strictly monitored as this is generally a progressive

disease and ineffective management can have disastrous consequences.



FOLLOW-UP

PATIENT MONITORING

- Diabetic dogs need to be managed with regular contact between the owner and their veterinary team. The frequency should be approximately 3–4 months if the animal is stable and clinical signs are controlled; or more frequently if control is poor or variable. Criteria effective in assessing adequate control are listed below.
- Clinical signs—assess degree of PU/PD, appetite, and body weight; if within acceptable limits, the disease is likely to be well regulated.
- Glycated proteins—fructosamine or glycosylated hemoglobin; the extent of glycation is directly related to the blood glucose concentration over the lifespan of the protein in the circulation (normally 10–20 days for fructosamine, 4–8 weeks for hemoglobin); thus they are not affected by vagaries of single blood glucose level nor by the effects of travel and/or hospitalization on gastric emptying and thus the interplay between the effects of the insulin and the meal on blood glucose levels.
- Glycated protein levels are modified by changes in albumin or hemoglobin concentrations and the amount of time they spend in circulation; anything that accelerates albumin turnover (e.g., glomerulonephropathy, liver dysfunction, GI disease) will lower the fructosamine level for a given average blood glucose.
- Glycated protein levels are best used for ongoing management of a relatively stable diabetic patient; a fructosamine in the upper third of the reference range reflects excellent diabetic control; a fructosamine in the lower third is more suggestive of overzealous diabetic control and possible increased risk of clinically significant hypoglycemia.
- Glucose curve—can provide information on insulin effectiveness, duration of action, nadir (lowest blood glucose level achieved during dosing interval), and potential for rebound hyperglycemia; results subject to outside influences; stress of hospitalization and multiple blood draws; used most frequently when establishing initial control, changing insulin type, dose, or frequency, or problem solving the difficult diabetic; duration of curve ideally matches dosing interval (12 or 24 hours); identification of nadir (to avoid iatrogenic hypoglycemia) and glucose level at the time of dosing are the most important aspects of curve; mimic “normal” conditions as closely as possible; can have owner feed and administer insulin at home prior to hospitalization although not ideal as introduces additional confounding factors related to gastric emptying; measure blood glucose q2h or q4h; goal is effective insulin

dose (decline in blood glucose to 100–200 mg/dL) for appropriate duration (majority of 12- or 24-hour dosing interval) with a nadir > 80 mg/dL and < 150 mg/dL.

- Home-glucose monitoring using serial blood glucose estimations with home-glucose monitoring kits; requires significant owner commitment, compliance, and competence; most useful as early indicator of need for reduction in dose in patients with well controlled clinical signs; should never be used by the owner to make independent adjustment of insulin dose. Owner-measured urine glucose levels are not particularly useful.

PREVENTION/AVOIDANCE

- Neuter females; avoid unnecessary use of megestrol acetate.
- No evidence exists to suggest obesity increases the risk of DM in neutered dogs.

POSSIBLE COMPLICATIONS

- Cataracts can occur even with good glycemic control.
- Weakness, especially with exercise; seizures or coma may occur with insulin overdose.

EXPECTED COURSE AND PROGNOSIS

- Dogs generally have permanent disease unless affected during an estrus cycle where neutering may resolve the diabetes for a period.
- Prognosis with twice daily insulin treatment and feeding aligned with insulin's maximum effects is excellent.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Urinary tract infection
- Cataracts

AGE-RELATED FACTORS

Juvenile DM is rare and may be more difficult to manage

PREGNANCY/FERTILITY/BREEDING

- DM can develop during pregnancy, in which case the pregnancy is difficult to maintain.
- Exogenous insulin administration may cause fetal oversize and dystocia.
- Insulin resistance develops, making hyperglycemia difficult to control.
- The pregnant bitch is prone to ketoacidosis; an emergency ovariohysterectomy may be necessary.
- Do not breed dogs with DM.

ABBREVIATIONS

- DM = diabetes mellitus
- IDDM = insulin-dependent diabetes mellitus
- NIDDM = non-insulin dependent diabetes mellitus

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Client Education Handout
available online

DIABETIC HEPATOPATHY



BASICS

OVERVIEW

D

- Liver lesion—severe degenerative vacuolar hepatopathy (VH, macrovesicular lipid and glycogen), parenchymal collapse causing marked hepatic nodularity; associated with syndromic pressure point dermatosis and usually diabetes mellitus (DM).
- Liver lesions—may precede cutaneous lesions and DM.
- May develop in some dogs treated chronically with phenobarbital.

SIGNALMENT

- Middle-aged to older dogs
- Males may have greater predilection
- Syndrome in Shih Tzu dogs recognized

SIGNS

Historical Findings

- Acute onset; may be few signs initially.
- Common signs—weight loss, lethargy, PU/PD, anorexia, diarrhea, vomiting, anicteric or jaundiced, lameness due to painful foot pad fissures.

Physical Examination Findings

- Lethargy, poor body condition, painful feet and elbow lesions compromise recumbent and standing postures, may be jaundiced.
- Cutaneous lesions—see Superficial Necrolytic Dermatitis.
- Normal, small to large hepatic size—rarely, may palpate irregular liver margin.
- Rare abdominal effusion.

CAUSES & RISK FACTORS

- Etiology—associated with hypoaminoacidemia; causal role in cutaneous lesions and possibly liver lesions.
- Secondary causal role—suggested for ill-defined deficiencies: zinc, fatty acid, or niacin.
- Hyperglucagonemia—originally proposed causal mechanism but inconsistent (~ 30%–40% of tested dogs demonstrate high plasma glucagon); poor correlation may reflect assay specificity or high hepatic glucagon extraction; pancreatic glucagon-producing tumor confirmed in < 25% of dogs.
- Insulin resistant DM.
- Similar cutaneous lesions described with primary hepatopathies caused by: phenobarbital or rarely, with chronic mycotoxicosis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cirrhosis—regenerative nodular hyperplasia with extensive connective tissue deposition and loss of architectural organization.

- Chronic hepatitis—inflammatory infiltrates; individual hepatocyte necrosis.
- Copper associated hepatopathy—high tissue copper associated initially with zone 3 necroinflammatory injury.
- Diffuse nodular hyperplasia—rare.
- Degenerative glycogen-type VH.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—mild to moderate non-regenerative to mild regenerative anemia; RBC microcytosis; neutrophilic leukocytosis reflects cutaneous lesions (infections).
- Biochemistry—high liver enzymes (especially ALP); hypoproteinemia with hypoalbuminemia; euglycemic to fasting hyperglycemia; variable cholesterol and BUN.
- Urinalysis—ammonium biurate crystalluria may reflect hepatic insufficiency.

OTHER LABORATORY TESTS

- Total serum bile acids—often increased.
- Insulin—inappropriately increased.
- Plasma glucagon—inconsistently high.
- Plasma amino acids—30%–50% of normal in dogs with cutaneous lesions; moderate reductions in dogs with liver lesions preceding skin lesions.

IMAGING

- Abdominal radiography—variable liver size, small, normal, to large liver; rare effusion.
- Abdominal ultrasonography—may see irregular liver margin; characteristic nodular pattern: hypoechoic foci in background hyperechoic parenchyma, “Swiss cheese pattern”; although suggested as pathognomonic, other severe degenerative VH also demonstrates this pattern; occasional diffuse nodularity cannot be imaged; pancreatic mass imaged < 20% of dogs.

DIAGNOSTIC PROCEDURES

- Aspiration sampling—hepatocytes show VH associated with glycogen and lipid.
- Liver biopsy—needle biopsy may compromise definitive diagnosis by limiting detection of proliferative foci of hepatocytes between massive vacuolated parenchyma; needle biopsy may be best option for dogs with extensive skin lesions; larger laparoscopic samples preferred; avoid laparotomy as dogs with cutaneous lesions may not promptly heal.
- If pancreatic mass imaged, resect for histology and immunohistochemical staining for glucagon and other products.
- Skin biopsy—see Superficial Necrolytic Dermatitis.



TREATMENT

- Diet—use high good-quality protein, energy-dense diet; but enteral or parenteral feeding may be required for inappetent dogs.

- If HE—improve nitrogen tolerance with lactulose and metronidazole (see Hepatic Encephalopathy) and use liver-specific diet.
- Oral protein hyperalimentation and periodic parenteral IV amino acid infusions need in most.
- Amino acid supplementation—egg yolk (3–6 yolks per day); anabolic whey protein powder (e.g., Beneprotein, used for body building muscle accretion) one serving ~ 7 g protein, 25–35 kcal; one serving/5–7 kg body weight; mix with diet; if HE use baseline diet formulated for hepatic insufficiency; IV infusion (3.5% to 10% solutions), e.g., 10% crystalline amino acid solution (Aminosyn, Abbott Laboratories; 100 mL delivers 10 g amino acids), 25 mL/kg body wt. over 8–12 h through a large central vein (i.e., jugular vein), unless coagulopathy; then use long jugular catheter threaded deeply into a peripheral vein); rare HE induction. Cutaneous lesions may resolve after only one amino acid treatment; if little response, repeat q7–10 days for 4 treatments; if no response, grave prognosis.
- Essential fatty acid supplementation—omega-3 fatty acids; double normal dose.
- Metastatic pancreatic tumors secreting glucagon may be controlled with long-acting somatostatin analog (octreotide: 2–3.7 µg/kg q6–12 h); prohibitively expensive.



MEDICATIONS

DRUG(S)

- Manage DM with insulin.
- See Dietary recommendations above.
- Cutaneous or nail bed infections—systemic antimicrobials or antifungals; germicidal baths.
- Zinc supplementation—2–4 mg/kg elemental zinc q24h; avoid zinc methionine if HE.
- Niacinamide—250–500 mg/dog q12h (500 mg for dogs > 10 kg); watch for toxic effects; avoid extended-release form.
- Topical glucocorticoids—if unresponsive inflammatory skin lesions, after infection managed (**caution:** systemic glucocorticoids may promote HE, enteric ulceration, infection, complicate DM management).
- Ketoconazole—for secondary yeast infection; anti-inflammatory and antipruritic effects
- Somatostatin—long-acting octreotide theorized as possible treatment; based on speculated endocrinologic cause; prohibitively expensive.
- Ursodeoxycholic acid—10–15 mg/kg PO daily, divided dose given with food.
- Antioxidants—Vitamin E (10 IU/kg daily PO); S-adenosylmethionine (SAMe) 20 mg/kg PO daily on empty stomach, other

(CONTINUED)

DIABETIC HEPATOPATHY

D

beneficial effects additional to antioxidant influence.

- If associated with phenobarbital, discontinue.

POSSIBLE INTERACTIONS

- HE induction: high protein diet supplements and amino acid infusions.
- Toxic effects of ketoconazole and its interference in drug metabolism.
- Toxic effects of niacinamide and zinc.

**FOLLOW-UP****PATIENT MONITORING**

- Weekly to monthly physical exam to assess need for amino acid supplements and treatment for secondary infections.
- Daily glucose monitoring at home.
- Fastidious management of diabetes mellitus.
- Weekly to monthly CBC, biochemistry, and urinalysis, initially.

POSSIBLE COMPLICATIONS

- Hyperosmolar amino acid solutions may cause thrombophlebitis.
- Ketoacidosis—uncommon.
- Hepatic encephalopathy.
- Sepsis—due to diabetes and skin lesions.
- Pain—from skin lesions require analgesics.

EXPECTED COURSE AND PROGNOSIS

- Some dogs achieve cutaneous remission ~ 2 year with described therapies; most have unremitting progression, necessitating euthanasia; improved liver lesions with treatment.

**MISCELLANEOUS****SYNONYMS**

- Superficial necrolytic dermatitis
- Necrolytic migratory erythema
- Metabolic epidermal necrosis
- Glucagonoma syndrome
- Hepatocutaneous syndrome

ABBREVIATIONS

- DM = diabetes mellitus
- HE = hepatic encephalopathy
- VH = vacuolar hepatopathy

Suggested Reading

Oberkirchner U, Linder KE, Zadronzny L, et al. Successful treatment of canine necrolytic migratory erythema (superficial necrolytic dermatitis) due to metastatic glucagonoma with octreotide. *Vet Dermatol* 2010, 21:510–516.

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DIAPHRAGMATIC HERNIA



BASICS

OVERVIEW

- D** • Protrusion of an abdominal organ through an abnormal opening in the diaphragm either as an acquired injury or as a congenital defect.
- Traumatic—most common acquired cause; usually the result of automobile trauma but also any forceful blow; sudden increase of pressure results in an abdominal-thoracic pressure gradient, causing a tear in the diaphragm, usually at a muscular portion.
 - Congenital—pleuroperitoneal or peritoneopericardial diaphragmatic hernia (PPDH); may note other congenital defects (e.g., umbilical hernia, cranoventral abdominal wall defects, cryptorchidism, cleft palate, ventricular septal defect, aortic stenosis, and portosystemic shunting).
 - Impaired lung expansion—because of lack of lung contact with parietal pleura.
 - Intrapulmonary changes (e.g., lung contusion, atelectasis, and capillary permeability changes causing edema)—contribute to poor gas exchange.
 - Rib fractures due to trauma—may contribute to hypoventilation because of pain or mechanical (flail chest) factors.
 - Myocardial trauma can result in various dysrhythmias—ventricular tachyarrhythmias: most common; seen within 24–72 hours after trauma; difficult to control with conventional treatment; commonly resolve within 5 days.
 - Various stages of shock—can cause multiple organ system failure.

SIGNALMENT

- Dogs and cats.
- Acquired—no breed predilection.
- Congenital (PPDH)—Weimaraners may be predisposed; Maine Coon and other longhaired cats may be overrepresented; can be diagnosed at any age because clinical signs are variable and intermittent; often diagnosed incidentally.
- Young animals at higher risk for both congenital and traumatic causes.

SIGNS

Traumatic

- Can be acute, subacute, or chronic (with no known history of trauma).
- Low-grade respiratory signs or vague history of gastrointestinal problems possible.
- Signs may be progressive.
- Tachypnea and respiratory distress—most common; acutely affected patients often in shock.
- Arrhythmias—may be detected.
- Muffled heart and lung sounds along with intestinal sounds—may be auscultated in the thorax.
- Abdomen—may feel empty on palpation.
- Acute incarceration of bowel or stomach—can cause vomiting, diarrhea, retching, bloating, pain, and acute collapse.

Congenital

- May not have clinical signs or develop clinical signs later in life.
- Referable to the

respiratory, cardiac, or gastrointestinal system.

- Difficulty breathing, muffled heart sounds, murmurs, and concurrent ventral abdominal wall defects—most common.
- Signs can be acute from strangulation of incarcerated bowel, liver, or spleen or rapid formation of pleural or pericardial effusion.

CAUSES & RISK FACTORS

Traumatic—lack of confinement and exposure to automobiles; any blunt trauma; roaming animals and male dogs at higher risk than others.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- See Dyspnea and Respiratory Distress
- See Panting and Tachypnea
- See Pleural Effusion

CBC/BIOCHEMISTRY/URINALYSIS

Non-specific changes due to ischemia or shock may be noted

IMAGING

- Standard two-view thoracic and abdominal radiography
- Horizontal beam radiography
- Ultrasonography
- Contrast radiography—upper gastrointestinal series or peritoneography
- CT sometimes needed

DIAGNOSTIC PROCEDURES

Thoracocentesis for pleural effusion.



TREATMENT

TRAUMATIC

- Inpatient—treat shock; improve ventilation and cardiac output; manage concurrent injury; stabilize patient before surgery.
- Surgery—early intervention indicated with persistent hypotension despite adequate fluid therapy, severe respiratory failure from excessive lung compression, severe liver failure secondary to organ entrapment, bowel rupture, or enlarging gas-filled bowel seen on radiographs; if patient cannot be stabilized, surgical repair will not necessarily improve cardiovascular and respiratory status.
- Intrathoracic gastric dilation—requires immediate decompression.

CONGENITAL

- Surgical repair—perform as early as possible to avoid adhesion formation and organ entrapment.
- Stabilize patients before surgery.



MEDICATIONS

DRUG(S)

Antiarhythmic agents—as indicated

CONTRAINdications/POSSIBLE INTERACTIONS

Take care when treating for shock with concurrent severe pulmonary contusion due to the risk for fluid overload; products such as hetastarch may be beneficial.



FOLLOW-UP

PATIENT MONITORING

Frequent or continuous electrocardiographic monitoring—advised; evaluate for postoperative arrhythmias.

POSSIBLE COMPLICATIONS

- Pneumothorax—may develop from excessive pressure on damaged lung tissue during anesthetic bagging or from failure to remove air from the chest cavity after diaphragmatic closure.
- Postoperative hyperthermia common in cats.
- Pulmonary edema—can develop from excessive fluid administration in the face of low oncotic pressure from blood loss, capillary permeability changes secondary to inflammation in response to pulmonary contusion, or lung reexpansion.

EXPECTED COURSE AND PROGNOSIS

Prognosis—always initially guarded; favorable after successful control of shock, elimination of any cardiac arrhythmias, successful surgery, and the lack of reexpansion pulmonary edema. Older cats with traumatic diaphragmatic hernia are less likely to survive surgical repair.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Congenital peritoneopericardial diaphragmatic hernias may be associated with other congenital midline defects, such as septal defects, cleft palates, umbilical hernias and abdominal wall defects.

ABBREVIATIONS

- CT = computed tomography
- PPDH = peritoneal pericardial diaphragmatic hernia

Suggested Reading

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DIARRHEA, ACUTE

D



BASICS

DEFINITION

Abrupt or recent onset of abnormally increased fecal water and/or solid content.

PATHOPHYSIOLOGY

- Caused by imbalance in the absorptive, secretory, and/or motility actions of the intestines.
- Mechanisms of diarrhea:
 - (1) Osmotic—excess molecules in the intestinal lumen draw in water, overwhelming the intestinal absorptive capacity (e.g., diet changes, malabsorption or overeating).
 - (2) Secretory—stimulation of small intestinal secretion that overwhelms the intestinal absorptive capacity (e.g., toxins). Stimulation of the parasympathetic nervous system or exposure to a variety of secretagogues can increase intestinal secretion.
 - (3) Exudative/permeability—leakage of tissue fluid, serum proteins, blood, or mucus from sites of infiltration or ulceration.
 - (4) Dysmotility—hypomotility (ileus) is more common than hypermotility. Hypermotility can be primary (irritable bowel syndrome) or secondary (obstruction, malabsorption leading to intestinal distention).
 - (5) Mixed.

SYSTEMS AFFECTED

- Cardiovascular—hypovolemia, tachycardia, pale mucous membranes, prolonged CRT and weak pulses; hypokalemia can cause arrhythmias.
- Endocrine/Metabolic—electrolyte and acid-base abnormalities, dehydration, and prerenal azotemia.
- Gastrointestinal—abdominal pain, hypokalemia can lead to decreased motility.
- Musculoskeletal—hypokalemia can lead to muscle weakness.

GENETICS

No genetic basis

INCIDENCE/PREVALENCE

Acute diarrhea is more common in younger animals and is more likely to resolve on its own. A fairly common problem, especially in dogs with dietary indiscretion.

GEOGRAPHIC DISTRIBUTION

Some infectious causes (e.g., salmon poisoning) may be regional.

SIGNALMENT

- Dogs and cats.
- Any animal can suffer from acute diarrhea; kittens and puppies are most frequently affected.

SIGNS

General Comments

- Acute diarrhea is usually self-limiting and is often isolated episode. Most animals with acute diarrhea are not affected systemically unless the animal has acute hemorrhagic diarrheal syndrome that can cause severe dehydration and hypovolemic shock.
- Sometimes an acute or peracute severe

disease, more common in dogs than cats (e.g., Parvovirus, *Clostridium perfringens*-associated acute hemorrhagic diarrheal syndrome).

- Signs of more severe illness (e.g., concurrent vomiting, abdominal pain, hematochezia, hemoptysis, severe dehydration, or lethargy) should prompt more aggressive diagnostic and therapeutic measures.

Historical Findings

- Increased fecal fluidity and/or volume and/or frequency of short duration.
- Owner may report fecal accidents, changes in fecal consistency and volume, blood or mucus in the feces, or straining to defecate.
- Owners may be able to report exposure to toxins, dietary changes, or dietary indiscretion.

Physical Examination Findings

- Varies with the disease severity.
- Dehydration or lethargy often present.
- Abdominal pain or discomfort, fever, signs of hypotension, nausea, and weakness may occur in more severely affected individuals.
- Rectal exam may reveal blood, mucous or altered consistency of stool.

CAUSES

- Systemic illness may also result in diarrhea as a secondary event.
- Dietary indiscretion—ingestion of garbage, non-food material, or spoiled food.
- Dietary changes—abrupt changes in amount or type of foodstuffs.
- Dietary intolerance—malassimilation of food, dietary hypersensitivity.
- Metabolic diseases—hypoadrenocorticism, liver disease, renal disease, and pancreatic disease can cause acute or chronic diarrhea.
- Obstruction—foreign bodies, intussusception, or intestinal/mesenteric volvulus.
- Idiopathic—hemorrhagic gastroenteritis.
- Viral—parvovirus, coronavirus, rotavirus, canine distemper virus.
- Bacterial—*Salmonella*, *Campylobacter*, *Clostridium* spp., *Escherichia coli*, etc.
- Parasitic—verminous (hookworms, ascarids, whipworms, and cestodes) or protozoal (*Giardia*, coccidia, *Tritrichomonas* and *Entamoeba*).
- Rickettsial—Salmon poisoning (*Neorickettsia*).
- Fungal—histoplasmosis.
- Drugs and toxins—heavy metals (e.g., lead), organophosphates, nonsteroidal anti-inflammatories, steroids, antimicrobials, antineoplastic agents, etc.

RISK FACTORS

Young dogs and cats present for diarrhea from dietary indiscretion, intussusception, foreign bodies, and infectious causes more often than older patients.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Patients should have a complete physical examination, fecal flotation, and assessment of their hydration status.
- Further diagnostic

tests depend on the extent of illness and other clinical signs.

CBC/BIOCHEMISTRY/URINALYSIS

- Generally normal; not necessary unless systemic involvement.
- Can see neutropenia with parvoviral enteritis and marked hemoconcentration with a discordant normal or low-normal plasma protein concentration with *C. perfringens* and *C. difficile*-associated hemorrhagic diarrhea.
- Electrolytes are commonly abnormal because of intestinal losses (hypokalemia, hypochloremia, hyponatremia).

OTHER LABORATORY TESTS

- Spec cPL (pancreatitis), TLI (EPI), cobalamin, and folate (altered absorption)—the latter are more commonly performed with chronic diarrhea.
- ELISA and IFA fecal testing is available for *Giardia* and *Cryptosporidium* spp.
- Diarrhea PCR panel—to evaluate for common specific infectious diseases (e.g., *Salmonella*, *Parvovirus*)

IMAGING

- Radiographs—generally not necessary in patients with mild illness.
- Abdominal radiographs can help identify or rule out intestinal foreign bodies or obstruction.
- More severe signs (e.g., abdominal pain or persistent vomiting) may increase the likely diagnostic benefit of abdominal imaging.
- Contrast abdominal radiography and ultrasonography may be useful with some patients, especially looking for an obstruction.

DIAGNOSTIC PROCEDURES

- Perform fecal flotation for parasites on all patients.
- Because helminth ova and *Giardia* cysts can be shed in low numbers or intermittently, multiple fecal analyses are recommended, and empiric treatment is advisable.
- The *Giardia* ELISA is a sensitive assay and should be combined with fecal flotation to increase the diagnostic yield of *Giardia* spp.
- Can perform fecal ELISA tests for parvovirus antigen in dogs.
- Endoscopy and biopsy—useful in select cases; more commonly needed in chronic diarrhea.

PATHOLOGIC FINDINGS

Dependent on etiology



TREATMENT

APPROPRIATE HEALTH CARE

Depends largely on the severity of illness; patients with mild illness can often be handled as outpatients with symptomatic therapy; patients with more-severe illness or that fail to respond to therapy should be treated more aggressively.

NURSING CARE

- Fluid therapy and correction of electrolyte imbalances is the mainstay of treatment in most cases.
- Can give crystalloid fluid

DIARRHEA, ACUTE

(CONTINUED)

D therapy (PO, SC or IV) as required. • Aim to return the patient to proper hydration status (over 12–24 hours) and replace ongoing losses. • Severe volume depletion can occur with acute diarrhea; aggressive fluid therapy may be necessary. • Use potassium supplementation (potassium chloride 20–40 mEq/L) in most patients, but not during shock fluid therapy. Hypokalemia can worsen ileus.

ACTIVITY

Animals should have limited activity until the diarrhea has stopped.

DIET

Patients with mild illness that are not vomiting can be managed with a fat-restricted, digestible intestinal diet, either homecooked (boiled rice and chicken in 4:1 ratio) or low-fat cottage cheese (1%) and rice or a commercial prescription intestinal diet.

CLIENT EDUCATION

- Limiting exposure to garbage, foods other than the patient's normal diet, and potential foreign bodies.
- Proper puppy and kitten vaccination and deworming schedules.

SURGICAL CONSIDERATIONS

Patients with obstructions may require surgery to evaluate the intestine and remove the foreign objects.



MEDICATIONS

DRUG(S) OF CHOICE

- Antidiarrheal drugs can be classified as motility-modifying drugs, antsecretory drugs, or intestinal protectants.
- Motility-modifying drugs generally operate by increasing segmental motility and thus increasing transit time (i.e. narcotic such as loperamide; 0.1 mg/kg PO q8–12h in dogs; 0.08 mg/kg PO q12h in cats) or by decreasing forward motility (i.e., anticholinergics); these medications are not necessary in mild disease, as it is generally self-limiting. Do not use these medications longer than 1–2 days because of adverse effects.
- Acute diarrhea that does not resolve with antidiarrheal drugs merits further investigation.
- Anthelmintics (e.g., fenbendazole 50 mg/kg PO q24h for 5 days) and antiprotozoal drugs (e.g., metronidazole 10–20 mg/kg PO q12h for 5 days) are recommended as empiric treatment for patients with acute diarrhea or those with positive fecal analyses. Can use coccidiostatic (e.g., sulfadimethoxine, ponazuril) drugs if fecal analysis warrants.
- Antibiotic therapy is unnecessary for most cases of mild illness and may actually exacerbate the diarrhea.
- Patients with bacterial enteritis, severe illness, concomitant leukopenia, or suspected breakdown of the gastrointestinal mucosal

barrier (as evidenced by blood in the feces) should be treated with antimicrobial agents.

- Probiotics may also be useful (*Lactobacillus*, *Enterococcus*). Probiotics have been shown to shorten the duration of acute, nonspecific diarrhea in some studies. Use probiotics from premium pet food companies in light of studies showing suboptimal quality of probiotics that have not undergone rigorous testing.

CONTRAINdications

- Anticholinergics in patients with suspected intestinal obstruction, glaucoma, or intestinal ileus.
- Narcotic analgesics—can cause CNS depression; undesirable in patients with more severe illness that are already depressed or lethargic.
- Narcotic analgesics in patients with liver disease and bacterial or toxic enteritis.

PRECAUTIONS

- Most cases of acute mild diarrhea resolve with minimal treatment; be cautious of excessive diagnostics and overtreating.
- Almost any drug can produce adverse effects (often including diarrhea and vomiting); these may be more severe than the initial problem.
- Cats can be sensitive to subsalicylates and should not be given high or frequent doses.

POSSIBLE INTERACTIONS

- Long term use of metronidazole can lead to neurologic complications.
- Some animals are sensitive to sulfa containing medications used for treatment of Coccidia.

ALTERNATIVE DRUG(S)

Kaolin pectin



FOLLOW-UP

PATIENT MONITORING

- Most acute diarrhea resolves within a few days.
- If clinical signs persist, additional diagnostics and treatments may be necessary.
- Upon completion of medication, recheck patients that exhibited parasites by fecal analysis.

PREVENTION/AVOIDANCE

- Animals should be fed a consistent high-quality diet.
- Owners should attempt to control indiscriminate eating and monitor for foreign body ingestion.

POSSIBLE COMPLICATIONS

- Intussusception is thought to be associated with increased intestinal motility.
- Monitor for this complication in patients with acute diarrhea, especially young dogs with parvoviral enteritis and parasitism.

EXPECTED COURSE AND PROGNOSIS

Most cases of acute diarrhea resolve spontaneously without treatment or with minimal treatment.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Acute vomiting commonly occurs concurrently with acute diarrhea.

AGE-RELATED FACTORS

- Young dogs and cats present for diarrhea from dietary indiscretion, intussusception, foreign bodies, and infectious causes more often than older patients.
- Younger and smaller animals are also more prone to dehydration and may require more-aggressive fluid therapy.

ZOONOTIC POTENTIAL

- *Campylobacter jejuni* is a zoonosis; however, most other *Campylobacter* spp. are non-pathogenic.
- Some strains of *Giardia* are zoonotic; however, this is uncommon.
- Parasitic larvae can cause visceral larval migrans (ascariids) and cutaneous larval migrans (hookworms) in humans, particularly children.

PREGNANCY/FERTILITY/BREEDING

Always be cautious using medication in pregnant animals.

SEE ALSO

- Diarrhea, Antibiotic Responsive
- Vomiting, Acute

ABBREVIATIONS

- CNS = central nervous system
- CPV = canine parvovirus
- CRT = capillary refill time
- ELISA = enzyme-linked immunosorbent assay
- EPI = exocrine pancreatic insufficiency
- Spec cPL = canine pancreatic lipase
- TLI = trypsin-like immunoreactivity

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Client Education Handout
available online

DIARRHEA, ANTIBIOTIC RESPONSIVE

D



BASICS

OVERVIEW

- Defined as antibiotic-responsive diarrhea without an identifiable underlying etiology.
- Antibiotic-responsive diarrhea was previously termed idiopathic (primary) small intestinal bacterial overgrowth (SIBO). This term is not used anymore as it was based on quantitative culture of bacteria in the upper GI tract which could not be confirmed by newer PCR-based methods. Secondary SIBO is a result of concurrent gastrointestinal diseases (e.g., exocrine pancreatic insufficiency).
- Current theories center on the possibility of immune dysregulation, possibly associated with abnormal CD4+ T-cells, IgA plasma cells, cytokine expression, and, in German shepherd dogs, mutations in pattern recognition receptors.

SIGNALMENT

Species

Dog

Breed Predilections

May be increased incidence in German shepherds, boxers, and Chinese Shar-peis.

Mean Age and Range

Recent studies show that the condition is more common in young dogs, with a median age of 2 years.

Predominant Sex

N/A

SIGNS

Historical Findings

- Small bowel signs—inappetence or anorexia, vomiting, weight loss, large-volume diarrhea.
- Large bowel signs—tenesmus, hematochezia, increased frequency of defecation.

Physical Examination Findings

Weight loss, poor body condition, borborygmus and flatulence may be detected; hematochezia may be present if there is large bowel involvement.

CAUSES & RISK FACTORS

- Genetic risk factors of mutations in pattern recognition genes (*TLR4* and *TLR5*) have been associated with the disease.
- Certain enteropathogenic bacteria (*Clostridium perfringens*, *E. coli*, and *Lawsonia intracellularis*) have been suspected but not proven to be etiologic agents.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Secondary SIBO
- EPI

- Parasitic infection
- IBD (including food-responsive diarrhea)
- Neoplasia

CBC/BIOCHEMISTRY/URINALYSIS

- Typically normal.
- Hypoalbuminemia is an uncommon finding.

OTHER LABORATORY TESTS

- Fecal examination for parasites should be performed.
- Serum cobalamin levels may be low and folate levels may be increased or decreased.
- Serum TLI levels (measured to rule out EPI) are normal.

IMAGING

Routine abdominal imaging (radiographs and ultrasound) should be performed to rule out other causes for diarrhea. Results of these tests are unremarkable in cases of ARD.

DIAGNOSTIC PROCEDURES

- There is no definitive test for the diagnosis of ARD other than resolution of gastrointestinal signs following antibiotic administration.
- Diagnosis depends upon ruling out all other causes for chronic diarrhea (especially food-responsive diarrhea) and a clinical response to an appropriate course of antibiotic therapy.



TREATMENT

- Hospitalization is generally not indicated and dogs may be managed on an outpatient basis.
- Restriction of physical activity is not indicated.
- The role of diet in ARD is unknown. Current recommendations are to feed a low-fat, highly digestible food or an elimination or hydrolyzed diet.



MEDICATIONS

DRUG(S)

- Several options for antibiotics are available:
 - Tylosin (5–10 mg/kg PO q24h); metronidazole (10–20 mg/kg PO q12h); oxytetracycline (10–20 mg/kg PO q8h).
 - In some cases, combination therapy may be necessary.
 - Antibiotic therapy should be administered for 4–6 weeks.
 - If serum cobalamin levels are decreased, cobalamin supplementation should be pursued. Dogs < 15 kg body weight: 500 µg parenteral cobalamin; dogs > 15 kg body weight: up to 1,500 µg parenteral cobalamin. Doses are given as subcutaneous injections once weekly for 6 weeks, then once every other week for 6 weeks. Serum

cobalamin levels should be reassessed at the end of therapy. Limited information is available regarding the effectiveness of oral cobalamin supplementation.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Oxytetracycline may cause staining of tooth enamel. Doses should be decreased in animals with hepatic or renal insufficiency. Oxytetracycline has been associated with a high incidence of bacterial transfer of resistance genes.
- Metronidazole undergoes extensive hepatic metabolism; dosages should be reduced in animals with hepatic insufficiency.



FOLLOW-UP

- Clinical resolution of diarrhea is the most important criterion.
- Weight gain may also be seen; hypoalbuminemia (if present) should resolve.
- Relapses usually occur when the antibiotics are discontinued. Many dogs can be maintained on very low doses of antibiotics long term, although long-term studies assessing antibiotic resistance are lacking.



MISCELLANEOUS

ABBREVIATIONS

- ARD = antibiotic responsive diarrhea
- EPI = exocrine pancreatic insufficiency
- IBD = inflammatory bowel disease
- SIBO = small intestinal bacterial overgrowth
- TLI = trypsin like immunoreactivity

Suggested Reading

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DIARRHEA, CHRONIC—CATS



BASICS

DEFINITION

- A change in the frequency, consistency, and volume of feces for more than 3 weeks or with a pattern of episodic recurrence.
- Can be either small bowel, large bowel, or mixed in origin.

PATHOPHYSIOLOGY

- High solute and fluid secretion—secretory diarrhea
- Low solute and fluid absorption—osmotic diarrhea
- High intestinal permeability
- Abnormal GI motility
- Many cases involve various combinations of these four basic pathophysiologic mechanisms for the development of diarrhea.

SYSTEMS AFFECTED

- Endocrine/Metabolic—fluid, electrolyte, and acid–base
- Exocrine • Gastrointestinal
- Lymphatic • Nutritional

SIGNALMENT

Cat

SIGNS

General Comments

- Underlying disease process determines extent of clinical signs.
- Normal feces is composed of about 68–75% water. As little as a 2–3% increase of water content results in poor stool quality and the gross description of diarrhea.
- Classification of small bowel and large bowel types of diarrhea is a convenient clinical tool but there is a significant overlap of these entities.

Historical Findings

Small Bowel

- Normal to increased volume
- Frequency of defecation—normal to moderately increased (2–4 times/day)
- Weight loss
- Normal to increased appetite (polyphagia)
- May be melena
- May have flatulence and borborygmus
- Vomiting—variable

Large Bowel

- Smaller volume.
- Frequency of defecation is moderately to markedly increased (> 4 times per day).
- Weight loss is less commonly seen.
- Often hematochezia and mucus.
- Tenesmus, urgency, dyschezia (painful defecation).
- Flatulence and borborygmus—variable.
- Vomiting—variable.

Physical Examination Findings

A complete physical examination, including rectal examination, auscultation and abdominal palpation is needed to assist in diagnosis of possible causes for diarrhea.

Small Bowel

- Poor body condition associated with malabsorption, maldigestion, and PLE.

- Variable dehydration.
- Abdominal palpation may reveal segmental or diffusely thickened small bowel loops associated with infiltrative disease, abdominal effusion, foreign body, neoplastic mass, intussusception, or enlarged mesenteric lymph nodes.
- Rectal palpation typically unremarkable.

Large Bowel

- Body condition is more typically unremarkable.
- Dehydration—uncommon.
- Abdominal palpation may reveal thickened large bowel, foreign body, neoplastic mass, intussusception, or enlarged mesocolic lymph nodes.
- Rectal palpation may reveal irregularity of the rectal mucosa, intraluminal or extraluminal rectal masses, rectal stricture, or sublumbar lymphadenopathy.

CAUSES

Small and Large Intestinal Diseases

Primary Disease

- Inflammatory bowel disease (e.g., lymphoplasmacytic enteritis, eosinophilic enteritis, granulomatous enteritis)
- Neoplasia (e.g., lymphoma, adenocarcinoma, mast cell neoplasia)
- Bacterial (e.g., *Salmonella* spp., enterotoxic *Escherichia coli*, other enterobacteriaceae species, *Clostridia* spp.)
- Viral (e.g., enteric corona virus, FIP, FeLV-associated, FIV-associated)
- Mycotic (e.g., histoplasmosis)
- Other (e.g., protothecosis, pythiosis)
- Parasites (e.g., *Giardia*, *Toxocara* spp., *Ancylostoma*, *Toxascaris leonina*, *Cryptosporidium* spp., *Cystoisospora* spp., *Tritrichomonas foetus*)
- Partial obstruction (e.g., foreign body, intussusception, neoplasia)
- Secondary lymphangiectasia
- Small intestinal bacterial overgrowth, intestinal microbial dysbiosis
- Short bowel syndrome
- Villous atrophy
- Duodenal ulcers

Maldigestion

- Hepatobiliary disease—lack of bile salts needed for intraluminal digestion.
- Exocrine pancreatic insufficiency

Dietary

- Dietary intolerance (food-responsive diarrhea)
- Food allergy
- Rapid diet change

Metabolic Disorders

- Hyperthyroidism
- Cobalamin deficiency
- Renal disease—uremia
- Hepatobiliary disease—liver failure
- Toxins (e.g., enterotoxins, aflatoxins, food poisoning)
- Adverse drug reactions

Congenital Anomalies

- Short colon
- Portosystemic shunt
- Persistent pancreaticomesojejunal ligament

RISK FACTORS

Dietary changes, feeding poorly digestible or high-fat diets



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

First localize the origin of the diarrhea to the small or large bowel (or both) on the basis of historical signs.

CBC/BIOCHEMISTRY/URINALYSIS

- Eosinophilia in some cats with parasitism, eosinophilic enterocolitis, hypereosinophilic syndrome, or mast cell tumor.
- Macrocytosis in some cats with hyperthyroidism or FeLV infection.
- Anemia that is variably regenerative and has microcytosis suggests chronic GI bleeding and iron deficiency.
- Leukopenia in some cats with FeLV or FIV infection.
- Panhypoproteinemia caused by protein-losing enteropathy is uncommon in cats with intestinal disease but can occur. Hypoalbuminemia can be seen.
- Biochemical profiles, hormonal assays, serum bile acid panel, and urinalysis abnormalities may suggest renal disease, hypoproteinemia, hepatobiliary disease, or endocrinopathy.

OTHER LABORATORY TESTS

Fecal and/or Rectal Scraping Exam

- Direct wet prep, routine centrifugation fecal flotation, fecal ELISA testing may indicate GI parasites.
- Cytologic examination of rectal scrapings may reveal specific organisms, such as *Histoplasma* or rare *Prototheca*.
- PCR fecal testing should be interpreted with caution because positive results for toxin genes or infectious agents may or may not correlate with clinical disease. Interpret PCR results in light of patient signalment, history, clinical presentation, vaccination history and other laboratory data.
- Culture feces if *Salmonella* is suspected—special media required.

Thyroid Function Tests

- High total T₄ or free T₄ concentration indicates hyperthyroidism.
- If hyperthyroidism is suspected but the T₄ is normal, perform a T₃ suppression test, repeat the T₄ a few months later, or perform a technetium scan of the thyroid glands.

Serologic Testing

Test for FeLV and FIV—especially if hematologic abnormalities are present.

Test for Exocrine Pancreatic Function

Feline-specific TLI—test of choice for diagnosis of EPI.

IMAGING

- Survey abdominal radiography may indicate intestinal obstruction, abnormal intestinal pattern, organomegaly, mass, foreign body, pancreatic disease, hepatobiliary disease, urinary disease, or abdominal effusion. Low yield in most cats with chronic diarrhea.

(CONTINUED)

- Contrast radiography (upper GI series or barium enema) may indicate bowel wall thickening, intestinal ulcers, mucosal irregularities, mass, radiolucent foreign body, or stricture. Procedure is performed infrequently in cats in light of advantages of abdominal ultrasonography. • Abdominal ultrasonography may demonstrate bowel wall thickening, abnormal bowel wall layering, GI or extra-GI masses, intussusception, foreign body, ileus, abdominal effusion, hepatobiliary disease, renal disease, or mesenteric or mesocolic lymphadenopathy. Abdominal sonography is used in conjunction with abdominal radiography.

DIAGNOSTIC PROCEDURES

- If malabsorptive (EPI), metabolic, parasitic, dietary, and infectious causes have been excluded, consider empiric dietary therapy utilizing an elimination diet for 2 weeks before performing endoscopy and biopsy or a laparotomy for definitive diagnosis. Consider PCR on intestinal biopsies (fluorescent in situ hybridization; FISH) to rule out infectious enteropathies with neutrophilic or granulomatous enteropathies.

Endoscopy/Laparoscopy

- Upper GI flexible endoscopy allows examination and biopsy of the gastric and duodenal mucosa; always obtain multiple (8–10) mucosal specimens from each segment/area. • Flexible colonoscopy allows examination of the entire rectum, colon, cecum; rigid coloproctoscopy limits examination to the descending colon and rectum and is done less frequently due to its limitation; always obtain multiple mucosal specimens (8–10) from each segment.
- Visual impressions of gastrointestinal mucosal detail may not reflect histopathologic changes; always take biopsies. • Endoscopic biopsies rely upon infiltrative and inflammatory diseases being represented in the first two layers of the intestinal wall, and the segments biopsied being representative of the disease process. • Full thickness biopsies can be obtained via laparoscopy from one or more segments of small intestine (not large intestine) via exteriorization of the segment(s).

Surgical Biopsy

A surgical approach is beneficial if biopsies of multiple organs (small intestine, lymph nodes, stomach, pancreas, liver) are desired.

Ultrasound-Guided GI Aspiration or Biopsy

- Can perform ultrasound-guided fine-needle aspiration on most GI lesions that present as reasonable targets but cytologic interpretation accuracy is subject to sample quality, expertise, and limitations of the technique
- Ultrasound guided microcore (true-cut) biopsy on non-cavitated lesions > 2 cm in diameter are performed less frequently.

- Paracentesis of peritoneal fluid for fluid analysis, culture, and cytology is recommended. • Concern has been expressed for risk of translocation of cancer cells or infective organisms with these procedures.



TREATMENT

APPROPRIATE HEALTH CARE

- Treat the underlying cause—Administration of an elimination diet (intact protein source or hydrolyzed protein) will resolve diarrhea in approximately 40–60% of cats with chronic enteropathies. Response should be detected within 2–3 weeks following dietary implementation. • Complete resolution of signs is not always possible in cats with IBD, neoplasia, or fungal disease despite proper treatment. Measurement of serum cobalamin is important in all cats with chronic enteropathies. Supplementation with cyanocobalamin at 250 µg SC per cat on a weekly basis for 6 consecutive weeks followed by every 3 weeks for the indefinite future.
- Repeated changes of diet that are made in order to maintain a symptom-free situation suggests that further testing is needed.

NURSING CARE

- Give fluid therapy with balanced electrolyte solution. • Correct electrolyte and acid-base imbalances.

SURGICAL CONSIDERATIONS

Pursue exploratory laparotomy and surgical biopsy if there is evidence of obstruction, an intestinal mass, mid-small bowel disease unreachable via ultrasound-guided procedure, or if a diagnosis based on endoscopic biopsy or ultrasound-guided procedure is questioned because of poor response to therapy.



MEDICATIONS

DRUG(S) OF CHOICE

- Disease-specific.
- Prednisolone or budesonide for management of IBD. Chlorambucil should be considered with prednisolone for management of small cell intestinal lymphoma.
- Cyanocobalamin.
- Probiotics can be beneficial in some patients with chronic nonspecific diarrhea.

CONTRAINdicATIONS

Anticholinergics exacerbate most types of chronic diarrhea and should not be used for empirical treatment.

PRECAUTIONS

Opiate antidiarrheals such as diphenoxylate and loperamide can cause hyperactivity and respiratory depression in cats and should not be used for more than 3 days.

DIARRHEA, CHRONIC—CATS



FOLLOW-UP

PATIENT MONITORING

- Assess changes in frequency and severity of diarrhea and body weight. • Resolution usually occurs within 2–3 weeks following successful implementation of dietary therapy, consider re-evaluating the diagnosis if diarrhea does not resolve.

D

POSSIBLE COMPLICATIONS

- Dehydration. • Lowered body condition.
- Abdominal effusions as related to specific cause of chronic diarrhea.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Toxoplasmosis • Giardiasis (low zoonotic potential) • Cryptosporidiosis • Salmonellosis • *Campylobacter jejuni*

SEE ALSO

Under "Causes"

ABBREVIATIONS

- B₁₂ = vitamin B₁₂, cobalamin • ELISA = enzyme-linked immunosorbent assay • EPI = exocrine pancreatic insufficiency • FeLV = feline leukemia virus • FIP = feline infectious peritonitis • FIV = feline immunodeficiency virus • GI = gastrointestinal • PCR = polymerase chain reaction • PLE = protein-losing enteropathy • TLI = trypsin-like immunoreactivity • TSH = thyroid stimulating hormone

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Author Mark E. Hitt

Consulting Editor Stanley L. Marks



Client Education Handout
available online

DIARRHEA, CHRONIC—DOGS



BASICS

DEFINITION

- A change in the frequency, consistency, and volume of feces for more than 3 weeks.
- Can be small bowel, large bowel, or mixed.

PATHOPHYSIOLOGY

- Secretory diarrhea • Osmotic diarrhea
- Increased permeability • Abnormal GI motility • Many cases involve combinations of these pathophysiologic mechanisms.

SYSTEMS AFFECTED

- Endocrine/Metabolic • Exocrine • Fluid Balance • Gastrointestinal • Lymphatic

SIGNALMENT

Dog

SIGNS

General Comments

- Disease processes determines extent of clinical signs.
- Normal feces is composed of about 68–75% water. A 2–3% increase of water content results in gross description of diarrhea.
- Classification of small, large and mixed bowel types of diarrhea may also have overlap of descriptive findings.

Historical Findings

Small Bowel

Can include:

- Normal to increased volume • Normal to moderately increased (2–4 times/day) defecation frequency • Weight loss
- Polyphagia • May be melena • No tenesmus or dyschezia (excepting irritation) • May be flatulence and borborygmus • Vomiting—variable

Large Bowel

- Smaller volume • Frequency of defecation is increased (> 4 times/day) • Typically little to no weight loss • Often hematochezia and mucus • Tenesmus, urgency, dyschezia
- Flatulence and borborygmus—variable
- Vomiting—variable

Physical Examination Findings

A complete physical examination, including rectal examination, auscultation, and abdominal palpation is needed to assist in diagnosis of possible causes for diarrhea.

Small Bowel

- Poor body condition associated with malabsorption, maldigestion, and PLE.
- Variable dehydration. • Abdominal palpation may reveal thickened small bowel loops (diffuse or segmental) associated with infiltrative disease, abdominal effusion, foreign body, neoplastic mass, intussusception, or enlarged mesenteric lymph nodes. • Rectal palpation typically unremarkable.

Large Bowel

- Body condition is more typically normal.
- Dehydration—uncommon. • Abdominal

palpation may reveal thickened large bowel, foreign body, neoplastic mass, intussusception, or enlarged mesocolic lymph nodes. • Rectal palpation may reveal irregularity of the colorectal mucosa, intraluminal or extraluminal rectal masses, rectal stricture, or sublumbar lymphadenopathy.

CAUSES

Small Bowel

Primary Small Intestinal Disease

- Inflammatory bowel disease (e.g., lymphoplasmacytic enteritis, eosinophilic enteritis, granulomatous segmental enteritis, immunoproliferative enteropathy of Basenjis)
- Primary or secondary lymphangiectasia
- Neoplasia • Bacterial (*Campylobacter jejuni*, *Salmonella* spp., invasive adherent or enterotoxic *Escherichia coli*, other enterobacteriaceae species) • Viral (e.g., coronavirus, parvoviruses, distemper virus, rotavirus) • Mycotic (e.g., histoplasmosis, aspergillosis) • Other (e.g., protothecosis, pythiosis) • Parasites (e.g., *Giardia*, *Toxocara* spp., *Ancylostoma*, *Toxascaris leonina*, *Cryptosporidium* spp., *Cystoisospora* spp.)
- Other (e.g., pythiosis) • Partial obstruction (e.g., foreign body, intussusception, and neoplasia) • Antibiotic-responsive diarrhea (ARD) (intestinal microbial dysbiosis) • Short bowel syndrome

Maldigestion

- Exocrine pancreatic insufficiency
- Hepatobiliary disease—lack of intraluminal bile

Dietary

- Food-responsive enteropathy. • Food allergy. • Gluten-sensitive enteropathy.
- Rapid diet change.

Metabolic Disorders

- Hepatobiliary disease
- Hypoadrenocorticism • Uremic gastroenteritis • Toxins—enterotoxins, aflatoxins, exotoxins, food poisoning
- Adverse drug reactions

Large Bowel

Primary Large Intestinal Disease

- Inflammatory bowel disease (e.g., lymphoplasmacytic colitis, eosinophilic colitis, histiocytic ulcerative colitis)
- Neoplasia • Infection (e.g., histoplasmosis, *Clostridium perfringens* and *C. difficile*, enteropathic adherent invasive *E. coli*, *Campylobacter jejuni*, *Prototheca*, and pythiosis) • Parasites (e.g., *Trichuris vulpis*, *Entamoeba histolytica*, and *Balantidium coli*) • Ileocolic intussusception and cecal inversion

Dietary

- Diet—dietary indiscretion, diet changes, food-responsive enteropathy, and foreign material (e.g., bones, plastic, wood, hair) • Fiber-responsive large bowel diarrhea

Miscellaneous

Irritable bowel syndrome

RISK FACTORS

Small Bowel

- Dietary changes, feeding poorly digestible or high-fat diets.
- Large-breed dogs, especially German shepherds, have the highest incidence of antibiotic-responsive diarrhea (ARD).
- Large-breed dogs have a higher risk of intestinal volvulus/torsion; may be seen in association with EPI.
- Pythiosis occurs most often in young, large-breed dogs living in rural areas with a higher incidence bordering the Gulf of Mexico.

Large Bowel

- Dietary changes or indiscretion, stress, and psychological factors may play a role.
- Histiocytic ulcerative colitis (invasive adherent *Escherichia coli*-associated)—boxers, French bulldogs < 3 years old.
- Pythiosis is more common in large-breed dogs that spend more time outside (roaming, hunting).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

First localize the origin to the small or large bowel (or both).

CBC/BIOCHEMISTRY/URINALYSIS

- Eosinophilia may be associated with parasitism, eosinophilic enterocolitis, hypoadrenocorticism, paraneoplastic causes, or pythiosis.
- Lymphopenia and hypocholesterolemia may be associated with lymphangiectasia.
- Anemia and microcytosis suggest chronic GI bleeding and iron deficiency.
- Panhypoproteinemia resulting from PLE is associated with infiltrative small bowel disorders and lymphangiectasia.
- Biochemical profiles, hormonal assays, serum bile acid panel, and urinalysis abnormalities may suggest renal disease, hepatobiliary disease, or endocrinopathy.

OTHER LABORATORY TESTS

Fecal and/or Rectal Scraping Exam

- Direct wet-prep examination, fecal ELISA testing, and zinc sulfate centrifugation (for *Giardia*) may indicate GI parasites. Multiple samples may be required for whipworm infestations.
- Cytologic examination of rectal scrapings may reveal specific organisms, such as *Histoplasma* or *Prototheca*.
- PCR fecal testing can be helpful when screening for uncommon or difficult to diagnose infections; interpret with caution as many of the microorganisms can be found in healthy, non-diarrheic animals (e.g., viral enteritis, cryptosporidiosis, Giardia, *Salmonella*, *C. perfringens* enterotoxin gene, *C. difficile*, *Campylobacter jejuni*). PCR testing should be interpreted in light of patient signalment, history, clinical presentation, vaccination history and other laboratory data.
- Culture feces if *Campylobacter* or *Salmonella* is

(CONTINUED)

DIARRHEA, CHRONIC—DOGS

D

suspected—special media required; check with your laboratory prior to submission.

Tests of Exocrine Pancreatic Function

Canine-specific TLI—test of choice for confirming EPI.

Tests for Malabsorption

- Serum folate—low serum folate may be associated with jejunal malabsorption; elevated folate may occur due to small intestinal bacterial overgrowth.
- Cobalamin (B_{12})—low serum B_{12} may be associated with EPI or ileal malabsorption; primary cobalamin deficiency syndromes are rare.

Tests for Metabolic Disease

- Resting cortisol—a value $< 2.0 \mu\text{g/dL}$ should be followed up with ACTH stimulation test to evaluate for hypoadrenocorticism.
- Fasting and 2-hour post-prandial serum bile acids—test if hepatobiliary disease is suspected; significantly increased values suggest hepatic dysfunction or portosystemic shunting.

IMAGING

- Survey abdominal radiography may indicate intestinal obstruction, abnormal intestinal pattern, organomegaly, mass, foreign body, pancreatic disease, hepatobiliary disease, urinary disease, or abdominal effusion.
- Contrast radiography (upper GI series or barium enema) may indicate bowel wall thickening, intestinal ulcers, mucosal irregularities, mass, radiolucent foreign body, or stricture. Utility of contrast radiography has been replaced with ultrasound in most patients.
- Abdominal ultrasonography may demonstrate bowel wall thickening, abnormal bowel wall layering, GI or extra-GI masses, intussusception, foreign body, ileus, abdominal effusion, hepatobiliary disease, or mesenteric or mesocolic lymphadenopathy.

DIAGNOSTIC PROCEDURES

If maldigestive (EPI), metabolic, parasitic, dietary, and infectious causes have been excluded, then consider a dietary trial using an elimination diet (novel, single protein source) for 2 weeks in stable dogs prior to performing advanced diagnostics (endoscopy or laparotomy and biopsy).

Endoscopy/Laparoscopy

- Upper GI flexible endoscopy allows examination and biopsy of the gastric and duodenal mucosa; always obtain multiple (8–10) mucosal specimens from each segment.
- Flexible colonoscopy allows examination of the rectum, colon, cecum, and variably ileum; always obtain multiple mucosal specimens (8–10) from each segment.
- The gross appearance of the mucosa does not always correlate with histopathology. Always take biopsies.
- Endoscopic biopsies rely upon diseases being represented in the first two layers of the intestinal wall and the segments biopsied being representative of others not reached.

- Full thickness biopsies can be obtained via laparoscopy from one or more segments of small intestine (not large intestine) via enlargement of puncture site and exteriorization of the segment(s) using punch biopsy(s) and sutures.

Surgical Biopsy

- Full-thickness biopsies can be obtained from clearly visualized segments/locations of the intestinal tract.
- A surgical approach can be the most advantageous/pragmatic approach if biopsies of multiple organs (e.g., small intestine, lymph nodes, stomach, pancreas, liver) are desired with the ability to correct abnormal findings.

Ultrasound-Guided GI Aspirates

- Ultrasound-guided fine-needle aspiration of GI mass lesions can be helpful for diagnosing mast cell tumors, carcinomas, and large-cell lymphoma.
- Seeding of neoplastic cells is a concern.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Treat the underlying cause symptomatic or empirical therapy with elimination diets can be beneficial in 40–60% of dogs with uncomplicated chronic enteropathies.
- Complete resolution of signs is not always possible in dogs with severe IBD, lymphangiectasia, intestinal neoplasia, and pythiosis.
- Feeding lower-fat, novel (for the patient) protein and carbohydrate source, highly digestible, or fiber supplemented diets for 3–4 weeks may resolve diarrhea that is due to dietary intolerance or allergy. Repeated changes of diet to maintain a symptom-free situation suggests further testing is needed.

NURSING CARE

- Fluid therapy with balanced electrolyte solutions as needed.
- Consider colloids for hypoproteinemic patients requiring fluid therapy.
- Correct electrolyte and acid-base imbalances.

SURGICAL CONSIDERATIONS

Pursue laparotomy and biopsy if there is evidence of obstruction, intestinal mass, or mid-small bowel disease unreachable via ultrasound-guided procedure or if a diagnosis based on endoscopic biopsy or ultrasound-guided procedure is questioned because of poor response to therapy.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Disease-specific.
- Prednisone and budesonide for IBD.
- Cyclosporine or Azathioprine as adjunctive therapy with corticosteroids for dogs with refractory IBD.

- The need for cyanocobalamin supplementation must be assessed in all dogs with chronic enteropathy.
- Tylosin or metronidazole for dogs with antibiotic-responsive enteropathy.
- Probiotics are beneficial in some dogs with chronic enteropathy.

CONTRAINDICATIONS

Anticholinergics can exacerbate the situation with many causes of chronic diarrhea; they are sometimes used to relieve cramping associated with irritable bowel syndrome.

**FOLLOW-UP****PATIENT MONITORING**

- Frequency and consistency of the stool, appetite, and body weight.
- In dogs with PLE—serum proteins, cholesterol and clinical signs (ascites, subcutaneous edema, pleural effusion).
- Resolution of diarrhea is usually gradual with treatment; if it does not resolve reevaluate the diagnosis.

POSSIBLE COMPLICATIONS

- Dehydration.
- Lowered body condition.
- Abdominal effusions as related to specific cause of chronic diarrhea.
- Ascites, subcutaneous edema and/or pleural effusion with hypoalbuminemia from PLEs.

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

- Giardiasis (low risk of transmission)
- Salmonellosis • *Campylobacter jejuni*
- Ascaridiasis

SEE ALSO

Under "Causes"

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone
- B_{12} = vitamin B_{12} , cobalamin
- CT = computed tomography
- ELISA = enzyme-linked immunosorbent assay
- EPI = exocrine pancreatic insufficiency
- GI = gastrointestinal
- PCR = polymerase chain reaction
- PLE = protein-losing enteropathy
- TLI = trypsin-like immunoreactivity

Suggested Reading

Willard MD, Mansell J, Fosgate GT, et al. Effect of sample quality on the sensitivity of endoscopic biopsy for detecting gastric and duodenal lesions in dogs and cats. *J Vet Intern Med* 2008; 22(5):1084–1089.

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DIGOXIN TOXICITY



BASICS

OVERVIEW

Not uncommon because of digoxin's narrow therapeutic index and prevalence of renal impairment in elderly patients with cardiac disease.

SIGNALMENT

- Dog and cat
- More common in geriatric patients

SIGNS

Historical Findings

- Anorexia
- Vomiting
- Diarrhea
- Lethargy
- Depression

Physical Examination Findings

Heart rate may range from severe bradycardia to severe tachycardia.

CAUSES & RISK FACTORS

- Renal disease—impairs digoxin elimination.
- Chronic pulmonary disease—results in hypoxia and acid-base disturbances.
- Obesity—if dosage not calculated on lean body weight.
- Hypokalemia, hypercalcemia, hypomagnesemia, and hypoxia predispose to arrhythmias.
- Drugs and conditions that alter digoxin metabolism or elimination (e.g., quinidine and hypothyroidism).
- Rapid IV digitalization.
- Overdosage or accidental ingestion of owner's medication.
- Administration of diuretic leading to hypokalemia.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Arrhythmias and conduction disturbances—may reflect structural heart disease, not digoxin toxicity.
- Anorexia—common in animals with heart failure.

CBC/BIOCHEMISTRY/URINALYSIS

Animals with hypokalemia, hypercalcemia, hypomagnesemia, and renal failure are predisposed to toxicity.

OTHER LABORATORY TESTS

- Consider checking thyroid status.
- Obtain digoxin serum concentration 8–10 hours after an oral dose—therapeutic

range is 0.5–1.5 ng/mL. A recent study in humans found digoxin levels greater than 1 mg/ml were associated with increased mortality; not all patients with concentrations > 1.5 ng/mL have signs of toxicity; some with values in the normal range have signs of toxicity, especially if hypokalemic. To minimize the risk of toxicity, I aim to achieve a digoxin level between 0.5 and 1 ng/mL.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

- Conduction disturbances—AV block, arrhythmias, and ST segment depression in some patients.
- Digoxin can cause any arrhythmia.



TREATMENT

- Discontinue digoxin until signs of toxicity resolve (24–72 hours); reevaluate need for the medication; if necessary, resume treatment at a dosage based on the serum digoxin concentration.
- Maintain hydration and correct any electrolyte disturbance (especially hypokalemia) with parenteral fluid administration.
- Discontinue drugs that slow digoxin metabolism or elimination (e.g., quinidine, verapamil, amiodarone).
- Severe arrhythmias (ventricular tachycardia) and conduction disturbances—can be life-threatening; require hospitalization for treatment and monitoring.



MEDICATIONS

DRUG(S)

- Treat clinically important bradyarrhythmias with atropine or a temporary transvenous pacemaker.
- Treat clinically important ventricular arrhythmias with lidocaine or phenytoin; phenytoin also reverses high-degree AV block.
- Digoxin-binding antibodies (e.g., Digibind) rapidly drop digoxin concentration in critically ill animals; the use of these products is limited in veterinary practice by their exorbitant cost.
- Thyroxin supplementation if hypothyroidism confirmed.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Avoid or discontinue drugs that slow digoxin elimination or metabolism (e.g., quinidine, verapamil, and diltiazem).
- Avoid drugs that could worsen conduction disturbances (e.g., beta-blockers and calcium channel blockers).
- Class 1A antiarrhythmic drugs (e.g., quinidine and procainamide) may worsen AV block.



FOLLOW-UP

- Monitor renal function and electrolytes frequently in patients receiving digoxin; lower digoxin dose if renal disease develops.
- Monitor serum digoxin concentration periodically.
- Monitor ECG periodically to assess for arrhythmias or conduction disturbances that may suggest digoxin toxicity.
- Monitor body weight frequently; alter digoxin dosage accordingly; patients with congestive heart failure often lose weight.



MISCELLANEOUS

SEE ALSO

- Atrioventricular Block, Complete (Third Degree)
- Atrioventricular Block, First Degree
- Atrioventricular Block, Second Degree—Mobitz I
- Atrioventricular Block, Second Degree—Mobitz II
- Ventricular Tachycardia

ABBREVIATIONS

- AV = atrioventricular
- ECG = electrocardiogram

Suggested Reading

Teerlink JR, Gersh BJ, Opie LH, Heart Failure. In: Opie LH, Gersh BJ, eds., Drugs for the Heart: 8th ed. Philadelphia: Elsevier Saunders, 2013, pp. 169–223.

Author Francis W.K. Smith, Jr.

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DIISOCYANATE GLUE (GORILLA GLUE) TOXICOSIS



BASICS

OVERVIEW

- Diisocyanate wood glue rapidly expands in the moist environment of the stomach causing bloat and foreign body obstruction. The glue is not absorbed and does not cause a systemic toxicity. Ingestions as small as 2 ounces (56 g) can require surgical intervention to resolve obstruction. Glue is also adhesive and an irritant to the paws, oral cavity, and stomach lining.
- Gorilla Glue is just one brand name. There are non-gorilla brand glue types that contain diisocyanate as the active ingredient and not all types of Gorilla Glue contain it. Confirm the actual product with the owner, using the packaging if necessary.
- Typically the owner finds a chewed bottle of glue and/or glue on the animal.

SIGNALMENT

Dogs and less commonly cats, birds, and small mammals. Young animals are more commonly affected.

SIGNS

- Ingestion: Lethargy, vomiting, hematemesis, abdominal distension, abdominal pain, anorexia, drooling.
- Inhalation: Coughing, sneezing, and increased secretions within 4–8 hours.
- Dermal: Irritation, redness, and rash.

CAUSES & RISK FACTORS

Pets with access to glue bottle.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

History of exposure and clinical signs generally facilitate diagnosis. Presenting signs are consistent with GDV, bloat, pancreatitis,

inflammatory bowel disease and other causes of foreign body obstruction. Radiographs are highly suggestive (see Web Figure 1).

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis—Inflammation.
- Elevated total proteins/prerenal azotemia—if pet is dehydrated due to vomiting or unable to eat and drink.
- Electrolyte disturbances—consistent with GI obstruction and anorexia.

IMAGING

Survey radiographs—Glue will appear as a mottled gas and soft tissue opacity distending the stomach. The appearance can resemble recent food ingestion (see Web Figure 1).



TREATMENT

- Emesis only if immediately after the ingestion. Gastric lavage rarely of benefit as glue expands rapidly.
- Stabilize patient with IV fluids as needed.
- Surgically remove the expanded glue foreign body.
- Wash exposed skin with warm soapy water, rub vegetable oil into the hair or clip hair to remove as much glue as possible. Glue can be left adhered to the skin if non-irritating and will fall off over time.



MEDICATIONS

- Antiemetic—Maropitant citrate 1 mg/kg SC q24h.
- H2 Blocker—to aid in the healing of gastric inflammation or ulceration. Famotidine 0.5 mg/kg PO or SQ BID.
- Sucralfate: If a gastric ulcer is present, 0.5–1 g PO TID on an empty stomach.

CONTRAINdications

- Emetics—emesis should not be performed unless done immediately after a witnessed ingestion. Expansion of the glue is rapid, late emesis stresses the stomach wall and could damage the esophagus.
- Do not dilute with water as exposure to moisture leads to rapid expansion of the glue.



FOLLOW-UP

PATIENT MONITORING

Monitor in hospital until eating and drinking normally. Recheck 10–14 days post surgery.

PREVENTION/AVOIDANCE

Prevent exposure.

EXPECTED COURSE AND PROGNOSIS

With removal of obstructive foreign body, prognosis is excellent. Without surgical removal the foreign body is not expected to resolve on its own.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Gastritis
- Dermatitis

ABBREVIATION

GDV = gastric dilatation-volvulus

Suggested Reading

Horstman CL, Eubig PA, Cornell KK, et al. Gastric outflow obstruction after ingestion of wood glue in a dog. J Am Anim Hosp Assoc 2003;39:47–51.

Author Catherine A. Angle

Consulting Editor Lynn R. Hovda



**Client Education Handout
available online**

DIOCTOPHYMA RENALE (GIANT KIDNEY WORM)



BASICS

OVERVIEW

- In dogs, adult female *D. renale* are significantly larger than males, reaching up to 100 cm in length and 1.2 cm in width. In contrast, males are only 20–40 cm in length and 6 mm in width.
- Adult male and female *D. renale* are typically blood red in color when they are alive but become brownish-black after they die and degenerate. The characteristic red color may be associated with a hemoglobin-like blood pigment (erythrocytokeratin).
- The eggs are lemon-shaped and constant in size. They have a light tan or rust color with deep pits in their shells except at the poles, which contain opercula. A typical female *D. renale* has been estimated to produce approximately 18–20 million eggs in its lifetime. The eggs may remain viable for up to 5 years. Desiccation and freezing temperatures are lethal to infective eggs of *D. renale*.
- Free-living annelids (*Lumbriculus variegatus*) are essential intermediate hosts. *Lumbriculus* spp. (aka blackworms and mudworms) are phylogenetically related to the earthworm. They can be readily found in Europe, North America, and South America. They often inhabit shallow water of the edges of ponds, lakes, and marshes where they feed on decaying vegetation and microorganisms. Any mammal that drinks water containing infected annelids has the potential of ingesting the infective third stage of *D. renale*.

EPIDEMIOLOGY

Cases of *D. renale* have been encountered in virtually every part of the world with a temperate climate. In North America, cases have frequently been encountered in Mississippi, Louisiana, Minnesota, Wisconsin, Michigan, and the central and eastern provinces of Canada. The giant kidney worm has been reported in many species of animals, including dogs, mink, coyotes, jackals, raccoons, foxes, wolves, beech martens, pine martens, otters, and weasels. Humans are accidental hosts; because of the aquatic portion of its life cycle, water is an essential element of the habitat of *D. renale*. Therefore it is not surprising that semiaquatic fish-eating mammals are the most common definitive hosts of *D. renale*. Fish and frogs often serve as paratenic hosts for this parasite. Mink are the most commonly infected mustelids, and are the principal definitive host in North America.

LIFE CYCLE

- To complete the life cycle, both males and females must be located in the same kidney of the host, and the urinary tract must be patent. Fertile eggs are passed with urine voided by

the host, and then embryonate in water. After 1–7 months, they produce first-stage larvae. The rate of their development is dependent on the temperature of the water. The optimal temperature for eggs to embryonate is 25–30°C. The eggs hatch only after being swallowed by the intermediate host, *L. variegatus*. This annelid is the only intermediate host needed to complete the life cycle. A period of ≥ 100 days in *L. variegatus* is required for the second and third (infective) stage of the parasite to develop. The definitive host becomes infected by ingesting the infective larvae in annelids.

- Paratenic hosts may also become a part of the life cycle. In the United States, frogs and northern black bullheads are paratenic hosts. The larvae encyst in the liver, mesentery, stomach wall, or abdominal muscles of the paratenic hosts.

• The definitive host becomes infected by ingesting raw fish, frogs, other paratenic hosts, or by ingesting *L. variegatus*. After being swallowed by the definitive host, the infective larvae penetrate the walls of the stomach or intestines and migrate to the submucosa. After approximately 5–7 days, they migrate to the liver and remain there for about 50 days. Migration to the right or the left kidney and invasion of the renal pelvis follows.

• *D. renale* have been found more frequently in the right kidney than in the left. The predilection for the right kidney has been attributed to the close anatomic relationship of the right kidney to the duodenum. According to some investigators, adult *D. renale* are found in the left renal pelvis when they penetrate the stomach at the greater curvature. Finding encysted *D. renale* around the liver is associated with larval penetration at the lesser curvature of the stomach. On occasion, *D. renale* have been encountered in the urinary bladder and/or ureter. The highest number of adults found in one dog is 34. The time required for infective larvae to become mature gravid females in the definitive host is 3.5–6 months. The entire life cycle requires approximately 2 years.

PATHOPHYSIOLOGY

Kidney

• Adult parasites have attained substantial size by the time they penetrate the kidney. The exact mechanisms involved with gaining access to the renal pelvis have not been reported. Entry of the parasite into the kidney probably results from the effects of enzymes released by the parasite. Potent collagenases, hyaluronidases, and cysteine proteases released by nematodes can easily digest host tissues. Glands containing these enzymes may be located adjacent to the esophagus.

• Available evidence does not support the theory that adult *D. renale* slowly devour the renal tissue of the host, reducing it to a hollow sack. The buccal cavity of the parasite is not

used for the ingestion of intact renal tissues; solid particles have not been detected in the esophagus of *D. renale*. Although the exact mechanism(s) of destruction is not known, obstruction caused by the growing adult parasite(s) and secondary hydronephrosis (or pyonephrosis) plays a major role. Light microscopic examination of sections of kidneys from dogs with unilateral renal infection reveals changes typical of advanced hydronephrosis (i.e., obliteration of the majority of renal tubules surrounded by chronic inflammatory tissue and persistence of the structural architecture of many glomeruli).

- Ova of *D. renale* may be observed in the renal parenchyma adjacent to the renal pelvis. The urothelium lining the renal pelvis is often hyperplastic in some areas and ulcerated in other areas.
- If only one kidney is affected with *D. renale*, the host retains adequate renal function due to compensatory hypertrophy and hyperplasia of the remaining kidney. If both kidneys are parasitized, or if one kidney is parasitized and the opposite kidney has substantial co-morbid dysfunction, varying stages of renal failure and uremia may occur. Eggs that are released by female worms pass through the urinary tract and provoke inflammation in the mucosa of the ureter and urinary bladder.

Peritoneal Cavity

• In dogs, viable parasites located in the abdominal cavity and/or between lobes of the liver have frequently been reported as an incidental finding during ovariohysterectomies. It is possible that under certain conditions the adult worms may remain in the peritoneal cavity for extended periods prior to penetration of a kidney.

• Eggs present in the peritoneal cavity can trigger development of chronic peritonitis. Examination of the abdominal viscera from dogs with *D. renale* in the peritoneal cavity revealed hemorrhage, granulomatous inflammation, and fibrosis frequently involving the omentum, the surface of the liver, and less frequently the surface of the spleen. Viable adult males (but not females) have been found in the peritoneal cavity of dogs without an associated inflammatory response, suggesting that females and/or their eggs stimulate a greater host inflammatory response than males.

• Ascites may occur in dogs with *D. renale* in the peritoneal cavity. The fluid detected in the abdominal cavity is usually hemorrhagic. The quantity of ascitic fluid reported to be removed from dogs infected with *D. renale* ranged from approximately 20 mL to 3.2 L.

SIGNALMENT

Species

Dog and cat

Breed Predilections

N/A

(CONTINUED)

DI OCTOPHYMA RENALE (GIANT KIDNEY WORM)**Mean Age and Range**

N/A

Predominant Sex

N/A

CLINICAL SIGNS

- The feeding of *L. variegatus* infected with *D. renale* to dogs typically induces vomiting due to effects of the parasite on the gastric mucosa.
- If only one kidney has been invaded with *D. renale* and the opposite kidney is normal, signs are often absent.
- Silent hematuria may be the first indication of an abnormality.
- Palpation of the abdomen may reveal an enlarged and/or misshapen hydronephrotic kidney.
- If both kidneys are parasitized, clinical signs attributable to renal failure or uremia may occur. However, the host will die before extensive hydronephrosis of both kidneys has time to develop. The degree of renal dysfunction is influenced by (1) number of parasites in the kidney, (2) duration of infection, (3) number of kidneys parasitized, and (4) presence and severity of co-morbid renal diseases.

CAUSES & RISK FACTORS

See "Life Cycle" and "Pathophysiology"

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

Any cause of hydronephrosis or renomegaly

CBC/BIOCHEMISTRY/URINALYSIS

- When a gravid female worm is present in one or both kidneys that have a patent track to the exterior, microscopic examination of urine voided by the host usually reveals ova of *D. renale*.
- Hematuria, pyuria, and proteinuria with or without eggs are indicative of an inflammatory response.
- Findings typical of chronic renal failure when both kidneys are parasitized or when one only kidney contains parasites and the contralateral kidney is diseased.

OTHER LABORATORY TESTS

N/A

IMAGING

- Radiography may reveal an enlarged hydronephrotic kidney. If intravenous urography is performed, it may be characterized by inability of the parasitized kidney to excrete the contrast agent.
- Ultrasonography may reveal that the affected kidney is hydronephrotic and contains excessive fluid. Ultrasound may also reveal characteristic hypoechoic loops associated with one or more of these parasites in the renal pelvis. Transverse plane sonographs of the affected kidney may reveal a thin hyperechoic rim that contains multiple circular structures of uniform diameter. The outer layers of these structures are hyperechoic; the inner portions are hypoechoic. In the longitudinal plane, the structures appear as elongated hyperechoic bands alternating with elongated hypoechoic bands. If viable parasites are in the peritoneal cavity, sonography may reveal hyperechoic curvilinear bands in the region of the right caudal lobe of the liver and/or the cranial pole of the right kidney. Serially performed sonographs may reveal movement of the parasite(s) from one location to another.
- CT and MRI scans may also be used to detect *D. renale* in the renal pelvis of one or both kidneys, in the peritoneal cavity, or in varying positions between the lobes of the liver.

DIAGNOSTIC PROCEDURES

N/A

**TREATMENT**

Nephrectomy is usually the treatment of choice when only one kidney is affected and the opposite kidney is capable of sustaining homeostasis. In patients with parasites in both kidneys, nephrotomy and removal of the parasites may be indicated if sufficient functional tissue remains in both kidneys to maintain a reasonable quality of life. Unfortunately by the time *D. renale* affecting both kidneys is recognized, the patients often have moderate-to-severe irreversible renal failure. Parasites that are incidental findings in the peritoneal cavity during celiotomy may be removed without further morbidity.

**MEDICATIONS****DRUG(S)**

Pharmacologic treatment of adults and/or infective larvae discovered in any species has been virtually non-existent. A report of a 44-year-old man with recurrent lumbar pain attributed to *D. renale* was cured following two regimens of ivermectin.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A

**FOLLOW-UP****PREVENTION/AVOIDANCE**

Dogs and cats should not be fed raw fish or fish viscera, especially in areas where *D. renale* is known to exist. Likewise, they should not be given access to lake or pond water likely to contain infective stages of *D. renale*.

**MISCELLANEOUS****ABBREVIATIONS**

- CT = computed tomography
- MRI = magnetic resonance imaging

INTERNET RESOURCES

<http://www.capcvet.org>

Suggested Reading

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Authors Carl A. Osborne and Hasan Albasan

Consulting Editor Carl A. Osborne

D

DISCOLORED TOOTH/TEETH



BASICS

DEFINITION

- Any color change from the norm—the normal color varies and depends on the shade, translucency, and thickness of enamel.
- Translucent enamel is bluish-white; opaque enamel is gray-white.
- Extrinsic—from surface accumulation of exogenous pigment.
- Intrinsic—secondary to endogenous factors discoloring the underlying dentin.

PATHOPHYSIOLOGY

Extrinsic Discoloration

- Bacterial stains—chromogenic bacteria give a green to black-brown to orange color, which is usually 1 mm above the gingival margin on the tooth.
- Plaque related—a black-brown stain; usually secondary to the formation of ferric sulfide from the interaction of bacterial ferric sulfide and iron in the saliva. Plaque on the dentition is usually white.
- Foods—charcoal biscuits and similar products penetrate the pits and fissures of the enamel; food that contains abundant chlorophyll can produce a green discoloration.
- Gingival hemorrhage—gives a green staining; results from the breakdown of hemoglobin into green biliverdin.
- Dental restorative materials—amalgam gives a black-gray discoloration.
- Medications—products containing iron or iodine give a black discoloration; those containing sulfides, silver nitrate, or manganese give a gray-to-yellow to brown-to-black discoloration; those containing copper or nickel give a green discoloration; products containing cadmium give a yellow-to-golden brown discoloration (e.g., 8% stannous fluoride combines with bacterial sulfides, giving a black stain; chlorhexidine gives a yellowish-brown discoloration).
- Metals—wear from chewing on cages or food dishes.
- From removed orthodontic brackets or bands.
- Crown fragments—less translucency due to dehydration of fragment.
- Discolored restorations.
- Tooth wear with dentin exposure—tertiary dentin, reparative dentin, secondary dentin.
- A calculus-covered crown ranges in color from a dark yellow to dark brown.

Intrinsic Discoloration

- Hyperbilirubinemia—affects all teeth; occurs during the developmental stages of the dentition (during dentin formation); bilirubin accumulation in the dentin occurs from excess red blood cell breakdown; extent of tooth discoloration depends on the length of hyperbilirubinemia (one can see lines of resolution on the teeth once the condition has been resolved); gives a green discoloration.
- Localized red blood cell destruction, usually one tooth—usually follows a traumatic injury to the tooth; discoloration comes from

hemoglobin breakdown within the pulp from a pulpitis and secondary release into adjacent dentinal tubules; discoloration goes from pink (pulpitis) to gray (pulpal necrosis or resolution) to black (liquefactive necrosis); blood factors that cause tooth discoloration are hemoglobin, methemoglobin, hematoidin, hemosiderin, hematin, hemin, and sulfmethemoglobin.

• Amelogenesis imperfecta—developmental alteration in the structure of enamel affecting all teeth; teeth have a chalky appearance and a pinkish hue; can be a problem in the formation of the organic matrix, mineralization of the matrix, or the maturation of the matrix.

- Dentinogenesis imperfecta—developmental alteration in the dentin formation; enamel separates easily from the dentin, resulting in grayish discoloration.
- Infectious agents (systemic)—parvovirus, distemper virus, or any infectious agent that causes a sustained body temperature rise; affects the formation of enamel; a distinct line of resolution is visible on the teeth; affects all teeth; results in enamel hypoplasia where the pitted areas have black edges and the dentin is brownish.
- Dental fluorosis—affects all teeth; excess fluoride consumption affects the maturation of enamel, resulting in pits (enamel hypoplasia) with black edges; the enamel is a lusterless, opaque white, with yellow-brown zones of discoloration.
- Tooth erosion from constant vomiting results in enamel pitting and darkened staining.
- Attrition—tooth-to-tooth wear results in crown loss and reparative dentin formation (yellow-brown color).
- Abrasion—tooth wear against another surface; chewing on tennis balls or chewing itself from a dermatologic condition. Reparative dentin (yellow-brown color) forms.
- Aging—older animals' dentition is more yellow and less translucent.
- Malnutrition (generalized, vitamin D deficiency, and vitamin A deficiency)—if severe can result in demarcated opacities on the enamel.

Internal/External Resorption

- Internal—follows pulpal injury (trauma) causing vascular changes with increased oxygen tension and a decreased pH, resulting in destruction (resorption) of the tooth from within the pulp from dentinoclasts; tooth has pinkish hue; usually one tooth affected.
- External—many factors cause this, such as trauma, orthodontic treatment, excessive occlusal forces, periodontal disease as well as treatment, tumors, and periapical inflammation; reabsorption can occur anywhere along the periodontal ligament and can extend to the pulp; osteoclasts resorb the tooth structure. Often the area is repaired by deposition of osteodentin.

Medications and Discoloration

- Tetracycline—binds to calcium, forming a calcium orthophosphate complex that is laid

down into the collagen matrix of enamel; occurs on all teeth; occurs only when the enamel is being formed; results in a yellow-brown discoloration. With long-term use of tetracycline drugs in mature animals, discoloration of the tooth occurs secondarily to the involvement of the underlying secondary dentin formation.

- Amalgam (as with extrinsic stains).
- Iodine/essential oils.
- From endodontically treated teeth with the mendicants penetrating the dentinal tubules.
- Macrolide antibiotic (reported in humans): due to increased number of karyopcytosis of the ameloblast at the transitional stage of development, resulting in vacuolar degeneration of the ameloblast and cystic change at maturation and hypocalcification, giving a white discolored lesion with horizontal stripes on the enamel.
- Bacterial "creeping" (leakage)—occurs around the margins of a restoration and usually is blackish in color.

SYSTEMS AFFECTED

Gastrointestinal—oral cavity

GENETICS

- Both amelogenesis imperfecta and dentinogenesis imperfecta in humans are inherited conditions that have many modes of inheritance: X-linked dominant, X-linked recessive, autosomal dominant, autosomal recessive. The mode of inheritance in animals has not been studied.
- Congenital hypothyroidism.
- Metabolic diseases.

INCIDENCE/PREVALENCE

- Discoloration of the teeth or a tooth is extremely common in all animals.
- Extrinsic staining is very common, especially bacterial stains; others are less common.
- Intrinsic staining is likewise very common, especially internal and external resorption, followed by localized red blood cell destruction; the other causes are rare.

GEOGRAPHIC DISTRIBUTION

- Heavy metals from mining operations.
- Fluoridation forms areas of excessive fluoride in the drinking water.
- Otherwise none.

SIGNALMENT

Species

Dogs and cats

Breed Predilections

None

Mean Age and Range

The reported age range varies—when the condition affects the maturing enamel or dentin it can be first noted after 6 months.

Predominant Sex

None

SIGNS

Historical Findings

Owner reports a variation in color of a tooth or teeth.

(CONTINUED)

DISCOLORED TOOTH/TEETH

D

Physical Examination Findings

- Abnormal coloration of tooth or teeth.
- Pitted enamel with staining. • Fractured tooth.
- Rings or lines of discoloration around tooth or teeth.
- Wear on crowns of the dentition or in selected areas as in behavioral causes (cage bitters—distal aspect of the canines is affected).
- Erosion of enamel.

CAUSES & RISK FACTORS

- Extrinsic discoloration—bacterial stains from plaque and calculus; foods; gingival hemorrhage; dental restorative materials, medications (chlorhexidine, 8% stannous fluoride), metal.
- Intrinsic discoloration—internal (trauma); external (feline osteoblastic resorptive lesions) resorption; localized red blood cell destruction in the tooth (trauma); systemic infections; medications (tetracycline); fluorosis; hyperbilirubinemia; amelogenesis imperfecta; dentinogenesis imperfecta.

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- Calculus on the teeth.
- Normal tooth aging—increased translucence
- Food debris lodged in the diastimal spaces

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia—blood-related disorders
- Bilirubin—increased with liver diseases

OTHER LABORATORY TESTS

- T₃/T₄—low in congenital hypothyroidism
- Specific metabolic enzyme decrease or absence—tyrosinemia

IMAGING

Dental radiography is extremely useful in identifying internal or external resorption, restorative materials, or bacterial stain from coronal percolation.

DIAGNOSTIC PROCEDURES

- If many teeth are affected, one tooth can be extracted and sent for histologic evaluation (see below).
- Transillumination with a strong fiber-optic light can benefit the clinician by distinguishing between a vital and necrotic pulp.
- Appropriate preoperative diagnostics when indicated prior to procedure.

PATHOLOGIC FINDINGS

- Tooth or teeth are discolored; enamel and/or dentin can be pitted or broken with staining.
- Extrinsic discoloration—all stain is in the enamel or exposed dentin, otherwise the tooth structure is normal.
- Intrinsic discoloration—hyperbilirubinemia; enamel

hypoplasia; lines of resolution on the tooth; all teeth affected.

- Localized red blood cell destruction—stain in dentinal tubules; pulpitis/liquefactive necrosis of the pulp.
- Internal resorption—well-circumscribed enlargement of an area of the endodontic system with granulation tissue containing many odontoclasts.
- External resorption—moth-eaten loss of tooth structure anywhere along the periodontal ligament; can extend into the endodontic system; areas of tooth resorption have granulation tissue with many osteoclasts.
- Fluorosis—enamel hypoplasia; enamel hypocalcification; medications; systemic (e.g., tetracycline has irregular matrix formation to the enamel and dentin), all teeth affected.
- Amelogenesis imperfecta—irregular formation of the enamel matrix, mineralization, or maturation.
- Dentinogenesis imperfecta—irregular formation of dentin; enamel may be separated from the dentin.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Extrinsic stain removal—mainly cosmetic
- Intrinsic stain treatment—functional and pain relieving

NURSING CARE

- Extrinsic stain—remove inciting cause
- Intrinsic stain—soft food; remove chew toys

ACTIVITY

Curtail or treat specific behavioral abnormalities (cage biting).

DIET

Intrinsic stain—soft food

CLIENT EDUCATION

- To prevent it in future animals or litters.
- Intrinsic causes—if untreated the tooth or teeth are more likely to accumulate plaque and calculus, leading to subsequent periodontal disease; tooth fracture is more prevalent, which could result in tooth abscessation.

SURGICAL CONSIDERATIONS

- Extrinsic stain (cosmetic)—internal and/or external bleaching; veneers or crowns.
- Polishing the affected teeth with 3% hydrogen peroxide in pumice will help remove external stain. Also good home care with plaque control will check redevelopment of some stains (plaque/calculus/bacteria stain).
- Intrinsic stain (functional and pain relief)—possible endodontic treatment

(internal resorption and localized red blood cell destruction).

- Restorative procedures such as crowns or veneers to protect both tooth and pulp.
- Extraction of affected teeth may be required, especially with external resorption.

**MEDICATIONS****DRUG(S) OF CHOICE**

N/A

**FOLLOW-UP****PREVENTION/AVOIDANCE**

- See “Pathophysiology”
- Good oral care at home will help prevent the reoccurrence of certain specific stains.

POSSIBLE COMPLICATIONS

See “Client Education”

EXPECTED COURSE AND PROGNOSIS

Varies dependent upon the etiology but can vary from just aesthetics to significant pain.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Juvenile purpura

AGE-RELATED FACTORS

Most common in young dogs and cats

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

- Tetracycline administration during pregnancy may result in permanent tooth discoloration in the offspring.
- See “Genetics.”

SYNONYMS

- Chlorhexidine staining
- Extrinsic staining
- Intrinsic staining
- Tetracycline staining

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Author Heidi B. Lobprise

Consulting Editor Heidi B. Lobprise

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DISCOSPONDYLITIS



BASICS

DEFINITION

A bacterial or fungal infection of the intervertebral discs and adjacent vertebral bodies.

PATHOPHYSIOLOGY

- Hematogenous spread of bacterial or fungal organisms—most common cause.
- Neurologic dysfunction—may occur; usually the result of spinal cord compression caused by proliferation of bone and fibrous tissue; less commonly owing to luxation or pathologic fracture of the spine, epidural abscess, or extension of infection to the meninges and spinal cord.

SYSTEMS AFFECTED

- Musculoskeletal—infection and inflammation of the spine
- Nervous—compression of the spinal cord

GENETICS

- No definite predisposition identified.
- An inherited immunodeficiency has been detected in a few cases.

INCIDENCE/PREVALENCE

Approximately 0.1–0.8% of dog hospital admissions

GEOGRAPHIC DISTRIBUTION

- More common in the southeastern United States.
- Grass awn migration and coccidiomycosis—more common in certain regions.

SIGNALMENT

Species

Dog; rare in cat

Breed Predilections

Large and giant breeds, especially German shepherd and Great Dane.

Mean Age and Range

- Mean age—4–5 years
- Range—5 months–12 years

Predominant Sex

Males outnumber females by ~2:1

SIGNS

Historical Findings

- Onset usually relatively acute; some patients have mild signs for several months before examination.
- Pain—difficulty rising, reluctance to jump, and stilted gait are most common signs.
- Ataxia or paresis.
- Weight loss and anorexia.
- Lameness.
- Draining tracts.

Physical Examination Findings

- Focal or multifocal areas of spinal pain in >80% of patients.

- Any disc space may be affected; lumbosacral space is most commonly involved.
- Paresis or paralysis, especially in chronic, untreated cases.
- Fever in ~30% of patients.
- Lameness.

CAUSES

- Bacterial—*Staphylococcus pseudintermedius* is the most common. Others include *Streptococcus*, *Brucella canis*, and *E. coli*, but virtually any bacteria can be causative.
- Fungal—*Aspergillus*, *Paecilomyces*, *Scedosporium apiospermum*, and *Coccidioides immitis*.
- Grass awn migration is often associated with mixed infections, especially *Actinomyces*; tends to affect the L2–L4 disc spaces and vertebrae.
- Other causes—surgery, bite wounds.

RISK FACTORS

- Urinary tract infection; reproductive tract infection
- Periodontal disease
- Bacterial endocarditis
- Pyoderma
- Immunodeficiency



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Intervertebral disc protrusion—may cause similar clinical signs; differentiated on the basis of radiography and myelography.
- Vertebral fracture or luxation—detected on radiographs.
- Vertebral neoplasia—usually does not affect adjacent vertebral end plates.
- Spondylosis deformans—rarely causes clinical signs; has similar radiographic features, including sclerosis, ventral spur formation, and collapse of the disc space; rarely causes lysis of the vertebral end plates.
- Focal meningomyelitis—often identified by CSF analysis.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram—often normal; may see leukocytosis.
- Urinalysis—may reveal pyuria and/or bacteriuria with concurrent urinary tract infections.

OTHER LABORATORY TESTS

- Aerobic, anaerobic, and fungal blood cultures identify the causative organism in about 35% of cases; obtain if available.
- Sensitivity testing—indicated if cultures are positive.
- Urine cultures—indicated; positive in about 30% of patients.
- Organisms other than *Staphylococcus* spp.—may not be the cause.
- Serologic testing for *Brucella canis*—indicated.

IMAGING

- Spinal radiography—usually reveals lysis of vertebral end plates adjacent to the affected disc, collapse of the disc space, and varying degrees of sclerosis of the end plates and ventral spur formation; may not see lesions until 3–4 weeks after infection.
- Myelography—indicated with substantial neurologic deficits; determine location and degree of spinal cord compression, especially if considering decompressive surgery; spinal cord compression caused by discospondylitis typically displays an extradural pattern.
- Computed tomography or magnetic resonance imaging—more sensitive than radiography; indicated when radiographs are normal or inconclusive.

DIAGNOSTIC PROCEDURES

- CSF analysis—occasionally indicated to rule out meningomyelitis; usually normal or reveals mildly high protein.
- Bone scintigraphy—occasionally useful for detecting early lesions; helps clarify if radiographic changes are infectious or degenerative (spondylosis deformans).
- Fluoroscopically guided fine-needle aspiration of the disc—valuable for obtaining tissue for culture when blood and urine cultures are negative and there is no improvement with empiric antibiotic therapy.

PATHOLOGIC FINDINGS

- Gross—loss of normal disc space; bony proliferation of adjacent vertebrae.
- Microscopic—fibrosing pyogranulomatous destruction of the disc and vertebral bodies.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—mild pain managed with medication.
- Inpatient—severe pain or progressive neurologic deficits require intensive care and monitoring.

NURSING CARE

Non-ambulatory patients—keep on a clean, dry, well-padded surface to prevent decubital ulceration.

ACTIVITY

Restricted

DIET

Normal

CLIENT EDUCATION

- Explain that observation of response to treatment is very important in determining the need for further diagnostic or therapeutic procedures.
- Instruct the client to immediately contact the veterinarian if clinical signs progress or recur or if neurologic deficits develop.

(CONTINUED)

SURGICAL CONSIDERATIONS

- Curettage of a single affected disc space—occasionally necessary for patients that are refractory to antibiotic therapy.
- Goals—remove infected tissue; obtain tissue for culture and histologic evaluation.
- Decompression of the spinal cord by hemilaminectomy or dorsal laminectomy—indicated for substantial neurologic deficits and spinal cord compression evident on myelography when there is no improvement with antibiotic therapy; also perform curettage of the infected disc space; it may be necessary to perform surgical stabilization if more than one articular facet is removed.

**MEDICATIONS****DRUG(S) OF CHOICE****Antibiotics**

- Selection based on results of blood cultures and serology.
- Negative culture and serology—assume causative organism is *Staphylococcus* spp.; treat with a cephalosporin (e.g., cefadroxil; dogs, 22 mg/kg PO q12h; cats, 22 mg/kg PO q24h) for 8–12 weeks.
- Acutely progressive signs or substantial neurologic deficits—initially treated with parenteral antibiotics (e.g., cefazolin; dogs and cats, 20–35 mg/kg IVq8h).
- Brucellosis—treated with tetracycline (dogs, 15 mg/kg PO q8h) and streptomycin (dogs, 3.4 mg/kg IM q24h) or enrofloxacin (dogs, 2.5–5 mg/kg PO q12h).

Analgesics

- Signs of severe pain—treated with an analgesic (e.g., oxymorphone; dogs, 0.05–0.2 mg/kg IV, IM, SC q4–6h).
- Taper dosage after 3–5 days to gauge effectiveness of antibiotic therapy.

CONTRAINDICATIONS

Glucocorticoids

PRECAUTIONS

Use NSAIDs and other analgesics cautiously—may cause a temporary resolution of clinical signs even when infection is progressing; when used, discontinue after 3–5 days to assess efficacy of antibiotic therapy.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

- Initial therapy—cephradine (dogs, 20 mg/kg PO q8h); cloxacillin (dogs, 10 mg/kg PO q8h).

- Refractory patients—clindamycin (dogs and cats, 10 mg/kg PO q12h), enrofloxacin (dogs, 5–20 mg/kg PO q24h; cats, 5 mg/kg PO q24h), orbifloxacin (dogs and cats, 2.5–7.5 mg/kg PO q24h).

**FOLLOW-UP****PATIENT MONITORING**

- Reevaluate after 5 days of therapy.
- No improvement in pain, fever, or appetite—reassess therapy; consider a different antibiotic, percutaneous aspiration of the affected disc space, or surgery.
- Improvement—evaluate clinically and radiographically every 4 weeks.

PREVENTION/AVOIDANCE

Early identification of predisposing causes and prompt diagnosis and treatment—help reduce progression of clinical symptoms and neurologic deterioration.

POSSIBLE COMPLICATIONS

- Spinal cord compression owing to proliferative bony and fibrous tissue.
- Vertebral fracture or luxation.
- Meningitis or meningomyelitis.
- Epidural abscess.

EXPECTED COURSE AND PROGNOSIS

- Recurrence is common if antibiotic therapy is stopped prematurely (before 8–12 weeks of treatment).
- Some patients require prolonged therapy (1 year or more).
- Prognosis—depends on causative organism and degree of spinal cord damage.
- Mild or no neurologic dysfunction (dogs)—usually respond within 5 days of starting antibiotic therapy.
- Substantial paresis or paralysis (dogs)—prognosis guarded; may note gradual resolution of neurologic dysfunction after several weeks of therapy; treatment warranted.
- *Brucella canis*—signs usually resolve with therapy; infection may not be eradicated; recurrence common.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

See "Risk Factors"

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

Brucella canis—human infection uncommon but may occur

DISCOSPONDYLITIS

D

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Diskitis
- Intervertebral disc infection
- Intradiskal osteomyelitis
- Vertebral osteomyelitis

SEE ALSO

Brucellosis

ABBREVIATIONS

- CSF = cerebrospinal fluid
- NSAID = nonsteroidal anti-inflammatory drug

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Client Education Handout
available online

DISSEMINATED INTRAVASCULAR COAGULATION



BASICS

DEFINITION

DA complex hemostatic defect arising from a variety of inciting causes that leads to uncontrolled activation and consumption of clotting factors. It results in widespread formation of microthrombi with clinical manifestations of thrombosis and/or hemorrhage.

PATHOPHYSIOLOGY

- DIC represents a complication of a variety of primary conditions. It begins with a hypercoagulable state that leads to microthrombi in many small vessels.
- The primary conditions primarily act through increased exposure/production of TF (Factor III) which activates the extrinsic coagulation pathway.
- TF is normally restricted from intravascular exposure. It is usually exposed when endothelium is damaged revealing subendothelial tissue, which localizes coagulation. Increased exposure/production mainly occurs through widespread endothelial injury and/or increased production secondary to inflammation.
- Inflammation activates endothelial cells, platelets, and monocytes leading to membrane expression of TF. Inflammatory cytokines also induce vesiculation of these membranes releasing large quantities of microparticles into circulation that are enriched with both TF and PS and that facilitate extensive dissemination of coagulation. Some neoplastic cells constitutively produce membrane TF and also release microparticles.
- Microparticles provide a suitable membrane surface for amplifying intrinsic and common pathway coagulation, potentially leading to uncontrolled production of thrombin that overwhelms coagulation inhibitors (AT, APC, TFPI). Thrombin's conversion of fibrinogen to fibrin contributes to vascular occlusion.
- Widespread microthrombus formation consumes coagulation factors and platelets while initiating fibrinolysis. By-products of fibrinolysis (FDPs) have anticoagulant properties and inhibit platelet function. Hemorrhage at a variety of sites can follow.
- Uncontrolled progression leads to widespread tissue hypoxia, multi-organ dysfunction, and death.

SYSTEMS AFFECTED

Multisystemic syndrome

GENETICS

N/A

INCIDENCE/PREVALENCE

Associated with severe systemic disease, often in the terminal stages

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dogs and cats; diagnosed more in dogs

Breed Predilections

None

Mean Age and Range

Depends on the primary disease

Predominant Sex

None

SIGNS

- Vary with the primary disease and with DIC-associated organ dysfunction
- Petechiae
- Bleeding from venipuncture sites, mucosa, or in body cavities
- Bleeding is infrequent in cats, possibly leading to under-diagnosis

CAUSES

- Gastric dilatation-volvulus
- Heart failure
- Heartworm disease
- Heat stroke
- Hemolysis, especially immune mediated
- Hemorrhagic gastroenteritis
- Infectious diseases, systemic (especially endotoxemia)
- Inflammation, severe—regardless of underlying cause
- Liver disease, if severe (e.g., ICH, xylitol toxicity in dogs; lipidosis in cats)
- Malignancies, especially hemangiosarcoma, mammary carcinoma, and pulmonary adenocarcinoma in dogs and lymphoma in cats
- Pancreatitis
- Protein-losing nephropathy (nephrotic syndrome)
- Shock, hypoxia, acidosis
- Thrombocytopenia, especially immune mediated
- Transfusion incompatibility
- Trauma
- Venom

RISK FACTORS

Vary with cause



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Key differentials: immune-mediated thrombocytopenia, anticoagulant toxicity, coagulation factor deficiency, paraproteinemia.
- Highly variable diagnostic pattern includes thrombocytopenia, prolonged clotting tests (PT, APTT), decreased fibrinogen, decreased AT, and increased fibrinolysis (FDPs, D-dimers). At least three abnormalities in animals affected by a predisposing condition (see "Causes") is considered diagnostic.
- Suspect DIC any time thrombocytopenia and prolonged clotting tests are seen together.

- Patients showing predisposing conditions should have laboratory monitoring every 24–48 hours. A sudden drop in platelet count and a 20–30% prolongation in APTT is very suspicious for DIC.

- Hepatic insufficiency may mimic DIC pattern. Decreased production of clotting factors is common. Decreased clearance of normal fibrin(ogen)olytic by-products may increase FDP values. Mild idiopathic thrombocytopenia may also be seen. Spontaneous bleeding is uncommon unless DIC is present.

CBC/BIOCHEMISTRY/URINALYSIS

- Inflammatory leukogram, often with a stress component.
- Thrombocytopenia; very consistent finding in dogs, less reliable in cats.
- Anemia is possible. RBC fragmentation (schistocytes) is a supportive finding.
- Biochemical changes reflect affected organs.

OTHER LABORATORY TESTS

- Prolonged clotting tests (PT, APTT); APTT is more sensitive.
- Hypofibrinogenemia, although inflammatory increase may mask consumption.
- Increased FDPs and D-dimers. D-dimers are very sensitive. DIC is unlikely if D-dimers are low/negative. Neither test is specific enough alone to diagnose DIC.
- Decreased AT; may be a positive acute phase reactant in cats, masking consumption.
- TEG reportedly identifies hypercoagulable and hypocoagulable states in DIC. Case fatality rate is significantly higher in the hypocoagulable state.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

None

PATHOLOGIC FINDINGS

- Usually related to the primary disease or DIC-affected organs
- Petechiae common



TREATMENT

APPROPRIATE HEALTH CARE

- Requires intensive inpatient treatment.
- Aggressive treatment of the primary disease is essential (e.g., antimicrobials for sepsis).

NURSING CARE

- Maintain tissue perfusion and oxygenation using fluids, transfusions, and oxygen therapy.
- Restore depleted factors by blood/plasma transfusions. Use fresh frozen plasma (6–20 mL/kg) to correct bleeding due to factor deficiency.

ACTIVITY

Limited by the disease severity

(CONTINUED)

DISSEMINATED INTRAVASCULAR COAGULATION

DIET

Maintain nutritional support as appropriate for the clinical condition of the patient.

CLIENT EDUCATION

Inform the owner that the condition is life-threatening with a guarded to poor prognosis.

SURGICAL CONSIDERATIONS

Related to primary disease. Plasma or whole blood transfusion to restore clotting factors is a presurgical consideration. Surgery may be contraindicated with uncontrolled bleeding.



MEDICATIONS

DRUG(S) OF CHOICE

- Successful drug protocols are mostly anecdotal and traditionally use heparin to effect (clinical improvement, test results).
- Heparin binds to and potentiates the action of AT. Plasma or blood transfusions are often needed to replenish AT for heparin to be effective.
- Heparin dosage depends on severity of signs and lab changes.
- Mild to moderate disease: heparin at 5–200 U/kg SC q8h or IV (q8h or continuous infusion)
- Severe disease: heparin at 300–1,000 U/kg SC q8h or IV (q8h or continuous infusion)

CONTRAINDICATIONS

Inhibitors of fibrinolysis should not be used. Fibrinolysis is important in the clearance of thrombi.

PRECAUTIONS

- High doses of heparin may cause fatal hemorrhage.
- Watch for overhydration in cases with renal or pulmonary compromise.
- Corticosteroids impair function of mononuclear phagocytes, possibly delaying removal of activated coagulation factors and FDPs. Avoid prolonged use.
- Use of antiplatelet medications (aspirin, clopidogrel) in thrombocytopenic patients warrants caution for hemorrhage even though platelet activation is a part of DIC pathogenesis.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

Low molecular weight heparin: many forms with variable activity are available. Fewer complications reported but very expensive. Most information is anecdotal.



FOLLOW-UP

PATIENT MONITORING

- Clinical improvement and the arrest of bleeding are key positive findings.
- Daily lab testing (e.g., coagulation tests, fibrinogen, platelet counts) is warranted in severe cases to identify positive or negative trends. Less frequent testing may suffice in milder cases.
- Coagulation times and fibrinogen often return to normal more rapidly than FDPs and platelet counts.

PREVENTION/AVOIDANCE

- Related to primary disease.

POSSIBLE COMPLICATIONS

Aside from the primary disease, DIC affected organs may have permanent dysfunction or marginal reserve capacity.

EXPECTED COURSE AND PROGNOSIS

Mortality rates for dogs range from 50% to 77%. For cats, rates may be > 90%.



MISCELLANEOUS

ASSOCIATED CONDITIONS

See "Causes"

AGE-RELATED FACTORS

Related to primary disease

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Unlike in humans, obstetric complications are not a common cause in dogs and cats.

SYNONYMS

- Consumption coagulopathy
- DIC

SEE ALSO

- Coagulation Factor Deficiency
- Thrombocytopenia

D

ABBREVIATIONS

- APC = activated protein C
- APTT = activated partial thromboplastin time
- AT = antithrombin
- DIC = disseminated intravascular coagulation
- FDP = fibrin degradation product
- ICH = infectious canine hepatitis
- PS = phosphatidylserine
- PT = prothrombin time
- RBC = red blood cell
- TF = tissue factor
- TFPI = tissue factor pathway inhibitor
- TEG = thromboelastography
- TNF = tumor necrosis factor

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Client Education Handout
available online

DROWNING (NEAR DROWNING)



BASICS

OVERVIEW

- Defined as process of experiencing respiratory impairment from submersion or immersion in liquid; near-drowning defined as water submersion followed by survival for at least 24 hours. Recent changes in terminology prefer the use of “death, morbidity or no morbidity following a drowning episode.”
- Following submersion, elevations in carbon dioxide levels in the bloodstream stimulate respiration, and subsequent aspiration of water occurs.
- Fresh water aspiration dilutes pulmonary surfactant, leading to alveolar collapse ± infectious pneumonia. Hypertonic seawater aspiration leads to diffusion of interstitial water into alveoli. Large volumes of water are not typically aspirated, but any amount results in ventilation-perfusion mismatch, hypoxemia, and metabolic acidosis.
- Submersion time, temperature of the water, and type of water (fresh vs. salt vs. chemical water) significantly affect development of organ damage.

SIGNALMENT

Dogs and cats. Approximately half of the animals involved in immersion accidents are less than 4 months of age.

SIGNS

- Noted acutely after exposure to water
- Cyanosis, apnea, respiratory distress
- Coughing ± clear to frothy red sputum
- Vomiting
- Obtunded to comatose
- Crackles or wheezes auscultated over chest
- Tachycardia or bradycardia, asystole

CAUSES & RISK FACTORS

- Greater risk near bodies of water (including pools, buckets, bathtubs) or ice.
- Owner negligence or inadequate safety precautions versus purposeful harm.
- Animals in or near water at the time of a seizure, head trauma, hypoglycemic event, cardiac arrhythmia, or syncopal episode are at risk of drowning.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hypothermia, neck trauma, and meningitis.
- With drowning secondary to a seizure, head trauma, hypoglycemic event, cardiac arrhythmia, or syncopal episode, history at the time of presentation may be informative.

CBC/BIOCHEMISTRY/URINALYSIS

- Fresh water inhalation/ingestion—hemodilution, hemolysis, and decreases in sodium, chloride, and urine specific gravity.
- Hypertonic salt water ingestion/inhalation—hemoconcentration and increases in sodium, chloride, and urine specific gravity.

OTHER LABORATORY TESTS

Arterial blood gas reveals hypoxemia ($\text{PaO}_2 < 80 \text{ mmHg}$), hypoventilation ($\text{PaCO}_2 > 50 \text{ mmHg}$), and acid-base derangements.

IMAGING

- Radiographic changes may not be detectable for 24–48 hours.
- Focal or diffuse alveolar pattern due to aspiration pneumonia or non-cardiogenic pulmonary edema.
- Mixed patterns may be present, ± a radiopaque material filling the airways (“sand bronchogram”).
- Foreign body inhalation may produce segmental atelectasis.
- Progression of pulmonary injury to ARDS is possible and may appear as bilateral, diffuse, symmetrical alveolar infiltrates.

DIAGNOSTIC PROCEDURES

- Endotracheal or transtracheal wash with cytologic evaluation and culture with sensitivity indicated if animal is stable.
- Electrocardiographic monitoring.
- Cervical radiographs, CT or MRI of brain, and BAER assessment in select cases.



TREATMENT

- Initiate mouth-to-muzzle resuscitation on-site.
- Emergency inpatient care is required.
- Airway clearance, if obstructed, is first priority.
- Cardiopulmonary resuscitation, if necessary.
- Oxygen supplementation.
- Intubation and mechanical ventilation with positive end-expiratory pressure may be required in animals with severe hypoxemia, hypercapnia, or imminent respiratory fatigue.
- Fluid therapy and acid-base/electrolyte management are crucial.
- Gradually rewarm (over 2–3 hours) hypothermic animals.
- Gravitational drainage or abdominal thrusts (Heimlich maneuver) are not recommended in the absence of airway obstruction owing to high risk of regurgitation and subsequent aspiration of stomach contents.



MEDICATIONS

DRUG(S) OF CHOICE

- Mannitol, 0.5 g/kg IV over 30 minutes, may be beneficial in animals with suspected cerebral edema.
- Broad-spectrum antibiotics (e.g., ampicillin, 22 mg/kg IV q8h, and enrofloxacin, 10–20 mg/kg IV q24h in the dog or 5 mg/kg IV q24h in the cat) for aspiration pneumonia.
- Beta-2 agonists may help animals with suspected bronchospasm.
- Pentoxifylline decreased incidence of lung injury in dogs with experimental freshwater aspiration.

CONTRAINDICATIONS

- Corticosteroid therapy not indicated; use could be detrimental in animals with aspiration pneumonia.
- Use of enrofloxacin in young animals may result in cartilage erosion.



FOLLOW-UP

PATIENT MONITORING

- Continuous monitoring of heart rate and rhythm, respiratory rate, MM color and CRT, urine output, arterial blood pressure, rectal temperature, and neurologic status.
- Arterial blood gas, complete blood count, biochemical profile, coagulation profile, and acid-base status checked as needed.

PREVENTION/AVOIDANCE

Close monitoring of animals (especially young and old/debilitated animals) near bodies of water. Place barriers around bodies of water, life jackets on animals, train owners to perform CPR.

POSSIBLE COMPLICATIONS

Aspiration pneumonia, non-cardiogenic pulmonary edema, ARDS, gastrointestinal bleeding, diarrhea, vomiting, acute kidney injury, permanent neurologic derangements, DIC, central diabetes insipidus.

EXPECTED COURSE AND PROGNOSIS

Directly related to animal's status at time of admission: animals that present comatose, severely acidotic ($\text{pH} < 7.0$), or requiring cardiopulmonary resuscitation or mechanical ventilation have a poor prognosis. Animals that present conscious have a good prognosis if no complications ensue; 37.5% mortality rate in 15 dogs and 1 cat with freshwater aspiration.



MISCELLANEOUS

ABBREVIATIONS

- ARDS = acute respiratory distress syndrome
- BAER = brainstem auditory evoked response
- CPR = cardiopulmonary resuscitation
- CT = computed tomography
- DIC = disseminated intravascular coagulation
- MRI = magnetic resonance imaging

Suggested Reading

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DUCTAL PLATE MALFORMATION (CONGENITAL HEPATIC FIBROSIS)



BASICS

DEFINITION

- Ductal plate malformations (DPMs) are noninflammatory hepatopathies recognized in juvenile and young adult dogs or cats reflecting developmental abnormalities of biliary structures.
- Diverse phenotypes defined by involved structures, coexistent hepatic fibrosis, portal hypertension, and acquired portosystemic shunts (APSS).
- Propensity for septic suppurative cholangitis, choledochitis, cholelithiasis, or extrahepatic bile duct obstruction (EHBDO) reflects structural malformations.
- Represent abnormal development, differentiation, and resorption of embryonic anlage of the ductal plate, the embryologic precursor of the portal tract and bile ducts.
- In humans (and knockout mouse models), DPMs represent gene mutations influencing structure or function of primary cilia.
- Primary cilia—solitary, non-motile organelles located on the apical surface of most mammalian cells. These function as mechano-, osmo-, and chemoreceptors and are involved in designation of planar cell polarity, in cell cycle control, and numerous additional signaling pathways. Pathomechanisms leading to DPM involves interrupted tubulogenesis.
- Polycystic kidney disease in Persian cats involves the polycystin-1 precursor gene; ~ 15% develop hepatic DPM.

Four Major DPM Phenotypes

- (1) *Choledochal cyst*—diverticulum protruding from the common bile duct (CBD) or cystic duct; has propensity for infection—similar to appendicitis in humans causing sepsis, EHBDO, and cranial abdominal mass effect.
- (2) *Caroli's malformation*—irregular sacculation and dilation of hepatic, interlobular and large intralobular bile ducts; ducts have variable morphology appearing elongate, irregular, lanceolate, or sacculated, usually with attenuated biliary epithelium and intraluminal debris; with chronicity may develop choleliths, dystrophic mineralization, and septic cholangitis.
- (3) *Diffuse intralobular bile duct malformation without OR with diffuse portal-to-portal bridging fibrosis; if fibrosis = congenital hepatic fibrosis (CHF)*—Abnormal tubulogenesis of small intralobular bile ducts reflect abnormal resorption of extraneous ductule anlage; results in retention of numerous small malformed proliferative ductules lacking luminal apertures, variously embedded in excessive extracellular matrix (ECM); amalgamation of proliferative ductules, numerous stout arterials, and ECM dimensionally expand portal tracts forming variable bridging partitions between portal regions; portal veins are often inconspicuous;

dense fibrosis may cause presinusoidal portal hypertension and formation of APSS in CHF phenotype.

(4) *von Meyenberg complexes*

(VMC)—isolated single microscopic DPM comprised of clusters of proliferative intralobular bile ductule profiles embedded in an expanded ECM profile; also called bile duct hamartoma; are inconsequential.

(5) Progressive presinusoidal fibrosis with aging can lead to gradual onset of portal hypertension, formation of APSS, ascites, and hepatic encephalopathy (HE).

PATHOPHYSIOLOGY

- DPMs are not associated with increased liver enzymes or jaundice until compromised by infection, choleliths, EHBDO, or choledochitis.
- As described, different phenotypes may involve different acquired disease manifestations.
- *Choledochal cysts*—not recognized until cystic luminal contents are contaminated by bacteria; ensuing infection, cyst expansion, choledochitis or EHBDO cause clinical signs; until compromised CBD, patient remains anicteric and asymptomatic.
- *Caroli's malformation*—serendipitously recognized on abdominal radiography (limy gallbladder, mineralized sacculated large bile ducts), or abdominal US, when obstructed by choleliths or infected (choledochitis).
- *Diffuse DPM without extensive bridging fibrosis or presinusoidal portal hypertension*—not typically associated with increased liver enzymes or jaundice and have normal total serum bile acids (TSBA); diagnosed when infection causing increase in liver enzymes leads to liver biopsy.
- *Diffuse DPM with bridging fibrosis (CHF) causes presinusoidal portal hypertension*—may present for ascites, increased TSBA, ± increased liver enzymes reflecting secondary cholangitis.

SYSTEMS AFFECTED

- Liver—microhepatia, normal, or large liver; gallbladder agenesis, maldevelopment of left liver lobes; rare concurrent congenital intrahepatic or extrahepatic congenital portosystemic vascular anomaly (shunt, PSVA); jaundice due to EHBDO from choledochal cyst, or cholelithiasis (Caroli's malformation, choledochal cyst), or increased liver enzymes from suppurative cholangitis.
- Gastrointestinal—anorexia; intermittent vomiting or diarrhea reflecting concurrent IBD or enteric hypertensive vasculopathy (splanchnic hypertension from presinusoidal ECM deposition).
- Nervous—episodic HE.
- Musculoskeletal—stunted growth and poor body condition; chronic disease, inappetence, enteric malassimilation. Urogenital—polyuria and polydipsia; possible polycystic renal phenotype; ammonium biurate urolithiasis reflects APSS or rare PSVA.
- Hemic/Lymphatic/Immune—RBC microcytosis due to APSS; neutrophilic leukocytosis with toxic neutrophils and left-shifted leukon in

suppurative cholangitis/choledochitis, choledochal cyst.

SIGNALMENT

- Dog and cat, no sex predilection.
- Juvenile and young adults; dogs: mean age 1.5–2.5 years (0.2–12) years.
- May affect multiple littermates.
- Boxer dogs may be predisposed.
- Persian cats with polycystic renal disease predisposed.

SIGNS

- May be asymptomatic.
- Stunted growth, poor body condition if APSS.
- GI signs: inappetence, emesis, diarrhea, enteric hemorrhage; especially if concurrent IBD.
- PU/PD if APSS or polycystic renal disease.
- ± Increased liver enzymes.
- ± Fever, leukocytosis, increased bilirubin: septic choledochitis, choledochal cyst, or cholelithiasis.
- ± Abdominal distention: ascites with APSS.
- ± Episodic CNS signs due to HE.
- ± Urolithiasis (ammonium urates) reflect hyperammonemia due to APSS or rare PSVA.

CAUSES & RISK FACTORS

- Congenital malformation; suspected gene mutations affecting structure or function of primary cilia have not been proven in dogs.
- Clinical signs usually caused by acquired complications, see previously.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Stunted growth, increased total serum bile acids—PSVA, portal atresia, splanchnic portal venous thromboembolism (TE).
- Increased liver enzymes with or without hyperbilirubinemia—chronic hepatitis, toxicity, cholangiohepatitis, choledochitis, cholecystitis.
- Jaundice—acute liver injury, toxic injury, chronic hepatitis, copper associated hepatopathy, cholelithiasis, ruptured gallbladder (if GB cannot be imaged), EHBDO, hemolysis—check RBC morphology for schistocytes, acanthocytes, spherocytes, Coombs' test.
- CNS signs—fungal disorders (distemper); toxicities (lead); hydrocephalus; epilepsy; metabolic disorders (hypoglycemia, hypokalemia, hyperkalemia, hypophosphatemia); Wernicke's encephalopathy (thiamine deficiency).
- Ascites—Pure Transudate, many causes (see Portal Hypertension).
- HE—APSS or PSVA or Portal TE.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—RBC microcytosis: reflects APSS; target cells in dogs.
- Biochemistry—if APSS: ± low albumin, cholesterol, BUN, variable globulin; all DPM phenotypes: ± increased ALP and ALT activity; hyperbilirubinemia: if EHBDO due to choledochal cyst or cholelithiasis or if septic.
- Urinalysis—

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ammonium biurate crystalluria if APSS in CHF phenotype.

OTHER LABORATORY TESTS

Routine Coagulation Tests

Variable abnormalities (see Coagulopathy of Liver Disease). Low protein C and antithrombin activity may reflect APSS in CHF phenotype.

TSBA

Increased with shunting pattern if APSS or rare PSVA.

Peritoneal Fluid Analysis

Pure transudate (protein < 2.5 g/dL); modified transudate if chronic—only in CHF phenotype.

IMAGING

Radiography

- Abdominal radiography: variable liver size (microhepatia to large liver, e.g., severe polycystic liver disease in cats). • Abdominal effusion: APSS in CHF phenotype.
- Ammonium biurate calculi—radiolucent unless radiodense mineral shell; implies APSS.
- Thoracic radiography—normal: rule out right-sided heart disease or pericardial tamponade.

Abdominal Ultrasonography

- Variable liver size: small to large. • GB may not be discovered: atresia possible. • May disclose parenchymal or biliary system changes due to malformations (sacculated or cystic ductal structures); variable liver texture; unremarkable vasculature to portal hypoperfusion. • Choledochal cyst—may be difficult to image owing to overlying enteric gas and confusion with CBD and cystic duct.
- Abdominal effusion: if APSS in CHF.
- APSS—confirm using color-flow Doppler; may confirm hepatofugal portal flow (away from the liver); tortuous APSS usually adjacent or caudal to left kidney, adjacent to splenic vasculature; rule out portal TE and hepatic AV malformations. • Uroliths: renal pelvis, urinary bladder; obstructive uropathy: urethral obstruction.

ADDITIONAL IMAGING

Colorectal (CRS) or Splenoportal (SPS) Scintigraphy

- Technetium-^{99m} pertechnetate; gamma camera imaging documents isotope appearance in heart before liver to confirm shunting; shunt fraction (time activity plot) is not quantitatively reliable; normal shunt fraction ≤ 15% CRS. Sensitive noninvasive test—confirms shunting; cannot differentiate PSVA from APSS or intrahepatic from extrahepatic PSVA. • SPS: requires splenic injection with contrast; same principle, can miss caudal PSVA.

Multisector CT

- Gold standard imaging to confirm APSS or PSVA; demonstrates arterial and portal circulations, may disclose asymmetric liver

development, GB atresia, choledochal cyst, sacculated interlobular and cystic ducts.

- Non-invasive test: IV contrast administration and short-term (20 minutes) general anesthesia.

DIAGNOSTIC PROCEDURES

- Fine-needle aspiration cytology—cannot diagnose DPM, can sometimes identify bacteria.
- Liver biopsy—open surgical wedge or laparoscopic cup samples from several liver lobes are best, record symmetry of liver lobes sampled, needle core samples can often diagnose DPM.

Echocardiography

Rule out right-sided heart disease and vena caval occlusion (see Portal Hypertension).

DIAGNOSTIC PROCEDURES

- Liver biopsy: as described above.
- Portal hypertension: > 13 cmH₂O attenuated by APSS; measurement may be hazardous and is not clinically useful.

PATHOLOGIC FINDINGS

- Gross—depends on phenotype.
 - (1) *Choledochal cyst*: variable size (as large as 10 cm); wall thick or thin; contents acholic and mucinous white bile; purulent, or bile laden; may be abscessed; may envelop CBD.
 - (2) *Caroli's malformation*: grossly distended hepatic, interlobular, and segmental bile ducts, thick walls if choledochitis, may be mineralized, may have pigment-calcium carbonate choleliths.
 - (3) *Diffuse DPM*: firm fibrotic parenchyma, fine nodular to smooth surface, may have splanchnic APSS if CHF phenotype.
 - (4) *von Meyenburg complexes*: inapparent or tiny pale foci. In phenotypes 2 and 3 above, possible GB atresia, PSVA, other vascular malformation, or left-sided liver agenesis.
- Microscopic—variable severity as previously described. Portal hypoperfusion with diffuse DPM and CHF phenotype; direct intersection of proliferative bile ductules and hepatocytes is a unique feature; islands of hepatocytes encircled by portal-to-portal bridging partitions of variable width in the CHF phenotype.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—for septic complications of choledochal cyst or DPM cholangitis or severe HE (see Hepatic Encephalopathy; Hepatitis, Suppurative and Hepatic Abscess; Cholangitis/Cholangiohepatitis Syndrome).
- Surgical intervention: choledochal cyst—best managed by resection; depends on anatomic malformation and location; may be marsupialized or anastomosed to intestine. Attempt to use alcohol ablation not advised.
- Outpatient—stable patients. • Avoid endoparasitism. • Treat infections promptly—DPM patients (except VMC)

predisposed to cholangitis, choledochitis due to blind ended non-contiguous ductal structures; in CHF portal venous hypoperfusion reduces Kupffer cell surveillance.

- In CHF: remain vigilant for ammonium biurate obstructive uropathies (all levels of urinary system); urethral obstruction (males) may require permanent urethrostomy.
- If APSS—avoid NSAIDs which may augment ascites (sodium and water retention) and gastrointestinal bleeding provoking HE.

NURSING CARE

Hepatic Encephalopathy

- Eliminate causal factors of HE; individualize diet, supplement water-soluble vitamins, vitamin E, and K depending on PT or PIVKA test; optimize HE management to individual response (see Hepatic Encephalopathy). Strive to maintain body condition and muscle mass—muscle mass attenuates ammonia toxicity as temporary storage site; provide multiple small feedings daily.
- Ascites (see Portal Hypertension).



MEDICATIONS

DRUG(S) OF CHOICE

Hepatic Encephalopathy

- Lactulose (0.5–1.0 mL/kg PO q8–12h)—goal to maintain several soft stools daily; may withdraw with optimal diet modifications.
- Oral antibiotics to modify encephalogenic enteric toxin production—first choices: metronidazole (7.5 mg/kg PO q12h) or amoxicillin (22 mg/kg PO q12h). Avoid neomycin (20 mg/kg PO q8–12h PO)—has potential for enteric absorption (esp. if concurrent IBD) causing ototoxicity (deafness) and nephrotoxicity [chronic neomycin: ~ 3% absorbed per dose].

Ascites (also see Portal Hypertension)

- *Dietary sodium restriction* (see Portal Hypertension; Portosystemic Shunting, Acquired)
- Diuretics: *Furosemide* (1–4 mg/kg PO, IM, or IV q12–24h)—potassium wasting effect modulated by *combination with spironolactone* (1–4 mg/kg PO q12h, loading dose then maintenance dose of 2–4 mg/kg; potassium sparing; less potent than furosemide (see Portal Hypertension; Portosystemic Shunting, Acquired).
- *Diuretic-resistant ascites*—consider therapeutic abdominocentesis, V₂ receptor antagonists, and angiotensin receptor blocker diuretic (see Portal Hypertension for details).
- *Antifibrotic*—in humans with DPM, traditional antifibrotics have no influence on age-related accrual of portal ECM causing presinusoidal portal hypertension. The only drug with some efficacy in rat model of adult polycystic renal disease (with CHF) is telmisartan.

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D

- *Telmisartan* is an angiotensin receptor blocker (ARB) used widely in humans as an antihypertensive with partial PPAR- γ agonist activity; it also is nephroprotective (diabetes, other forms of renal injury), prevents certain forms of drug-induced hepatotoxicity, and reduces hepatic fibrosis. ARBs—selectively antagonize the angiotensin-1 receptor, bypassing intermediary activation steps within the RAAS cascade. Telmisartan administration PO to healthy dogs at 1.0 mg/kg/day significantly increased urine volume and sodium excretion and was safely used (single case report) for amelioration of pathologic proteinuria in a dog; effective, non-toxic at escalating doses of 0.43 mg/kg PO q24h to 0.9 mg/kg/day.

Antioxidant Medications

Indicated in dogs with chronic cholangitis, increased liver enzymes, or CHF (see Cirrhosis and Fibrosis of the Liver).

Bleeding Tendencies

See Coagulopathy of Liver Disease. Rare in CHF; may encounter in chronic EHBDO caused by choledochal cyst or cholelithiasis.

Gastrointestinal Hemorrhage

See Cirrhosis and Fibrosis of the Liver; Portal Hypertension. Hypertensive enteric vasculopathy may be encountered with CHF because of APSS.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Avoid or reduce dosage of drugs relying on hepatic biotransformation or first pass hepatic metabolism; avoid drugs reacting with GABA-benzodiazepine receptors; avoid drugs inhibiting biotransformation and metabolism of other drugs (e.g., cimetidine, chloramphenicol, quinidine, some calcium channel blockers). • Avoid metoclopramide if spironolactone used as a diuretic (augments aldosterone).



FOLLOW-UP

PATIENT MONITORING

- Biochemistry—initially, monitor q2–4 weeks until stable in animals presenting

with sepsis or EHBDO, then q4–6 months or if cyclically ill or febrile; monitor for recurrent septic cholangitis/choledochitis, development of septic effusion; HE decompensation. If colchicine used for fibrosis (NOTE: not recommended), monitor CBC for bone marrow suppression and observe for enteric toxicity and neurotoxicity.

POSSIBLE COMPLICATIONS

CHF associated with HE—requires indefinite nutritional and medical management.

EXPECTED COURSE AND PROGNOSIS

- Long-term survival (years) possible.
- Short-term or life-long treatments may be required—antibiotics, unknown long-term benefit from antifibrotics, necessary nutritional modifications if APSS in CHF, ancillary treatments for HE and hypertensive portal vasculopathy (enteric hemorrhage, inappetence), and ascites. • Occasional flare-ups of HE and ascites may require hospitalizations for adjustment of nutritional and medical interventions. Sodium restriction and diuretics may require titration to achieve optimal control of ascites.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Hepatic encephalopathy • Ascites
- Gastrointestinal bleeding • APSS

AGE-RELATED FACTORS

- Prognosis depends on: (1) degree of fibrosis and APSS in CHF, (2) severity of relapsing septic cholangitis or choledochal cyst infection, (3) intrahepatic infectious cholelithiasis, and (4) evidence of hepatic insufficiency at initial diagnosis. • Fibrosis likely progressive with aging.

ZOONOTIC POTENTIAL

N/A

SEE ALSO

- Hepatic Encephalopathy • Portosystemic Shunting, Acquired • Ascites • Hypertension, Portal

ABBREVIATIONS

- ACT = activated clotting time
- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- APSS = acquired portosystemic shunts
- APTT = activated partial thromboplastin time
- AV = arteriovenous
- BUN = blood urea nitrogen
- CBD = common bile duct
- CHF = congenital hepatic fibrosis
- CNS = central nervous system
- DPM = ductal plate malformation
- GI = gastrointestinal
- HE = hepatic encephalopathy
- IBD = inflammatory bowel disease
- MVD = hepatoportal microvascular dysplasia
- NSAID = nonsteroidal anti-inflammatory drug
- PIVKA = proteins invoked by vitamin K absence or antagonism
- PSVA = portosystemic vascular anomaly
- PT = prothrombin time
- TE = thromboembolism
- TSBA = total serum bile acids
- VMC = von Meyenberg complex

Suggested Reading

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DYSAUTONOMIA (KEY-GASKELL SYNDROME)



BASICS

OVERVIEW

- Failure of autonomic function in multiple organs with minimal motor or sensory involvement.
- Young adult, rural, Midwestern dogs at greatest risk.
- Treatment is symptomatic and the prognosis guarded.

SIGNALMENT

- Dog and less commonly cat.
- No breed or sex predilection.
- Median age is 18 months but any age animal may be affected.

SIGNS

- Acute to subacute onset (5–14 days).
- Various combinations of signs may be present but both sympathetic and parasympathetic signs in various organs are necessary to be confident of a diagnosis.
- Sensory or motor deficits are minimal.

Presenting Complaints

- Most commonly GI signs of vomiting or regurgitation, diarrhea, or occasionally constipation.
- Straining to urinate and dribbling urine.
- Photophobia and third-eyelid elevation.
- Dyspnea, coughing, and purulent nasal discharge.
- Depression, anorexia, and weight loss.

Examination Findings

- Variable combinations of autonomic dysfunction.
- Loss of anal sphincter tone.
- Dry nose and mucous membranes; lack of tear production.
- Distended, easily expressed bladder.
- Pupils midrange to maximally dilated with no pupillary light reflex but intact vision.
- Third-eyelid elevation, ptosis, and enophthalmos.
- Lack of gut sounds and occasional abdominal pain.
- Heart rate and blood pressure typically in the low end of normal range but do not rise in response to stress.
- Secondary aspiration pneumonia or rhinitis.
- Cachexia.
- Occasionally mild proprioceptive deficits or weakness.

CAUSES & RISK FACTORS

- Cause unknown.
- Highest incidence in Missouri, Oklahoma, and Kansas as well as Wyoming and northern Colorado, but occasional cases reported throughout United States.
- Free-roaming, rural dogs at greatest risk.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Anticholinergic toxicity.
- Other differential diagnoses depend upon the specific clinical

signs; e.g., urinary tract infection for dysuria, corneal ulcer for photophobia, dehydration for dry mucous membranes.

CBC/BIOCHEMISTRY/URINALYSIS

Unremarkable

IMAGING

- Megaeosophagus ± aspiration pneumonia
- Distended bowel loops with no peristalsis
- Distended urinary bladder
- Echocardiography may show systolic dysfunction as a reduced fractional shortening.

DIAGNOSTIC PROCEDURES

- If pupils affected, 0.05% pilocarpine drops in one eye will produce miosis within 60 minutes. Rules out anticholinergic toxicity.
- Atropine (0.03 mg/kg IV) may not produce a rise in heart rate; suggests loss of vagal tone.
- Intradermal histamine may produce no response or a wheal but no flare; demonstrates loss of sympathetic innervation of arterioles.



TREATMENT

- Symptomatic.
- IV fluids to prevent dehydration.
- High calorie food. Feeding tube to ensure adequate nutrition if megaesophagus is present. If GI motility is absent, parenteral nutrition may be necessary.
- Lubricating eye drops if tear production is insufficient.
- Humidification of the air may help with dry mucous membranes.
- Manual bladder expression.



MEDICATIONS

DRUG(S)

- Antibiotics as needed to treat secondary infections.
- Prokinetic drug such as metoclopramide if GI motility affected.
- Bethanechol to stimulate lacrimation and urination (start at 0.05 mg/kg q8–12h and adjust dose based on response); manual expression of bladder more reliable.
- Ocular pilocarpine to relieve photophobia.
- Pimobendan if poor cardiac contractility.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Animals with dysautonomia develop denervation supersensitivity to direct acting cholinergic or adrenergic drugs.
- Great care must be exercised in using such drugs, particularly adrenergic drugs that could

precipitate fatal tachyarrhythmias. It is best to start at < 10% of the low end of the dose range when using direct-acting drugs and escalate the dose as needed to produce the desired effect.



FOLLOW-UP

- Prognosis is guarded. Most animals die of aspiration pneumonia or euthanasia due to poor quality of life.
- Animals who survive often have some degree of permanent autonomic dysfunction that may require constant care.



MISCELLANEOUS

- Necropsy identification of neuronal loss in ganglia confirms the diagnosis.
- Clinical diagnosis based on autonomic failure in multiple organs without underlying cause or significant motor or sensory involvement and appropriate response to pharmacologic testing.

ABBREVIATION

- GI = gastrointestinal

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DYSCHEZIA AND HEMATOCHEZIA



BASICS

DEFINITION

- Dyschezia—painful or difficult defecation
- Hematochezia—bright red blood in or on the feces

PATHOPHYSIOLOGY

Results from inflammatory, infectious, or neoplastic conditions affecting the colon, rectum, or anus.

SYSTEMS AFFECTED

Gastrointestinal

SIGNALMENT

- Dog and cat
- No breed or sex predilection

SIGNS

Historical Findings

- Vocalizing and whimpering during defecation.
- Tenesmus.
- Decreased frequency of defecation in association with severe dyschezia (animal resists defecating due to pain) resulting in constipation or obstipation.
- Mucoid, bloody diarrhea with a marked increase in frequency and scant fecal volume in patients with colitis.
- Scooting behavior in association with anal gland infection or impaction.

Physical Examination Findings

- Rectal examination may reveal hard feces (constipation or obstipation), diarrhea (colorectal disease), colorectal masses, anorectal thickening, rectal or colonic strictures, anal sac enlargement/pain, prostatomegaly, or perineal hernias.
- Fistulous tracts around anus occur with perianal fistulae.
- Anal occlusion with matted hair and feces occurs with pseudocoprostasis.

CAUSES

Rectal/Anal Disease

- Stricture or spasm
- Anal sacculitis or abscess
- Perianal fistulae
- Rectal or anal foreign body
- Pseudocoprostasis
- Rectal prolapse
- Trauma—bite wounds, etc.
- Neoplasia—adenocarcinoma, lymphoma, and anal sac tumors
- Rectal polyps
- Mucocutaneous lupus erythematosus

Colonic Disease

- Neoplasia—adenocarcinoma, lymphoma, other tumors
- Idiopathic megacolon—cats
- Inflammation—IBD, infectious parasitic agents, colitis secondary to dietary-responsive enteropathy (see Colitis and Proctitis)

- Constipation (see Constipation and Obstipation)

Extraintestinal Disease

- Fractured pelvis or pelvic limb
- Prostatic disease
- Perineal hernia
- Intrapelvic neoplasia

RISK FACTORS

- Ingestion of hair, bone, foreign material may contribute to constipation and subsequent dyschezia.
- Environmental factors such as a dirty litter pan, infrequent outside walks may contribute to constipation and subsequent dyschezia.



DIAGNOSIS

It is pivotal to recognize that hematochezia in animals can be seen with both diffuse colitis as well as with focal or discrete colorectal neoplasms. The fundamental differences in the clinical presentation between the two disorders can usually be recognized during the history and following a thorough physical examination, including a rectal examination. Dogs with colorectal neoplasms do not have diarrhea, and the most important and frequent clinical sign is hematochezia in the absence of an increase in defecation frequency or change in stool consistency. Pencil-thin or ribbon-like stools can be seen when the colorectal neoplasm is advanced, causing a change in the shape of the stool. *A rectal examination must be performed on every patient with a history of hematochezia or dyschezia.*

DIFFERENTIAL DIAGNOSIS

- Dysuria, stranguria, or hematuria—abnormal findings on urinalysis, such as pyuria, crystalluria, bacteriuria. The history and physical examination should differentiate whether the animal is having difficulty urinating or defecating.
- Dystocia—differentiate with history and imaging.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually unremarkable, unless there is a history of chronic blood loss with secondary iron deficiency causing a microcytic and hypochromic non-regenerative anemia.
- Mild neutrophilia (with or without a left shift) with infection or inflammation.

OTHER LABORATORY TESTS

Centrifugation fecal flotation to help rule out parasitic causes of colitis

IMAGING

- Pelvic radiographs may reveal intrapelvic disease, foreign body, or fracture.
- Ultrasonography may demonstrate prostatic disease or caudal abdominal masses; however, a portion of the descending colon cannot be visualized because of the pelvis.

DIAGNOSTIC PROCEDURES

Colonoscopy/proctoscopy to evaluate for inflammatory or neoplastic disease



TREATMENT

- Depends on the underlying cause.
- Colonic strictures secondary to neoplasms can be managed via surgical excision or balloon catheter dilation.
- Consider laxatives (lactulose) to ease defecation and discomfort in animals with colorectal strictures or masses.
- Colorectal masses are best removed surgically or via endoscopy (snare and cauterization for polyps).



MEDICATIONS

DRUG(S) OF CHOICE

- Antibiotics—if bacterial infection (e.g., anal sac abscess); amoxicillin/clavulanic acid 15 mg/kg PO q12h for 7–10 days.
- Anti-inflammatory drugs—sulfasalazine or prednisone (dogs) and prednisolone (cats) if colitis is present (see Colitis chapters).
- Cyclosporine (5 mg/kg q12h for 3–4 months with gradual taper thereafter) for dogs with perianal fistulae.
- Laxatives—lactulose, 1 mL/4.5 kg PO q8–12h to effect; docusate sodium or docusate calcium—dogs, 50–100 mg PO q12–24h; cats, 50 mg PO q12–24h.
- Cisapride—prokinetic indicated for cats with moderate to severe megacolon (and no evidence of obstruction) in conjunction with lactulose and dietary therapy at a dose of 5 mg per cat q12h.

CONTRAINdications

Avoid agents that cause increased fecal bulk (insoluble fiber), unless specifically indicated (colitis).

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

- The need for follow-up depends on the underlying cause. Dogs and cats that are undergoing balloon dilation of colorectal strictures usually require multiple procedures to manage the stricture properly. Animals should always be rechecked at suture removal

DYSCHEZIA AND HEMATOchezIA

(CONTINUED)

or 10–14 days following surgical resection of colorectal masses.

- Animals with hematochezia secondary to colitis should have a marked improvement or resolution of their clinical signs within 5–7 days following implementation of elimination dietary therapy.

PATIENT MONITORING

D Daily monitoring by the owner with periodic phone calls to the clinician every 2–3 weeks during the beginning of treatment.

POSSIBLE COMPLICATIONS

- May see fecal incontinence following surgical resection of anal sacs or colorectal tumors if anal sphincter is compromised.
- Secondary megacolon may occur if obstipation is severe and long-term.

**MISCELLANEOUS ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Caution with corticosteroids, antibiotics

SEE ALSO

- Colitis and Proctitis
- Constipation and Obstipation

ABBREVIATIONS

- IBD = inflammatory bowel disease

Suggested Reading

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BASICS

DEFINITION

- Dysphagia refers to abnormal swallowing and is far more commonly seen in dogs compared to cats.
- Dysphagia is divided into 3 main categories: oropharyngeal, esophageal, and gastroesophageal causes.
- Oropharyngeal causes of dysphagia can be further subcategorized into oral, pharyngeal, or cricopharyngeal causes.
- Any disorder causing difficulty with prehension or mastication can cause dysphagia.
- Odynophagia refers to painful swallowing and is most commonly seen in association with esophageal foreign bodies or to severe esophagitis.
- Esophageal dysphagia is discussed in the chapters on MegAESOPHAGUS and Regurgitation.

PATHOPHYSIOLOGY

- The *oral preparatory phase* is voluntary and begins as food or liquid enters the mouth. Mastication and lubrication of food are the hallmarks of this phase. Abnormalities of the oral preparatory phase usually are associated with dental disease, xerostomia, weakness of the lips (cranial nerves V and VII), tongue (cranial nerve XII), and cheeks (cranial nerves V and VII).
- The *oral phase* of swallowing consists of the muscular events responsible for movement of the bolus from the tongue to the pharynx and is facilitated by the tongue, jaw, and hyoid muscle movements.
- The *pharyngeal phase* begins as the bolus reaches the tonsils and is characterized by elevation of the soft palate to prevent the bolus from entering the nasopharynx, elevation and forward movement of the larynx and hyoid, retroflexion of the epiglottis and closure of the vocal folds to close the entrance into the larynx, contraction of the muscles of the pharynx, and relaxation of the cricopharyngeus muscle that makes up much of the proximal esophageal sphincter (PES) to allow passage of the bolus into the esophagus. Respiration is briefly halted (apneic moment) during the pharyngeal phase.
- Abnormalities of the pharyngeal phase of swallowing are associated with pharyngeal weakness secondary to neuropathies or myopathies, pharyngeal tumors or foreign bodies, cricopharyngeus muscle disorders.
- The *esophageal phase* is involuntary and begins with the relaxation of the PES and movement of the bolus into the esophagus.

SYSTEMS AFFECTED

- Gastrointestinal
- Nervous

- Neuromuscular
- Respiratory

GENETICS

Breeds that have a hereditary predisposition or a high incidence of dysphagia include the golden retriever (pharyngeal weakness), cocker and springer spaniels (cricopharyngeal dysphagia), Bouvier des Flandres and Cavalier King Charles spaniel (muscular dystrophy), and boxer (inflammatory myopathy). In addition, large and giant-breed dogs are predisposed to acquired megaesophagus.

INCIDENCE/PREVALENCE

Variable depending on underlying etiology. Megaesophagus is one of the most common causes of dysphagia in dogs.

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

- Dog and cat.
- Congenital disorders that cause dysphagia (e.g., cricopharyngeal achalasia, cleft palate, hiatal hernia) are usually diagnosed in animals < 1 year old.
- Acquired esophageal dysmotility and pharyngeal weakness is more common in older patients.

SIGNS

Historical Findings

- Drooling (due to pain or inability to swallow saliva), gagging, ravenous appetite, repeated or exaggerated attempts at swallowing, swallowing with the head in an abnormal position, nasal discharge (due to nasal reflux of food and liquids into the nasopharynx), coughing (due to aspiration), regurgitation, painful swallowing, and occasionally anorexia and weight loss are all possible. If the tongue is not functioning normally, problems with prehension and mastication may be seen.
- Ascertain onset and progression. Foreign bodies cause acute dysphagia; pharyngeal dysphagia may be chronic and insidious in onset.

Physical Examination Findings

- Physical examination must include careful examination of the oropharynx using sedation or anesthesia if necessary to help rule out morphologic abnormalities such as dental disease, foreign bodies, cleft palate, glossal abnormalities, and oropharyngeal tumors.
- Evaluation of cranial nerves should be performed, including assessment of tongue and jaw tone, and assessment of laryngeal function.
- A complete physical and neurologic examination may identify clinical signs supporting a generalized neuromuscular disorder, including muscle atrophy, stiffness, or decreased or absent spinal reflexes.
- Evaluate the gag reflex by placing a finger in the pharynx; however, the presence or absence

of a gag reflex does not correlate with the efficacy of the pharyngeal swallow nor the adequacy of deglutitive airway protection.

- The importance of the clinician's carefully observing the dysphagic animal while it is eating (kibble and canned food) and drinking in the hospital is pivotal, and such observation helps to localize the problem to the oral cavity, pharynx, or esophagus.

ORAL DYSPHAGIA

- Modified eating behavior (e.g., eating with head tilted to one side or having difficulty prehending the bolus or opening the mouth).
- Tongue paralysis or dystrophy, dental disease, masticatory muscle myositis, temporal muscle atrophy, or pain, and food packed in the buccal folds suggest oral dysphagia.

PHARYNGEAL DYSPHAGIA

- Prehension of food is normal.
- Repeated attempts at swallowing with food falling out of the mouth, and excessive gagging suggest pharyngeal dysphagia.
- Saliva-coated food retained in the buccal folds, a diminished gag reflex, and nasal discharge may also exist.

CRICOPHARYNGEAL DYSPHAGIA

- Patients make repeated, nonproductive efforts to swallow, gag, and cough, then forcibly regurgitate immediately after swallowing.
- Gag reflex and prehension are normal.
- Nasal reflux is commonly observed when food hits the closed PES.

ESOPHAGEAL DYSPHAGIA

- Most common causes include megaesophagus, esophagitis, esophageal stricture, esophageal foreign bodies, and esophageal dysmotility.
- Diagnosis made with survey radiographs of the thorax and neck followed by videofluoroscopy.

GASTROESOPHAGEAL DYSPHAGIA

Most common cause is a sliding hiatal hernia that is often associated with gastroesophageal reflux and subsequent esophagitis.

CAUSES

- Anatomic or mechanical lesions include pharyngeal inflammation (e.g., abscess, inflammatory polyps, and oral eosinophilic granuloma), neoplasia, pharyngeal and retropharyngeal foreign body, sialocele, temporomandibular joint disorders (e.g., luxation, fracture, and craniomandibular osteopathy), mandibular fracture, cleft or congenitally short palate, cricopharyngeal achalasia, lingual frenulum disorder, and pharyngeal trauma.
- Pain as a result of dental disease (e.g., tooth fractures and abscess), mandibular trauma, stomatitis, glossitis, and pharyngeal inflammation may disrupt normal prehension, bolus formation, and swallowing. Stomatitis, glossitis, and pharyngitis may be

DYSPHAGIA

(CONTINUED)

D

- secondary to feline viral rhinotracheitis, FeLV/FIV, pemphigus, SLE, uremia, and ingestion of caustic agents or foreign bodies.
- Neuromuscular disorders that impair prehension and bolus formation include cranial nerve deficits (e.g., idiopathic trigeminal neuropathy CN V, lingual paralysis CN XII) and masticatory muscle myositis.
- Pharyngeal weakness, paresis, or paralysis can be caused by infectious polymyositis (e.g., toxoplasmosis and neosporosis), immune-mediated polymyositis, muscular dystrophy, polyneuropathies, and myoneuron junction disorders (e.g., myasthenia gravis, tick bite paralysis, and botulism).
- Other CNS disorders, especially those involving the brainstem.
- Rabies can cause dysphagia by affecting both the brainstem and peripheral nerves.

RISK FACTORS

Many of the causative neuromuscular conditions have breed predispositions.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Differentiate vomiting from regurgitation.
- Vomiting is associated with abdominal contractions; dysphagia is not.

CBC/BIOCHEMISTRY/URINALYSIS

- Inflammatory conditions often cause a leukocytosis, sometimes with a left shift.
- High serum creatine kinase activity is usually suggestive of a myopathy.
- May find evidence of renal disease (e.g., azotemia and low urine concentration) in patients with oral and lingual ulcers secondary to uremia.

OTHER LABORATORY TESTS

- Type 2M muscle antibody serology (masticatory muscle myositis).
- Acetylcholinesterase receptor antibody serology (acquired myasthenia gravis).
- Antinuclear antibody serology (immune-mediated diseases).
- T_4 , free T_4 , TSH, anti-thyroglobulin antibodies to rule out hypothyroidism.
- Resting cortisol and/or ACTH stimulation test to rule out Addison's disease.

IMAGING

- Obtain survey radiographs of the thorax and neck in all dysphagic animals for which an oral cause of dysphagia has been ruled out.
- Ultrasonography of the pharynx may be useful in patients with mass lesions and for obtaining ultrasound-guided biopsy specimens.
- Fluoroscopy with barium is useful in evaluating pharyngeal and esophageal motility as well as proper coordination of the upper and lower esophageal sphincters.

- CT and/or MRI for a suspected intracranial mass.
- Esophagram (liquid barium administered orally followed by immediate survey radiographs of the thorax) is helpful for diagnosing radiolucent esophageal foreign bodies and esophageal strictures, but is insensitive for diagnosing eosophageal functional disorders.

OTHER DIAGNOSTIC PROCEDURES

- Endoscopy of the nasopharynx—retroflexion of the endoscope over the soft palate to look for foreign bodies and evaluate the esophagus and lower esophageal sphincter.
- Electromyography of skeletal musculature to confirm the presence of a myopathy.
- Repetitive nerve stimulation and edrophonium chloride (0.1–0.2 mg/kg IV) test for suspected myasthenia gravis.
- Cerebrospinal fluid analysis in patients with a CNS disorder.

PATHOLOGIC FINDINGS

Variable depending on underlying etiology. Myopathies can be inflammatory or dystrophic.



TREATMENT

APPROPRIATE HEALTH CARE

- Determine the underlying cause to optimize therapy and outcome.
- Most patients can be managed on an outpatient basis unless there are other complicating factors such as aspiration pneumonia, dehydration or weakness.

NURSING CARE

- Supportive care may be necessary if the patient is dehydrated (IV fluids).
- Other supportive modalities may be necessary in the case of aspiration pneumonia (oxygen, coupage, etc.).
- For patients with generalized weakness due to myopathies, good nursing care is required, such as rotating position, good padding, and physical therapy.

ACTIVITY

Alterations in activity should be based on the underlying etiology.

DIET

- Nutritional support is important for all dysphagic patients.
- Elevating the head and neck during feeding and for 10–15 minutes after feeding may help patients with esophageal disease. Consider altering the consistency of the diet. Dogs with cricopharyngeal dysphagia are able to handle kibble better than canned food or water.
- If nutritional requirements cannot be met orally, a gastrostomy tube may be necessary.

CLIENT EDUCATION

- Variable dependent on the underlying cause.
- Educate the client that not all diseases can be cured, but managed.
- Changes in feeding (see above section) may be long-term.
- Clients should be taught to monitor for signs of possible aspiration pneumonia (mucopurulent nasal discharge, respiratory rate, coughing, dyspnea, tachypnea).

SURGICAL CONSIDERATIONS

- Cricopharyngeal myectomy may benefit patients with cricopharyngeal dysphagia; a correct diagnosis is essential using videofluoroscopy before surgery.
- Hiatal hernia surgery generally involves a left-sided gastropexy with esophageal hiatal plication and esophagopexy.



MEDICATIONS

DRUG(S) OF CHOICE

Dysphagia is not immediately life-threatening; direct drug therapy at the underlying cause.

PRECAUTIONS

- Use barium sulfate with caution in patients with evidence of aspiration.
- Use corticosteroids with caution or not at all in patients with evidence of, or at risk for, aspiration.



FOLLOW-UP

PATIENT MONITORING

- Daily for signs of aspiration pneumonia (e.g., lethargy, fever, mucopurulent nasal discharge, coughing, and dyspnea).
- Body condition and hydration status daily; if oral nutrition does not meet requirements, use gastrostomy tube feeding.

POSSIBLE COMPLICATIONS

Aspiration pneumonia and malnutrition.

EXPECTED COURSE AND PROGNOSIS

Variable dependent on the cause



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Aspiration pneumonia
- Megaesophagus
- Malnutrition

AGE-RELATED FACTORS

- Puppies are more likely to have congenital abnormalities such as cricopharyngeal achalasia, congenital megaesophagus, vascular ring anomalies, and cleft palates.

(CONTINUED)

- Puppies with vascular ring anomalies will typically present with signs of regurgitation shortly after being weaned onto solid food at 6–8 weeks of age.
- Puppies with cleft palates usually have milk or food refluxing from the nasal passage during mastication and swallowing.
- Puppies with cricopharyngeal achalasia typically present with repeated bouts of swallowing, gagging, and retching during swallowing with nasal reflux of water or food.
- Puppies are more likely to ingest foreign objects that can lodge in the esophagus and cause esophagitis and stricture formation.
- Older dogs, in particular Labrador retrievers, are more likely to have esophageal dysmotility secondary to a polyneuropathy.

ZOONOTIC POTENTIAL

- Consider rabies in any patient with oropharyngeal dysphagia, especially if the

animal's rabies vaccination status is unknown or questionable or it has been exposed to a potentially rabid animal.

- If a dysphagic animal dies of rapidly progressive neurologic disease, submit the head to a qualified laboratory designated by the local or state health department for rabies examination.

SEE ALSO

- MegAESOPHAGUS
- Pneumonia, Bacterial
- Regurgitation

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- CNS = central nervous system
- CNs = cranial nerves
- CT = computed tomography
- MRI = magnetic resonance imaging
- SLE = systemic lupus erythematosus
- TSH = thyroid stimulating hormone

Suggested Reading

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**Client Education Handout
available online**

D

DYSPNEA AND RESPIRATORY DISTRESS



BASICS

DEFINITION

Dyspnea—a subjective term that in human medicine means “an uncomfortable sensation in breathing” or a sensation of air hunger; in veterinary medicine, it is used to indicate difficulty breathing or respiratory distress.

PATHOPHYSIOLOGY

Dyspnea and respiratory distress are believed to occur when the central nervous system notes a difference between the afferent feedback from a given efferent motor drive signal (ventilation demanded) and what the brain had anticipated would be the appropriate afferent response (ventilation achieved).

SYSTEMS AFFECTED

Respiratory

SIGNALMENT

Dogs and cats; age, breed, and sex predisposition vary with inciting cause.

SIGNS

Historical Findings

- Acute or chronic onset.
- Often associated with coughing, tachypnea, exercise intolerance.

Physical Examination Findings

- General signs of respiratory distress—increased abdominal effort, nasal flaring, open-mouth breathing, cyanosis, orthopnea (neck extension, elbow abduction); other signs depend on underlying cause.
- Nasal disease—stertor, nasal discharge, lack of airflow through nostrils; dyspnea improves with open-mouth breathing.
- Upper airway disease—stridor, cough, hyperthermia, respiratory effort and noise on inspiration.
- Tracheal collapse—honking cough, tracheal sensitivity.
- Lower airway disease—cough, expiratory wheezes on auscultation,
- Pulmonary parenchymal disease—may have crackles, harsh or moist lung sounds on auscultation; may be normal.
- Pneumonia—fever, may have tracheal sensitivity.
- Cardiogenic pulmonary edema—heart murmur, arrhythmia, hypothermia, pale mucous membranes, prolonged capillary refill time.
- Pleural space disease—diminished breath sounds: ventrally—fluid; dorsally—air; unilaterally—space-occupying lesions or pyothorax/chylothorax. Often paradoxical respiratory pattern (inward movement of the abdominal wall during inspiration).
- Thoracic wall disease—can have paradoxical respiratory pattern, visible or palpable trauma.
- PTE—may have clinical signs of the underlying disease predisposing to thrombosis, e.g., hyperadrenocorticism, IMHA, neoplasia.
- Other signs will pertain to the underlying disease, e.g., shock, trauma.

CAUSES & RISK FACTORS

Upper Airway Disease

- Nasal obstruction—stenotic nares, nasopharyngeal polyp or stenosis, infection, inflammation, neoplasia, trauma, foreign body, coagulopathy.
- Pharynx—elongated soft palate, foreign body, neoplasia, granuloma.
- Larynx—laryngeal paralysis, everted laryngeal saccules, edema, collapse, foreign body, neoplasia, trauma, webbing.
- Trachea—collapse, stenosis, trauma, foreign body, neoplasia, parasites, extraluminal compression (lymphadenopathy, enlarged left atrium, heart-base tumors).

Lower Airway Disease

Inflammatory, infectious (*Mycoplasma*), parasitic, neoplastic (bronchogenic carcinoma).

Pulmonary Parenchymal Disease

- Edema—cardiogenic or non-cardiogenic.
- Pneumonia—infectious; parasitic; aspiration; eosinophilic; interstitial.
- Neoplasia (primary or metastatic).
- Inflammatory—ARDS; uremic pneumonitis; smoke inhalation.
- Hemorrhage—trauma; coagulopathy.
- PTE—IMHA; PLN or PLE; heartworm disease; hyperadrenocorticism; neoplasia.
- Others—lung lobe torsion, atelectasis.

Pleural Space Disease

- Pneumothorax—traumatic; iatrogenic; secondary to pulmonary parenchymal disease; ruptured bulla; migrating foreign body; primary spontaneous (no underlying cause).
- Pleural effusion—transudates, exudates; hemothorax; chylothorax.
- Soft tissue—neoplasia; diaphragmatic hernia.
- Fibrosing pleuritis.

Thoracic Wall Disease

- Open pneumothorax—trauma; flail segment—trauma; neoplasia; paralysis due to cervical spinal disease, botulism, polyradiculoneuritis, tick bite paralysis, myasthenia gravis, elapid snake envenomation.

Diaphragmatic Disease

- Trauma—rupture; hernia
- Phrenic nerve disease
- Neoplasia
- Fibrosis

Abdominal Distention

- Organomegaly—hyperplasia; neoplasia, pregnancy; obesity; ascites; gastric dilatation, torsion



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Inspiratory dyspnea—suggests extrathoracic upper airway disease.
- Expiratory dyspnea—suggests intrathoracic airway disease.
- Dyspnea on inspiration and expiration can occur with fixed upper airway obstructions and severe intrathoracic disease.
- Congestive

heart failure—murmur, arrhythmia, tachycardia, poor pulse quality, jugular pulses, hypothermia, crackles on auscultation, fluid dripping from nose.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia—can cause non-respiratory dyspnea.
- Polycythemia—chronic hypoxia.
- Inflammatory leukogram—pneumonia, pyothorax.
- Eosinophilia—hypersensitivity or parasitic airway disease.
- Thrombocytosis—hyperadrenocorticism predisposes to PTE.
- Sodium:potassium ratio < 27—can be seen with pleural or abdominal effusions.
- Azotemia—if severe may lead to uremic pneumonitis.
- Proteinuria—can predispose to PTE.
- Multiple organ dysfunction—ARDS.
- Hypoproteinemia—may suggest protein-losing disease that can predispose to PTE or hydrothorax.

OTHER LABORATORY TESTS

- Pleural fluid analysis.
- Fecal examination for parasites
- Serum antigen or antibody titers—heartworm, toxoplasmosis, distemper, FeLV, FIV.
- Increased urine protein:creatinine ratio with PLN could indicate loss of antithrombin and hypercoagulability resulting in PTE.
- PaO_2 —partial pressure of oxygen dissolved in arterial blood; normoxemia: PaO_2 80–120 mmHg (room air, sea level); hypoxemia: PaO_2 < 80 mmHg; $F_1\text{O}_2$ —fraction of inspired oxygen ranges from 0.21 (room air) to 1.0; $\text{PaO}_2/F_1\text{O}_2$ ratio—measure of lung efficiency; $\text{PaO}_2/F_1\text{O}_2 \geq 500$ —normal lung efficiency; 300–500—mild insufficiency; 200–300—moderate insufficiency; < 200—severe insufficiency. Reduction in lung efficiency is most commonly due to pulmonary parenchymal disease.
- PaCO_2 or PvCO_2 —partial pressure of CO_2 dissolved in arterial or venous blood; measure of ventilation; normal 30 mmHg < PCO_2 < 40 mmHg. Hypercapnia = hypoventilation = decreased alveolar minute ventilation (MV).
- Coagulation testing—if suspect hemothorax and/or pulmonary hemorrhage.
- Plasma NT-proANP, BNP, ET-1, and cTNI concentrations may aid in differentiation of cardiac and non-cardiac causes of dyspnea.

IMAGING

- Cervical and thoracic radiography: upper airway disease—soft palate elongation, large airway narrowing, lymphadenopathy, intraluminal abnormalities. Lower airway disease—bronchial thickening, middle lung lobe consolidation (cats), atelectasis, hyperinflation and diaphragmatic flattening (primarily cats). Pneumonia—alveolar infiltrates; lobar sign—lung lobe torsion, foreign body pneumonia, neoplasia; cardiogenic pulmonary edema—enlarged cardiac silhouette, pulmonary venous distention, enlarged left atrium with perihilar pulmonary infiltrates in dogs; infiltrates can

(CONTINUED)

DYSPNEA AND RESPIRATORY DISTRESS

be of any distribution in cats. Non-cardiogenic pulmonary edema—caudodorsal distribution. ARDS—diffuse, symmetrical alveolar infiltrates. Pulmonary vascular abnormalities—PTE, heartworm disease. Pleural space disease—pneumothorax, pleural effusion, mass lesions, diaphragmatic hernias. Thoracic wall disease—rib fractures, neoplasia. • Thoracic ultrasonography: evaluation of distribution of pleural effusion, pneumothorax (absence of “glide sign”), and parenchymal disease (presence of “comet tail” artifact). Pulmonary mass identification—guide fine-needle aspiration; mediastinal evaluation. • Echocardiography: evaluate cardiac function if cardiogenic pulmonary edema or pleural effusion suspected; elevated pulmonary artery pressure and right ventricular overload can support diagnosis of PTE; visualize heart-based masses.

- Abdominal radiography or ultrasound: evaluation of abdominal distention.
- Fluoroscopy: evaluate tracheal and bronchial collapse; evaluate diaphragmatic function.
- Computed tomography: airway, pulmonary parenchymal, and pleural space disease can be evaluated; can detect lesions not clearly defined on radiographs.
- Pulmonary vascular angiography: gold standard for diagnosis of PTE.
- Ventilation perfusion scintigraphy: abnormal perfusion scan is considered supportive of PTE.

DIAGNOSTIC PROCEDURES

- Pulse oximetry—SpO₂ of hemoglobin saturated with oxygen. The relationship between PaO₂ and SpO₂ is defined by the oxygen hemoglobin dissociation curve; PaO₂ of 60 mmHg = SpO₂ of 90%; PaO₂ of 80 mmHg = SpO₂ of 95%; PaO₂ of > 100 mmHg = SpO₂ of 100%. Below 95%, small changes in SpO₂ signify large changes in PaO₂. SpO₂ measurements in animals on high inspired oxygen lack sensitivity.
- Thoracocentesis—fluid analysis and culture.
- Laryngoscopy/nasopharyngoscopy/tracheoscopy—visualize foreign bodies and masses.
- Bronchoscopy—evaluate upper and lower airways; perform bronchoalveolar lavage for cytology and culture. Requires anesthesia, perform only when stabilized.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Inpatient care until the cause is identified and treated or determined not to be life-threatening; therapy dependent on underlying cause.
- ALWAYS administer oxygen and keep patient in sternal recumbency until ability to oxygenate is determined.
- Lower airway disease—bronchodilators; oxygen therapy until stable;

systemic corticosteroids may be required to stabilize cats with acute bronchoconstriction.

- Pulmonary parenchymal disease—oxygen therapy, antibiotics if pneumonia; treat coagulation disorders; cardiogenic edema requires furosemide ± vasodilators.
- Non-cardiogenic edema requires oxygen therapy, may require positive-pressure ventilation.
- Pleural space disease—thoracocentesis for air and fluid. Place a chest tube if repeated thoracocentesis is necessary to keep patient stable.
- Thoracic wall disease—surgery as indicated, particularly if open chest wound is present; flail chest may require surgery if medical management fails or there is a severe displacement of fractures.
- Thoracic wall paralysis/muscle fatigue—positive-pressure ventilation if severely hypercapnic.
- Abdominal distention—drain ascites as needed; relieve gastric distention.

NURSING CARE

- Oxygen therapy via cage, nasal cannula, E-collar covered in plastic wrap, mask, or flow-by. Humidify oxygen source if giving oxygen therapy for more than a few hours.
- Maintain in sternal recumbency and turn hips every 3–4 hours if patient cannot tolerate lateral recumbency.
- Monitor temperature regularly, as excess work of breathing results in hyperthermia, which augments respiratory distress.

DIET

Weight-reducing diet if obesity is a contributing cause.

SURGICAL CONSIDERATIONS

- Anesthesia must be carefully tailored to the patient. Securing an airway is essential and rapid intravenous induction is important. The ability to positive-pressure ventilate patients is often required.
- Animals with upper airway obstruction are fragile and can rapidly decompensate. Have multiple-sized endotracheal tubes available.
- Dyspnea associated with a laryngeal mass can respond to debulking surgery but edema and hemorrhage can lead to worsened obstruction. Warn owners of increased likelihood of aspiration pneumonia complications in animals with laryngeal disease.
- Avoid positive-pressure ventilation in patients with a closed pneumothorax. Must monitor oxygenation status of anesthetized patients with pulse oximetry and when possible arterial blood gases.

**MEDICATIONS****DRUG(S)**

Varies with underlying cause (see “Appropriate Health Care”).

**FOLLOW-UP****PATIENT MONITORING**

- Patients receiving oxygen therapy can be monitored by assessing the degree of respiratory effort. As the animal stabilizes, perform a room air trial and reevaluate the level of respiratory difficulty. Arterial and venous blood gases can be a useful assessment.
- Pulse oximetry is an effective and noninvasive tool for monitoring patients on room air.
- Repeat radiographs are often indicated in assessing pulmonary parenchymal disease and pleural space disease.

**MISCELLANEOUS****SEE ALSO**

- Acute Respiratory Distress Syndrome
- Asthma, Bronchitis—Cats
- Brachycephalic Airway Syndrome
- Congestive Heart Failure, Left-Sided
- Congestive Heart Failure, Right-Sided
- Laryngeal Diseases
- Pneumonia
- Pneumothorax
- Pulmonary Edema, Noncardiogenic

ABBREVIATIONS

- ARDS = acute respiratory distress syndrome
- BNP = brain natriuretic peptide
- cTNI = cardiac troponin-I
- ET-1 = endothelin-1
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- IMHA = immune-mediated hemolytic anemia
- MV = minute ventilation
- NT-proANP = n-terminal pro-atrial natriuretic peptide
- PLE = protein-losing enteropathy
- PLN = protein-losing nephropathy
- PTE = pulmonary thromboembolism

Suggested Reading

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Prosek R, Sisson DD, Oyama M, Solter PF. Distinguishing cardiac and noncardiac dyspnea in 48 dogs using plasma atrial natriuretic factor, B-type natriuretic factor, endothelin and cardiac troponin-I. *J Vet Intern Med* 2007; 21:238–242.

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Client Education Handout
available online

DYSTOCIA



BASICS

DEFINITION

Difficult birth

PATHOPHYSIOLOGY

- Dystocia may occur as a result of maternal or fetal factors and may occur during any stage of labor.
- Abnormal presentation, posture, and position; may be causal. Normal: anterior or posterior longitudinal, dorsosacral, and head and feet extended.
- Three stages of labor:

Stage 1

- Early onset of uterine contractions and relaxation of the cervix; ends with rupture of first chorioallantoic sac—averages 6–12 h (up to 36 h in nervous, primiparous bitch).
- Bitch—may be restless, nervous, shiver, pant, pace, and nest.
- Queen—tend to vocalize initially; purr and socialize as Stage 1 progresses.

Stage 2

- Delivery of the fetuses.
- Bitch—obvious abdominal contractions; from beginning of stage 2 to delivery of first offspring usually <4 h; time between delivery of subsequent fetus usually 20–60 min (may be as long as 2–3 h).
- Queen—average length of parturition is 16 h, with a range of 4–42 h (up to 3 d in some cases may be normal); important to consider this variability when intervening.
- Number of fetuses present may significantly affect the length of stages 2 and 3.

Stage 3

- Delivery of the fetal membranes.
- May alternate between stage 2 and 3 with multiple fetuses.

INCIDENCE/PREVALENCE

- Dog: incidence unknown; difficult to estimate due to breed variability and breeder intervention.
- Cat: reported average ranges from 3.3–5.8%; mixed-breed cats 0.4%; increased with pedigree cats, to a high of 18.2% in the Devon rex.

SIGNALMENT

Breed Predilections

Dogs

- Higher incidence with miniature and small breeds due to small litter size with concurrent large fetal size; may occur in large breeds with large or singleton litters.
- Brachycephalic—broad head and narrow pelvis—Bulldog, Boston terrier, pug.
- Large fetal head: maternal pelvis ratio—Sealyham terrier, Scottish terrier.
- Uterine inertia—Scottish terrier, dachshund, border terrier, Aberdeen terrier, Labrador retriever (see Uterine Inertia).
- Miscellaneous breeds with overall increased incidence of dystocia—Chihuahua, dachshund, Pekingese, Yorkshire terrier, miniature poodle, Pomeranian.

Cats

- Brachycephalic—Persian, Himalayan
- Dolichocephalic—Devon rex

SIGNS

Historical Findings

- Indicators of dystocia include:
 - More than 30 min of persistent, strong, abdominal contractions without fetal delivery.
 - More than 4 h from the onset of stage 2 to delivery of first fetus (bitches).
 - More than 2 h between delivery of fetuses (bitch).
 - Failure to commence labor within 24 h of the drop in rectal temperature below 37.2°C (99°F) or within 36 h of serum progesterone < 2 ng/mL (bitch).
 - Female cries, displays signs of pain, and constantly licks the vulvar area when contracting.
 - Prolonged gestation—more than 72 d from day of first mating (bitch); more than 59 d from the first day of cytologic diestrus (bitch); more than 66 d from LH peak (bitch); more than 68 d from the day of mating (queen).

Physical Examination Findings

- Presence of greenish-black discharge (uteroverdin) preceding the birth of first fetus by more than 2 h.
- Presence of bloody discharge prior to delivery of first fetus.
- Diminished or absent Ferguson's reflex (stimulation or pressure to dorsal vaginal wall to elicit abdominal straining: "feathering") indicates uterine inertia.

CAUSES

Fetal

- Oversize; fetal monsters, fetal anasarca; fetal hydrocephalus; prolonged gestation due to inability of a singleton fetus to initiate labor.
- Abnormal presentation, position, or posture of fetus in the birth canal.
- Fetal death.

Maternal

- Inadequate uterine contractions (primary or secondary uterine inertia)—myometrial defect; biochemical imbalance; psychogenic disturbance; exhaustion.
- Ineffective abdominal press—pain; fear; debility (exhaustion); diaphragmatic hernia; age.
- Placentitis, metritis, endometritis.
- Pregnancy toxemia, gestational diabetes.
- Abnormal pelvic canal—previous pelvic injury; abnormal conformation; pelvic immaturity.
- Congenitally small pelvis—Welsh corgis; brachycephalic breeds.
- Inguinal hernia.
- Abnormality of the vaginal vault—stricture; septae; vaginal hyperplasia; hypoplastic vagina; intraluminal or extraluminal cysts; neoplasia.
- Abnormality of the vulvar opening—stricture; small vulva; fibrosis from trauma; neoplasia.
- Insufficient cervical dilation.
- Lack of adequate lubrication.
- Uterine torsion.
- Uterine rupture.
- Uterine neoplasia, cysts, or adhesions.

RISK FACTORS

- Age
- Brachycephalic and toy breeds
- Persian, Himalayan, and Devon rex breeds

- Obesity
- Abrupt changes in environment peripartum
- Previous history of dystocia



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Uterine inertia—hypocalcemia versus hypoglycemia

PHYSICAL EXAMINATION

- Complete physical examination—determine concurrent or contributing problems (e.g., hypoglycemia, hypocalcemia, dehydration, fever); perform careful abdominal palpation to confirm the existence of fetuses.
- Digital vaginal examination—presence of a fetus or fetal membranes in the vaginal canal; abnormalities of the maternal pelvic canal; assess Ferguson's reflex.
- Bitches unresponsive to oxytocin or lacking Ferguson's reflex—uterine inertia more likely than obstructive dystocia, except if obstructed for several hours.

CBC/BIOCHEMISTRY/URINALYSIS

Minimum database—PCV, total protein, BUN, serum glucose, and calcium concentrations (ionized preferable to total serum calcium).

OTHER LABORATORY TESTS

Progesterone concentration

IMAGING

- Radiography—determine pelvic conformation, number and position of fetuses, evidence of fetal obstruction, fetal oversize, and fetal death; may require two views.
- Radiographic evidence of fetal death—collapse of fetal skeletons, abnormal association of fetal bones to the axial skeleton, presence of air/gas surrounding a fetus, fetal balling.
- Ultrasonography—recommended for monitoring fetal viability; fetal stress (e.g., fetal heart rate sustained at < 180 bpm) or death; sustained tachycardia (> 260 bpm) indicates need for more frequent monitoring; placental separation, and character of fetal fluids (presence of meconium or blood in amniotic fluid); fetal heart rate is normally two to three times that of the dam in bitches.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—until delivery of all fetuses and the dam is stabilized.
- Uterine inertia—initiate medical treatment if no evidence of fetal stress.
- Ecbolic agents contraindicated in the face of possible obstructive dystocia—may accelerate placental separation and fetal death, or cause uterine rupture.
- Hypocalcemia—bitch: administer 10% calcium gluconate at 0.2 mL/kg slowly IV (over 5–10 minutes; monitor for arrhythmia);

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may be repeated q4-6h as needed; queen: 0.5–1.0 mL calcium gluconate IV slowly—use with caution in cats as risk of uterine rupture is increased due to strong uterine contractions following calcium administration. • Hypoglycemia—administration of balanced electrolyte solution with 5–10% dextrose at a rate of 60–80 mL/kg/day IV. • Oxytocin—once calcium and glucose deficits are treated, microdoses of oxytocin (0.5–4.0 IU IM, SC depending on the size of the bitch and response to treatment); may be repeated at 30-minute intervals as long as delivery progresses. Consider C-section if more than three doses of oxytocin per fetus are required or more than four fetuses remain. If the bitch is not contracting adequately on her own, allow a minimum of 30 min between delivery of a fetus and the next dose of oxytocin.

- WhelpWise™ system monitors fetal heart rates and uterine contraction patterns; extremely useful for bitches with a history of uterine inertia or with large litters to determine the need for, and response to, medical treatment.

Manual Delivery

- To deliver a fetus lodged in vaginal vault:
 - Apply lubrication liberally.
 - Digital manipulation—least amount of damage to fetus and dam. Apply traction in a postero-ventral direction.
 - Instrument delivery not recommended due to inadequate space—undesirable sequelae include fetal mutilation and laceration of the dam.
 - Never apply traction to the distal extremities of a live fetus.
 - Failure to deliver a fetus located in the vaginal canal within 30 minutes—C-section indicated.

SURGICAL CONSIDERATIONS

- Indications for C-section—uterine inertia unresponsive to oxytocin or a uterine inertia with more than four fetuses remaining *in utero* (maximizes fetal survivability); pelvic or vaginal obstruction; inability to correct fetal malposition; fetal oversize; fetal stress; *in utero* fetal death.
- Elective C-section—breeds prone to dystocia; bitches with a history of dystocia; bitches with singleton or large litter size; often performed to maximize fetal survivability.

General Comments

- Provide fluid therapy with a balanced electrolyte solution before, during, and after surgery.
- The gravid uterus can compress great vessels, compromise venous return, and place pressure on diaphragm, resulting in decreased tidal volume.
- Pregnant bitches have lower systolic BP, PO₂, PCV; and higher PCO₂, respiratory rates, and incidence of

acidosis.

- Pre-oxygenation of patients improves maternal and neonatal outcome.
- Premedication with glycopyrrolate if fetal heart rates are normal (bitches: 0.01 mg/kg IV, IM; queens: 0.005–0.01 mg/kg IV, IM); or if fetal bradycardia exists with atropine (bitches: 0.02–0.04 mg/kg IM; queens: 0.04 mg/kg IM); induction with propofol (4–6 mg/kg IV), intubate and maintain with sevoflurane (or isoflurane) preferred; propofol CRI until fetuses delivered, then switch to sevoflurane/isoflurane.
- If propofol is unavailable, premedication with diazepam (0.1–0.4 mg/kg IV, IM) and butorphanol (0.2–0.4 mg/kg IM) followed by masking with sevoflurane (or isoflurane).
- Ketamine—not recommended in the bitch due to fetal depression; may be used in the queen where ketamine affects the fetus in a dose-dependent manner. With appropriate premedication a low-dose induction (1 mg/kg IV or 5 mg/kg IM) may be adequate.
- Epidural—bitch: (0.2 mg/kg 0.5% bupivacaine and 0.1 mg/kg preservative-free morphine or 0.1–0.3 mL/kg 2% lidocaine without epinephrine given to desired effect but not to exceed 10 mg/kg total lidocaine dose; queen: 2% lidocaine (0.2 mL/kg) given to desired effect plus butorphanol (0.2–0.4 mg/kg IV, IM); local anesthesia may also be utilized. Disadvantages of local/regional anesthesia are the inability to oxygenate adequately without an endotracheal tube and increased regional blood flow making hemostasis more difficult. Severely depressed or exhausted queen—premedication with diazepam (0.2–0.4 mg/kg IV, IM) or midazolam (0.066–0.22 mg/kg IV, IM) and either butorphanol (0.2–0.4 mg/kg IV, IM) or oxymorphone (0.1–0.4 mg/kg IV, IM); followed by propofol induction and maintenance with sevoflurane or isoflurane.
- Butorphanol (0.1–0.4 mg/kg IV, IM) or buprenorphine (0.005–0.01 mg/kg IV/IM) for postoperative analgesia.
- Premedications—if using diazepam, reverse neonates with flumazenil (0.01 mg/kg IV); if using opiates, reverse neonates with naloxone (0.04 mg/kg IV, IM, SC); repeat dosing until medications are fully metabolized in the neonate. Avoid premedication if fetal stress exists.



MEDICATIONS

CONTRAINDICATIONS

Oxytocin—contraindicated with obstructive dystocia, fetal stress, long-standing *in utero* fetal death, uterine rupture, uterine torsion.



FOLLOW-UP

PREVENTION/AVOIDANCE

- Schedule elective C-section for bitches with abnormal pelvic canal; small pelvis; vaginal vault abnormalities; breeds predisposed to dystocia; dams with previous history of uterine inertia.
- Scheduling of surgery—extremely important that D1 diestrus, LH peak, or ovulation is identified during breeding to ensure acceptable fetal survivability (see Breeding, Timing). If ovulation timing is not available, gestational aging and maturation assessment via ultrasonography is necessary.

EXPECTED COURSE AND PROGNOSIS

- If dystocia is identified promptly and intervention is successful—good to fair for life of the dam; fair for survival of fetuses.
- If dystocia unrecognized or untreated for 24–48 h—poor to guarded for life of the dam; unlikely that any fetuses will survive.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

History of dystocia may or may not impact future fertility. Dystocia may recur depending on cause (anatomic abnormalities, primary uterine inertia). Resolution of dystocia by C-section does not preclude natural whelping during future deliveries.

SEE ALSO

- Breeding, Timing
- Uterine Inertia
- Vaginal Malformations and Acquired Lesions

ABBREVIATIONS

- C-section = cesarean section
- LH = luteinizing hormone
- PCO₂ = partial pressure of carbon dioxide
- PCV = packed cell volume
- PO₂ = partial pressure of oxygen

Suggested Reading

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**Client Education Handout
available online**

DYSURIA AND POLLAKIURIA



BASICS

DEFINITION

- Dysuria—difficult or painful urination.
- Pollakiuria—voiding small quantities of urine with increased frequency of micturition.

PATHOPHYSIOLOGY

The urinary bladder and urethra normally serve as a reservoir for storage and periodic release of urine. Inflammatory and non-inflammatory disorders of the lower urinary tract may decrease bladder compliance and storage capacity by damaging structural components of the bladder wall or by stimulating sensory nerve endings located in the bladder or urethra. Sensations of bladder fullness, urgency, and pain stimulate premature micturition and reduce functional bladder capacity. Dysuria and pollakiuria are caused by lesions of the urinary bladder and/or urethra and provide unequivocal evidence of lower urinary tract disease; these clinical signs do not exclude concurrent involvement of the upper urinary tract or disorders of other body systems.

SYSTEMS AFFECTED

Renal/Urologic—bladder, urethra, and prostate gland

SIGNALMENT

Dog and cat

SIGNS

N/A

CAUSES

Urinary Bladder

- Urinary tract infection—bacterial, viral, fungal, parasitic, or mycoplasmal.
- Urocystolithiasis.
- Neoplasia—e.g., transitional cell carcinoma.
- Trauma.
- Anatomic abnormalities—e.g., ureterocele, persistent uterus masculinus, perineal hernias containing the urinary bladder, and spay granulomas.
- Detrusor atony—e.g., chronic partial obstruction and dysautonomia.
- Chemicals/drugs—e.g., cyclophosphamide.
- Iatrogenic—e.g., catheterization, palpation, reverse flushing, overdistension of the bladder during contrast radiography, urohydropropulsion, urethrocystoscopy, and surgery.
- Idiopathic—e.g., idiopathic feline lower urinary tract disease.

Urethra

- Urinary tract infection—see previous section.
- Urethrolithiasis—see previous section.
- Urethral plugs—e.g., matrix and matrix-crystalline.
- Neoplasia—see previous section; local invasion by malignant neoplasms of adjacent structures.

- Trauma.
- Anatomic anomalies—e.g., congenital or acquired strictures, urethrorectal fistulas, and pseudohermaphrodites.
- Urethral sphincter hypertonicity—e.g., upper motor neuron spinal cord lesions, reflex dyssynergia, and urethral spasm.
- Iatrogenic—see previous section.
- Idiopathic—see previous section.

Prostate Gland

- Prostatitis or prostatic abscess
- Neoplasia—adenocarcinoma and transitional cell carcinoma
- Cystic hyperplasia
- Paraprostatic cysts

RISK FACTORS

- Diseases, diagnostic procedures, or treatments that (1) alter normal host urinary tract defenses and predispose to infection, (2) predispose to formation of uroliths, or (3) damage the urothelium or other tissues of the lower urinary tract.
- Mural or extramural diseases that compress the bladder or urethral lumen.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiating from Other Abnormal Patterns of Micturition

- Rule out polyuria—increased frequency and volume of urine $> 50 \text{ mL/kg/day}$.
- Rule out urethral obstruction—stranguria, anuria, overdistended urinary bladder, signs of post-renal uremia.
- Rule out urinary incontinence—involuntary urination, urine dribbling, enuresis, incomplete bladder emptying.
- Rule out urine spraying or marking—voiding small amounts of urine on vertical surfaces or other socially significant places.

Differentiate Causes of Dysuria and Pollakiuria

- Rule out urinary tract infection—hematuria; malodorous or cloudy urine; small, painful, thickened bladder.
- Rule out urolithiasis—hematuria; palpable uroliths in urethra or bladder.
- Rule out neoplasia—hematuria; palpable masses in urethra or bladder.
- Rule out neurogenic disorders—flaccid bladder wall; residual urine in bladder lumen after micturition; other neurologic deficits to hind legs, tail, perineum, and anal sphincter.
- Rule out prostatic diseases—urethral discharge, prostatomegaly, pyrexia, depression, tenesmus, caudal abdominal pain, stiff gait.
- Rule out cyclophosphamide cystitis—history.
- Rule out iatrogenic disorders—history of catheterization, reverse flushing, contrast

radiography, urohydropropulsion, urethrocystoscopy, or surgery.

CBC/BIOCHEMISTRY/URINALYSIS

- Results of CBC and biochemistries are often normal. Lower urinary tract disease complicated by urethral obstruction may be associated with azotemia, hyperphosphatemia, acidosis, and hyperkalemia. Patients with concurrent pyelonephritis may have impaired urine-concentrating capacity, leukocytosis, and azotemia. Patients with acute prostatitis or prostatic abscesses may have leukocytosis. Dehydrated patients may have elevated total plasma protein.
- Disorders of the urinary bladder are best evaluated with a urine specimen collected by cystocentesis. Urethral disorders are best evaluated with a voided urine sample or by comparison of results of analysis of voided and cystocentesis samples. (Caution: cystocentesis may induce hematuria.)
- Pyuria, hematuria, and proteinuria indicate urinary tract inflammation, but these are non-specific findings that may result from infectious and non-infectious causes of lower urinary tract disease.
- Identification of bacteria, fungi, or parasite ova in urine sediment suggests, but does not prove, that urinary tract infection is causing or complicating lower urinary tract disease. Consider contamination of urine during collection and storage when interpreting urinalysis results.
- Identification of neoplastic cells in urine sediment indicates urinary tract neoplasia. Use caution in establishing a diagnosis of neoplasia based on urine sediment examination. Urinary tract inflammation or extremes in urine pH or osmolality can cause epithelial cell atypia that is difficult to differentiate from neoplasia.
- Crystalluria occurs in normal patients, patients with urolithiasis, or patients with lower urinary tract disease unassociated with uroliths. Interpret the significance of crystalluria cautiously.
- Hematuria, proteinuria, and variable crystalluria occur in cats with non-obstructive idiopathic lower urinary tract disease. Significant pyuria is rare in these patients.

OTHER LABORATORY TESTS

- Quantitative urine culture—the most definitive means of identifying and characterizing bacterial urinary tract infection; negative urine culture results suggest a non-infectious cause (e.g., uroliths and neoplasia) or inflammation associated with urinary tract infection caused by fastidious organisms (e.g., mycoplasmas or viruses).
- Cytologic evaluation of urine sediment, prostatic fluid, urethral or vaginal discharges or biopsy specimens obtained by catheter or needle aspiration—may help in evaluating patients with localized urinary tract disease; may establish a definitive diagnosis of urinary tract neoplasia, but cannot rule it out.

(CONTINUED)

IMAGING

Survey abdominal radiography, contrast urethrocytography and cystography, urinary tract ultrasonography, and excretory urography are important means of identifying and localizing causes of dysuria and pollakiuria.

DIAGNOSTIC PROCEDURES

- Use urethrocytscopy in patients with persistent lesions of the lower urinary tract for which no definitive diagnosis has been established by other, less-invasive, means.
- Use light microscopic evaluation of tissue biopsy specimens from patients with persistent lesions of the urinary tract for which no definitive diagnosis has been established by other, less-invasive, means. Tissue specimens may be obtained by catheter biopsy, urethrocytscopy and forceps biopsy, or surgery.

**TREATMENT**

- Patients with non-obstructive lower urinary tract diseases are typically managed as outpatients; diagnostic evaluation may require brief hospitalization.
- Dysuria and pollakiuria associated with systemic signs of illness (e.g., pyrexia, depression, anorexia, vomiting, and dehydration) or laboratory findings of azotemia or leukocytosis warrant aggressive diagnostic evaluation and initiation of supportive and symptomatic treatment.
- Treatment depends on the underlying cause and specific sites involved. See specific chapters describing diseases listed in section on causes.
- Clinical signs of dysuria and pollakiuria often resolve rapidly following specific treatment of the underlying cause(s).

**MEDICATIONS****DRUG(S) OF CHOICE**

- Patients with urge incontinence, severe or persistent signs, or untreatable lower urinary tract disease may benefit from symptomatic therapy with propantheline, oxybutynin, or dicyclomine anticholinergic agents that may reduce the force and frequency of uncontrolled detrusor contractions.
- Propantheline—dogs: 0.2 mg/kg PO q6–8h; cats: 0.25–0.5 mg/kg PO q12–24h.

Oxybutynin—dogs: 0.2 mg/kg PO q8–12h; cats: 0.5–1.25 mg/cat PO q8–12h.
Dicyclomine—dogs: 5–10 mg/dog PO q8h.

- Patients with transitional cell carcinoma of the urinary bladder or urethra may be symptomatically managed with the nonsteroidal anti-inflammatory drug piroxicam (0.3 mg/kg PO q24h), which reduces the severity of clinical signs, improves quality of life, and in some cases, induces tumor remission.

CONTRAINdications

- Glucocorticoids or other immunosuppressive agents in patients suspected of having urinary or genital tract infection.
- Potentially nephrotoxic drugs (e.g., gentamicin) in patients that are febrile, dehydrated, or azotemic or that are suspected of having pyelonephritis, septicemia, or preexisting renal disease.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

- Monitor response to treatment by status of clinical signs, serial physical examinations, laboratory testing, and radiographic and ultrasonic evaluations appropriate for each specific cause.
- Refer to specific chapters describing diseases listed, under "Causes."

POSSIBLE COMPLICATIONS

- Dysuria and pollakiuria may be associated with formation of macroscopic vesicourachal diverticula.
- Refer to specific chapters describing diseases listed, under "Causes."

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Hematuria, pyuria, and proteinuria
- Disorders predisposing to urinary tract infection

- Disorders predisposing to formation of uroliths
- Macroscopic vesicourachal diverticula

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Feline urological syndrome
- Lower urinary tract disease

SEE ALSO

- Feline Idiopathic Lower Urinary Tract Disease
- Lower Urinary Tract Infection, Bacterial
- Lower Urinary Tract Infection, Fungal
- Urinary Retention, Functional
- Urinary Tract Obstruction
- Urolithiasis chapters
- Vesicourachal Diverticula

Suggested Reading

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Authors John M. Kruger and Carl A. Osborne

Consulting Editor Carl A. Osborne

D

EAR MITES



BASICS

OVERVIEW

Otodectes cynotis mites infest primarily the external ear canal and cause variable degrees of otic discharge and pruritus.

E

SIGNALMENT

- Common in young dogs and cats, although it may occur at any age.
- No breed or sex predilection.

SIGNS

- Pruritus is usually present, but can be minimal.
- Pruritus primarily located around the ears, head, and neck; occasionally generalized.
- Thick, red-brown or black otic exudate ("coffee grounds" appearance)—usually seen in the outer ear.
- Otic exudate and pruritus demonstrate individual variability.
- Crusting and scales may occur on the neck, rump, and tail (dogs).
- Excoriations on the convex surface of the pinnae often occur, owing to the intense pruritus.

CAUSES & RISK FACTORS

Otodectes cynotis



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pediculosis
- *Pelodera* dermatitis
- Sarcoptic mange
- Notoedric mange
- Chiggers
- Otitis externa secondary to allergy/hypersensitivity
- Flea bite hypersensitivity

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Ear swabs placed in mineral oil—usually effective means of identification.
- Skin scrapings—may identify mites if signs are generalized.
- Mites may be visualized in external ear canal.
- Diagnosis may be made by response to treatment.



TREATMENT

- Outpatient.
- Diet and activity—no alteration necessary.
- Very contagious—all animals in contact with the affected animal must be treated.
- Thoroughly clean and treat the environment.



MEDICATIONS

DRUG(S)

- Ears should be thoroughly cleaned with a commercial ear cleaner.
- Otic parasiticides should be used for 7–10 days to eradicate mites and eggs; effective topical commercial products contain pyrethrins, thiabendazole, ivermectin, amitraz and milbemycin; treat during alternative weeks for two to three treatment cycles recommended to prevent reinfection from eggs.
- Selamectin : per label instructions or repeated at 2 weeks.
- Imidacloprid/moxidectin (Advantage Multi/Advocate): per label instructions.
- Ivermectin 200–300 µg/kg PO (three treatments) or SC (two treatments) at 14-day intervals: non-FDA-approved usage.

- Flea treatments should be applied to animal for elimination of ectopic mites.

- Mites may persist in the environment; environmental treatment may be helpful.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Ivermectin and moxidectin—do not use orally or by injection in collies, shelties, their crosses, or other herding breeds; use only if absolutely necessary in animals <6 months of age; an increasing number of toxic reactions have been reported in kittens.
- Ivermectin and milbemycin—cause elevated levels of monoamine neurotransmitter metabolites, which could result in adverse drug interactions with amitraz and benzodiazepines.



FOLLOW-UP

- Ear swab and physical examination should be done 1 month after therapy commences.
- Prognosis is good.
- If signs persist after treatment, an additional, underlying cause may be present.
- Repeat infestation indicates an uncontrolled source of mites.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Transient papular dermatitis in human beings

Suggested Reading

Miller WH, Griffin CE, Campbell K.L. Muller & Kirk's Small Animal Dermatology, 7th ed. St. Louis, MO: Elsevier Mosby, 2013.

Thomas RC. Treatment of ectoparasites. In: Bonagura JD, Twedt DC, eds. Current Veterinary Therapy XV. St. Louis, MO: Elsevier Saunders, 2014, pp. 428–432.

Author Karen A. Kuhl

Consulting Editor Alexander H. Werner

EBSTEIN'S ANOMALY



BASICS

OVERVIEW

- Atrialization of the right ventricle—an apical displacement of the tricuspid valve complex into the right ventricle.
- Accompanied by various degrees of tricuspid insufficiency or stenosis.
- Major pathophysiology related to the degree of tricuspid insufficiency or stenosis.
- An abnormal accessory pathway may lead to supraventricular tachycardias.

SIGNALMENT

- Very rare—occasionally encountered in dogs and cats.
- No breed or sex predilection.
- Murmur auscultated at a young age, though can be very difficult to auscult with stenosis.

SIGNS

- Animals with mild tricuspid insufficiency or stenosis are asymptomatic.
- Animals with moderate insufficiency or stenosis are often exercise intolerant.
- Animals with severe insufficiency or stenosis have R-CHF with pleural effusion and/or ascites.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Tricuspid dysplasia

CBC/BIOCHEMISTRY/URINALYSIS

Results usually normal

OTHER LABORATORY TESTS

N/A

IMAGING

Thoracic Radiography

- Right atrial and ventricular enlargement
- Hepatomegaly

Echocardiography

- Two-dimensional echocardiography reveals an apically displaced tricuspid valve with an enlarged right atrium and small right ventricle.
- Color Doppler shows tricuspid insufficiency and/or tricuspid stenosis.
- Spectral Doppler confirms tricuspid stenosis and estimates right ventricular pressure.

OTHER DIAGNOSTIC PROCEDURES

Electrocardiography

- Simultaneous intracardiac pressure and ECG tracings may be needed to verify the diagnosis.
- Accessory conduction pathway (ventricular preexcitation) or supraventricular tachycardia.



TREATMENT

- Medical management currently the only practical approach.
- Surgical replacement of the tricuspid valve can be successfully performed at a few institutions.
- Restrict sodium intake only if right heart failure develops.



MEDICATIONS

DRUG(S)

- Patients with R-CHF—start furosemide (2–4 mg/kg q6–12h) and enalapril (0.5 mg/kg q12h).
- Patients with tricuspid stenosis—gradually increase atenolol dose (0.1–1 mg/kg q12h) to obtain low normal heart rate to facilitate ventricular filling.
- Patients with supraventricular tachycardia (WPW syndrome)—start procainamide (15 mg/kg q8h).

- If WPW syndrome persists, consider a calcium channel blocker (i.e., verapamil or diltiazem) or a beta-blocker (e.g., propranolol or atenolol).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Do not use calcium channel blockers and beta-blockers concurrently

E



FOLLOW-UP

Monitor with serial echocardiography



MISCELLANEOUS

SEE ALSO

Atrioventricular Valve Dysplasia

ABBREVIATIONS

- ECG = electrocardiography
- R-CHF = right-sided congestive heart failure
- WPW = Wolff-Parkinson-White (syndrome)

Suggested Reading

Bonagura JD, Lehmkuhl LB. Congenital heart disease. In: Fox PR, Sisson D, Moise NS, eds., *Textbook of Canine and Feline Cardiology*. 2nd ed. Philadelphia: Saunders, 1999, pp. 471–535.

Webb GD, Smallhorn JF, Therrien J, Redington AN. Congenital heart disease. In: Bonow RO, Mann DC, Zipes DP, Libby P, eds., *Braunwald's Heart Disease*. 9th ed. Philadelphia: Elsevier Saunders, 2012, pp. 1450–1452.

Author Jean M. Betkowski

Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

Acknowledgment The author and editors acknowledge the prior contribution of Carroll Loyler.

ECLAMPSIA



BASICS

OVERVIEW

- Post-parturient hypocalcemia.
- Usually develops 1–4 weeks postpartum; may occur at term, prepartum, or during late lactation.
- Alters cell membrane potentials, causing spontaneous discharge of nerve fibers and tonic-clonic contraction of skeletal muscles.
- Life-threatening tetany and convulsions, leading to hyperthermia.
- Cerebral edema possible.

SIGNALMENT

- Dog—postpartum bitch; most common in toy breeds; higher incidence with first litter.
- Most common prior to day 40 postpartum; occasionally occurs prepartum.
- Breeds at increased risk: Chihuahua, miniature pinscher, Shih Tzu, miniature poodle, Mexican hairless, Pomeranian.
- Cat—rare.

SIGNS

Historical Findings

- Poor mothering
- Restlessness, nervousness
- Panting, whining
- Vomiting, diarrhea
- Ataxia, stiff gait, limb pain
- Facial pruritis
- Muscle tremors, tetany, convulsions
- Recumbency, extensor rigidity—usually seen 8–12 hours after onset of signs.

Physical Examination Findings

- Hyperthermia
- Rapid respiratory rate
- Dilated pupils, sluggish pupillary light responses
- Muscle tremors, muscular rigidity, convulsions

CAUSES & RISK FACTORS

- Calcium supplementation during gestation, including dairy products
- Inappropriate Ca:P ratio in gestational diet
- Low body weight:litter size ratio
- Poor prenatal nutrition
- First litter
- Large litter size



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hypoglycemia—may be concurrent; hypoglycemia alone does not cause muscular rigidity.

- Toxicosis—distinguished by signalment and history.

- Epilepsy or other neurologic disorder—differentiated by signalment; calcium concentration diagnostic.

CBC/BIOCHEMISTRY/URINALYSIS

- Total serum calcium < 9 mg/dL in bitches; < 8 mg/dL in queens.
- Although ionized calcium (< 2.4–3.2 mg/dL) is the form important for normal neuromuscular function, measurement of total serum calcium is usually sufficient for diagnosis.
- Hypoglycemia—may be concurrent.
- Hypomagnesemia has been reported in 44% of affected bitches; may promote tetany.
- Serum potassium elevated in 56% of cases, due to metabolic acidosis or respiratory alkalosis.

IMAGING

N/A

OTHER LABORATORY TESTS

N/A

DIAGNOSTIC PROCEDURES

ECG shows prolonged QT interval, bradycardia, tachycardia, or ventricular premature complexes.



TREATMENT

- Emergency inpatient.
- Hyperthermia—cool with cool water soak and fans; use caution with cool water enemas.
- Puppies—remove from dam onto a foster dam or hand-raise; if not possible or undesirable due to behavioral need for contact with dam, remove pups from dam for 24 hours, or until serum calcium is stabilized, and provide supplementation for remainder of lactation; continue to monitor serum calcium level.



MEDICATIONS

DRUG(S)

- Calcium gluconate—10% solution 0.22–0.44 mL/kg IV given slowly to effect over 5 minutes; monitor heart rate or ECG during administration.
- Correct hypoglycemia.
- Diazepam 5 mg IV; for unresponsive seizures.
- Cerebral edema—treat, if indicated.
- Send home on calcium carbonate, or gluconate 10–30 mg/kg PO q8h until lactation ends (calcium carbonate (TUMS) 500 mg tablets supply 200 mg calcium).

- Magnesium supplementation may be helpful in hypomagnesemic bitches.
- Start puppies/kittens on solid food at 3–4 weeks of age.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Corticosteroids—avoid; cause decreased intestinal absorption and increased renal excretion of calcium.



FOLLOW-UP

PATIENT MONITORING

- Serum calcium concentration—monitor until it is stabilized in the normal range.
- Avoid calcium supplementation during gestation.
- Diet—maternal: ensure a calcium:phosphorus ratio of 1:1 or 1.2:1; avoid high-phytate foods (e.g., soybeans); puppies: supplement feeding for large litters.

POSSIBLE COMPLICATIONS

- Cerebral edema
- Death
- Hand-raising of puppies

EXPECTED COURSE AND PROGNOSIS

- Probably will recur with subsequent litters; calcium supplementation can be started after parturition for bitches with history of eclampsia in prior litters.
- Prognosis—good with immediate treatment; poor with delayed treatment.



MISCELLANEOUS

ABBREVIATION

ECG = electrocardiogram

Suggested Reading

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Author Joni L. Freshman
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ECTOPIC URETER



BASICS

OVERVIEW

- Congenital anomaly of the urinary system. The ureteral orifice(s) is/are inappropriately positioned caudal to the bladder trigone (i.e., trigone, urethra, vagina, vestibule, uterus, or prostate), resulting in urinary incontinence.
- A common cause of urinary incontinence in juvenile female dogs. Also seen in adult dogs.
- Anomalous differentiation of the mesonephric and metanephric ducts resulting in inappropriate ureteral termination.
- Dogs—> 95% tunnel intramurally, traversing the urethra in the submucosa.
- Male dogs—most commonly associated with severe hydronephrosis and hydroureter due to ureteral opening stenosis.
- Commonly associated with multiple anomalies of the urinary tract: > 75% have concurrent USMI, > 90% have PPMR, chronic UTIs (~ 80%), hydroureter (35–50%), hydronephrosis (25–50%), short urethral/intrapelvic bladders (~ 20%).

SIGNALMENT

- Dog and cat. • Juvenile incontinent dogs (commonly). • Infrequently reported in cats and male dogs; 20:1 ratio of female:male dogs. • Dog breeds may be predisposed: retrievers, Siberian huskies, Newfoundlands, poodles, terriers.

SIGNS

- Constant or intermittent incontinence since birth. • Normal voiding in some. • Chronic UTIs. • May be asymptomatic (male dogs) and can have moderate to severe hydroureter/hydronephrosis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- USMI—urethral pressure profilometry.
- Inappropriate urination—urge incontinence, “overactive bladder,” behavioral (conscious urination).
- UTI—pollakiuria and urge incontinence.
- Vaginal pooling—leakage after urination when patient stands up from recumbent position.
- Congenital hydroureter/hydronephrosis—male dogs with EU often continent.
- Short urethra/intrapelvic bladder syndrome.

CBC/BIOCHEMISTRY/URINALYSIS

Urine specific gravity and serum creatinine or urea nitrogen concentration often normal. Abnormal with concurrent anomalies (e.g., renal dysplasia, pyelonephritis).

OTHER LABORATORY TESTS

Urine bacterial culture and sensitivity—via cystocentesis.

IMAGING

- Cystoscopy (96% sensitivity): diagnostic method of choice.
- Helical computed tomography (91% sensitivity): more accurate than standard radiography.
- Urinary tract ultrasonography (60–91% sensitivity) can provide accurate diagnosis and anatomical information of the upper urinary tract.
- Excretory urography (50–75% sensitivity) with positive contrast cystogram or a pneumocystogram, followed by a vaginourethrogram (female) or urethrogram (male); may diagnose associated hydroureter/hydronephrosis, ureterocele, and/or absent or abnormal kidneys.
- Retrograde urethrography (47% sensitivity).

DIAGNOSTIC PROCEDURES

- Cystourethrogastroscopy—definitive diagnosis of EU, short urethral syndrome, location of ectopic orifice in the genitourinary tract; identifies multiple fenestrations, troughs.
- UPP—may detect concurrent USMI, but intramural ectopic ureter may confound results and therefore should not guide treatment of concurrent EU.



TREATMENT

- Cystoscopic-guided laser ablation (CLA): performed for intramural EU only; simultaneous diagnosis and treatment; opens ureteral tract in a minimally invasive manner; addresses concurrent vaginal defects (~ 95%).
- Surgical: neoureterostomy (with or without distal tract dissection/reconstruction), reimplantation, or ureteronephrectomy; complication rates range between 14% and 25% including ureteral strictures, leakage, and infection.
- Never consider ureteronephrectomy if ipsilateral renal function remains.
- Warn owners that incontinence may continue in ~ 45–70% of patients after surgery. Many patients become continent with the addition of medications, bulking agent augmentation, and/or placement of an artificial urethral sphincter.



MEDICATIONS

DRUG(S)

- Use if incontinence persists after surgery.
- Phenylpropanolamine: an α -blocker (1–1.5 mg/kg PO q8h) will improve continence after surgery/laser therapy in 10–20% of dogs, improving continence levels to 50–60%.
- Diethylstilbestrol: initially 0.1–0.3 mg/kg q24h for 7 days, then once weekly; 0.1–1 mg PO for 3–5 days, then 1 mg per week thereafter. Gradually titrate to the lowest effective dose. DES is potentially toxic to the

bone marrow and can cause blood dyscrasias. Estriol tablets: 2 mg once daily and then titrated to lowest effective dose. Combination of estrogen and PPA therapy may be more effective.

- Testosterone propionate (2.2 mg/kg IM q2–3 days) or methyltestosterone (0.5 mg/kg/day) is administered to male dogs initially to see if replacement therapy will be effective. For longer action, testosterone cypionate (2.2 mg/kg IM q30 days) can be used.
- Not advised in immature animals.
- Estriol: can be used for estrogen-responsive urinary incontinence. The dose is 2 mg once daily per dog (regardless of body weight) for 14 days, followed by the lowest effective daily dose tapered every 7 days.

OTHER

After surgery/laser ablation (1) transurethral submucosal bulking agent injections: can improve continence to ~60–65%; (2) placement of an artificial urethral sphincter (called a hydraulic occluder) can improve continence to ~80–90%.



FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS

- Dogs—with surgery (25–50%) or laser ablation (40–55%) alone, continence rates range from 25% to 55%, which improves to 60% with medications, 65% with bulking-agent injection, and ~80–90% with the placement of a hydraulic occluder.
- Care should be taken in evaluation of hydroureter/hydronephrosis after surgery as ureteral strictures have been reported, which can result in permanent loss of the ipsilateral kidney.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Hydronephrosis, hydroureter, ureterocele, pelvic bladder, persistent paramesonephric remnant, vaginal septum, renal dysplasia, renal agenesis, USMI, short urethra/intrapelvic bladder.

SEE ALSO

- Incontinence, Urinary • Pelvic Bladder

ABBREVIATIONS

- CLA = cystoscopic-guided laser ablation
- DES = diethylstilbestrol • EU = ectopic ureter(s)
- PPA = phenylpropanolamine
- UPP = urethral pressure profilometry
- USMI = urethral sphincter mechanism incompetence • UTI = urinary tract infection

Author Allyson C. Berent

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ECTROPION



BASICS

OVERVIEW

- Eversion or rolling out of the eyelid margin, resulting in exposure of the palpebral conjunctiva.
- Ophthalmic system (exposure and poor tear retention/distribution)—may predispose patient to irritation, recurrent infections, and sight-threatening corneal disease).

SIGNALMENT

- Dogs, seldom cats.
- Breeds with higher than average prevalence—sporting breeds (e.g., spaniels, hounds, and retrievers); giant breeds (e.g., Saint Bernards and mastiffs); any breed with loose facial skin (especially bloodhounds).
- Developmental—genetic predisposition in listed breeds; may occur in dogs < 1 year old.
- Acquired—noted in other breeds; occurs late in life secondary to age-related loss of facial muscle tone and developing skin laxity.
- Intermittent—caused by fatigue; may be observed after strenuous exercise or when drowsy.

SIGNS

- Eversion of the lower eyelid with lack of contact of the lower lid to the globe and exposure of the palpebral conjunctiva and third eyelid—usually obvious.
- Facial staining caused by poor tear drainage—tears spill over onto the face instead of passing from the eye to the nose via the nasolacrimal ducts.
- History of mucoid to mucopurulent discharge owing to conjunctival exposure.
- Recurrent foreign body irritation due to debris localizing between lid and globe in inferior cul-de-sac.
- History of bacterial conjunctivitis.

CAUSES & RISK FACTORS

- Usually secondary to breed-associated alterations in facial conformation and eyelid support.
- Marked weight loss or muscle mass loss about the head and orbits—may result in acquired disease.
- Tragic facial expression in hypothyroid dogs.
- Scarring of the eyelids secondary to injury or after overcorrection of entropion—may result in cicatricial disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Usually clinically obvious.
- Look for any underlying disorder in non-predisposed breeds and patients with late-age onset.
- Loss of orbital or periorbital mass—may cause condition in patients with masticatory myositis.
- Palpebral nerve paralysis—condition associated with lack of muscle tone of the orbicularis oculi muscles.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

- Possible masticatory myositis—test for auto-antibodies against type 2M muscle fibers.
- Palpebral nerve paralysis or tragic facial expression—consider testing for hypothyroidism.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Palpebral nerve paralysis—full neurologic evaluation; potential for hypothyroidism.
- Secondary conjunctivitis—consider bacterial culture or cytologic examination to help select an appropriate topical antibiotic.
- Fluorescein or rose bengal staining of the cornea and conjunctiva—may document corneal ulcerations; may reveal severity of the exposure problem.



TREATMENT

- Supportive care (topical lubricant or antibiotic-containing ointments) and good ocular and facial hygiene—sufficient for most mild disease.
- Surgical treatment—eyelid shortening or radical facelift; necessary for severely affected patients that have chronic ocular irritation.
- Intermittent, fatigue-induced condition—do not treat surgically.



MEDICATIONS

DRUG(S)

- Topical broad-spectrum ophthalmic antibiotics—bacterial conjunctivitis or corneal ulceration. Neomycin/polymyxin B/bacitracin (or others based on bacterial culture and sensitivity) q6–8h.
- Lubricant eye drops and ointments—reduce conjunctival and corneal desiccation secondary to exposure.
- Hypothyroid and masticatory myositis-induced conditions—may respond well to appropriate medical treatment of the underlying disease.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- May become more severe as patient ages.
- Non-surgically treated patient—monitor for signs of infectious conjunctivitis, exposure keratopathy, corneal ulceration, and facial dermatitis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Hypothyroidism
- Myopathy, focal Inflammatory—masticatory myositis and extraocular myositis

AGE-RELATED FACTORS

Old animals more likely to have ectropion secondary to loss of facial muscle tone.

SEE ALSO

- Hypothyroidism
- Myopathy, Inflammatory—Masticatory Myositis and Extraocular Myositis

Suggested Reading

Stades FC, van der Woerdt A. Diseases and Surgery of the Canine Eyelid. In: Gelatt KN, Gilger BC, Kern TJ, eds., Veterinary Ophthalmology, 5th ed. Ames, IA: Wiley-Blackwell, 2013, pp. 853–864.

Author J. Phillip Pickett

Consulting Editor Paul E. Miller

EHRLICHIOSIS (ANAPLASMA)



BASICS

DEFINITION

Caused by *Ehrlichia* spp.—tick-borne rickettsial disease

Dogs

- Within the family Anaplasmataceae—three pathogenic genera: *Ehrlichia*, *Anaplasma*, and *Neorickettsia*.
- *Ehrlichia* spp.—divided into three groups: (1) *E. canis*: ehrlichiosis found intracytoplasmically in circulating leukocytes; (2) *E. ewingii*: canine granulocytic ehrlichiosis; like *A. phagocytophilum*, infects granulocytic cells in dogs, but differs in geographic distribution (mainly found in southeastern and south-central United States); (3) *E. chaffeensis*: like *E. canis*, tropism for mononuclear cells; mainly a human pathogen but causes disease in dogs; disease distribution based on vector (mainly *Amblyomma americanum*) range.
- *Anaplasma* spp.—two organisms of importance: (1) *A. phagocytophilum*: infects mainly horses but also the granulocytic cells of dogs; mainly found in northeastern and upper midwestern states and California based on distribution of vectors (hard ticks *Ixodes* spp.); (2) *A. platys*: tropism for platelets; shares serologic cross-reactivity with *A. phagocytophilum*.
- Although usually found in defined ranges, serologic evidence suggests *E. canis* and *A. phagocytophilum* occur in all 48 contiguous states.
- *Neorickettsia* spp.—two organisms of importance: (1) *N. risticii*: causes Potomac horse fever in horses but also infects dogs and cats; infections acquired by ingesting infected snails, free nematode life stages, or aquatic insects with encysted metacercaria; grazing or drinking from standing water explains why horses become infected more often than dogs; infected dogs have negative *E. canis* titers; (2) *N. helminthoeca*: causes salmon poisoning disease in dogs.

Cats

- Feline mononuclear ehrlichiosis (and *E. risticii* extremely rarely) can cause clinical disease.
- Serologic evidence for *A. phagocytophilum* infection but no disease.
- Serologic evidence—suggests a species that cross-reacts with *E. canis* can cause illness.

PATHOPHYSIOLOGY

- *E. canis* • *Rhipicephalus sanguineus*—brown dog tick; transmits disease to dogs in saliva; 1- to 3-week incubation period; three stages of disease:
 - Acute—spreads from bite site to the spleen, liver, and lymph nodes (causes organomegaly); then subclinical with mild thrombocytopenia; mainly endothelial cells affected; vasculitis; antiplatelet antibodies may exacerbate thrombocytopenia; variable leukopenia; mild anemia; severity depends on organism.
 - Subclinical—organism persists; antibody response increases

(hyperglobulinemia); thrombocytopenia persists.

- Chronic—impaired bone marrow production (platelets, erythroid suppression); marrow hypercellular with plasma cells.

SYSTEMS AFFECTED

- Bleeding tendencies—thrombocytopenia and vasculitis.
- CNS, eyes (anterior uveitis), and lungs—rarely affected by vasculitis.
- Lymphadenopathy.
- Multisystemic.
- Splenomegaly.

INCIDENCE/PREVALENCE

- Occurs throughout the year; insidious.
- Average duration from onset to presentation—usually > 2 months.
- Prevalence depends on geographic locality.

GEOGRAPHIC DISTRIBUTION

- Worldwide.
- North America—mainly Gulf Coast and eastern seaboard; also the Midwest and California.

SIGNALMENT

Species

- Dogs—can be infected with a number of species; *E. canis*, *A. platys*, *A. phagocytophilum*, *E. ewingii*, and *E. chaffeensis* produce main disease entities.
- Cats—*E. risticii*; serology suggests a species like *E. canis*, and *A. phagocytophilum*.

Breed Predilections

Chronic (*E. canis*)—seems more severe in Doberman pinschers and German shepherds.

Mean Age and Range

- Average age—5.22 years
- Range 2 months–14 years

SIGNS

General Comments

Duration of clinical signs from initial acute illness to presentation—usually > 2 months.

Historical Findings

- Lethargy, depression, anorexia, and weight loss
- Fever
- Spontaneous bleeding—sneezing, epistaxis
- Respiratory distress
- Ataxia, head tilt
- Ocular pain (uveitis)

Physical Examination Findings

Acute

- Bleeding diathesis (petechiation of mucous membranes as a result of thrombocytopenia) associated with fever (with depression, anorexia, weight loss) and generalized lymphadenopathy should raise suspicions.
- Ticks—found in 40% of cases.
- Respiratory—dyspnea (even cyanosis); increased bronchovesicular sound.
- Diffuse CNS disease (meningitis).
- Ataxia with upper motor neuron dysfunction.
- Vestibular dysfunction.
- Generalized or local hyperesthesia.
- Most dogs recover without treatment and enter a subclinical state.

Chronic

- In non-endemic areas.
- Spontaneous bleeding.
- Anemia.
- Generalized lymphadenopathy.
- Scrotal and limb edema.
- Splenomegaly.
- Hepatomegaly.
- Uveitis, usually bilateral (75%), can sometimes be the

only presenting sign.

- HypHEMA.
- Retinal hemorrhages and detachment with blindness.
- Corneal edema.
- Arthritis (rare).
- Seizures (rare).

RISK FACTORS

Concurrent infection with *Babesia*, *Haemobartonella*, *A. platys*, and *Hepatozoon canis*—worsens clinical syndrome.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Rocky Mountain spotted fever (*Rickettsia rickettsii*)—usually seasonal between March and October; serologic testing for diagnosis; responds to same treatment as ehrlichiosis.
- Immune-mediated thrombocytopenia—not usually associated with fever or lymphadenopathy; serologic testing best distinguishes; may treat for both until results are known.
- Systemic lupus erythematosus—ANA test usually negative with ehrlichiosis; serologic testing for diagnosis.
- Multiple myeloma—serologic testing to differentiate and determine cause of hyperglobulinemia.
- Chronic lymphocytic leukemia—differentiate by lymphocytosis and cytology of bone marrow.
- Brucellosis—serologic testing for diagnosis.

CBC/BIOCHEMISTRY/URINALYSIS

Acute

- Thrombocytopenia—before onset of clinical signs.
- Anemia.
- Leukopenia—from lymphopenia and eosinopenia.
- Leukocytosis and monocytosis—as disease becomes more chronic.
- Morulae—intracytoplasmic inclusions in leukocytes rare; buffy coat smear increases the sensitivity of finding morulae.
- Nonspecific changes—mild increases in ALT, ALP, BUN, creatinine, and total bilirubin (rare).
- Hyperglobulinemia—progressively increases 1–3 weeks post-infection.
- Hypoalbuminemia—usually from renal loss.
- Proteinuria—with or without azotemia; about half of patients.

Chronic

- Pancytopenia—typical; monocytosis and lymphocytosis may be present.
- Hyperglobulinemia—magnitude of globulin increase correlates with duration of infection; usually polyclonal gammopathy, but monoclonal (IgG) gammopathies occur.
- Hypoalbuminemia.
- High BUN and creatinine from primary renal disease.

OTHER LABORATORY TESTS

Serologic Testing

- Most clinically useful and reliable method.
- IFA highly sensitive; poor specificity with cross-reactivity between *E. canis* and *A. phagocytophila*, but not between *E. canis* and *A. platys*.
- More specific tests being developed.
- Titers—reliable 3 weeks after infection; > 1:10 diagnostic.
- Coombs’

EHRlichiosis (ANAPLASMA)

(CONTINUED)

positive anemia—may be seen; may confuse the diagnosis. • Test for other accompanying pathogens—*Babesia*, *Mycoplasma haemofelis*, *A. platys*, and *Hepatozoon canis*. • Point-of-care screening serology testing for single or multiple agents are both practical, sensitive, and specific for IFA titers greater than 320. Positive tests should be confirmed with IFA and other testing (CBC) before treatment is initiated as false-positive results frequently occur. Immunoblotting can be used to distinguish cross-reactions (especially between *E. canis* and *E. ewingii*). • PCR—more reliable than finding circulating morulae. • PCR of blood for *E. canis* provides a species-specific diagnosis and is positive by day 7 post-infection, usually before the development of clinical disease (9–12 days post-infection) in experimental settings. It is less reliable in natural infections and should not be used as the only screening method of diagnosis. Real-time PCR techniques are proving to be more sensitive and may hold a place in initial diagnostic testing as more data on accuracy becomes available.

DIAGNOSTIC PROCEDURES

Bone Marrow Aspirate

- Acute—hypercellularity of megakaryocytic and myeloid series.
- Chronic—often erythroid hypoplasia with increased M:E ratios and plasmacytosis.
- Increased numbers of mast cells seen on marrow smears.

PATHOLOGIC FINDINGS

- Acute—petechial hemorrhages on serosal and mucosal surfaces of most organs; generalized lymphadenopathy (brownish discoloration), splenomegaly, hepatomegaly, and red bone marrow (hypercellularity).
- Chronic—pale marrow (hypoplastic); subcutaneous edema; histologically, perivascular plasma cell infiltrate in numerous organs most characteristic; multifocal non-suppurative meningoencephalitis with lymphoplasmacytic cell infiltrate into the meninges common.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—initial medical stabilization for anemia and/or hemorrhagic tendency resulting from thrombocytopenia.
- Outpatient—stable patients; monitor blood and response to medication frequently.

NURSING CARE

- Balanced electrolyte solution is indicated for dehydration.
- Blood transfusion is indicated for anemia.
- Platelet-rich plasma or a blood transfusion is indicated for hemorrhage resulting from thrombocytopenia.

CLIENT EDUCATION

- Acute—prognosis excellent with appropriate therapy.
- Chronic—response

may take 1 month; prognosis poor if the bone marrow is severely hypoplastic. • Progression from acute to chronic can be easily prevented by early, effective treatment; but many dogs remain seropositive and may relapse (even years later). • German shepherds and Doberman pinschers—more chronic and severe form of disease.



MEDICATIONS

DRUG(S) OF CHOICE

- Doxycycline (treatment of choice)—5 mg/kg PO q12h for 4 weeks; give IV for 5 days if the dog is vomiting.
- Glucocorticoids—prednisolone or prednisone; 1–2 mg/kg PO q12h for 5 days; may be indicated when thrombocytopenia is life-threatening (thought to be a result of immune-mediated mechanisms); because immune-mediated thrombocytopenia is a principal differential diagnosis, may be indicated until results of serologic tests are available.
- Androgenic steroids—to stimulate bone marrow production in chronically affected dogs with hypoplastic marrows; oxymetholone (2 mg/kg q24h PO until response) or nandrolone decanoate (1.5 mg/kg IM weekly).

CONTRAINdications

- Tetracycline (and derivatives)—do not use in dogs < 6 months old (permanent yellowing of teeth occurs); do not use with renal insufficiency (try doxycycline because it can be excreted via the gastrointestinal tract).
- Enrofloxacin not effective against *Ehrlichia* spp. but is against *Anaplasma* spp.

PRECAUTIONS

Glucocorticoids—prolonged use at immunosuppressive levels may interfere with the clearance and elimination of *E. canis* after use of tetracycline.

ALTERNATIVE DRUG(S)

- Oxytetracycline and tetracycline—22 mg/kg PO q8h for 21 days; effective and less expensive; minocycline (10 mg/kg PO q12h for 4 weeks) is effective if doxycycline is difficult to obtain.
- Chloramphenicol—20 mg/kg PO q8h for 14 days; for puppies < 6 months of age; avoids yellow discoloration of erupting teeth caused by tetracyclines; warn client of public health risks; avoid in dogs with thrombocytopenia, pancytopenia, or anemia.



FOLLOW-UP

PATIENT MONITORING

- Platelet count—every 3 days after initiating antirickettsial agent until normal;

improvement is rapid in acute cases.

- Serologic testing—repeat in 9 months; most dogs will become seronegative; positive titer suggests reinfection or ineffective treatment (reinstitute treatment regimen).

PREVENTION/AVOIDANCE

- Control tick infestation—dips or sprays containing dichlorvos, chlорfenvinphos, dioxathion, propoxur, or carbaryl; flea and tick collars may reduce reinfestation but reliability unproven; avoid tick-infested areas.
- Removing ticks by hand—use gloves (see “Zoonotic Potential”); ensure mouth parts are removed to avoid a foreign body reaction.

EXPECTED COURSE AND PROGNOSIS

- Acute—excellent prognosis with appropriate and early treatment.
- Chronic—may take 4 weeks for a clinical response; prognosis poor with hypoplastic marrow.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- *Babesia* • *Haemobartonella* • *A. platys*

ZOONOTIC POTENTIAL

- Serologic evidence indicates that *E. canis* (or possibly a related species) occurs in people; probably not directly infected from dogs; tick exposure thought to be necessary; *R. sanguineus* probably not the vector in humans.
- Most cases in the southern and south-central United States.

SYNOMYS

- Canine hemorrhagic fever • Canine rickettsiosis • Canine typhus • Lahore canine fever • Nairobi bleeding disease • Tracker dog disease • Tropical canine pancytopenia

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine transaminase
- ANA = antinuclear antibody
- CNS = central nervous system
- IFA = indirect fluorescent antibody
- PCR = polymerase chain reaction

Suggested Reading

Stillman BA, Monn M, Liu J, et al.

Performance of a commercially available in-clinic ELISA for detection of antibodies against *Anaplasma phagocytophilum*, *Anaplasma platys*, *Borrelia burgdorferi*, *Ehrlichia canis*, and *Ehrlichia ewingii* and *Dirofilaria immitis* antigen in dogs. J Am Vet Med Assoc 2014, 245:80–86.

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**Client Education Handout
available online**

ELBOW DYSPLASIA



BASICS

DEFINITION

A series of four developmental abnormalities that lead to malformation and degeneration of the elbow joint.

PATHOPHYSIOLOGY

- Four abnormalities—UAP, OCD, FMCP, and incongruity; alone or in combination; may be seen in one or both elbows; bilateral disease common (50% of cases).
- UAP—delayed closure of the growth plate between the anconeal process and the proximal ulnar metaphysis (olecranon) by 5 months of age; may be the result of abnormal mechanical stress on the anconeal process.
- OCD—affects the medial aspect of the humeral condyle; a disturbance in endochondral ossification causes retention of articular cartilage and subsequent mechanical stress leads to a cartilage flap lesion.
- FMCP—chondral or osteochondral fragmentation or fissure of the medial coronoid process of the ulna; likely a manifestation of osteochondrosis of the coronoid process; the coronoid does not have a separate ossification center; may be the result of abnormal mechanical stress on the medial coronoid process.
- Incongruity—asynchronous proximal growth between the radius and ulna may lead to abnormal loading, wearing, and erosion of cartilage in the humeroulnar compartment; possible malformation of the trochlear notch of the ulna; a slightly elliptical trochlear notch with a decreased arc of curvature is too small to articulate with the humeral trochlea, which results in major points of contact in areas of the anconeal process, coronoid process, and medial humeral condyle and little or no contact in other areas of the trochlea.

SYSTEMS AFFECTED

Musculoskeletal

GENETICS

- Inherited disease.
- High heritability—heritability index ranges between 0.25 and 0.45.

INCIDENCE/PREVALENCE

- Most common cause for elbow pain and lameness.
- One of the most common causes for forelimb lameness in large-breed dogs.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog

Breed Predilections

Large and giant breeds—Labrador retrievers; rottweilers; golden retrievers; German

shepherds; Bernese mountain dogs; chow chows; bearded collies; Newfoundlands.

Mean Age and Range

- Age at onset of clinical signs—typically 4–10 months
- Age at diagnosis—generally 4–18 months.
- Onset of symptoms related to DJD—any age.

Predominant Sex

- FMCP—males predisposed
- UAP, OCD, incongruity—none established

SIGNS

General Comments

- Lameness—if no distinct abnormalities noted on physical examination or radiographs, early intervention may demand advanced imaging.
- Not all patients are symptomatic when young.
- Intermittent episodes of elbow lameness due to advanced DJD changes in a mature patient—common.

Historical Findings

Intermittent or persistent forelimb lameness—exacerbated by exercise; progressed from a stiffness seen only after rest.

Physical Examination Findings

- Pain—elicited on elbow hyperflexion or extension; elicited when holding the elbow and carpus at 90° while pronating and supinating the carpus.
- Affected limb—tendency to be held in abduction and supination.
- Joint effusion and capsular distension—especially noted between the lateral epicondyle and olecranon.
- Crepitus—may be palpated with advanced DJD.
- Diminished range of motion.

CAUSES

- Genetic
- Developmental
- Nutritional

RISK FACTORS

- Rapid growth and weight gain
- High-calorie diet



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Trauma
- Septic arthritis
- Panosteitis
- Avulsion or calcification of the flexor muscles
- Synovial sarcoma

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

Radiography

- Image both elbows—high incidence of bilateral disease.
- Elbow DJD recognized by osteophytes on the cranial margin of the radial head and epicondyles (medial and lateral), and medial coronoid process; also commonly see sclerosis of the ulna caudal to the coronoid process and trochlear notch and a staircase between the joint surface of the radius and lateral coronoid; may see these changes with UAP, OCD, FMCP, and incongruity.
- UAP—best diagnosed from the mediolateral hyperflexed view; may easily see lack of bony union. Comparison to the contralateral elbow may be helpful although the high incidence of bilateral disease should be kept in mind.
- OCD—best diagnosed from the craniocaudal and craniocaudal-lateromedial oblique views; reveals a radiolucent defect or flattening of the medial aspect of the humeral condyle.
- FMCP—may not be visualized in some cases; diagnosis is then presumptive based on DJD and the lack of UAP or OCD lesions; commonly see early osteophyte formation on the proximal caudal surface of the anconeal process with FMCP.

Other

CT, MRI, and linear tomography—can provide more definitive evidence for fissures and non-displaced fragments. CT is necessary in many cases of FMCP as survey radiographs have low sensitivity.

DIAGNOSTIC PROCEDURES

- Joint tap and analysis of synovial fluid—confirm involvement of joint.
- Synovial fluid—should be straw-colored with normal to decreased viscosity; cytology reveals < 5,000 nucleated cells/ μL (> 90% are mononuclear cells); normal results do not necessarily rule out the diagnosis.
- Arthroscopy—may help diagnose UAP, FMCP, and OCD.

PATHOLOGIC FINDINGS

- UAP—fibrous union between anconeal process and proximal ulnar metaphysis; fibrous tissue invasion and degeneration of the anconeal process; DJD.
- OCD—chondral flap on medial humeral condyle; sclerosis of underlying subchondral bone with fibrous tissue invasion; erosive lesion on apposing coronoid cartilage; DJD.
- FMCP—chondral or osteochondral fragmentation of the cranial tip or lateral margin of the medial coronoid; erosive lesion on cartilage of the apposing medial aspect of the humeral condyle; DJD.
- Incongruity—erosive lesions involving part or all of medial coronoid process and the apposing articular cartilage of the medial aspect of the humeral condyle; DJD; linear striations in the articular cartilage.

E

ELBOW DYSPLASIA

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

Surgery—controversial but recommended for most patients

E

NURSING CARE

- Cold packing the elbow joint—perform immediately post-surgery to help decrease swelling and control pain; perform at least 5–10 minutes q8h for 3–5 days.
- Range-of-motion exercises—beneficial until the patient can bear weight on the limb(s).

ACTIVITY

Restricted for all patients postoperatively

DIET

- Weight control—important for decreasing the load and stress on the affected joint(s).
- Restricted weight gain and growth in young dogs—may decrease incidence and severity.

CLIENT EDUCATION

- Discuss the heritability of the disease.
- Discuss the likelihood of DJD progression regardless of intervention.
- Discuss the influence of excessive intake of nutrients that promote rapid growth.

SURGICAL CONSIDERATIONS

- Severity of DJD and advanced age of patient—negatively influence outcome. Generally DJD progresses faster without treatment.
- UAP—four options: removal, lag screw fixation, dynamic proximal ulnar osteotomy, and lag screw fixation plus dynamic proximal osteotomy; base decision on degree of DJD, patient's age, and surgical expertise.
- OCD and FMCP—medial approach to elbow (diagnostic differentiation not necessary); removal of loose fragment(s).
- Incongruity—controversial; four options: no surgery, coronoidectomy, dynamic proximal ulnar osteotomy, intra-articular osteotomy; base decision on type of incongruity, degree of DJD, patient's age, and surgical expertise.
- Arthroscopic diagnosis and treatment—excellent option for FMCP, OCD, and incongruity; benefits: superior visualization, minimally invasive.



MEDICATIONS

DRUG(S) OF CHOICE

- None that promotes healing of osteochondral or chondral fragments.
- NSAIDs—minimize pain, decrease inflammation, symptomatically treat associated DJD.
- Deracoxib (3–4 mg/kg PO q24h, chewable).
- Carprofen (2.2 mg/kg PO q12h or q24h).

- Etodolac (10–15 mg/kg PO q24h).
- Meloxicam (load 0.2 mg/kg PO, then 0.1 mg/kg PO q24h—liquid).
- Tepoxalin (load 20 mg/kg, then 10 mg/kg PO q24h).

CONTRAINDICATIONS

Avoid corticosteroids—potential side effects; articular cartilage damage associated with long-term use.

PRECAUTIONS

NSAIDs—gastrointestinal irritation may preclude use in some patients.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Chondroprotective drugs (e.g., polysulfated glycosaminoglycans, glucosamine, and chondroitin sulfate)—may help limit cartilage damage and degeneration; may help alleviate pain and inflammation.



FOLLOW-UP

PATIENT MONITORING

- Post-surgery—limit activity for a minimum of 4 weeks; encourage early, active movement of the affected joint(s).
- Yearly examinations—recommended to evaluate progression of DJD.

PREVENTION/AVOIDANCE

- Discourage breeding of affected animals.
- Do not repeat dam-sire breedings that result in affected offspring.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

- Progression of DJD—expected
- Prognosis—fair to good for all forms



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

Middle-aged to old dogs with advanced DJD are not candidates for surgical intervention.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYS

Elbow osteochondrosis

SEE ALSO

Osteochondrosis

ABBREVIATIONS

- CT = computed tomography
- DJD = degenerative joint disease

- FMCP = fragmented medial coronoid process

- MRI = magnetic resonance imaging

- NSAID = nonsteroidal anti-inflammatory drugs
- OCD = osteochondritis dissecans
- UAP = un-united anconeal process

INTERNET RESOURCES

<http://www.offa.org/elbowinfo.html>.

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Client Education Handout
available online

ELECTRIC CORD INJURY



BASICS

OVERVIEW

- Electric cord injury is an uncommon event that occurs when an animal bites an electric cord.
- Other causes of electrocution are uncommon in dogs and cats but can occur.
- Household electrical currents are alternating (60 Hz) or 120 volts and dangerous.
- Injury can be caused due to thermal injury or due to disruption of normal electrophysiologic activity of excitable tissue.
- Pulmonary edema can be a sequelae to electrocution and the pathophysiology is thought to be neurogenic and centrally mediated, leading to pulmonary hypertension.
- Cataract formation is reported following electrocution.

SIGNALMENT

- Seen in dogs and cats.
- Most commonly seen in dogs.
- Most commonly seen in young animals. In published report age ranged from 5 months to 1.5 years.
- No breed or sex predilections.
- No genetic basis.

SIGNS

- Burns associated with gingiva, tongue, palate
- Singed hair or whiskers
- The most common clinical signs are related to acute dyspnea
- Coughing
- Tachypnea
- Orthopnea
- Increased respiratory effort
- Cyanosis
- Crackles during pulmonary auscultation
- Tachycardia
- Muscle tremors
- Tonic-clonic activity
- Collapse

CAUSES & RISK FACTORS

- Chewing electrical cord
- Young animals
- Primarily dogs but also reported in cats



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Left-sided congestive heart failure—may be due to congenital or acquired heart disease. The presence of cardiac murmur or dysrhythmia may help differentiate; however, dysrhythmias may be seen with electric cord injury.
- Vitamin K antagonist, rodenticide intoxication history (pulmonary hemorrhage).
- Thoracic trauma (pulmonary contusions)—history, thoracic radiographs.
- Other causes of non-cardiogenic pulmonary edema.
- Pleural space disease—muffled lung sounds during auscultation, thoracic radiographs.
- Thermal or chemical injuries—history, physical examination, thoracic radiographs.
- Exposure to fire and smoke inhalation—history, physical examination.
- Atypical pneumonia—history, physical examination, thoracic radiographs.

CBC/BIOCHEMISTRY/URINALYSIS

May help rule out other systemic causes of non-cardiogenic pulmonary edema.

OTHER LABORATORY TESTS

Arterial blood gas analysis may be useful to document hypoxemia. This may be difficult to perform in unstable patients.

IMAGING

• Thoracic radiographs may help distinguish between cardiogenic and non-cardiogenic causes of pulmonary edema.

• The radiographic pattern is usually a generalized, mixed alveolar bronchial pattern. The edema is often most notable in the caudal dorsal lung fields.

• Pulmonary venous congestion is absent with non-cardiogenic pulmonary edema.

Echocardiography may help identify or rule out underlying cardiac disease.

DIAGNOSTIC PROCEDURES

- Electrocardiogram—may help distinguish cardiogenic disease from non-cardiogenic disease; however, dysrhythmias may be seen with electrocution and other causes of non-cardiogenic pulmonary edema.
- Echocardiography should help identify heart failure as a cause.

PATHOLOGIC FINDINGS

- Pink, frothy fluid in airways
- Fluid-filled, congested lungs
- Subendocardial and subepicardial petechia
- Circumscribed, pale gray or tan oral lesions



TREATMENT

- If patient is close to live wire, turn off electricity and/or remove patient to safe area.
- Establish patent airway if patient is unconscious.
- Oxygen supplementation.
- Mechanical ventilation may be required.
- Establish venous access.



MEDICATIONS

DRUG(S)

- If in shock—treat with intravenous crystalloids (90 mL/kg/h in dog, 45–60 mL/kg/h in cat) or colloids (20 mL/kg in dogs, 5–10 mL/kg in cats).
- If pulmonary edema is present—furosemide I/V (2–4 mg/kg); this is controversial as this is a form of non-cardiogenic pulmonary edema.
- Anxiolytic therapy if dyspneic—butorphanol 0.1–0.2 mg/kg IV.
- Corticosteroids have been employed but are controversial and of unknown value.
- Inotropic support if required.

- Antiarrhythmic therapy if required.
- Oral and cutaneous burns—treated symptomatically.



FOLLOW-UP

PATIENT MONITORING

- Patient should be monitored until stable.
- Physical examination.
- Oral lesion should be monitored and may prevent the animal from eating.
- Electrocardiography.
- Central venous pressure.
- Blood pressure.
- Arterial blood gas.
- Thoracic radiographs.

PREVENTION/AVOIDANCE

- Damaged electric cords should be discarded.
- Avoid animal exposure to electric cords.
- Follow child safety rules for a safe home.

POSSIBLE COMPLICATIONS

- Infected burn wounds can occur but are uncommon.
- Oral-nasal fistula due to severe burns.

EXPECTED COURSE AND PROGNOSIS

- The prognosis is based on the response to therapy.
- Pulmonary edema can develop as soon 1 hour and as late as 36 hours after incident.
- Pulmonary edema associated with electrocution is associated with high mortality (38.5%).
- If patient survives first 24 hours the prognosis improves.
- Resolution of pulmonary edema may take 3–5 days.
- Most oral lesions resolve.
- Inappetence related to oral lesions resolves.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Cataracts have been reported in one dog 18 months after electrocution.

Suggested Reading

Brightman AH, Brogdon JD, Helper LC, Everds N. Electrical cataracts in the canine: A case report. *J Am Anim Hosp Assoc* 1984, 20:895–898.

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ENAMEL HYPOPLASIA/HYPOCALCIFICATION



BASICS

OVERVIEW

- Enamel hypoplasia refers to inadequate deposition of enamel matrix. This can affect one or several teeth and may be focal or multifocal. The crowns of the affected teeth can have areas of normal enamel next to areas of hypoplastic or missing enamel.
- Apparent defect in enamel surfaces, often pitted and discolored; focal or generalized.
- Defects due to disruption of normal enamel formation.
- Systemic influences during enamel formation (e.g., distemper, fever) over an extended time may cause generalized changes; local or focal influences (e.g., trauma, even from deciduous tooth extraction) over a short time may cause specific patterns or bands.
- Most cases are primarily aesthetic; some patients can have extensive structural damage, even root involvement.
- Enamel hypocalcification is a more correct description, since the amount of enamel is adequate (not hypoplastic), but defects in calcification lead to enamel defect.
 - Enamel hypocalcification refers to the inadequate mineralization of enamel matrix. This often affects several or all teeth. The crowns of affected teeth are covered by soft enamel that may be worn easily away.
- Teeth may be more sensitive with exposed dentin, and occasionally fractures of severely compromised teeth occur; usually they remain fully functional.

SIGNALMENT

- Dogs and less commonly cats.
- Often apparent at time of tooth eruption (after 6 months of age) or shortly thereafter (with signs of wear).

SIGNS

Historical Findings

Discolored teeth

Physical Examination Findings

- Irregular, pitted enamel surface with discoloration of diseased enamel and potential exposure of underlying dentin (light brown).
- Early or rapid accumulation of plaque and calculus on roughened tooth surface; possible gingivitis and/or accelerated periodontal disease.

CAUSES & RISK FACTORS

- Insult during enamel formation.
- Canine distemper virus, fever, trauma (e.g., accidents, excessive force during deciduous tooth extraction).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Enamel staining—discolored but smooth surface (tetracycline).
- Carious lesions—cavities with decay.
- Amelogenesis imperfecta—genetic and/or developmental formation and maturation abnormalities other than hypomineralization.
- Tooth resorption—similar to those found in cats.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal.
- Appropriate preanesthetic diagnostic when indicated.

OTHER LABORATORY TESTS

N/A

IMAGING

- Intraoral radiographs are necessary to determine the structure and viability of roots.
- Cases reported of abnormal root formation, no root formation, or separated crown and root.

DIAGNOSTIC PROCEDURES

None



TREATMENT

- Treatment depends upon extent of lesions and equipment and materials available.
- Goal is to provide the smoothest surface possible.
- Appropriate preoperative antimicrobial and pain management therapy when indicated.

Optimal treatment

- Ideal treatment is to gently remove diseased enamel (enamel scrub) with white stone burs or finishing disks on high-speed handpiece (adequate water coolant)—handle with care!
- Take care not to damage the tooth—excess enamel/dentin removal; hyperthermic damage to pulp.
- Focal defects may be amenable to composite restoration, but long-term success is poor; metallic crown restoration is preferred; many restorative materials (bonding agents, composites) require use of light-curing units and appropriate skill levels.
- Bonding agent recommended to seal exposed dentinal tubules and protect surfaces.

Alternative treatment

- Without a high-speed handpiece and appropriate attachments, treatment can be more challenging.

- The soft, diseased enamel can sometimes be removed with ultrasonic scalers, but take care to avoid damage and hyperthermia.

- A strong fluoride treatment (in-hospital, on a dry tooth surface; varnish or strong sodium fluoride paste) can be used to decrease sensitivity and enhance enamel strength.



MEDICATIONS

DRUG(S)

N/A

CONTRAINdications/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

Inform the owner that further degeneration of remaining enamel may occur, necessitating additional therapy in the future.

PREVENTION/AVOIDANCE

- Recommend regular professional dental cleaning and a routine homecare program (brushing); may include weekly application of stannous fluoride at home (minimize ingestion because of toxicity).
- Avoid excessive chewing on hard objects.



MISCELLANEOUS

INTERNET RESOURCES

<http://www.avdc.org/Nomenclature.html>.

Suggested Reading

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ENCEPHALITIS



BASICS

DEFINITION

Inflammation of the brain that may be accompanied by spinal cord and/or meningeal involvement.

PATHOPHYSIOLOGY

- Inflammation—caused by an infectious agent or by the patient's own immune system.
- Immune-mediated—immune system derangement generally of unknown cause.

SYSTEMS AFFECTED

- Nervous • Multisystemic signs—may be noted in patients with infectious diseases

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

Varies with the cause or agent implicated

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Granulomatous meningoencephalitis—mostly small-breed dogs, especially terriers and miniature poodles; large-breed dogs also affected. • Pug encephalitis—pugs.
- Pyogranulomatous meningoencephalitis—German shorthaired pointers. • Maltese encephalitis—Maltese. • Yorkshire terrier necrotizing encephalitis—Yorkshire terriers.

SIGNS

Historical Findings

Acute onset of clinical signs that rapidly progress.

Physical Examination Findings

With mycotic, rickettsial, viral, and protothecal organisms—fundic lesions frequent.

Neurologic Examination Findings

- Rostral fossa—seizures; circling; pacing; personality change; decreasing level of responsiveness. • Caudal fossa—abnormalities related to the brainstem (e.g., somnolence, head tilt, facial paresis/paralysis, incoordination). • Progression (e.g., anisocoria, pinpoint pupils, decreasing level of consciousness, poor physiologic nystagmus)—suggests tentorial herniation.

CAUSES

Dogs

- Idiopathic, immune-mediated—GME; pug encephalitis; Maltese encephalitis; YNE; eosinophilic meningoencephalitis. • Viral—canine distemper virus; rabies; herpes; parvovirus; adenovirus; pseudorabies; West Nile virus; Eastern and Venezuelan equine encephalomyelitis virus. • Post-vaccinal encephalomyelitis—canine distemper virus; rabies; canine coronavirus-parvovirus.
- Rickettsial—Rocky Mountain spotted fever;

ehrlichiosis. • Mycotic—cryptococcosis; blastomycosis; histoplasmosis; coccidioidomycosis; aspergillosis; phaeohyphomycosis. • Bacterial—anaerobic and aerobic. • Protozoal—toxoplasmosis; neosporosis; encephalitozoonosis

- Spirochetes—borreliosis. • Parasite migration—*Dirofilaria immitis*; *Toxocara canis*; *Ancylostoma caninum*; *Cuterebra*; cysticercosis. • Migrating foreign body—plant awn; others. • Protothecosis. • PME.

Cats

- Idiopathic, immune-mediated—GME; EME. • Idiopathic polioencephalomyelitis.
- Viral—FIP; rabies; FIV; pseudorabies; panleukopenia; rhinotracheitis. • Mycotic—cryptococcosis; blastomycosis; phaeohyphomycoses. • Bacterial—anaerobic and aerobic. • Protozoal—toxoplasmosis.
- Parasite migration—*Dirofilaria immitis*; *Cuterebra*.

RISK FACTORS

- Immunosuppressive drugs and FIV or FeLV infection—infectious encephalitides. • Tick-infected areas—rickettsial and *Borrelia* infections. • Travel history—mycotic infections.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Fungal encephalitides—frequently accompanied by systemic signs. • Protozoal diseases—systemic; may have a chronic history. • Rickettsial diseases—CBC abnormalities common. • FIP—patients usually < 3 years of age; protracted course; characteristic CSF results. • Canine distemper virus—commonly seen as acute encephalitis with systemic signs in patients < 1 year old; can be difficult to confirm antemortem.
- Primary CNS neoplasia—signs may be similar to encephalitis. • Degenerative disorders—usually slow, insidiously progressive onset. • Metabolic or toxic encephalopathy—bilateral, symmetrical neurologic abnormalities that relate to the cerebrum; confirm toxins by laboratory tests or serum assay.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—frequently normal; leukocytosis may be seen in diseases that produce systemic signs; may see lymphopenia in early stages of canine distemper virus and rickettsial infection; rickettsial encephalitis may be accompanied by thrombocytopenia and anemia. • Biochemistry—frequently normal; hyperproteinemia with polyclonal gammopathy often with FIP and chronic systemic infections; creatine kinase may be moderately high with *Neospora* infection.

OTHER LABORATORY TESTS

- Serology—available for fungal, protozoal, rickettsial, and viral diseases; helpful but must

be interpreted with caution because a positive titer does not always indicate active disease (e.g., toxoplasma in cats) and a negative titer does not always rule out active disease (e.g., FIP). • Indirect fluorescent antibody—a single positive titer of 1:10 or greater confirms ehrlichiosis. • ELISA—a four-fold rise between acute and convalescent IgG titers when the first titer is > 1:128 confirms Rocky Mountain spotted fever; an IgM titer of > 1:256 suggests infection within the previous 16 weeks by *Toxoplasma gondii* and may indicate exacerbation of chronic infection.

- Latex agglutination antigen—a single positive titer from serum or CSF confirms Cryptococcus. • Agar-gel immunodiffusion—diagnose blastomycosis with a high degree of accuracy. • Local production of canine distemper virus-specific antibody (IgG and IgM)—in CSF after virus infects the CNS.
- Positive *Neospora caninum* titer—correlates well with active disease. • Positive FIP titer—indicates only infection with a coronavirus; may not be pathogenic. • Positive *Borrelia burgdorferi* titer—indicates exposure to the organism, not necessarily active disease.

IMAGING

- Thoracic radiographs—may confirm lung abnormalities. • Skull radiographs—may confirm sinusitis/rhinitis in some cats with cryptococcosis. • CT or MRI of the brain—may detect multifocal or single mass lesions.

DIAGNOSTIC PROCEDURES

- CSF—perform on all animals with clinical signs that suggest encephalitis; results almost always abnormal; normal results do not rule out acute viral encephalitis that is limited to the parenchyma; with pleocytosis, culture for bacteria (aerobic and anaerobic). • CSF—neutrophils indicate acute active inflammatory process; small lymphocytes indicate an antigenic response; eosinophils indicate an allergic response or a reaction to foreign material (tumor, parasite).

PATHOLOGIC FINDINGS

The lesions are a function of the brain response to the infectious agent or other cause.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient—diagnosis and initial therapy

NURSING CARE

- Symptomatic treatment—control brain edema and seizure activity as necessary.
- Cerebral edema—20% mannitol (2.2 g/kg IV over 30–45 minutes); may repeat within 1–2 hours to achieve maximum response; limit parenteral fluids to prevent rebound cerebral edema; short-term (72-hour) corticosteroid treatment can be added for further control (dexamethasone sodium

ENCEPHALITIS

(CONTINUED)

phosphate at 0.5 mg/kg IV q12h for 24 hours; then reduce to 0.25 mg/kg q12h for 48 hours). • Seizures—treat with antiepileptic drugs; with boluses or constant-rate infusion.

ACTIVITY

As tolerated

DIET

If severe depression or vomiting—nothing oral until condition improves to prevent aspiration.

CLIENT EDUCATION

Inform client that relapse is possible with idiopathic or immune-mediated encephalitis when therapy is discontinued.

SURGICAL CONSIDERATIONS

Brain biopsy—may be needed in specific cases.



MEDICATIONS

DRUG(S) OF CHOICE

- Apply specific therapy once diagnosis is reached or highly suspected.
- Idiopathic and immune-mediated—2 mg/kg prednisone q12h initially; tapered over 6 months.
- Rickettsial and borreliosis—doxycycline.
- Protozoal—clindamycin.
- Mycotic—requires treatment for 1–2 years; itraconazole (5 mg/kg PO q12h with food) or fluconazole (6.25–12.5 mg/kg PO or IV q12h); corticosteroids often needed during the first 4–6 weeks to control cerebral edema.
- Viral and post-vaccinal—none definitive; treat symptomatically.
- Bacterial—broad-spectrum antibiotics that penetrate the blood-brain barrier; if agent is unknown, try a combination of enrofloxacin (5–10 mg/kg PO or IV q12h) and ticarcillin-clavulanate (50 mg/kg IV q8h) or amoxicillin-clavulanate (13.75 mg/kg PO q8h).

CONTRAINDICATIONS

- Bacterial and Rocky Mountain spotted fever—corticosteroids contraindicated.
- Puppies < 6 months of age with a rickettsial disease—use chloramphenicol (doxycycline-induced tooth discoloration). • Puppies < 8 months of age—enrofloxacin contraindicated (cartilage damage); use amoxicillin-clavulanate or ticarcillin-clavulanate alone.
- CNS infections—do not use aminoglycosides and first-generation cephalosporins because CNS penetration is poor.

PRECAUTIONS

- Administer mannitol intravenously 10 minutes prior to anesthesia for CSF collection to decrease intracranial pressure.
- Corticosteroids—observe closely for worsening signs that suggest an infectious cause.

POSSIBLE INTERACTIONS

- Chloramphenicol and cimetidine—do not use concurrently with phenobarbital to avoid toxic serum phenobarbital levels due to interference with liver metabolism.
- Corticosteroids alter CSF results if used for 12 hours or more.

ALTERNATIVE DRUG(S)

- Leflunomide 1.5–4 mg/kg PO q24h individualized based on its active metabolite, teriflunomide, blood level done 24h post-medication 7 days after therapy initiated due to long half-life. Safe therapeutic range is 20–40 µg/mL. Often effective for immune-mediated encephalitis unresponsive to conventional therapy. Leukopenia, thrombocytopenia, and hemorrhagic colitis are possible adverse effects. CBCs done monthly; treatment is for 1.5 years.
- Mycophenolate mofetil 10–16 mg/kg PO or IV q12h can be used in addition to leflunomide and prednisone in dogs with immune-mediated encephalitis to achieve further immune suppression. Adverse effects are similar to leflunomide. A CBC should be done 2 weeks after onset of therapy and then monthly.



FOLLOW-UP

PATIENT MONITORING

- Frequent neurologic evaluations in the first 48–72 hours to monitor progress. • Relapse as medication is withdrawn—repeat CSF analysis. • Measure serum titer of cryptococcus capsular antigen every 3 months until negative.

PREVENTION/AVOIDANCE

- A method of effective tick control should be used on animals that live in endemic areas.
- Avoid vaccination of dogs that have had GME.

POSSIBLE COMPLICATIONS

- Long-term corticosteroid therapy—signs of iatrogenic hyperadrenocorticism. • CSF collection or natural course of the disease—tentorial herniation and death.

EXPECTED COURSE AND PROGNOSIS

- Resolution of signs—generally gradual (2–8 weeks). • Protozoal—almost always progresses to death. • Immune-mediated—fair to good prognosis for complete remission with aggressive immunosuppression.
- Rickettsial, mycotic, bacterial, protozoal, and spirochete infections—fair chance of survival. • Parasite migration, migrating foreign bodies, PME, YNE, and polioencephalomyelitis—usually fatal. • Pug and Maltese encephalitis—may be fatal; course varies greatly; some patients respond to steroid treatment for long periods.
- Post-vaccinal encephalomyelitis—may resolve on its own; often permanent damage and death.



MISCELLANEOUS

AGE-RELATED FACTORS

- Young (< 2 years) and old (> 8 years) animals—more risk for infectious diseases.
- Dogs < 6 years of age—immune-mediated and idiopathic encephalitides.

ZOONOTIC POTENTIAL

- Rabies—consider in endemic areas if the patient is an outdoor animal that has rapidly progressive encephalitis.
- Humans may be infected by the same vector tick that affected the patient.
- Exudates from animals with mycosis can revert to the spore-forming, infectious mycelial stage.
- Cultures are highly contagious and should be handled with great care.

SEE ALSO

- Under “Causes”
- Seizures (Convulsions, Status Epilepticus—Cat)
- Seizures (Convulsions, Status Epilepticus—Dog)
- Stupor and Coma

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- ELISA = enzyme-linked immunosorbent assay
- EME = eosinophilic meningoencephalitis
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- GME = granulomatous meningoencephalitis
- MRI = magnetic resonance imaging
- PME = pyogranulomatous meningoencephalitis
- YNE = Yorkshire terrier necrotizing encephalitis.

INTERNET RESOURCES

<http://www.ivis.org/advances/Vite/toc.asp>

Suggested Reading

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Client Education Handout
available online

ENCEPHALITIS SECONDARY TO PARASITIC MIGRATION



BASICS

OVERVIEW

- Aberrant parasitic migration into the CNS.
- Parasites usually affect another organ system of the same host (e.g., *Dirofilaria immitis*, *Taenia*, *Ancylostoma caninum*, *Angiostrongylus*, or *Toxocara canis*), or a different host species (e.g., raccoon roundworm, *Baylisascaris procyonis*; skunk roundworm, *B. columellaris*; *Coenurus* spp.; or *Cysticercus cellulosae*).
- Access to CNS—hematogenously (dirofilariasis) or through adjacent tissues, including the middle ear, skull foramina, cribriform plate through nasal cavities, or open fontanelles (cuterebraiasis).

SIGNALMENT

- Dirofilariasis—adult animals only.
- Other parasites—young dogs and cats with access to outdoors—rare and sporadic occurrence.

SIGNS

- Vary with the portion of CNS affected.
- Likely asymmetrical.
- May suggest a focal mass lesion or a multifocal disease process.
- Cuterebraiasis—seasonal (July–October) acute or peracute onset of behavior changes, seizures, visual deficits, etc. A previous history of respiratory disease is common.
- Rat parasite, *Angiostrongylus cantonensis* (Australia)—lumbosacral syndrome (hind limbs, tail, and bladder paralysis/paresis) in puppies that may ascend to thoracic limbs and cranial nerves.

CAUSES & RISK FACTORS

Housing in a cage previously occupied by wildlife (raccoons, skunks).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Rule out other causes of focal encephalopathy—infectious diseases (viral, bacterial, protozoan, or fungal); granulomatous meningoencephalomyelitis; brain tumor.
- Diagnosis often made on necropsy.

CBC/BIOCHEMISTRY/URINALYSIS

Normal unless the parasite also affects non-neural tissues.

OTHER LABORATORY TESTS

CSF—may show an eosinophilic, neutrophilic, or mononuclear pleocytosis (also found in protozoal, fungal, and

protozoa encephalitides); may be normal (strictly parenchymal lesions).

IMAGING

CT or MRI—brain; focal lesion and/or cerebral infarction from occlusion of cerebral vessels. Non-specific and often inconclusive but could lead to surgical exploration and removal of migrating parasite.

PATHOLOGIC FINDINGS

- The parasite or its tracts may or may not be identified.
- Infarction, vascular rupture and hemorrhage or vascular emboli may cause local to extensive necrosis and malacia. There may be granulomatous proliferation or/and obstructive hydrocephalus.
- *Dirofilaria immitis*—intravascular or extravascular.
- Worms produce focal inflammation.
- Cuterebraiasis is the suspected cause of feline ischemic encephalopathy.



TREATMENT

- Surgical removal of intracranial Cuterebra.
- Parasiticides (see below) could potentiate illness.
- Supportive and nursing care.



MEDICATIONS

DRUG(S)

- Dirofilariasis and neural angiostrongylosis—ananthelmintic treatment may cause worsening of signs and sometimes death.
- Mild neural angiostrongylosis—puppies may recover with supportive care and corticosteroid therapy.
- A single dose of ivermectin (400 mg/kg SC) may kill cuterebra larvae in cats with suspected cuterebraiasis. Pretreatment with diphenhydramine (4 mg/kg) and intravenous dexamethasone (0.1 mg/kg) may mitigate allergic/anaphylactic reactions to dead or dying larvae.
- Treat inflammation and secondary infections: corticosteroids/NSAIDs, antibiotics.



FOLLOW-UP

PATIENT MONITORING

As necessary

PREVENTION/AVOIDANCE

- Keep pets indoors or/and segregated from wildlife.
- Use preventive anthelmintics and dirofilaricides.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

Acute or insidious onset, then usually progressive.



MISCELLANEOUS

SEE ALSO

- Encephalitis
- Microsporidiosis (Encephalitozoonosis)
- Feline Ischemic Encephalopathy
- Heartworm Disease—Cats
- Heartworm Disease—Dogs

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- MRI = magnetic resonance imaging

INTERNET RESOURCES

- Braund KG. Neurovascular disorders (updated 2003) In: Clinical Neurology in Small Animals—Localization, Diagnosis and Treatment. www.ivis.org.
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ENDOCARDITIS, INFECTIVE



BASICS

DEFINITION

The invasion of the cardiac endocardium, usually the valves, by infectious agents. Usually Gram-positive bacteria, especially staphylococci or streptococci. Occasionally *Rickettsia* or *Bartonella* in dogs. Rarely fungi in dogs. Culture-negative cases may be due to *Bartonella* or fungi (e.g., *Aspergillus*). Less likely due to *Brucella*, *Coxiella*, and *Chlamydia*.

PATHOPHYSIOLOGY

- Bacteremia develops from various portals of entry; bacteria invade and colonize the heart valves—usually the aortic, occasionally the mitral, and rarely the tricuspid and pulmonic valves.
- Endocardial ulceration exposes collagen causing platelet aggregation, activation of the coagulation cascade, and formation of vegetations.
- Vegetations on heart valves are composed of an inner layer of platelets, fibrin, RBCs, and bacteria; a middle layer of bacteria; and an outer layer of fibrin.
- Valvular insufficiency develops in virtually all patients; aortic insufficiency almost invariably leads to intractable LS-CHF within weeks to several months.
- CHF is less frequent and latent when only the mitral valve is affected.
- Vegetative lesions may dislodge causing infarction or metastatic infection to any organ; organs commonly infected include the spleen, kidneys, brain, and skeletal muscles.

SYSTEMS AFFECTED

- Cardiovascular—valvular insufficiency; arrhythmias, myocarditis.
- CNS—para/tetraparesis; cranial nerve deficits; abnormal mentation.
- Hemic/Lymphatic/Immune—hypercoagulation; DIC.
- Musculoskeletal—septic or immune-mediated polyarthropathy; hypertrophic osteopathy; discospondylitis.
- Renal/Urologic—renal infarction; immune-mediated glomerulonephritis; urinary tract infections.
- Respiratory—pulmonary edema and/or emboli.

SIGNALMENT

Species

Dogs; rarely cats

Breed Predilections

- Middle-sized to large breeds
- Breeds predisposed to subaortic stenosis

Mean Age and Range

Most affected dogs are 4–8 years of age; infection can occur at any age.

Predominant Sex

Most studies report male predominance—may be as great as 2:1.

SIGNS

General Comments

- Gram-negative bacteremia results in

peracute or acute clinical signs; Gram-positive bacteremia results in subacute or chronic clinical signs.

- Systemic signs are secondary to infarction, infection (inflammation), toxemia, or immune-mediated damage; usually override cardiac signs.

Historical Findings

- Infectious disease involving the skin, oral, GI, and genital tract (e.g., prostatitis).
- History of predisposing factors—immunosuppressive drug therapy, aortic stenosis, recent surgery, infected wounds, abscesses, or pyoderma.
- Common reasons for presentation include lethargy, paresis, fever, anorexia, GI disturbances, and lameness.

Physical Examination Findings

- Usually diverse and misleading—"the great imitator."
- Pyrexia and general malaise.
- Dyspnea caused by CHF.
- Arrhythmias (usually ventricular, supraventricular, or heart block).
- Single or shifting leg lameness.
- Systolic heart murmur.
- "To-and-fro" murmur—associated with aortic valve vegetation causing systolic turbulence and diastolic regurgitation.
- Diastolic murmur component with hyperdynamic femoral pulses are a strong indication of advanced aortic valve endocarditis.

CAUSES

- Bacterial infection associated with the oral cavity, bone, prostate, skin, and other sites.
- Invasive diagnostic or surgical procedures forcing bacteria into the bloodstream.

RISK FACTORS

- Congenital subaortic stenosis.
- Immunosuppression from long-term or high-dose corticosteroids, neoplasia, or cytotoxic drug administration.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Bacteremia of any cause.
- Polysystemic, immune-mediated disorders.
- Left-sided CHF caused by dilated cardiomyopathy or congenital subaortic stenosis.

CBC/BIOCHEMISTRY/URINALYSIS

- Active, severe infection associated with an inflammatory leukogram (i.e., neutrophilia, left shift, and monocytosis)—patients with chronic, relatively inactive, or walled-off infection may have normal or nearly normal leukogram; those with chronic infection may have mature neutrophilia with monocytosis.
- Nonregenerative anemia.
- Thrombocytopenia—variable severity.
- Low-normal or low albumin, low-normal or low glucose, and high SAP/bilirubin activity are inconsistently associated with sepsis (septic triad).
- Renal azotemia—secondary to renal embolization, pyelonephritis, and/or hypovolemia-induced renal failure.

- Proteinuria caused by septic embolization, immune-mediated glomerulonephritis, or infarction of the kidneys; hematuria, pyuria, and granular casts associated with pyelonephritis.

OTHER LABORATORY TESTS

- Blood culturing—three samples taken at least 1 hour apart over 24 hours; at least two should yield the same microbe; both aerobic and anaerobic cultures recommended; antibiotic removal systems available for diagnosis of patients given antibiotics.
- PCR with bacterial 16S primers, in combination with blood culturing, increases the likelihood of identification of bacteria in blood.
- Culture-negative bacteremia often due to prior antibiotic administration or fastidious microbes, especially *Bartonella*.
- Catheter tips—culture.
- Urine cultures (not a substitute for blood cultures)—easy; often yield positive results; do not necessarily incriminate the urinary tract as the source of infection.
- Tests for prostate, kidney, and bone infection may be warranted.
- Positive antinuclear antibody, lupus erythematosus, rheumatoid factor, and Coombs' test results occasionally found—non-specific; tend to confound the diagnosis.
- Bartonella* alpha-Proteobacteria growth medium (BAPGM) and PCR—for *Bartonella*.

IMAGING

Radiographic Findings

Left heart enlargement; rarely, calcification of one or more heart valves.

Echocardiography

Best test—vegetative endocarditis of the aortic valve is easily discerned; mitral valve infection may be difficult to differentiate from myxomatous degeneration. Hyperechoic with chronicity.

DIAGNOSTIC PROCEDURES

Joint taps for cytologic examination and culture—cytologic examination usually does not differentiate septic from immune-mediated arthritis; either, usually not septic, can exist with infective endocarditis. Neutrophils are usually non-degenerate regardless of cause.

Electrocardiographic Findings

- ECG—may be normal; occasionally reflects left heart enlargement; often detects ventricular tachyarrhythmias; occasionally heart block of variable severity or supraventricular tachyarrhythmias.
- Heart block suggests aortic valve involvement with infection or infarction of the adjacent septum.

PATHOLOGIC FINDINGS

- Cardiomegaly, almost always left sided when present.
- Vegetative lesions and blood clots on one or more valves.
- Infection, hemorrhage, and infarction of adjacent myocardium.
- Renal infarcts are always present and lead to proteinuria and possibly renal failure.
- Primary or secondary sites of

(CONTINUED)

infection, especially kidneys and spleen.
• Pulmonary hemorrhage or edema.



TREATMENT

Early index of suspicion with aggressive, rapid diagnostic testing, followed by appropriate treatment are imperative for cure. Cure is a reasonable expectation when mitral valve (alone) IE is identified early in its course and treatment is aggressive.

NURSING CARE

- Aggressive fluid therapy—overt or impending CHF limits fluid volumes that can be administered; this problem is virtually insurmountable in patients with concomitant renal failure.
- Imminent CHF—provide no more than maintenance volumes of fluid; alternate D5W with LRS (or 2.5% dextrose in half-strength LRS); potassium supplementation usually required.

CLIENT EDUCATION

Guarded prognosis if only mitral valve involved. The prognosis is grave if the aortic valve is involved.



MEDICATIONS

DRUG(S) OF CHOICE

Treatment variable—depends on severity of sepsis and presence or absence of CHF.

Antibiotics

- Backbone of treatment but usually do not eradicate infection before irreversible aortic valve damage occurs; more than minimal damage to the aortic valve is life-threatening because aortic insufficiency tends to be a lethal complication.
- High-dose IV administration of bactericidal antibiotics is imperative and recommended for as long as feasible (at least 1 week), followed by SC administration for 1 or more weeks.
- Oral administration—recommended only after at least 4 weeks of injectable therapy and at least 1 week after hematologic and clinical signs of infection and inflammation have disappeared; long-term (> 4 months) treatment required to eradicate the infection from the vegetations.
- Selection determined by both the urgency of septic complications and results of bacterial culture; coagulase-positive staphylococci and streptococci are most often incriminated, so choices can be logically made before culture results are obtained.
- Coagulase-positive staphylococci—usually resistant to penicillin, hetacillin, amoxicillin, and ampicillin.
- Streptococci—often resistant to aminoglycosides and fluoroquinolones.

- Gram-negative bacteria—often sensitive to third-generation cephalosporins, fluoroquinolones, and aminoglycosides.
- Bartonella*—only aminoglycosides appear cidal; can try doxycycline, fluoroquinolone, rifampin, or azithromycin.
- First-generation cephalosporins—reasonable choice for stable patients until culture results are obtained.
- Treat life-threatening sepsis immediately with drug combinations. Pending culture results, one of three regimens is recommended: (1) Penicillin, ampicillin, ticarcillin, or a first-generation cephalosporin is combined with an aminoglycoside. Aminoglycosides are not good choices for animals with overt or impending CHF or those with renal azotemia. Gentamicin (2 mg/kg q8h) is recommended for only 5–10 days because of renal toxicity. A fluoroquinolone may be substituted for an aminoglycoside. (2) Clindamycin (2–10 mg/kg IV q8h) plus enrofloxacin (10 mg/kg q24h given diluted 1:1 in sterile water and injected slowly over 15–20 minutes). (3) Advanced-generation cephalosporins or ticarcillin-clavulanic acid (Timentin)—high dosages, but only normal dosages if patient has renal failure.

Treatment of CHF

- Pimobendan, ACE inhibitor, spironolactone, amlodipine, and furosemide indicated for patients with overt or impending CHF.
- Oxygen, nitroglycerin, high-dose furosemide (2–8 mg/kg IV), and hydralazine (1–2 mg/kg q12h) for patients with acute, severe pulmonary edema.

CONTRAINDICATIONS

- Avoid antibiotics that cannot penetrate fibrin (e.g., sulfonamides).
- Corticosteroids.

OTHER DRUGS

- Anticoagulant therapy—controversial in the prevention of embolization. Heparin not recommended in human medicine as it increases risk of hemorrhage.
- Aspirin (5–7 mg/kg PO q24h) and/or dalteparin (100 U/kg SC q8h) and/or clopidogrel (2–4 mg/kg PO q24h)—may reduce bacterial dissemination and embolization.



FOLLOW-UP

PATIENT MONITORING

- Emergence of antibiotic resistance—relapsing fever and inflammatory leukogram; imperative to adjust treatment on the basis of culture results.
- Frequent examination and CBC after discharge.
- Repeat blood cultures 1 week after antibiotics are discontinued or if fever recurs.

ENDOCARDITIS, INFECTIVE

PREVENTION/AVOIDANCE

- Indwelling catheters—restrict to appropriate indications; aseptic placement; replace within 3–5 days.
- Administer antibiotics to dog with moderate to severe subaortic stenosis during dentistry or “dirty” procedures.
- Avoid careless use of corticosteroids.

POSSIBLE COMPLICATIONS

- CHF
- Renal failure
- Septic embolization of many tissues and organs
- Persistent or latent immune-mediated polyarthropathy

EXPECTED COURSE AND PROGNOSIS

- Best prognosis associated with short history of bacteremia, rapid diagnosis, and aggressive treatment.
- Mortality relatively higher in animals recently given corticosteroids.
- Grave prognosis for patients with aortic valve endocarditis.
- Patients with mitral valve endocarditis can be saved with appropriate treatment.
- Latent CHF can occur with advance, late diagnosis or inadequate treatment for mitral valve endocarditis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Congenital heart defects (usually subaortic stenosis) in some animals.

SYNONYMS

- Bacterial endocarditis
- Infective endocarditis
- Vegetative endocarditis

SEE ALSO

- Bartonellosis
- Congestive Heart Failure, Left-Sided
- Discospondylitis
- Prostatitis and Prostatic Abscess
- Renal Failure, Acute
- Sepsis and Bacteremia

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- APTT = activated partial thromboplastin time
- CHF = congestive heart failure
- BAPGM = *Bartonella* alpha-Proteobacteria growth medium
- CNS = central nervous system
- DIC = disseminated intravascular coagulation
- ECG = electrocardiogram
- GI = gastrointestinal
- IE = infective endocarditis
- PCR = polymerase chain reaction
- RBC = red blood cell
- SAP = (serum) alkaline phosphatase

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Authors Justin D. Thomason and Clay A. Calvert

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Client Education Handout
available online

ENDOMYOCARDIAL DISEASES—CATS



BASICS

OVERVIEW

- Endomyocarditis—acute cardiopulmonary disease that typically develops following a stressful event; characterized by interstitial pneumonia and endomyocardial inflammation; pneumonia is usually severe and commonly causes death; one report recorded the incidence of endomyocarditis at post-mortem to be equivalent to that of hypertrophic cardiomyopathy.
- Endocardial fibroelastosis—congenital heart disease in which severe fibrous endocardial thickening leads to heart failure secondary to diastolic and systolic failure.
- Excessive moderator bands (EMBs)—a rare and unique pathologic disease. Moderator bands are normal muscular bands in the right ventricle, but they can sometimes occur in the left ventricle.

SIGNALMENT

- Cats.
- Endomyocarditis—predominantly males (62%) age 1–4 years.
- Endocardial fibroelastosis—early development of biventricular or left heart failure, usually prior to 6 months of age.
- EMBs—can be seen in any age cat.

SIGNS

Historical Findings

Endomyocarditis

- Dyspnea following a stressful event in a young, healthy cat.
- Respiratory signs usually occur 5–21 days after the stressor.
- In one report, 73% of cases presented between August and September.

Endocardial Fibroelastosis and EMBs

- Lethargy, weakness, collapse, syncope
- Poor appetite and weight loss
- Dyspnea
- Tachypnea
- Cyanosis
- Abdominal distention
- Paresis or paralysis; signs of thromboembolic disease.

Physical Examination Findings

Endomyocarditis

- Severe dyspnea
- Occasional crackles
- May be murmur or gallop; murmur may vary in intensity
- May be evidence of thromboembolic disease
- Typically no significant abnormalities prior to the stressful event.

Endocardial Fibroelastosis and EMB

- Gallop
- Systolic murmur, possible mitral regurgitation
- Dyspnea and increased lung sounds or crackles

- Paresis or paralysis with weak or absent femoral pulses.
- Arrhythmias possible.

CAUSES & RISK FACTORS

- Cause unknown for all three diseases.
- Risk factors for endomyocarditis include stressful incidents such as anesthesia (commonly associated with neutering or declawing), vaccination, relocation, or bathing.
- Endocardial fibroelastosis may be familial in Burmese and Siamese cats.
- The appearance of EMBs in a young cat would suggest a congenital malformation.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other Causes of Cardiac Disease

Hypertrophic cardiomyopathy, unclassified cardiomyopathy, restrictive cardiomyopathy, dilated cardiomyopathy, congenital heart malformations.

Other Causes of Dyspnea

- Other forms of cardiac disease, hypertrophic cardiomyopathy, unclassified cardiomyopathy, restrictive cardiomyopathy, dilated cardiomyopathy, congenital malformations
- Primary respiratory disease
- Pleural space disease
- Mediastinal disorders, infection, trauma, neoplasia
- Hemoglobin disorders, anemia, methemoglobinemia, causes of central cyanosis.

Other Causes of Collapse, Weakness, or Syncope

- Arrhythmias
- Neurologic or musculoskeletal disease
- Metabolic disease or electrolyte disorders
- Other forms of paresis or paralysis
- Arterial thromboembolism secondary to any form of cardiac disease or neoplasia
- Neurologic or musculoskeletal disease
- Neoplasia.

CBC/BIOCHEMISTRY/URINALYSIS

Not diagnostic

OTHER LABORATORY TESTS

N/A

IMAGING

Thoracic Radiographic Findings for All Three Diseases

- Cardiomegaly
- Interstitial or alveolar infiltrates or pleural effusion if congestion has developed.

Echocardiographic Findings

Endomyocarditis

- Normal to mildly large left atrium
- Left ventricular wall thickness can be normal to mildly thick (0.6–0.7 cm)

- Hyperechoic endomyocardium reported—incidence seems to vary and is subjective; in one report it was as high as 86%.

Endocardial Fibroelastosis

- Limited data available
- Reduced left ventricular function and enlarged left atrium.

Excessive Moderator Bands

- Many findings can overlap restrictive cardiomyopathy. A network of false tendons can sometimes be imaged with two-dimensional echocardiography.

DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

- Endomyocarditis—sinus tachycardia common; ventricular premature complexes, atrial premature complexes, bundle branch block, and complete AV block reported.
- Endocardial fibroelastosis—evidence for left-sided enlargement; sinus rhythm typically present, but various arrhythmias possible.
- EMBs—various electrocardiographic findings have been reported: AV block, sinus bradycardia, right bundle branch block, and left axis deviation.

PATHOLOGIC FINDINGS

Endomyocarditis

- Interstitial pneumonia.
- Left heart enlargement and opacity of the left ventricular endomyocardium with foci of hemorrhage; fibroplasia of the endocardium is striking.
- Varying degrees of endomyocardial inflammation with infiltrates of neutrophils, lymphocytes, plasma cells, histiocytes, and macrophages seen histologically.

Endocardial Fibroelastosis

- Left ventricular and atrial dilation with severe diffuse white opaque thickening of the endocardium.
- Diffuse hypocellular, fibroelastic thickening of the endomyocardium; prominent endomyocardial edema with dilation of lymphatics.

Excessive Moderator Bands

- Changes typically include an irregular left ventricular endocardial contour with a rounded apex and numerous irregular left ventricular false tendons. Heart weights can be greater than normal. The moderator bands are composed of central Purkinje fibers and collagen.



TREATMENT

ENDOMYOCARDITIS

- No single therapy protocol to date.
- Small percentage of cats have survived; these cats are not on long-term therapy.
- Supportive care with oxygen and possibly ventilation.

(CONTINUED)

ENDOMYOCARDIAL DISEASES—CATS**ENDOCARDIAL FIBROELASTOSIS AND EMBS**

- Oxygen therapy via cage delivery is least stressful.
- Thoracocentesis if pleural effusion.

**MEDICATIONS****DRUG(S) OF CHOICE***Endomyocarditis*

Steroids, furosemide, and vasodilators have been tried, but efficacy is still unknown.

*Endocardial Fibroelastosis and EMB**Acute CHF*

- Parenteral administration of furosemide, 0.5–1 mg/kg IV or IM, q1–6h.
- Dermal application of 2% nitroglycerin ointment, one-eighth to one-fourth inch q4–6h.
- Arrhythmias may resolve with stabilization. If there is rapid atrial fibrillation (heart rate > 200), a calcium channel blocker or beta-blocker can be given to help control the ventricular response. If there is dilated cardiomyopathy, digoxin may be a better choice for controlling the atrial fibrillation rate. For other supraventricular arrhythmias and ventricular arrhythmias, waiting for a response to heart failure therapy may be wise before starting antiarrhythmic therapy.
- Intractable edema—nitroprusside, 1–5 µg/kg/minute, may be helpful.

Chronic CHF

- Treat as other CHF, with furosemide and enalapril.
- Digoxin can be added when patient is stable and eating.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A

**FOLLOW-UP****EXPECTED COURSE AND PROGNOSIS**

- Endomyocarditis—poor, although some animals survive; animals that survive respiratory phase may progress to left ventricular endocardial fibrosis.
- Endocardial fibroelastosis and EMBS—medical treatment of CHF may prolong life, but recovery is unlikely.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Aortic thromboembolism.
- Relationship possible between endomyocarditis and left ventricular endocardial fibrosis.

SEE ALSO

- Aortic Thromboembolism
- Congestive Heart Failure, Left-Sided
- Congestive Heart Failure, Right-Sided
- Myocarditis

ABBREVIATIONS

- AV = atrioventricular
- CHF = congestive heart failure
- EMB = excessive moderator band

Suggested Reading

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ENTROPION



BASICS

OVERVIEW

- Inversion of part or all of one or more eyelid margins.
- Frictional irritation of the cornea, because of contact by the eyelashes or eyelid hair, may result in corneal ulceration or perforation or pigmentary keratitis.
- Ophthalmic system (vision may be threatened).

SIGNALMENT

- Common in dogs; occasionally seen in cats.
- Cats—usually seen in brachycephalic breeds (e.g., Persian and Himalayan).
- Dogs—seen in chow chow, shar-pei, Norwegian elkhound, sporting breeds (e.g., spaniel, retriever), brachycephalic breeds (e.g., English bulldog, pug, Pekingese), toy breeds (e.g., poodle, Yorkshire terrier), and giant breeds (e.g., mastiff, Saint Bernard, Newfoundland).
- Age—seen in puppies as early as 2–6 weeks old (especially chow chow and shar-pei); usually identified in dogs < 1 year old; may be seen in any age cat.

SIGNS

- Depends on type and degree of condition.
- Mild, medial—chronic epiphora and medial pigmentary keratitis (toy dogs and brachycephalic dogs and cats).
- Mild, lateral—chronic mucoid to mucopurulent ocular discharge (giant-breed dogs).
- Upper lid, lower lid, or lateral canthal—severe blepharospasm, purulent discharge, pigmentary or ulcerative keratitis, and potential cornea rupture (chow chows, shar-peis, bloodhounds, and sporting breeds).

CAUSES & RISK FACTORS

- Primarily genetic predisposition based on facial conformation and eyelid support.
- Brachycephalic breeds (dogs and cats)—excessive tension on the ligamentous structures of the medial canthus coupled with nasal folds and facial conformation defects results in rolling inward of the medial aspects of the upper and lower eyelids at the medial canthus.
- Giant breeds and breeds with heavy/loose facial skin (bloodhounds) or excessive facial folds (chow chows, shar-peis)—laxity of the lateral canthal ligamentous structures allows for entropion of the upper and lower eyelids and the lateral canthus.
- Chronic infectious conjunctivitis or keratitis (cats)—may lead to functional entropion caused by chronic blepharospasm (spastic entropion).
- Predisposed breeds (dogs)—spastic entropion, if ocular irritation (e.g., distichia, ectopic cilia, trichiasis, foreign body, and irritant conjunctivitis) leads to excessive blepharospasm.
- Non-predisposed breeds—may be the result of a primary irritant causing secondary spastic entropion.

- Severe weight loss or muscle atrophy caused by masticatory myositis (dogs)—loss of orbital fat or periorbital musculature may lead to enophthalmos and entropion.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Usually obvious clinically—underlying causes of spastic entropion (lash anomalies, foreign bodies, infectious keratitis/conjunctivitis) should be ruled out and corrected, if possible, before an attempt at surgical correction is made.
- Puppies—common for first-time breeders of chows and shar-peis to mistakenly think that the eyelids have not opened at 4–5 weeks of age, when puppies actually have severe blepharospasm and spastic entropion.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Application of a topical anesthetic may reduce spastic component and allow for differentiation of spastic versus physiologic entropion.



TREATMENT

PUPPIES

- Young (especially shar-peis and chows)—do NOT initially perform skin resection surgery.
- If cornea is ulcerated—topical antibiotic (e.g., neomycin/polymyxin B/bacitracin) ointment q6–8h.
- If mildly entropic and cornea not ulcerated, lubricate with artificial tear ointment q8–12h.
- If moderate to severe entropion, temporarily evert eyelid margins with sutures to try to break the spasm-irritation-spasm cycle; if successful, permanent procedure is unnecessary. May need to be repeated every 2–4 weeks until an adult facial conformation is achieved.
- Permanent skin resection technique—postponed until patient's facial conformation matures (usually 6 months of age in most breeds), as this increases success rates.

MEDIAL ENTROPION

- Temporary eversion of the medial canthus with sutures may aid in determining the contribution of medial entropion to epiphora in toy dog breeds and brachycephalic dogs/cats.
- Medial canthal reconstruction should be performed if the entropion results

in pigmentary keratitis, chronic epiphora, or corneal scarring.

MATURE DOGS AND CATS

- Chronic entropion—requires some type of eyelid margin—everting surgery; ranges from simple Hotz-Celsius procedure or more radical lateral canthoplasty procedures.
- No history of previous entropion and clinical signs of acute condition—examine meticulously for cause of spastic condition and correct; may attempt a temporary eversion suture technique before performing permanent skin resection, if necessary.



MEDICATIONS

DRUG(S)

- Topical ophthalmic ointment—triple antibiotic or antibiotic based on culture and sensitivity testing of corneal ulcer bed/conjunctival surfaces; q6–12h; may be used if the cornea is ulcerated, postoperatively, or as a presurgical lubricant.
- Topical petrolatum-based artificial tear ointments (Duratears, Puralube, or Lacrilube) q8–12h may be used temporarily in mild cases in which the cornea is not ulcerated.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

Temporary eversion suture technique—entropion may revert when sutures are removed or spontaneously pull through the skin; repeat as necessary until the patient is mature enough to undergo a more permanent form of skin resection repair (approximately 6 months of age).



MISCELLANEOUS

Suggested Reading

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EOSINOPHILIC GRANULOMA COMPLEX



BASICS

DEFINITION

- Cats—also called feline eosinophilic skin disease; often confusing term for four distinct syndromes: eosinophilic plaque, eosinophilic granuloma, indolent ulcer, and allergic miliary dermatitis; grouped primarily according to their clinical similarities, their frequent concurrent (and recurrent) development, and their positive response to corticosteroids.
- Dogs—eosinophilic granuloma in dogs (EGD) rare; not part of a disease complex; specific differences from cats listed separately.

PATHOPHYSIOLOGY

- Eosinophilic plaque—hypersensitivity reaction, most often to insects (fleas, mosquitos); less often to food or environmental allergens; exacerbated by mechanical trauma; often associated with secondary bacterial infection.
- Eosinophilic granuloma—multiple causes, including genetic predisposition and hypersensitivity.
- Indolent ulcer—may have both hypersensitivity and genetic causes; often associated with secondary bacterial infection.
- Allergic miliary dermatitis—very common hypersensitivity reaction, most often to fleas.
- Eosinophil—major infiltrative cell for eosinophilic granuloma, eosinophilic plaque, and allergic miliary dermatitis, but not indolent ulcer; leukocyte located in greatest numbers in epithelial tissues; most often associated with allergic or parasitic conditions, but has a more general role in the inflammatory reaction.
- EGD—may have both a genetic predisposition and a hypersensitivity cause (especially in non-genetically susceptible breeds).

SYSTEMS AFFECTED

Skin/Exocrine

GENETICS

- Related affected individuals and disease development in a colony of specific pathogen-free cats indicate that genetic predisposition (possible inheritable dysfunction of eosinophilic regulation) is a significant component for development of eosinophilic granuloma and indolent ulcer.
- Genetically predisposed development of hypersensitivity.

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

Seasonal incidence in some geographic locations—Insect or environmental allergen exposure.

SIGNALMENT

Species

- Cats—eosinophilic granuloma and plaque, indolent ulcer, allergic miliary

dermatitis. • Dogs and cats—eosinophilic granuloma.

Breed Predilections

- Cats—none. • Dogs—EGD: Siberian husky (76% of cases), Cavalier King Charles spaniel, possibly German shepherd dog.

Mean Age and Range

- Eosinophilic plaque—2–6 years of age
- Genetically initiated eosinophilic granuloma—< 2 years of age
- Allergic disorder—> 2 years of age
- Indolent ulcer—no age predisposition reported
- EGD—usually < 3 years of age

Predominant Sex

- Cats—predilection for females reported
- EGD—males (72% of cases)

SIGNS

General Comments—Cats

• Distinguishing among the syndromes depends on both clinical signs and histopathologic findings. • Lesions of more than one syndrome may occur simultaneously.

Historical Findings—Cats

- Lesions of all four syndromes may develop spontaneously and acutely.
- Development of eosinophilic plaques may be preceded by periods of lethargy.
- Seasonal incidence possible (related to insects and allergy).
- Waxing and waning of clinical signs common in all four syndromes.

Physical Examination Findings

- Eosinophilic plaque—alopecic, erythematous, erosive patches or well-demarcated, steep-walled plaques; usually occur in the inguinal, perineal, lateral thigh, ventral abdomen, and axillary regions; frequently moist or glistening; may appear striated due to pattern of licking; regional lymphadenopathy common.
- Eosinophilic granuloma—five, occasionally overlapping presentations:
 - Distinctly linear orientation (linear granuloma) on the caudal thigh.
 - Individual or coalescing plaques located anywhere on the body; ulcerated with a “cobblestone” or coarse pattern; white or yellow, possibly representing collagen degeneration.
 - Lip margin and chin swelling (“pouting”).
 - Footpad swelling, pain, and lameness (more common in cats under 2 years of age).
 - Oral cavity ulcerations (especially on the tongue, palate, and palatine arches); cats with oral lesions may be dysphagic, have halitosis, and may drool.
- Spontaneous regression—especially in young cats with the inheritable form.
- Allergic miliary dermatitis—multiple brown/black crusted and erythematous papules; lesions more often palpated than visualized; may be associated with alopecia; usually associated with pruritus; frequently affects the dorsum.
- Indolent ulcer—classically concave and indurated ulcerations with a granular, orange-yellow color, confined to the upper lips adjacent to the philtrum; affected cats are

rarely painful or pruritic.

- EGD—ulcerated plaques and masses; dark or orange color; most often affects the tongue and palatine arches; uncommon cutaneous lesions on the digits, prepuce and flanks.
- Cavalier King Charles spaniels—lesions on the soft palate or near the tonsils.

CAUSES

- Hypersensitivity—flea or insect (mosquito bite), food hypersensitivity, and atopy; a heritable dysfunction of eosinophil proliferation has been proposed.
- EGD—unknown; genetics in susceptible breeds; a hypersensitivity reaction often suspected (insect bite) in non-genetically susceptible breeds.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Includes the other diseases in the complex.
- Herpes virus dermatitis.
- FeLV or FIV.
- Unresponsive lesions—pemphigus foliaceus, dermatophytosis and deep fungal infection, demodicosis, pyoderma, and neoplasia (metastatic adenocarcinoma, squamous cell carcinoma, and epitheliotrophic lymphoma).
- EGD—neoplasia, histiocytosis, infectious and non-infectious granuloma, trauma.

CBC/BIOCHEMISTRY/URINALYSIS

CBC—mild to moderate eosinophilia

OTHER LABORATORY TESTS

FeLV and FIV—pruritic diseases associated with these viruses

DIAGNOSTIC PROCEDURES

- Impression smears from lesions—large numbers of eosinophils.
- Comprehensive flea and insect control—assist in excluding flea or mosquito bite hypersensitivity.
- Food-elimination trial and provocation—appropriate in all cases.
- Atopy—intradermal skin testing (preferred); serum allergy testing if intradermal testing not available; followed by immunotherapy.

PATHOLOGIC FINDINGS

- Histopathologic diagnosis—required for distinguishing the syndromes.
- Eosinophilic plaque—severe epidermal and follicular spongiosis and mucinosis with eosinophilic exocytosis; intense perivascular to diffuse dermal eosinophilic infiltrate; eroded or ulcerated epidermis.
- Eosinophilic granuloma—distinct foci of eosinophilic degranulation and collagen degeneration similar to granuloma formation (“flame figures”); keratinocyte apoptosis associated with eosinophils; eroded, ulcerated, and exudative acanthotic epidermis.
- Indolent ulcer—severe ulceration of the epidermis or mucosa with eosinophilic degranulation at the level of necrosis; fibrosing dermatitis and neutrophilic inflammation; significant

EOSINOPHILIC GRANULOMA COMPLEX

(CONTINUED)

eosinophilic infiltration unusual. • Allergic miliary dermatitis—discrete foci of epidermal erosion and necrosis with brightly eosinophilic crusts; dermal perivascular to interstitial eosinophil-rich infiltrate. • EGD—foci of palisading granulomas and flame figures surrounding collagen fibers; infiltrate with eosinophils mixed with macrophages, mast cells, plasma cells, and lymphocytes.



TREATMENT

APPROPRIATE HEALTH CARE

- Most patients treated as outpatients unless severe oral disease prevents adequate fluid intake.
- Identify and eliminate offending allergen(s) before providing medical intervention.
- Atopy: hyposensitization of intradermal skin-test-positive cats—successful in a majority of cases; preferable to long-term corticosteroid administration.

NURSING CARE

Discourage patient from damaging lesions by excessive grooming.

ACTIVITY

No restrictions

DIET

No restrictions unless a food allergy is suspected. Elimination diet—suspected food allergy.

CLIENT EDUCATION

- Inform clients about the possible allergic or heritable causes.
- Discuss the waxing and waning nature of these diseases.

SURGICAL CONSIDERATIONS

EGD—individual lesions may be excised if being mechanically traumatized and medically unresponsive.



MEDICATIONS

DRUG(S) OF CHOICE

- Cases may improve with antibiotics: cephalaxin 22 mg/kg q12h, amoxicillin trihydrate-clavulanate 12.5 mg/kg q12h, or clindamycin 11 mg/kg q24h.
- Injectable methylprednisolone 20 mg/cat, repeat in 2 weeks (if needed—maximum two injections); most common treatment; steroid tachyphylaxis common with repeated injections; not advised for long-term therapy.
- Oral corticosteroids—ongoing treatment necessary unless the primary cause is controlled; prednisolone (2–4 mg/kg q48h

then as required to control lesions); steroid tachyphylaxis may occur and may be specific to the drug administered; may be useful to change the form; other drugs: dexamethasone (0.1–0.2 mg/kg q24–72h) and triamcinolone (0.1–0.2 mg/kg q24–72h); higher induction dosages may be required but should be tapered as quickly as possible.

- Cyclosporine 7 mg/kg q24–48h.
- Topical: fluocinolone/DMSO (Synotic lotion) to individual lesions; not practical and/or may cause systemic effects in patients with large numbers of lesions.

Alternate Therapies

- Chlorambucil 0.1–0.2 mg/kg q48–72h.
- Doxycycline 5–10 mg/kg q24h.
- α -interferon 300–1000 IU/day; limited success.
- Megestrol acetate 2.5–5 mg every 2–7 days; significant incidence of side effects (e.g., diabetes, mammary cancer) preclude use in all but severe, recalcitrant cases.

EGD

- Oral prednisolone 0.5–2.2 mg/kg/day initially; then taper gradually.
- Intralesional corticosteroids 5 mg/lesion methylprednisolone.
- Cessation of therapy without recurrence is common.



FOLLOW-UP

PATIENT MONITORING

- Corticosteroids—baseline and frequent hemograms, serum chemistry profiles, and urinalyses with culture; excessive or too-frequent use of corticosteroids increases risk for development of diabetes mellitus and acquired skin fragility.
- Cyclosporine—baseline and frequent hemograms, serum chemistry profiles, and urinalyses with culture; measurement of plasma cyclosporine levels as needed to establish dosage within therapeutic levels (especially cats).
- Selective immunosuppressant drugs—frequent hemograms (biweekly at first, then monthly or bimonthly as therapy continues) to monitor for bone marrow suppression; routine serum chemistry profiles and urinalyses with culture (monthly at first, then every 3 months) to monitor for complications (renal disease, diabetes mellitus, and urinary tract infection).

EXPECTED COURSE AND PROGNOSIS

- Lesions should resolve permanently if a primary cause can be identified and controlled.
- Most lesions wax and wane, with

or without therapy; an unpredictable schedule of recurrence should be anticipated.

- Drug dosages should be tapered to the lowest possible level (or discontinued, if possible) once the lesions have resolved.
- Lesions in cats with the inheritable disease may resolve spontaneously after several years.
- EGD—lesions may be recalcitrant to medical intervention.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Systemic glucocorticoids and immunosuppressive drugs should not be used during pregnancy.

SYNONYMS

- Eosinophilic granuloma—feline collagenolytic granuloma; feline linear granuloma.
- Indolent ulcer—eosinophilic ulcer; rodent ulcer; feline upper lip ulcerative dermatitis.

SEE ALSO

- Atopic Dermatitis
- Food Reactions, Dermatologic

ABBREVIATIONS

- EGD = eosinophilic granulomas in dogs
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus

Suggested Reading

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**Client Education Handout
available online**

EPIDIDYMITIS/ORCHITIS**BASICS****OVERVIEW**

- Epididymitis—inflammation of the epididymis; most significant and severe clinical sign of brucellosis.
- Orchitis—inflammation of the testis.
- May be acute or chronic.
- Direct trauma to the scrotum—most common cause of acute form.
- May occur separately or concurrently (orchiepididymitis); extension into the vaginal tunics possible (periorchiepididymitis).

SIGNALMENT

- Not uncommon in dogs; rare in cats
- No genetic basis or breed predilections
- Mean age 3.7 years; range 11 months–10 years

SIGNS

- Swollen testis
- Pain (acute)
- Licking of the scrotum—may lead to dermatitis
- Listlessness
- Anorexia
- Reluctance to walk
- Reluctance to breed
- Open wound or abscess
- Infertility
- Pyrexia

CAUSES & RISK FACTORS

- *Brucella canis*—predilection for infecting the tail of the epididymis.
- Distemper.
- Rocky Mountain spotted fever.
- Ascending infection—associated with prostatitis (especially in brucellosis) and cystitis.
- Retrograde urine contamination of the ductus deferens—sequel to high intra-abdominal pressure as caused by automobile trauma.
- Bite wounds and other puncture wounds—isolated from infected testes: *Staphylococcus*, *Streptococcus*, *Escherichia coli*, *Proteus*, and *Mycoplasma*.
- Auto-immune response to spermatozoa antigens—secondary to trauma or inflammation.
- Lymphocytic auto-immune thyroiditis and orchitis—familial in beagles.

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- Inguinoscrotal hernia
- Scrotal dermatitis
- Torsion of the spermatic cord
- Hydrocele

- Sperm granuloma
- Testicular neoplasia
- Prostatitis
- Cystitis

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis—may be found with acute or infectious orchitis.
- Pyuria, hematuria, proteinuria—may be found if epididymitis/orchitis is secondary to prostatitis or cystitis.

OTHER LABORATORY TESTS

- *B. canis* antibodies—perform immediate testing in any dog with scrotal enlargement (see Brucellosis).
- Rapid slide agglutination test—used as a screen; sensitive but not specific (D-Tec® CB, Zoetis, (888)-963-8471).
- If positive results—recommend recheck by an agar gel immunodiffusion test (Cornell University Diagnostic Laboratory, (607)253-3900) or bacterial culture of whole blood or lymph node aspirate.

IMAGING

- Ultrasonographic evaluation of the prostate—guided aspiration for cytologic examination and bacterial culture.
- Ultrasonographic evaluation of the testes and epididymides—inflamed testes have patchy hypoechoic areas; inflamed epididymides have irregular contours and hypoechoic or hyperechoic areas; obtain measurements for future comparisons.

DIAGNOSTIC PROCEDURES

- Semen—collect if possible; cytologic evaluation; bacterial culture.
- Cytology (semen)—leukocytes; bacteria; spermatozoa with coiled tails, detached heads, and retained proximal and distal cytoplasmic droplets; head-to-head agglutination (*B. canis*).
- Prostatic massage—cytologic examination; bacterial culture; sample collected aseptically by urethral catheter.
- Open wounds—bacterial culture.
- Fine-needle aspirate—sample enlarged testes/epididymides for cytology and culture; leukocytes vary from numerous neutrophils (suppurative) to minimal inflammatory cells (granulomatous).
- Postmortem diagnosis—bacteria can be isolated from the non-gravid pregestational uterus and spleen in bitches, and the prostate gland in male dogs.

**TREATMENT**

- If fertility is not a concern—culture appropriate specimen; medically stabilize; administer needed antibiotics preoperatively to avoid scirrhouss cord; castrate.

- If fertility is a concern (unilateral orchitis)—unilateral castration when the patient's future as a sire must be maintained; administer appropriate antibiotics preoperatively.

**MEDICATIONS****E****DRUG(S)**

- Antibiotics—Brucellosis.
- Combined regimes generally more successful; if culture and sensitivity is available, use appropriate antibiotics; treatments may fail to completely eliminate the bacteria; therefore, reproductive sterilization is strongly recommended.
- Reported success with doxycycline (10 mg/kg PO q12h), gentamicin (5 mg/kg SC q24h for 7 days and repeated every 3 weeks), rifampin (5 mg/kg PO q24h), enrofloxacin (5 mg/kg PO q12h) for 1–3 months.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

N/A

**FOLLOW-UP**

- Prognosis for fertility—guarded to poor, especially with bilateral orchitis.
- Testicular heating causes testicular degeneration—degeneration in contralateral testis can result from primary disease or from elevated intrascrotal temperature following unilateral castration.
- Trauma or inflammation can cause obstruction of efferent tubules or epididymal duct, leading to spermatocele or sperm granuloma.
- Semen (dogs)—evaluate characteristics 3 months after treatment for orchitis is completed.

**MISCELLANEOUS****SEE ALSO**

Brucellosis

Suggested Reading

Hollott RB. Canine brucellosis: outbreaks and compliance. Theriogenology 2006, 66(3):575–587.

Johnston SD, Root Kustritz MV, Olson PNS. Disorders of the canine testis and epididymes. In: Johnston SD, Kustritz MVR, Olson PN, eds., Canine and Feline Theriogenology. Philadelphia: Saunders, 2001, pp. 313–317.

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EPILEPSY, GENETIC (IDIOPATHIC)—DOGS



BASICS

DEFINITION

Syndrome that is only epilepsy, with no demonstrable underlying brain lesion or other neurologic signs or symptoms; age-related; assumed genetic. The term 'idiopathic' replaced by 'genetic' according to the ILAE classification. (See Appendix VIII.)

PATHOPHYSIOLOGY

- Exact mechanism unknown.
- Likely different mechanisms between breeds.

SYSTEMS AFFECTED

Nervous

GENETICS

Genetic basis suspected in Australian shepherd, beagle, Belgian shepherd (Groenendael and Tervuren), Bernese mountain dog, border collie, dachshund, English springer spaniel, Finnish Spitz, German shepherd, golden retriever, Keeshond, Irish wolfhound, Italian spinone, Labrador retriever, Shetland sheepdog, standard poodle, vizsla.

INCIDENCE/PREVALENCE

0.5–2.3% of all dogs

GEOGRAPHIC DISTRIBUTION

Widespread

SIGNALMENT

Species

Dog

Breed Predilections

Beagles; all shepherds (German, Australian, Belgian); Bernese mountain dogs; boxers; cocker spaniels; border collies; dachshunds; golden retrievers; Irish setters; Labrador retrievers; poodles (all sizes); Saint Bernards; Shetland sheepdogs; Siberian huskies; springer spaniels; Welsh corgis; wirehaired fox terriers. Can occur in any breed.

Mean Age and Range

- Mean age 10 months–3 years
- Range 6 months–5 years

Predominant Sex

Male predisposition in Bernese mountain dog.

SIGNS

General Comments

• Seizures may be generalized (convulsive) from onset, or have a short aura (focal onset) with rapid secondary generalization. • An aura (animal appears frightened, dazed, seeks attention, or hides, etc.) frequently precedes the generalized seizure. • Focal seizures reported in the border collie, Finnish spitz dog, English springer spaniel, Labrador retriever, vizsla, Belgian shepherd, standard poodle.

Historical Findings

- First seizure—between 6 months and 5 years.
- Seizures—often when patient is

resting or asleep; often at night or early morning; frequency tends to increase if left untreated; affected animal falls on its side, becomes stiff, chomps its jaw, salivates profusely, urinates, defecates, vocalizes, and paddles with all limbs in varying combinations. Short duration (30–90 seconds). • Postictal behavior—confusion, disorientation; aimless, compulsive, blind, pacing; frequent polydipsia and polyphagia; recovery immediate or may take up to 24 hours. • Dogs with established epilepsy might have clustered generalized seizures at intervals of 1–4 weeks. • No asymmetry should be observed during seizure, e.g., twitching more pronounced on one side, limb contractions on one side, compulsive circling just prior or after the seizure. • Stimulus-induced seizures: seizures only upon specific stimulus (sound, event).

Physical Examination Findings

- Patients often have recovered at time of presentation.
- Patients may have postictal behavior.

CAUSES

Genetic in some breeds; of unknown cause in others.

RISK FACTORS

Known epilepsy in the family line



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Seizure pattern (breed, age at onset, type and frequency of seizures)—most important factor toward diagnosis.
- Acute onset of cluster seizures or status epilepticus—rule out toxicity or structural brain disease.
- > 2 seizures within the first week of onset—consider diagnosis other than genetic epilepsy.
- Seizures at < 6 months or > 5 years of age—consider metabolic, or intracranial structural disease; rule out hypoglycemia in older dogs.
- Focal seizures, or presence of neurologic deficits—rule out intracranial structural disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal
- Perform before initiating drug therapy as baseline data.

OTHER LABORATORY TESTS

Bile acids to rule out hepatic encephalopathy unnecessary in dogs with seizures without accompanying episodic abnormal behavior.

IMAGING

MRI—if seizure pattern does not fit genetic (idiopathic) epilepsy, neurologic deficits are present, or intracranial structural disease is suspected.

DIAGNOSTIC PROCEDURES

- CSF—for suspected structural intracranial diseases.
- Electroencephalography—may see

interictal spikes, polyspikes, and spike slow wave complexes.

PATHOLOGIC FINDINGS

- No primary lesion.
- Secondary neuronal loss and gliosis from prolonged seizures.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—recurrence of isolated seizures.
- Inpatient—for cluster seizures (> 1 seizure q24h) or status epilepticus.

NURSING CARE

Inpatients with seizure disorders require constant monitoring.

DIET

- Dogs on chronic PB and KBr treatment often become overweight; weight-reducing program as necessary.
- KBr treatment—insure steady levels of salt in diet; an increase in salt causes an increase in bromide excretion preferentially over chloride, with subsequent decreased serum KBr levels. Alternatively, a decrease salt content increases KBr serum level.
- Trial with high-fat, low-carbohydrate diet—no improvement in seizure control.

CLIENT EDUCATION

- Severe cluster seizures and status epilepticus are life-threatening emergencies requiring immediate medical attention.
- Keep a seizure calendar noting date, time, length, and severity of seizures to assess response to treatment.
- Once treatment instituted, medication is life-long in most cases.
- Abrupt drug withdrawal may cause seizures.



MEDICATIONS

DRUG(S) OF CHOICE

- Initiate treatment at second generalized seizure if dog < 2 years; when interictal period gradually shortens in the others.
- Antiepileptic treatment—decreases frequency, severity, and length of seizures; perfect control rarely achieved.
- Tolerance and refractoriness to treatment may develop.

Phenobarbital

- Most efficacious AED in the dog.
- Traditional first-line drug; initial dosage 3–5 mg/kg PO q12h; steady-state reached at 12–15 days but levels decrease significantly in the first 6 months owing to activation of lysosomal enzymes.
- Optimal therapeutic serum levels—100–120 µmol/L or 23–28 µg/mL.
- Oral loading dose (if needed)—6–10 mg/kg PO q12h for 2–3 days to reach therapeutic range rapidly.

Zonisamide

- First-line drug when seizure frequency allows (< 1/week); 5 mg/kg PO q12h; 10 mg/kg PO q12h as add-on to PB; half-life

(CONTINUED)

EPILEPSY, GENETIC (IDIOPATHIC)—DOGS

E

15 hours; steady state 4 days; therapeutic range in human 10–45 µg/mL.

Levetiracetam

- First-line drug when seizures have focal onset; < 1 seizure/week; 20 mg/kg PO q8h; must be given q8h to reach adequate levels; no hepatic metabolism; safe; steady state 3 days; therapeutic range in human 10–40 µg/mL.

Potassium Bromide

- Traditional first-line drug; initial dosage 30 mg/kg PO q24h or divided q12h; half-life 24–46 days; steady-state 3–4 months; varies with salt concentration in diet; bioavailability differs between dogs.
- Optimal therapeutic serum levels—20–25 mmol/L or 1.6–2 mg/mL; if sole antiepileptic drug, 25–32 mmol/L or 2–2.25 mg/mL can be safely used.
- Add-on to PB if seizures uncontrolled with optimal PB level—beneficial and synergistic effect.
- Loading dose—may cause vomiting, diarrhea, profound longstanding sedation; if needed, double daily PO doses for 2 weeks.
- Renal insufficiency decreases bromide elimination; half initial dosage.

Diazepam (At-Home Use)

- To abort ongoing seizures—dogs with cluster seizures or status epilepticus.
- Insert 0.5–1 mg/kg injectable drug in rectum via 1-inch teat cannula as soon as a seizure occurs; repeat 20 and 40 minutes later for a total of 3 insertions within 40 minutes; can be safely repeated once more in a 24-hour period.
- Given early in the course of ongoing seizures, help abort subsequent seizures.

CONTRAINDICATIONS

Aminophylline, theophylline

PRECAUTIONS

α -adrenergic agonists (e.g., phenylpropanolamine)—central nervous system excitation

POSSIBLE INTERACTIONS

- Cimetidine and chloramphenicol—interfere with PB metabolism; may cause toxic PB levels.
- PB lowers serum levels of zonisamide and levetiracetam.
- PB may lower T₄ and cause an upward trend in TSH without signs of hypothyroidism.
- PB does not interfere with low-dose dexamethasone suppression tests regardless of dose and treatment.
- Zonisamide decreases total T₄.
- Whenever animals on lifetime medication, refer to manufacturer's drug profile or to a pharmacist for interaction information.

ALTERNATIVE DRUG(S)

- With polypharmacy, initiate add-on gradually to avoid sedation.
- Gabapentin 10–20 mg/kg PO q8h; low efficacy as add-on.
- Newer analog pregabalin may be more efficacious (2–4 mg/kg q8h PO).
- Clorazepate 0.5–1 mg/kg PO q8h.
- Felbamate 30–70 mg/kg q12h–8h.
- Topiramate 2–10 mg/kg PO q12h.
- Phenytoin, valproic acid, carbamazepine, and ethosuximide—unsuitable

pharmacokinetics in dogs.

- Others—acupuncture, vagal nerve stimulation, transcranial magnetic motor stimulation.

**FOLLOW-UP****PATIENT MONITORING**

- Serum drug levels—preferentially at trough, at same time for each sampling; use same laboratory.
- Phenobarbital—measure PB level 4 weeks after initiating therapy; adjust dose as needed; then repeat level every 2 weeks until optimal levels reached; with chronic use perform CBC, biochemistry, and PB level every 6–12 months; tabulate albumin, liver enzymes and serum drug levels to monitor trend; drug essentially hepatotoxic; most dogs eventually develop hepatotoxicity if serum levels > 140 µmol/L (> 33 µg/mL) for long time (> 6–8 months). If hepatotoxicity suspected, perform bile acids.
- KBr—serum level (along with PB level) 4–6 weeks after initiating (should be 8–12 mmol/L or 0.5–1 mg/mL) and at 3–4 months. If diet change required, consider diet salt content; monitor level accordingly. Monitor KBr level closely if renal insufficiency (isosthenuria or azotemia).
- Zonisamide—measure level at 1 week. Monitor electrolytes and acid-base status to check for renal tubular acidosis.
- Levetiracetam—measure level at 4 days.

PREVENTION/AVOIDANCE

- Abrupt discontinuation of medication may precipitate seizures.
- Avoid salty treats in dogs treated with KBr.

POSSIBLE COMPLICATIONS

- Recurrent episodes of cluster seizures and status epilepticus.
- PB and KBr—polyuria, polydipsia, polyphagia, weight gain.
- Phenobarbital-induced C-AP occurs frequently; may be an early sign of hepatotoxicity but of less concern if ALT is within reference range.
- Phenobarbital-induced hepatotoxicity—after chronic treatment at high serum levels (> 140 µmol/L or > 33 µg/mL); often insidious in onset; only biochemical abnormality may be a decreased albumin.
- Higher incidence of pancreatitis in patients treated with PB and/or KBr; once pancreatitis develops, recurrence is frequent.
- Phenobarbital—rare bone marrow suppression with severe neutropenia (\pm sepsis) early in the course of treatment; discontinue drug.
- Paradoxical hyperexcitability; discontinue drug. Risk factor for superficial necrotolytic dermatitis.
- KBr—when levels are > 22 mmol/L or > 1.8 mg/mL, owners may complain of patient's unsteadiness while managing stairs.
- Zonisamide—mild sedation, decreased appetite, gastrointestinal signs.
- One case of renal tubular acidosis and one case of acute idiosyncratic hepatic necrosis reported.
- Levetiracetam—transient sedation.

EXPECTED COURSE AND PROGNOSIS

- Treatment for life.
- Some dogs are well controlled with same drug and dosage for years; others remain poorly controlled despite polypharmacy.
- Patient may develop status epilepticus and die.
- Early treatment does not decrease occurrence of status epilepticus.
- Normal expected lifespan but survival time shorter if episodes of status epilepticus.
- Treatment with 2 AEDs not linked to poor prognosis.
- Increased risk of premature death.
- Marked breed differences in incidence and mortality rates.
- Prognosis depends on combined veterinary expertise, therapeutic success, and owner's motivation.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Idiopathic epilepsy can be a reason for euthyroid sick syndrome in dogs.

AGE-RELATED FACTORS

If onset < 2 years of age, epilepsy more likely to be difficult to control; condition may becomes intractable.

PREGNANCY/FERTILITY/BREEDING

- Avoid breeding affected animals.
- Reported association between estrus and onset of seizures in intact bitches with presumptive 'idiopathic' epilepsy; two hormonally based patterns recognized: (1) during heat and (2) during a specific time point at the end of diestrus.

SEE ALSO

- Seizures (Convulsions, Status Epilepticus)—Dogs
- Seizures (Convulsions, Status epilepticus)—Cats

ABBREVIATIONS

- AED = antiepileptic drug
- ALT = alanine aminotransferase
- C-AP = corticosteroid alkaline phosphatase
- CSF = cerebrospinal fluid
- KBr = potassium bromide
- ILAE = International League Against Epilepsy
- MRI = magnetic resonance imaging
- PB = phenobarbital
- TSH = thyroid stimulating hormone

INTERNET RESOURCES

<http://www.canine-epilepsy.net/>

Suggested Reading

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Podell M. Antiepileptic drug therapy and monitoring. *Top Companion Anim Med* 2013, 28:59–66.

Author Joane M. Parent

Consulting Editor Joane M. Parent



Client Education Handout
available online

EPIPHORA



BASICS

DEFINITION

Abnormal overflow of the aqueous portion of the precorneal tear film.

E

PATHOPHYSIOLOGY

Caused by one of three common problems:

- (1) Overproduction of the aqueous portion of tears (usually in response to ocular irritation).
- (2) Poor eyelid function secondary to eyelid malformation or deformity.
- (3) Blockage of the nasolacrimal drainage system.

SYSTEMS AFFECTED

Eye and periocular skin

SIGNALMENT

See "Causes"

SIGNS

N/A

CAUSES

Overproduction of Tears Secondary to Ocular Irritants

Congenital

- Distichiasis or trichiasis—common in young shelties, shih tzus, Lhasa apsos, cocker spaniels, miniature poodles.
 - Entropion—shar-peis, chow chows, Labrador retrievers.
 - Eyelid agenesis—domestic shorthair cats.
- ###### Acquired
- Corneal or conjunctival foreign bodies—usually young, large-breed, active dogs.
 - Eyelid neoplasms—old dogs (all breeds).
 - Blepharitis—infectious or immune mediated.
 - Conjunctivitis—infectious or immune mediated.
 - Ulcerative keratitis.
 - Anterior uveitis.
 - Glaucoma.

Eyelid Abnormalities or Poor Eyelid Function

- Tears never reach the nasolacrimal puncta but instead spill over the eyelid margin.
- eyelid function does not direct tears to the medial canthus and nasolacrimal puncta.

Congenital

- Macropalpebral fissures—brachiocephalic breeds.
- Ectropion—Great Danes; bloodhounds; spaniels.
- Entropion—brachycephalic dogs—medial lower eyelid; Labrador retrievers—lateral lower eyelid.

Acquired

- Post-traumatic eyelid scarring.
- Facial nerve paralysis.

Obstruction of the Nasolacrimal Drainage System

Congenital

- Imperforate nasolacrimal puncta—cocker spaniels, bulldogs, poodles.
- Ectopic nasolacrimal openings—extra openings along the side of the face ventral to the medial canthus.
- Nasolacrimal atresia—lack of distal openings into the nose.

Acquired

- Rhinitis or sinusitis—causes swelling adjacent to the nasolacrimal duct.
- Trauma or fractures of the lacrimal or maxillary bones.
- Foreign bodies—grass awns, seeds, sand, parasites.
- Neoplasia—of the third eyelid, conjunctiva, medial eyelids, nasal cavity, maxillary bone, or periocular sinuses.
- Dacryocystitis—inflammation of the canaliculi, lacrimal sac, or nasolacrimal ducts.

RISK FACTORS

- Breeds prone to congenital eyelid abnormalities (see "Causes").
- Active outdoor dogs—at risk for foreign bodies.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other ocular discharges (e.g., mucous or purulent)—epiphora is a watery, serous discharge.
- Eye—usually red when caused by overproduction of tears; quiet when secondary to impaired outflow.
- Irritative causes and some congenital causes of obstruction—thorough ocular examination.
- Acute onset, unilateral condition with ocular pain (blepharospasm)—usually indicates a foreign body or corneal injury.
- Chronic, bilateral condition—usually indicates a congenital problem.
- Facial pain, swelling, nasal discharge, or sneezing—may indicate nasal or sinus infection; may indicate obstruction from neoplasm.
- With mucous or purulent discharge at the medial canthus—may indicate dacryocystitis.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

- Skull radiographs—may show a nasal, sinus, or maxillary bone lesion.
- Dacryocystorhinography—radiopaque contrast material to help localize obstruction.

- MRI or CT—may help localize obstruction (usually with contrast media) and characterize associated lesions.

DIAGNOSTIC PROCEDURES

- Bacterial culture and sensitivity testing and cytologic examination of the material—with purulent material at the medial canthus (e.g., dacryocystitis); performed before instilling any substance into the eye.
- Topical fluorescein dye application to the eye—most physiologic test for nasolacrimal function; should be performed first (after culture); dye flows through the nasolacrimal system and reaches the external nares in approximately 10 seconds in normal dogs.
- Nasolacrimal irrigation—see information below.
- Rhinoscopy—with or without biopsy or bacterial culture; may be indicated if previous tests suggest a nasal or sinus lesion.
- Surgical exploratory—may be the only way to obtain a definitive diagnosis.
- Temporary tacking out of the lower medial eyelid with suture—may help determine whether repair of medial lower entropion or repositioning of the eyelid would reduce epiphora secondary to eyelid conformational abnormalities.

Nasolacrimal Irrigation

- Confirms obstruction.
- May dislodge foreign material.
- A nasolacrimal cannula is inserted into the upper nasolacrimal punctum.
- Eyewash is irrigated through the cannula—if fluid does not exit the lower nasolacrimal punctum, the obstruction is in the upper or lower canaliculi, the nasolacrimal sac, or the lower punctum (imperforate).
- Lower punctum is manually obstructed—if flushed fluid does not exit the external nares, the obstruction is in the nasolacrimal duct or at its distal opening (atresia or blockage from a nasal sinus lesion).



TREATMENT

- Remove cause of ocular irritation—removal of a conjunctival or corneal foreign body; treatment of the primary ocular disease (e.g., conjunctivitis, ulcerative keratitis, and uveitis); cryosurgery or electroepilation for distichiasis, entropion correction; medial or lateral canthoplasty (for medial trichiasis and macropalpebral fissures); correction of cicatricial eyelid abnormalities.
- Treat primary obstructing lesion (e.g., third eyelid mass, nasal or sinus mass, and infection)—do initially; successful management may allow normal nasolacrimal flow to resume.

(CONTINUED)

EPIPHORA

- Warn client that patient is predisposed to nasolacrimal obstruction and that recurrence is common.
- Inform client that early detection and intervention provide a better long-term prognosis.

SURGICAL CONSIDERATIONS***Imperforate Puncta***

- Surgical opening of the puncta is indicated.
- If one of the puncta is patent (usually the upper punctum), flushing eyewash through the upper opening will cause “tenting” of the conjunctiva at the site of the lower punctum. Place patient under topical or general anesthesia. Grasp conjunctiva overlying the lower canaliculi with forceps and cut with scissors to leave a patent punctum. Puncta closed by conjunctival scarring (sympblepharon) caused by severe conjunctivitis (e.g., herpesvirus conjunctivitis in cats)—use same procedure. Recurrent disease—may be necessary to suture Silastic tubing in place to prevent stricture formation.

Obstructed or Obliterated Distal Nasolacrimal Duct

- Dacryocystorhinotomy or conjunctivorhinostomy—create an opening to drain the tears into the nasal cavity.
- See “Suggested Reading” for surgical technique.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Topical broad-spectrum antibiotic ophthalmic solutions—while awaiting diagnostic test results (e.g., bacterial culture and sensitivity testing; diagnostic radiographs); q4–6h; may try neomycin, gramicidin, polymyxin B triple ophthalmic antibiotic solution, or ophthalmic ciprofloxacin solution.
- Dacryocystitis—based on bacterial culture and sensitivity test results; continued for at least 21 days.

CONTRAINDICATIONS

- Topical corticosteroids or antibiotic—corticosteroid combinations—avoid unless a definitive diagnosis has been made.
- Topical corticosteroids—never use if the cornea retains fluorescein stain.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Tetracycline 5 mg/kg PO q24h; may help reduce idiopathic tear staining of the periocular facial hair; staining recurs when the drug is discontinued.

**FOLLOW-UP****PATIENT MONITORING*****Dacryocystitis***

- Reevaluate every 7 days until the condition is resolved.
- Continue treatment for at least 7 days after resolution of clinical signs to help prevent recurrence.
- Problem persists more than 7–10 days with treatment or recurs soon after cessation of treatment—indicates a foreign body or nidus of persistent infection; requires further diagnostics (e.g., dacryocystorhinography).
- Nasolacrimal catheter.
- Commonly required for persistent dacryocystitis.
- Maintains patency of the duct and prevents structuring.
- Catheter—Silastic or polyethylene (PE90) tubing; left in place 2–4 weeks.
- Procedure—pass 2-0 nylon via the upper punctum and thread it through the nasolacrimal duct to exit the external nares; pass tubing retrograde over the suture; suture the upper and lower portions of the tubing to the face.
- Most dogs tolerate the tubing well, however, an Elizabethan collar may be needed to prevent self-trauma.
- Continue topical antibiotics as before.

Dacryocystorhinotomy/Conjunctivo-Rhinostomy

- Tubing—reevaluate every 7 days to ensure it remains intact; may need to resuture if it becomes loosened or dislodged.
- After tubing has been removed—reevaluate in 14 days; for this and future examinations, place fluorescein on the eye and check nasolacrimal patency by examining the external nares for fluorescein; may evaluate the nasolacrimal system further by cannulating and flushing with eyewash.
- Dacryocystorhinography contrast study—repeated 3–4 months after surgery to evaluate size of the nasal opening; repeated for recurrence or with no nasolacrimal fluorescein drainage.

POSSIBLE COMPLICATIONS

Recurrence—most common complication; caused by recurrence of ocular irritation (e.g., corneal ulceration, distichiasis, entropion), recurrence of dacryocystitis, or closure of the dacryocystorhinotomy or conjunctivorhinostomy openings into the nasal cavity.

E

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Chronic conjunctivitis—cats
- Chronic conjunctivitis—dogs
- Recurrent eye “infections”
- Moist dermatitis (hot spots) ventral to the medial canthus
- Nasal discharge

AGE-RELATED FACTORS

N/A

ZOONOTIC

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Conjunctivitis—Cats
- Conjunctivitis—Dogs
- Eyelash Disorders (Trichiasis/Distichiasis/Ectopic Cilia)
- Keratitis, Ulcerative
- Third Eyelid Protrusion

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging

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Client Education Handout available online

EPISCLERITIS



BASICS

OVERVIEW

- Focal or diffuse infiltration of the episclera and/or scleral stroma by a varying mix of inflammatory cells and fibroblasts.
- Primary—affects only the eye; probably immune mediated; appears either as a perilimbal episcleral/scleral nodule (nodular episcleritis) or as a diffuse thickening of the episclera (diffuse episcleritis); nodular form may affect cornea and third eyelid with similar-appearing nodules.
- Secondary—usually diffuse; from the spillover of inflammatory cells into the episclera from other ocular disorders (e.g., endophthalmitis and panophthalmitis); may affect virtually any other organ system.

SIGNALMENT

- Dog
- Young to middle-aged collie, Shetland sheepdog

SIGNS

- Nodular—typically appears as a smooth, painless, localized, raised, pink-tan, firm episcleral/scleral mass.
- Diffuse—less common; appears as a diffuse reddening and thickening of the entire episclera/sclera; accompanied by variable amounts of ocular pain.
- Secondary—uveitis often pronounced.
- Conjunctiva—usually moves freely over the surface of the lesion.
- Nodules—tend to be slowly progressive, bilateral, and prone to recurrence.

CAUSES & RISK FACTORS

- Nodular and diffuse primary—idiopathic; believed to be immune mediated.
- Secondary—may result from deep fungal or bacterial ocular infection, lymphoma, systemic histiocytosis in Bernese mountain dogs, chronic glaucoma, and ocular trauma.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of a red eye—differentiated by careful ophthalmic examination and tonometry.
- Other mass-like lesions—differentiated by biopsy or cytologic examination.
- Neoplasia—lymphoma; squamous cell carcinoma; extension of an intraocular mass; other tumors.
- Granuloma—deep fungal infection; retained foreign body.
- Granulation tissue—trauma; healing corneal ulcer; globe perforation with uveal prolapse.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal if the lesion is confined to eye or adnexa.
- Secondary—may see abnormalities consistent with other systemic diseases (e.g., deep fungal or systemic histiocytosis).

OTHER LABORATORY TESTS

- Rheumatoid factor, antinuclear antibody, and lupus erythematosus cell preparations—usually not helpful.
- Serologic testing—may help rule out deep fungal infection.

IMAGING

- Abdominal ultrasound or thoracic/abdominal radiographs—may help rule out deep fungal infection or disseminated neoplasia.
- Ocular ultrasound—may help reveal other ocular abnormalities if ocular media opacities prevent a thorough ocular examination.

DIAGNOSTIC PROCEDURES

- Incisional biopsy and histopathologic examination of affected tissue.
- Nodular—typified by varying numbers of histiocytes, lymphocytes, plasma cells, and fibroblasts.
- If uveitis prominent—perform a uveitis workup (see Anterior Uveitis—Dogs).



TREATMENT

- Try to verify the diagnosis histologically or cytologically before treatment.
- Primary nodular—tends to have a benign course; observation alone may be appropriate with mild disease.
- Outpatient treatment if ocular pain, diffuse scleral involvement, eyelid function is disrupted, cornea is affected, or vision threatened.



MEDICATIONS

DRUG(S)

- Progress down the list only if the previous modality was ineffective.
- Topical 1% prednisolone acetate q4h for 1 week, then q6h for 2 weeks, then tapered.
- Systemic prednisolone 1–2 mg/kg/day; tapered with improvement.
- Systemic azathioprine 1–2 mg/kg/day for 3–7 days; then tapered to as low a dosage as possible.
- Cryosurgery or attempt excision.
- Alternative to listed drugs or surgery—may try a combination of tetracycline and niacinamide (q8h PO); 250 mg each for dogs < 10 kg; 500 mg each for dogs > 10 kg; may not observe good clinical response for at least

8 weeks; side effects uncommon and primarily the result of gastrointestinal upset by niacinamide.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Avoid systemic immunosuppressive drugs with deep fungal infections.
- Systemically administered prednisolone or azathioprine—may precipitate pancreatitis; potentially hepatotoxic.
- Azathioprine—may induce potentially fatal myelosuppression.
- Niacin—do not substitute for niacinamide.



FOLLOW-UP

PATIENT MONITORING

- Primary—monitor for nodule regression or reduction in episcleral thickening or reddening every 2–3 weeks for 6–9 weeks and then as needed; prognosis usually good; may require therapy for months to rest of life.
- Secondary—follow-up, prognosis, and complications usually depend on the primary disease.
- Azathioprine—repeat CBC, platelet count, and measurement of liver enzymes every 1–2 weeks for the first 8 weeks, then periodically.

POSSIBLE COMPLICATIONS

- Vision loss
- Chronic ocular pain
- Uveitis
- Secondary glaucoma



MISCELLANEOUS

SYNOMYMS

- Collie granuloma
- Fibrous histiocytoma
- Limbal granuloma
- Necrogranulomatous sclerouveitis
- Nodular fasciitis
- Nodular granulomatous episcleritis
- Proliferative keratoconjunctivitis

Suggested Reading

- Maggs DJ. Cornea and sclera. In: Maggs DJ, Miller PE, Ofri R, Slatter's Fundamentals of Veterinary Ophthalmology, 5th ed. St. Louis: Saunders, 2013, pp. 184–219.
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BASICS

DEFINITION

Bleeding from the nose

PATHOPHYSIOLOGY

Results from one of three abnormalities—coagulopathy; local disease or space-occupying lesion; vascular or systemic disease.

SYSTEMS AFFECTED

- Respiratory—hemorrhage; sneezing
- Gastrointestinal—melena
- Hemic/Lymphatic/Immune—anemia

GENETICS

Varies depending on underlying cause

INCIDENCE/PREVALENCE

Varies depending on underlying cause

SIGNALMENT

Species

Dog and cat

Age, Breed, and Sex Predilections

Varies depending on underlying cause

SIGNS

Historical Findings

- Nasal hemorrhage—unilateral or bilateral possible.
- Sneezing and/or stertorous respiration.
- Melena.
- With coagulopathy—hematochezia, melena, hematuria, or hemorrhage from other areas of the body.
- With hypertension—possibly blindness, intraocular hemorrhage, neurologic signs, cardiac or renal signs.

Physical Examination Findings

- Nasal hemorrhage.
- Melena—from swallowing blood or concurrent upper GI hemorrhage.
- Nasal stridor—may be present with neoplasia, foreign body or advanced inflammatory disease.
- With coagulopathy—possibly petechiae, ecchymosis, hematomas, intracavitory bleeds, hematochezia, melena, and hematuria.
- With coagulopathy or hypertension—possibly retinal or intraocular hemorrhages or retinal detachment; with hypertension—possibly heart murmur or arrhythmia.

CAUSES

Coagulopathy

THROMBOCYTOPENIA

- Immune-mediated disease—idiopathic disease; drug reaction; MLV vaccine reaction.
- Infectious disease—ehrlichiosis; anaplasmosis; Rocky Mountain spotted fever, babesiosis, FeLV or FIV-related illness.
- Bone marrow disease—neoplasia; aplastic anemia; infectious (fungal, rickettsial, or viral).
- Paraneoplastic disorder.
- DIC.

THROMBOPATHIA

- Congenital—von Willebrand disease; thrombasthenia; thrombopathia.
- Acquired—NSAIDs; clopidogrel;

hyperglobulinemia (*Ehrlichia*, multiple myeloma); uremia; DIC.

COAGULATION FACTOR DEFECTS

- Congenital: hemophilia A (factor VIIIc deficiency) and hemophilia B (factor IX deficiency).
- Acquired: anticoagulant rodenticide (warfarin) intoxication, hepatobiliary disease, DIC.

Local Lesion

- Foreign body.
- Trauma.
- Infection—fungal (*Aspergillus*, *Cryptococcus*, *Rhinosporidium*); viral or bacterial. Usually blood-tinged mucopurulent exudate rather than frank hemorrhage.
- Neoplasia—adenocarcinoma; carcinoma; chondrosarcoma; squamous cell carcinoma; fibrosarcoma; lymphoma; transmissible venereal tumor.
- Dental disease—oronasal fistula, tooth root abscess.
- Lymphoplasmacytic rhinitis.

Vascular or Systemic Disease

- Hypertension—renal disease; hyperthyroidism; hyperadrenocorticism; pheochromocytoma; idiopathic disease.
- Hyperviscosity—hyperglobulinemia (multiple myeloma, *Ehrlichia*); polycythemia.
- Vasculitis—immune-mediated and rickettsial diseases.

RISK FACTORS

Coagulopathy

- Immune-mediated disease—young to middle-aged, small-to medium-sized female dogs.
- Infectious disease—dogs living in or traveling to endemic areas; tick exposure.
- Thrombasthenia—Otter hounds.
- Thrombopathia—Basset hounds, Spitz.
- von Willebrand disease—Doberman pinschers, Airedales, German shepherds, Scottish terriers, Chesapeake Bay retrievers, and many other breeds; cats.
- Hemophilia A—German shepherds and many other breeds; cats.
- Hemophilia B—Cairn terriers, coonhounds, St Bernards, and other breeds; cats.

Space-Occupying Lesions

- Aspergillosis—German shepherds, rottweilers, mesocephalic and dolichocephalic breeds.
- Neoplasia—dolichocephalic breeds.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

See "Causes"

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia—if enough hemorrhage has occurred.
- Thrombocytopenia—possible.
- Neutrophilia—infection; neoplasia.
- Pancytopenia—if bone marrow disease.
- Hypoproteinemia—if enough hemorrhage has occurred.
- High BUN with normal creatinine—possible, owing to blood ingestion.
- Hyperglobulinemia—possible

with ehrlichiosis, multiple myeloma.

- Azotemia—with renal failure-induced hypertension.
- High ALT, AST, and total bilirubin—with coagulopathy from severe hepatic disease.
- Urinalysis—usually normal; possible to see hematuria (if coagulopathy), isosthenuria (if renal failure-induced hypertension), and proteinuria (if glomerulotubular disease and hypertension).

OTHER LABORATORY TESTS

- Coagulation profile—prolonged times with coagulation factor defects; normal with thrombocytopenia and thrombopathia.
- Platelet function testing (e.g., buccal mucosal bleeding time, von Willebrand factor analysis)—may be abnormal with platelet dysfunction (platelet count and coagulation profile may be normal).
- Ehrlichia*, *Anaplasma*, Rocky Mountain spotted fever, or *Babesia* testing—may be positive in thrombocytopenia or thrombopathia-induced epistaxis.
- Aspergillus* serology—may help establish a diagnosis of fungal rhinitis; false negative results are common so results must be interpreted in light of other clinical and diagnostic findings.
- Thyroid hormone assay—elevated in cats with epistaxis due to hyperthyroid-induced hypertension.

IMAGING

- Thoracic radiograph—screen for metastasis.
- Nasal series—under anesthesia, including open-mouth ventrodorsal and skyline sinus views when space-occupying or local lesion is suspected; osteolysis with neoplasia and fungal sinusitis; foreign bodies usually not seen; dental disease may be identified.
- CT or MRI—more sensitive than radiographs.

DIAGNOSTIC PROCEDURES

- Blood pressure evaluation—indicated when coagulopathies and space-occupying lesions have been ruled out and particularly when azotemia or proteinuria is noted.
- Rhinoscopy, nasal lavage, nasal biopsy (blind or guided via rhinoscopy or CT)—indicated for space-occupying disease; aimed at removing foreign bodies and evaluating and sampling nasal tissue for a causal diagnosis (e.g., evaluate nasal tissue samples for neoplasia, inflammation, and infection via cytology and/or histopathology and bacterial/fungal culture and sensitivity testing).
- Bone marrow aspiration biopsy—indicated if pancytopenia identified.



TREATMENT

APPROPRIATE HEALTH CARE

- Coagulopathy—usually inpatient management.
- Space-occupying lesion or vascular or systemic disease—outpatient or inpatient management, depending on the disease and its severity.
- Nasal tumors—radiotherapy; various response rates.

EPISTAXIS

(CONTINUED)

NURSING CARE

Provide basic supportive care if needed (fluids, nutrition).

ACTIVITY

Minimize activity or stimuli that precipitate hemorrhage episodes.

CLIENT EDUCATION

- Inform client about the disease process.
- Teach client how to recognize a serious hemorrhage (e.g., weakness, collapse, pallor, and blood loss > 30 mL/kg body weight).

SURGICAL CONSIDERATIONS

- Surgery indicated if a foreign body is unable to be removed by rhinoscopy or blind attempt.
- Fungal rhinitis (e.g., *Aspergillus* and *Rhinosporidium*) require debulking (also see "Medications").



MEDICATIONS

DRUG(S) OF CHOICE

General

- Whole blood, packed RBC, or hemoglobin solution transfusion—can be needed with severe anemia.
- Acepromazine (0.05–0.1 mg/kg SC, IV if normothermic and no platelet disorder present) to lower blood pressure and promote clotting; may help control serious hemorrhage.
- Discontinue all NSAIDs.

Coagulopathy

- Immune-mediated thrombocytopenia—prednisone (1.1 mg/kg q12h; taper over 4–6 months); other drugs can be used in addition to prednisone for refractive cases (see Immune Mediated Thrombocytopenia).
- Infectious disease—rickettsial disease (doxycycline, 5 mg/kg PO q12h for 3–6 weeks); *Babesia* (imidocarb, 6.6 mg/kg SC, 2 doses 2 weeks apart, diminazene acetate 5 mg/kg IM once, or 10 days of atovaquone 13.3 mg/kg PO q8h with azithromycin 10 mg/kg PO q24h).
- Bone marrow neoplasia—see Myeloproliferative Disorders.
- Thrombopathia and thrombasthenia—no treatment unless lymphoproliferative disease.
- von Willebrand disease—plasma or cryoprecipitate for acute bleeding; DDAVP 1 µg/kg SC or IV diluted in 20 mL of 0.9% NaCl given over 10 minutes may help control or prevent hemorrhage prior to invasive procedures (intranasal formulation [less expensive] may be used after passing through a bacteriostatic filter).
- Hemophilia A—plasma or cryoprecipitate for acute bleeding; no long-term treatment.
- Hemophilia B—plasma for acute bleeding; no long-term treatment.
- Anticoagulant rodenticide intoxication—plasma for acute bleeding; vitamin K at 5 mg/kg loading dose followed by 1.25 mg/kg q12h for 1 week (if warfarin formulation) to 4 weeks (longer-acting formulation).
- Hyperglobulinemia—

plasmapheresis.

- Polycythemia—phlebotomy; hydroxyurea.
- Liver disease and DIC—treat and support the underlying cause; plasma may be beneficial.

Space-Occupying Lesion

- Secondary bacterial infection—antibiotics based on culture and sensitivity testing.
- Fungal infection—for aspergillosis, topical treatment of nasal cavity and frontal sinuses with 1% clotrimazole in polyethylene glycol (see "Precautions") or 1–5% enilconazole (see Aspergillosis, Nasal, for protocol); for cryptococcosis—oral and injectable antifungal agents (see Cryptococcosis); for rhinosporidiosis—surgery followed by dapsone (1 mg/kg PO q8h for 2 weeks, then 1 mg/kg PO q12h for 4 months).

Vascular or Systemic Disease

- Hyperviscosity—treat underlying disease (e.g., ehrlichiosis, multiple myeloma, or polycythemia); plasmapheresis.
- Vasculitis—doxycycline for rickettsial disease (5 mg/kg q12h for 3–6 weeks); prednisone for immune-mediated disease (1.1 mg/kg q12h; taper over 4–6 months).

Hypertension

- Treat underlying disease—renal disease, hyperthyroidism, hyperadrenocorticism.
- Reduce weight if over-conditioned.
- Restrict sodium.
- Calcium channel blockers—amlodipine (dogs, 0.1 mg/kg PO q12–24h; cats, 0.625–1.25 mg/cat PO q12–24h)—treatment of choice.
- ACE inhibitors—benazepril (0.5 mg/kg q24h); enalapril (0.25–0.5 mg/kg q12–24h).
- β-blockers—propranolol (0.5–1 mg/kg q8h); atenolol (0.25–1.0 mg/kg q12–24h).
- Diuretics—hydrochlorothiazide (2–4 mg/kg q12h); furosemide (0.5–2 mg/kg q8–12h).
- Phenoxybenzamine 0.2–1.5 mg/kg q12h for pheochromocytoma.

CONTRAINDICATIONS

- Avoid drugs that may predispose patient to hemorrhage—NSAIDs; heparin; clopidogrel; phenothiazine tranquilizers.
- Topical antifungals—do not use in patients with disruption of the cribriform plate.

PRECAUTIONS

- Chemotherapeutic drugs (Immune-mediated thrombocytopenia therapy, e.g., azathioprine)—monitor neutrophil counts and liver enzymes weekly until a pattern has been established that shows that the patient is tolerating the drug.
- Enalapril and/or diuretics—closely monitor patients with renal failure; avoid severe salt restriction when using ACE inhibitors.
- Avoid topical clotrimazole preparations with propylene glycol as life-threatening mucosal irritation, ulceration, and nasopharyngeal swelling can occur.



FOLLOW-UP

PATIENT MONITORING

- Platelet count with thrombocytopenia
- Coagulation profile with coagulation factor defects
- Blood pressure with hypertension
- Clinical signs

PREVENTION/AVOIDANCE

- Restrict access to areas that might contain anticoagulant rodenticides.
- Practice dental preventative care.

POSSIBLE COMPLICATIONS

Anemia and collapse (rare)

EXPECTED COURSE AND PROGNOSIS

Varies depending on underlying cause.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Avoid teratogenic drugs (e.g., itraconazole).

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- ALT = alanine transaminase • AST = aspartate aminotransferase • CT = computed tomography • DDAVP = 1-desamino-8-d-arginine vasopressin • DIC = disseminated intravascular coagulation
- FeLV = feline leukemia virus • FIV = feline immunodeficiency virus • MLV = modified live virus • MRI = magnetic resonance imaging • NSAID = nonsteroidal anti-inflammatory drug • RBC = red blood cell

Suggested Reading

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Client Education Handout
available online



BASICS

OVERVIEW

- American Veterinary Dental College (AVDC) nomenclature: the term “epuli” (epulides) is a general term referring to a gingival mass lesion of any type.
- Classically considered as tumors of non-odontogenic origin that arise from periodontal connective tissue stroma and do not metastasize.
- Categories of epulides are fibromatous (FE), ossifying (OE), and acanthomatous (AE).
- FE and OE have been grouped together as variants of a fibromatous category. FE compared to and deemed equivalent to human peripheral odontogenic fibroma (POF).
- World Health Organization’s (WHO) “Histological classification of tumors of odontogenic origin of domestic animals” describes FE:
 - Primarily composed of periodontal ligament-type stroma: presence of regularly positioned stellate mesenchymal cells, smooth fibrillar collagen matrix, and regularly positioned and dilated but empty blood vessels.
 - Commonly observed cords of odontogenic epithelium and cell-poor collagen matrix resembling alveolar bone, cementum or even dentin.
 - Benign tumors.
- Recent retrospective study subdivided the WHO FE category into focal fibrous hyperplasia (FFH) and POF based on the presence of odontogenic epithelium.
 - FFH: inflammatory lesion, nonneoplastic; reactive lesions resulting from irritation caused by plaque and calculus. Dense fibrous connective tissue with mature fibroblasts widely scattered. Foci of dystrophic calcification and cellular fibrous tissue. Absence of odontogenic epithelium. Strands of surface epithelium often visible within the fibrous tissue. Superficial aspect may be ulcerated with associated inflammation.
 - Canine FE and human POF: equivalent. Mass of cellular, fibroblastic connective tissue separated from surface epithelium by a zone of histologically normal fibrous connective tissue, often in the form of strands of interwoven epithelium within a looser connective matrix; connective tissue highly vascular. Rest of odontogenic epithelium in the connective tissue may vary in number. Bone and collagenous matrix (osteoid, dentoid or cementum-like) present in variable amounts.
- Acanthomatous lesions are most distinct: termed either AE or canine (peripheral) acanthomatous ameloblastomas (CAA). Consists of islands and cords of squamous

epithelium that have invaded irregularly through a connective tissue stroma. Basal cells arranged in palisades, vacuolated cytoplasm with reverse polarization. No precise human equivalent. AE/CAA has clear clinicopathologic, morphologic and biologic differences from other categories. Characteristic aggressive infiltrative growth of epithelial cell components in spite of minimal cell atypia and few mitotic figures.

SIGNALMENT

- Dog—fourth most common oral malignancy
- Cat—rare
- Most common in brachycephalic breeds
- Boxers have a higher incidence of FE/fibrous changes
- Mean age—7 years
- No sex predisposition
- Fiani retrospective study (see “Suggested Reading”)
 - CAA: 45% (higher than other studies, but possibly based on more referral cases). Rostral mandible most common site (2.3 to 1 compared to maxilla). Mean 8.8 years. Golden retriever, Akita, cocker spaniels, shelties.
 - POF: 31%. Rostral maxilla (1.7 to 1 compared to mandible). Male to female ratio 1.8 to 1. Mean 8.5 years.
 - FFH: 16% (lower than other studies). Rostral mandible. Mean 9.0 years.

SIGNS

Historical Findings

- Often minimal—incidental finding detected on routine physical examination.
- If severe (AE, CAA): Excessive salivation, halitosis, dysphagia, bloody oral discharge, weight loss.

Physical Examination Findings

- Oral mass—in early cases, may appear as small pedunculated masses.
- Displacement of tooth structures due to the expansile nature of the mass (AE/CAA).
- Possible facial deformity due to asymmetry of the maxilla or mandible.
- Occasionally cervical lymphadenopathy.

CAUSES & RISK FACTORS

None identified



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Fibroma
- Benign polyp
- Ameloblastoma
- Malignant oral tumor
- Gingival hyperplasia/enlargement
- Abscess
- Differentiated from other types of masses by excisional biopsy coupled with radiographic appearance.

CBC/BIOCHEMISTRY/URINALYSIS

Results usually normal

OTHER LABORATORY TESTS

Cytologic preparations are rarely diagnostic

IMAGING

- Determine tumor borders by intraoral radiographs.
- Radiographs of AE/CAA typically demonstrate significant osseous changes with expansion into adjacent tissues; POF/FE-OE do not have well-defined borders on radiographs; tooth structures are usually displaced; may have ossified component.
- CT scan may be necessary to detail the invasiveness of a canine (peripheral) acanthomatous ameloblastoma.

DIAGNOSTIC PROCEDURES

A large, deep tissue biopsy (down to bone) is required to differentiate from other oral malignancies—fibroma, fibrosarcoma, or low-grade fibrosarcoma.



TREATMENT

DIET

Soft foods may be recommended to prevent tumor ulceration or after conservative or radical oral excision.

SURGICAL CONSIDERATIONS

- POF—surgical excision with at least 1 cm margins is usually curative; these tumors are of periodontal ligament stromal origin, so extraction of affected teeth and curettage of the alveolar socket are indicated; more advanced cases may require en bloc tooth and bone excision.
- Ossifying lesion—characteristically have a bony matrix and excision is often more difficult.
- Peripheral acanthomatous ameloblastoma—because of the aggressiveness of this tumor, at least 2 cm margins are recommended; partial mandibulectomy or maxillectomy is often indicated by the location of the tumor.
- Radiotherapy offers long-term control in dogs with a peripheral acanthomatous ameloblastoma deemed inoperable; most radiotherapy plans attempt 40–60 Gy over 3–6 weeks.



MEDICATIONS

DRUG(S)

- Efficacy of outpatient chemotherapy is unreported; most tumors of mesenchymal origin respond poorly.
- Local control (palliation) with intrathecally administered cisplatin has been reported.

EPULIS

(CONTINUED)

- Bleomycin injected locally has been successful in treating acanthomatous epulis.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Chemotherapy can be toxic; seek advice before initiating treatment if you are unfamiliar with cytotoxic drugs.

E**FOLLOW-UP****PATIENT MONITORING**

- Thorough oral, head, and neck examination regularly after treatment.
- Periodic intraoral radiographs, especially for AE/CAA.

EXPECTED COURSE AND PROGNOSIS

- AE/CAA are highly invasive into bone.
- Good prognosis expected when excisional margins are free of neoplastic cells.
- Mean survival time after surgery of peripheral acanthomatous ameloblastoma is 43 months (range, 6–134 months); mean survival times for patients with peripheral acanthomatous ameloblastoma, ossifying, and peripheral odontogenic fibroma are 52, 29, and 47 months, respectively. Survival times above are from different sources.

- Mean survival after radiotherapy in dogs with peripheral acanthomatous ameloblastoma ranges from 1–102 months (median, 37 months); the 1-year survival rate is 85%; the 2-year survival rate is 67%.

- Malignant transformation of an acanthomatous epulis (peripheral acanthomatous ameloblastoma) has been reported in up to 20% of irradiated patients years after treatment, suggesting that it may be a precancerous lesion.

**MISCELLANEOUS****SYNOMYMS**

- Peripheral ameloblastoma
- Peripheral acanthomatous ameloblastoma
- Peripheral odontogenic fibroma

SEE ALSO

Oral Masses

ABBREVIATIONS

- AE = acanthomatous epulis
- CAA = canine acanthomatous ameloblastoma
- CT = computed tomography
- FE = fibrous epulis

- FFH = focal fibromatous hyperplasia
- OE = ossifying epulis
- POF = peripheral odontogenic fibroma

INTERNET RESOURCES

<http://www.avdc.org/Nomenclature.html>.

Suggested Reading

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ESOPHAGEAL DIVERTICULA



BASICS

OVERVIEW

- Pouch-like sacculations of the esophageal wall that accumulate fluids and ingesta.
- Diverticula may be congenital or acquired and are rare.
- Pulsion diverticula occur secondary to increased intraluminal pressure. Seen with esophageal obstructive disorders such as foreign body or mass lesions.
- Traction diverticula occur secondary to periesophageal inflammation where fibrosis and contraction pull out the wall of the esophagus into a pouch.
- Diverticuli most commonly occur at the thoracic inlet or near the hiatus.
- Organ systems affected include the gastrointestinal (regurgitation), musculoskeletal (weight loss), and respiratory (aspiration pneumonia).

SIGNALMENT

- Rare; more common in dog than cat
- Congenital or acquired (no genetic basis proven)
- No important breed or sex predisposition

SIGNS

- Postprandial regurgitation, dysphagia, anorexia, coughing
- Weight loss, respiratory distress

CAUSES & RISK FACTORS

Pulsion Diverticulum

- Embryonic developmental disorders of the esophageal wall.
- Esophageal foreign body, mass or focal motility disturbances (uncommon).

Traction Diverticulum

- Inflammatory processes associated with the trachea, lungs, hilar lymph nodes, or pericardium; resultant fibrous connective tissue adheres to the esophageal wall.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Esophageal Redundancy

Barium contrast accumulation in the region of the thoracic inlet can occur normally in young dogs (especially brachycephalic breeds and Chinese Shar-Pei).

Periesophageal Mass

Esophagram or esophagoscopy should differentiate the presence of a mass causing luminal narrowing.

CBC/BIOCHEMISTRY/URINALYSIS

Usually within normal limits

OTHER LABORATORY TESTS

N/A

IMAGING

- Thoracic radiography—may show air or soft tissue opacity cranial to the diaphragm or cranial to the thoracic inlet.
- Contrast esophagram—shows contrast accumulation within the diverticulum.
- Videofluoroscopy—useful to evaluate for disturbances in esophageal motility.

DIAGNOSTIC PROCEDURES

Esophagoscopy confirms ingesta/debris within outpouchings of the esophagus.



TREATMENT

- If the diverticulum is small and not causing significant clinical signs, treat conservatively with elevated feedings of a soft, bland diet followed by copious liquids.
- If the diverticulum is large or is associated with significant clinical signs, surgical resection is recommended.
- Client education should include the importance of dietary management and the potential for aspiration pneumonia.
- Fluid therapy, antibiotics, and aggressive nursing, if concurrent aspiration pneumonia is present; alternative enteral nutrition via gastrostomy tube may be necessary in patients with aspiration pneumonia.
- Treat for esophagitis if present.



MEDICATIONS

DRUG(S)

- Drug therapy for esophagitis, if present.
- Give H₂ histamine antagonists (e.g., ranitidine 2 mg/kg PO q12h or famotidine 0.5–1 mg/kg PO q12h) if the patient has concurrent esophagitis.

- Proton pump inhibitors such as omeprazole are more potent and effective antacids than the H₂ histamine antagonists for management (0.7–1.5 mg/kg PO q24h) of severe esophagitis.

- Use broad-spectrum antibiotics if the patient has concurrent aspiration pneumonia; if severe pneumonia is present, base antibiotic selection on culture and sensitivity of samples obtained by transtracheal wash or bronchoalveolar lavage.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Evaluate for evidence of infection or aspiration pneumonia.
- Maintain positive nutritional balance throughout disease process.

POSSIBLE COMPLICATIONS

Patients with diverticula and impaction are predisposed to perforation, fistula, stricture, and postoperative incisional dehiscence.

EXPECTED COURSE AND PROGNOSIS

Prognosis is guarded in patients with large diverticula and overt clinical signs.



MISCELLANEOUS

INTERNET RESOURCES

Veterinary Information Network:
www.vin.com/VIN.plx.

Suggested Reading

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ESOPHAGEAL FOREIGN BODIES



BASICS

DEFINITION

Ingestion of foreign material or foodstuffs too large to pass through the esophagus, causing partial or complete luminal obstruction.

E

PATHOPHYSIOLOGY

Esophageal foreign bodies cause mechanical obstruction, mucosal inflammation with edema, and possibly ischemic necrosis and esophageal stricture formation.

SYSTEMS AFFECTED

- Gastrointestinal
- Respiratory—if aspiration pneumonia

GENETICS

N/A

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Due to the indiscriminate eating habits of many dogs, they have a higher incidence than cats.

Breed Predilections

More common in small-breed dogs; terrier breeds often overrepresented.

Mean Age and Range

More common in young to middle-aged animals

Predominant Sex

N/A

SIGNS

General Comments

The pet may have been observed ingesting a foreign body.

Historical Findings

Most common include retching, gagging, lethargy, anorexia, ptalism, regurgitation, restlessness, dysphagia, odynophagia, and persistent gulping.

Physical Examination Findings

- Ptyalism.
- Can be unremarkable.
- Occasional discomfort when palpating the neck or cranial abdomen.

CAUSES

Occurs most often with an object whose size, shape, or texture does not allow free movement through the esophagus, causing it to become lodged before it can pass.

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Esophagitis
- Esophageal stricture
- Esophageal neoplasia
- Megaeosophagus
- Other esophageal disorders

CBC/BIOCHEMISTRY/URINALYSIS

- Usually unremarkable.
- Occasionally, electrolyte abnormalities, an inflammatory leukogram, and/or hemoconcentration, depending upon the severity of signs and degree of dehydration.

OTHER LABORATORY TESTS

N/A

IMAGING

Thoracic Radiography

- Most esophageal foreign bodies are radiodense and are readily visualized. These objects most commonly lodge at points of minimal esophageal distension including the thoracic inlet, base of the heart, and the esophageal hiatus.
- Esophageal distension with air may be visualized cranial to the foreign body. Retained air in the esophagus is not always associated with esophageal foreign bodies.
- A contrast esophagram or videofluoroscopy is required to identify radiolucent objects. If perforation is suspected, use an aqueous organic iodide contrast agent for imaging studies.
- Air and/or fluid in the mediastinum or pleural space suggests esophageal perforation; depending on severity, this can be an indication for surgery instead of esophagoscopy.
- Pulmonary infiltrates suggest aspiration pneumonia.

DIAGNOSTIC PROCEDURES

Esophagoscopy affords direct visualization of both the foreign object and the esophageal mucosa, allowing assessment of the extent of esophageal injury. It also allows for visual interrogation of the mucosa for trauma post-foreign body removal.

PATHOLOGIC FINDINGS

N/A



TREATMENT

APPROPRIATE HEALTH CARE

- Emergencies—treat as inpatient and perform endoscopy as soon as possible after diagnosis.

- If endoscopic retrieval of the foreign body succeeds and esophageal damage is minimal, the patient may be discharged the same day.

NURSING CARE

- If the procedure to remove the foreign body is atraumatic and the esophagus has sustained minimal damage, no special aftercare is needed.
- Severe mucosal trauma may require placing a gastrostomy tube for enteral nutritional support during esophageal healing. Fluid therapy may also be required to maintain normal hydration status during periods of prolonged esophageal rest.

ACTIVITY

The patient may resume normal activity after a foreign body has been routinely removed.

DIET

No change needed other than, perhaps, altering the food to a more liquid consistency.

CLIENT EDUCATION

Discuss the possibility of complications and repeat offenders.

SURGICAL CONSIDERATIONS

- Endoscopic foreign body extraction is much less traumatic and invasive than surgery.
- Surgery is indicated when endoscopy fails to retrieve the foreign body; when endoscopy enables advancement of the object into the gastric lumen but it is too large to pass through the gastrointestinal tract; or when a large esophageal perforation or area of necrosis requires resection.
- It is often less traumatic to advance a bone foreign body into the stomach than to attempt retrieval transorally via endoscopy. Gastrostomy, if required, may then be performed.
- Most bone foreign bodies can be safely left to dissolve in the stomach without need for surgical removal. Non-digestible foreign objects (wood, metal, plastic) passed into the stomach may need to be removed surgically.



MEDICATIONS

DRUG(S) OF CHOICE

- If there is significant mucosal injury (i.e., esophagitis), recommendations include:
- Sucralfate slurry (0.5–1 g/dog PO q8h) for mucosal cytoprotection and healing.
- Proton pump inhibitor (omeprazole or pantoprazole at 1 mg/kg q24h) for robust suppression of gastric secretions which may contribute to reflux esophagitis. H₂-receptor antagonists (e.g., ranitidine, 1–2 mg/kg PO, IV, SC q12h, or famotidine, 0.5–1 mg/kg, PO q12h) may be used in animals with less severe esophagitis.

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ESOPHAGEAL FOREIGN BODIES

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- Broad-spectrum antibiotics (amoxicillin or Clavamox) may be administered to animals having small mucosal perforations.
- Metoclopramide (0.2–0.5 mg/kg IV, SC, PO q8h) or cisapride (0.5 mg/kg q8–12h PO) to stimulate gastric motility and minimize reflux esophagitis.
- Gastrostomy tube placement for enteral nutrition in animals with severe mucosal trauma.
- Viscous lidocaine gel administered with water and given 2–3 times daily can be used to help reduce esophageal pain if warranted.

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

- Examine the esophagus closely via endoscopy for mucosal damage post-foreign body removal.
- Mild erythema/erosions are not uncommon and tend to heal uneventfully.
- If an esophageal laceration/perforation is detected—parenteral nutrition or gastrostomy tube feedings allow esophageal rest and healing.

- Advise post-procedural survey thoracic radiographs to assess for pneumomediastinum/pneumothorax.
- Monitor at least 2–3 weeks for evidence of stricture formation.
- Esophageal stricture—most common clinical sign is regurgitation with evidence of odynophagia in many animals; esophagram or videofluoroscopy and/or esophagoscopy may be indicated to confirm a stricture.

PREVENTION/AVOIDANCE

Carefully monitor the environment and what is fed to the pet.

POSSIBLE COMPLICATIONS

- Approximately 25% of patients with foreign bodies develop complications.
- Complications most frequently encountered include esophageal perforation, esophageal strictures, esophageal fistulas, and severe esophagitis. Focal, transient esophageal motility disturbances can occur secondary to esophageal trauma.
- Pneumomediastinum, pneumothorax, pneumonia, pleuritis, mediastinitis, and bronchoesophageal fistulas can all occur secondarily to perforation.

EXPECTED COURSE AND PROGNOSIS

- Most patients do well and recover uneventfully.
- With complications, the prognosis is guarded.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

None

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Esophageal Diverticula
- Regurgitation

INTERNET RESOURCES

Veterinary Information Network:
www.vin.com/VIN.plx

Suggested Reading

Pratt CL, Reineke EL, Drobatz KJ. Sewing needle foreign body ingestion in dogs and cats: 65 cases (2000–2012). J Am Vet Med Assoc 2014, 245(3):302–308.

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Author Albert E. Jergens

Consulting Editor Stanley L. Marks



**Client Education Handout
available online**

ESOPHAGEAL STRICTURE



BASICS

DEFINITION

An abrupt fixed narrowing of the esophagus due to scar tissue, resulting in partial or complete obstruction.

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PATHOPHYSIOLOGY

- Benign strictures occur when there is severe esophagitis, occurring for greater than 270° of the esophageal circumference. Regardless of the initiating event, once esophagitis develops, there is a decrease in LES tone. This results in more acid reflux and subsequent worsening of the esophagitis. Once severe esophagitis is present, damage can extend to the lamina propria and muscularis layers. This incites a fibroblastic proliferation and contraction, leading to stricture formation.
- Malignant strictures occur rarely in dogs and cats, and stricture results from direct tumor invasion.

SYSTEMS AFFECTED

- Gastrointestinal—the esophagus is usually affected focally, although multiple strictures can occur.
- Respiratory—regurgitation is common with strictures, with secondary aspiration pneumonia.

GENETIC

None.

INCIDENCE/PREVALENCE

Uncommon

GEOGRAPHIC DISTRIBUTION

Spirocercus lupi granuloma occurs in the southern USA, parts of Europe, South Africa, and Israel. There is no other geographic distribution.

SIGNALMENT

Dog and cat. No known breed or sex predilections. Puppies and kittens with vascular ring anomaly become symptomatic at weaning.

SIGNS

- Pain during swallowing (odynophagia), dysphagia, increased salivation, regurgitation, anorexia, and weight loss. Signs tend to be progressive as the stricture progressively narrows.
- If regurgitation leads to aspiration pneumonia, cough and dyspnea can develop.

CAUSES

- Reflux during anesthesia is the most common cause of benign esophageal stricture, accounting for about ~65% of cases. It is presumed that decreased LES tone occurring during anesthesia allows for gastroesophageal reflux, which results in subsequent acid injury to the esophageal mucosa.
- Severe esophageal foreign bodies (if > 270° mucosal damage occurs).
- Tablets and capsules can induce esophagitis leading to stricture. The most commonly incriminated drugs are doxycycline, clindamycin and aspirin.

- Gastroesophageal reflux independent of anesthesia.
- Prolonged vomiting of gastric contents.
- Swallowing of caustic substances.
- Esophageal neoplasia (squamous cell carcinoma and lymphoma most common).
- Vascular ring anomaly (congenital).
- Spirocercus lupi* granuloma.

RISK FACTORS

- General anesthesia, especially with drugs that decrease LES tone or when the table is tilted head-down.
- Oral medications given with a dry swallow (60–80% of capsules do not pass into the stomach after 5 minutes following a “dry” swallow)
- Foreign body ingestion.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Megaesophagus
- Esophageal foreign body
- Esophageal neoplasia
- Extrinsic esophageal compression (mass, abscess)
- Gastroesophageal reflux
- Vomiting (any cause)
- Oropharyngeal dysphagia

CBC/BIOCHEMISTRY/URINALYSIS

Usually unremarkable. May have neutrophilic leukocytosis if secondary aspiration pneumonia develops.

OTHER LABORATORY TESTS

Usually unremarkable

IMAGING

- Thoracic radiographs—usually unremarkable, unless secondary aspiration pneumonia develops. Occasionally gas-filled dilation cranial to the stricture may be seen.
- Videofluoroscopic barium swallow—procedure of choice. If videofluoroscopy is not available, barium swallow of liquid, paste, or food followed immediately by radiography is performed. Peristalsis proximal to the stricture site can be abnormal with concurrent esophagitis. Usually recognize an abrupt narrowing of the esophageal lumen at the stricture site. Most easily demonstrated with canned food or kibble mixed with barium. May demonstrate more than one stricture.
- Most cases of reflux-induced strictures are between the heart base and diaphragm. Most cases of pill-induced strictures are near the thoracic inlet (especially cats).

DIAGNOSTIC PROCEDURES

Endoscopy—There is an abrupt decrease in luminal diameter at the stricture site. Usually the mucosa is normal (smooth and pink), but can appear hyperemic and ulcerated if esophagitis is present. Often the scope cannot be advanced beyond the stricture without balloon dilation. The location of the stricture should be measured from the upper canine teeth.

PATHOLOGIC FINDINGS

If an esophageal mass is present, biopsy with histopathology is warranted. Otherwise, benign strictures do not need to be biopsied. Variable degree of esophagitis may be seen.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient medical management is only successful for mild strictures. More severe strictures will lead to progressive malnutrition and possible aspiration pneumonia, and require inpatient intervention. If there are complications (esophageal perforation, aspiration pneumonia), then inpatient care is required.

NURSING CARE

With mild strictures, gruel feeding (ideally partially elevated) may be possible. With more severe strictures, oral alimentation is not possible. Intravenous fluids may be necessary if animal is dehydrated. Other medications depend on the presence of esophagitis, complications, and results of dilation.

ACTIVITY

Mild exercise restriction may be necessary after dilation. If pneumonia is present, the degree of hypoxia will determine appropriate activity level.

DIET

With mild strictures, gruel feeding (ideally partially elevated) may be possible. Recommend feeding a fat-restricted diet to enhance gastric emptying. Canned food can be fed in small frequent amounts following dilation, even when severe esophageal tearing occurs. In some cases, re-strictureting occurs necessitating percutaneous endoscopic gastrostomy (PEG) tube feeding while multiple dilations are employed.

CLIENT EDUCATION

- With mild strictures, gruel feeding (ideally partially elevated) may be possible. Otherwise dilation procedures are necessary.
- Owners should be aware that dilation procedures are not always successful, and that multiple attempts are required in some patients. It is important that medical management for esophagitis be diligently employed following dilation procedures to reduce the risk of re-stricture.
- Most cases have a successful outcome.
- If there is failure after ~5–8 attempts, rescue procedures (such as stent placement) should be considered.
- Patients with esophageal neoplasia have a poor prognosis.

SURGICAL CONSIDERATIONS

- The first-line treatment of benign esophageal strictures is mechanical dilatation of the stricture. Techniques have evolved from rigid bougienage, to flexible bougies, to

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balloon dilation. The latter technique is generally thought to be superior to bougienage, but objective evidence for this is lacking in human and veterinary patients. The theoretical advantage of balloon dilatation is that the forces applied to the stricture are a radial stretch, whereas some of the forces applied with bougienage are also longitudinal, resulting in greater potential for esophageal perforation. • Esophageal dilatation balloons are made of special plastic that makes the balloon extremely rigid when maximally inflated at high pressures, generally up to 45 psi. Balloons are positioned within the stricture under direct endoscopic visualization. The balloon is slowly inflated until it reaches the manufacturer's rated pressure for that balloon. Sequentially larger balloons are used until the clinician subjectively judges the degree of mucosal tearing to be acceptable. • The technique is very subjective in veterinary medicine, with many variables not defined by controlled studies. These include the sequence of dilatation, the optimal final dilation diameter, use of corticosteroids intralesionally, post-dilation drugs, post-dilation feeding regime, the elective use of percutaneous endoscopic gastrostomy (PEG) tubes, and repeat elective dilatations (and at what interval). Typically, an initial balloon diameter is selected that is 50–100% larger than the estimated stricture diameter. If there is doubt, selection of a smaller balloon with gradually larger subsequent dilations is safest. The sequence of subsequent larger dilations is then determined by the degree of mucosal tearing. The final dilation diameter is usually chosen by the degree of mucosal tearing and the size of the patient. As a general guideline, the end diameter is as follows: cats and dogs < 8 kg, 12 mm; dogs 8–15 kg, 16 mm; dogs 15–30 kg, 20 mm; dogs 30–50 kg, 25 mm; and dogs > 50 kg, 30 mm. This is subjective, and is a balance between the desire to achieve a large enough lumen at the completion of procedure and the risk of perforation when too large a balloon is used. • Injection of intralesional submucosal triamcinolone in a 4-quadrant pattern just prior to dilation may reduce the frequency of re-stricture. Similarly, topical application of mitomycin-C may also reduce the frequency of re-stricture. Both methods can be employed in the same patient. • Some authors recommend elective dilations at 1-week intervals to decrease the likelihood of re-stricture formation. I do not routinely recommend this since the published median number of dilations required for successful treatment is 2 (range 1–5). If 3 dilations are required, then I often recommend an elective dilation 1 week later. • If >5–8 dilations have been performed with subsequent stricture recurrence, a salvage procedure with placement of a self-expanding covered metal stent can be employed. It is

important that the stent be secured with sutures to prevent stent migration. • Surgical management (resection and anastomosis) is only performed as a last resort.



MEDICATIONS

DRUG(S) OF CHOICE

- Following dilation, give sucralfate suspension (0.5–1 gram/patient PO q6h) to reduce esophagitis and pain. Medications for esophagitis are used, including cisapride (0.5–0.75 mg/kg PO q8h) to increase LES tone and enhance gastric emptying, and omeprazole (1 mg/kg PO q12h) to decrease gastric acid. • Broad-spectrum antibiotics are used if aspiration pneumonia is present.

CONTRAINDICATIONS

Caustic substances and emetic medications

PRECAUTIONS

Esophageal perforation can occur with overzealous balloon dilation of the stricture. Therefore sequentially increase diameter of balloons.

POSSIBLE INTERACTIONS

Sucralfate may inhibit the absorption of other drugs.

ALTERNATIVE DRUG(S)

Metoclopramide can be used to increase LES tone (although cisapride is superior). Histamine H₂-receptor blockers can be used to decrease gastric acid (although proton pump inhibitors are superior).



FOLLOW-UP

PATIENT MONITORING

- Clinical signs are monitored for stricture recurrence (mainly regurgitation). An appropriate consistency food should be fed. Repeat stricture dilation should be considered based on recurrence of clinical signs.
- Aspiration pneumonia is monitored by clinical signs and radiographic resolution.

PREVENTION/AVOIDANCE

- Peanesthetic administration of cisapride decreases the number of reflux events in anesthetized dogs, but the low incidence of stricture may make this an overly aggressive part of routine preanesthetic management.
- Peanesthetic administration of omeprazole will minimize the likelihood of acid reflux and potentially decrease the likelihood of stricture formation. • Medications with ulcerogenic potential (such as doxycycline, clindamycin, and aspirin) should be given with at least 6 mL of water or food (a "wet swallow").

POSSIBLE COMPLICATIONS

- Complications of balloon dilatation include perforation, severe mucosal tearing and

ESOPHAGEAL STRicture

esophagitis, and re-stricture. • Aspiration pneumonia secondary to regurgitation.

- Complications of stent placement include stent migration, tissue ingrowth into the stent resulting in stent occlusion, food obstruction, hemorrhage, perforation, airway compression, pressure necrosis/fistula formation, dysphagia, and pain.

EXPECTED COURSE AND PROGNOSIS

- The overall successful treatment rate of balloon dilatation is reported to be between 70% and 88% in dogs and cats. The median number of dilations required for successful treatment is 2, but can require up to 5–8 before considered a failure. Prognosis is poorer with narrower and more chronic strictures. The prognosis for esophageal neoplasia is poor.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Aspiration pneumonia, esophagitis.

AGE-RELATED FACTORS

None.

ZOONOTIC POTENTIAL

None.

SYNOMYMS

- Esophageal narrowing • Esophageal blockage or obstruction

SEE ALSO

- Regurgitation • Megaeosophagus
- Dysphagia • Esophageal foreign body
- Esophagitis • Gastroesophageal reflux

ABBREVIATION

LES = lower esophageal sphincter

Suggested Reading

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Zacuto AC, Marks SL, Osborn J, et al. The influence of esomeprazole and cisapride on gastroesophageal reflux during anesthesia in dogs. J Vet Intern Med 2012, 26(3):518–525.

Author Keith Richter

Consulting Editor Stanley L. Marks



Client Education Handout
available online

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ESOPHAGITIS



BASICS

DEFINITION

- Inflammation of the esophagus typically affecting the esophageal body and gastroesophageal sphincter (lower esophageal sphincter, LES); most commonly due to gastroesophageal reflux (GER) or secondary to vomiting; the cricopharyngeal sphincter (proximal esophageal sphincter) is less commonly affected.
- Varies from mild self-limiting esophagitis to severe ulcerative esophagitis involving the submucosa and muscularis which can result in stricture formation.

PATOPHYSIOLOGY

- Physiologic defense mechanisms protecting the esophagus from inflammation are the esophageal mucosal barrier (stratified squamous epithelium, intracellular tight junctions, mucus gel, surface bicarbonate), the LES, clearance by esophageal motility, and the neutralizing effect of alkaline saliva.
- Disruption of these esophageal defense mechanisms can result in esophageal inflammation with erosion, and/or ulceration.
- Esophagitis can result in impaired esophageal motility and LES incompetence which may result in further GER perpetuating esophagitis and esophageal damage.

SYSTEMS AFFECTED

- Gastrointestinal (GI)—esophagus (esophageal body and LES most commonly affected) and in the vomiting patient primary or secondary GI disease.
- Respiratory—with regurgitation aspiration pneumonia may develop and possibly laryngitis, pharyngitis and rhinitis (reflux rhinitis).

INCIDENCE/PREVALENCE

Unknown—relatively common clinical diagnosis based on the history or clinical circumstances; incidence probably underestimated, as most cases are not definitively diagnosed.

GEOGRAPHIC DISTRIBUTION

Esophagitis caused by *Pythium* spp. (typically in states that border the Gulf of Mexico) and rarely *Spirocerca lupi* (southern states).

SIGNALMENT

Species

Dog and cat

Breed Predilections

Reflux esophagitis resulting from upper airway obstruction in brachycephalic breeds; thought to occur due to negative intrathoracic pressure upon inspiration resulting in GER and possibly hiatal hernia.

Mean Age and Range

- Animals of any age can be affected.
- Young animals with congenital esophageal

hiatal hernia and older animals that are anesthetized are at greater risk of developing GER and reflux esophagitis.

Predominant Sex

None

SIGNS

Historical Findings

- Regurgitation.
- Ptyalism.
- Dysphagia (difficulty swallowing, gagging, retching).
- Odynophagia (pain when swallowing, repeated swallowing efforts and extension of the head and neck during swallowing).
- Hyporexia or anorexia.
- Weight loss.
- Coughing and/or nasal discharge if there is aspiration pneumonia or nasopharyngeal reflux.

Physical Examination Findings

- Often normal physical examination.
- Oral and pharyngeal inflammation and/or ulceration if caustic or irritating substances have been ingested.
- Fever and pain in some patients with severe ulcerative esophagitis or aspiration pneumonia.
- Halitosis, ptyalism, and possibly pain on palpation of neck and esophagus.
- Cachexia and weight loss, chronic esophagitis or esophageal stricture.
- Respiratory signs including nasal discharge, cough, increased bronchovesicular sound, pulmonary crackles and dyspnea as well as systemic signs including lethargy and fever in patients with aspiration pneumonia.

CAUSES

- Most commonly GER secondary to general anesthesia, hiatal hernia, persistent or chronic vomiting, gastrointestinal disease resulting in delayed gastric emptying and malpositioned esophageal tubes.
- Gastroesophageal reflux disease (GERD) secondary to a primary LES abnormality is poorly understood in veterinary patients.
- Esophageal retention of tablets or capsules (doxycycline most common in cats, clindamycin, NSAIDs).
- Esophageal foreign body.
- Infectious agents—pythiosis, *Spirocerca lupi*, *Candida* infection secondary to immune-suppression.
- Uncommon causes of esophagitis include esophageal tumors, radiation injury, megaeosophagus, vascular ring anomalies and gastrinoma (Zollinger-Ellison syndrome).
- Eosinophilic esophagitis—has emerged as a common cause of esophagitis in children and adults and is one of the most common causes of esophagitis in humans; reported but rare in veterinary patients.
- Idiopathic.

RISK FACTORS

- Anesthetic premedications, induction agents, and maintenance drugs including all opioid class drugs, glycopyrrolate, atropine, acepromazine, diazepam, xylazine, propofol, and halogenated anesthetic agents have been associated with decreased LES tone and GER.
- Hiatal hernia—increases risk for gastroesophageal reflux.
- Preanesthetic fasting for prolonged periods (≥ 24 h) puts patients at greater risk for gastroesophageal reflux and increased gastric acidity.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Esophageal foreign body—usually detected by survey radiography or esophagoscopy.
- Esophageal stricture—segmental narrowing revealed by barium contrast radiography or esophagoscopy.
- Oropharyngeal dysphagia—diagnosed by evaluating swallowing of barium under fluoroscopy.
- Hiatal hernia—usually recognized as a gas- or fluid-filled opacity in the caudodorsal thoracic cavity at the level of the esophageal hiatus; contrast studies with fluoroscopy may be required to document a hiatal hernia.
- Megaeosophagus—survey radiography usually reveals diffuse dilation of the esophageal body.
- Esophageal diverticula—focal pouches detected by survey or contrast radiography or esophagoscopy.
- Vascular ring anomaly—usually revealed by barium contrast radiography as a focal dilation of the proximal esophageal body.
- Caudal esophageal neoplasia—esophageal mass effect with possible esophageal dilation.

CBC/BIOCHEMISTRY/URINALYSIS

Usually unremarkable; patients with ulcerative esophagitis or aspiration pneumonia may have leukocytosis and neutrophilia.

IMAGING

- Survey thoracic radiography—often unremarkable but may reveal mild esophageal dilation or fluid accumulation in the distal esophagus; aspiration pneumonia may be evident in the dependent portions of the lung; potentially dilation of the esophagus cranial to a stricture, an esophageal foreign body, hiatal hernia or an intraluminal or extraluminal mass may be detected.
- Barium contrast esophagram (static images and/or fluoroscopic)—may reveal esophageal dilation with retention of barium in esophagus, strictures, foreign bodies or masses; fluoroscopic studies allow for evaluation of swallowing, esophageal motility, strictures which may not be apparent on a static esophagram, sliding hiatal hernia and

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ESOPHAGITIS

E

GER (the latter two conditions may require abdominal compressions to demonstrate).

DIAGNOSTIC PROCEDURES

- Endoscopy and biopsy—most reliable means of diagnosis; mild cases of esophagitis may be endoscopically normal; visual findings of mucosal hyperemia and edema are common and in more severe cases ulceration and active bleeding; in patients with GER changes are usually most apparent in the distal third of the esophagus. Gastroduodenoscopy should also be performed to evaluate for GI causes of vomiting which can be associated with esophagitis.
- Diagnostic quality esophageal biopsies are difficult to obtain endoscopically due to the composition of the esophageal mucosa which has a tough stratified squamous epithelium. Histopathology provides the most definitive evidence of esophagitis; endoscopy and biopsies are usually reserved for cases unresponsive to therapy.
- Most cases of aspiration pneumonia will resolve when treated with supportive care and broad-spectrum antibiotics; endotracheal or transtracheal aspiration and/or bronchoscopy with bronchoalveolar lavage for cytology, and culture and sensitivity testing may be performed in patients not responding to therapy.

PATHOLOGIC FINDINGS

- Mucosal squamous hyperplasia or dysplasia with erosions and ulcers and lymphocytic plasmacytic and neutrophilic inflammation more in the acute phase.
- Barrett's esophagus (squamous metaplasia associated with chronic GERD which can lead to dysplasia and esophageal cancer in humans) has been reported in cats.

**TREATMENT****APPROPRIATE HEALTH CARE**

Mildly affected animals can be managed as outpatients; those with more severe esophagitis (persistent regurgitation, dehydration) and complications (aspiration pneumonia) require hospitalization. Eliminating predisposing factors such as hiatal hernia and management of any underlying GI or metabolic/endocrine disease that may result in vomiting or gastric hyperacidity is imperative. Treatment of esophagitis involves protecting the esophageal mucosa from further injury and reducing GER by increasing LES pressure and promoting gastric emptying with prokinetic drugs and suppressing gastric acid production.

NURSING CARE

- Intravenous fluids to maintain hydration—more severe cases.
- Medications—may need to be given parenterally during hospitalization.

- Oxygen therapy—may be necessary in patients with severe aspiration pneumonia.

DIET

- Severe esophagitis— withhold food and water until regurgitation is resolved; severe cases may require gastrostomy tube feedings or rarely total parenteral nutrition.
- For patients that can be fed orally:
 - Feed small amounts in multiple feedings.
 - A highly digestible-low residue diet that is moderately fat restricted and has a soft or gruel consistency is recommended; Hill's i/d, Purina EN, Iams Intestinal Plus Low-Residue, and Royal Canin Gastrointestinal Moderate Calorie are appropriate choices.

CLIENT EDUCATION

- Discuss need to restrict food intake in patients with severe esophagitis.
- Discuss potential complications, including aspiration pneumonia, esophageal stricture, esophageal perforation, and/or esophageal motility abnormalities.

SURGICAL CONSIDERATIONS

Percutaneous endoscopic gastrostomy (PEG) or surgical gastrostomy tube placement is indicated in severe cases.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Given parenterally (except for sucralfate) in severe cases; when administered enterally, dissolve in water and administer orally with a syringe or dropper, or by gastrostomy tube.
- Gastric acid suppressants and GI prokinetic drugs are the most established treatments for esophagitis and GER.
 - H_2 receptor antagonists (H_2 RAs)—famotidine 0.5–1.0 mg/kg PO, SC, IV q12h; ranitidine 2.0 mg/kg PO, SC, IV q8–12h; less effective than famotidine, may have prokinetic activity; cimetidine and nizatidine used less commonly.
 - Proton pump inhibitors (PPIs) provide superior gastric acid suppression compared to H_2 RAs—omeprazole 0.7–1.0 mg/kg PO q24h or 1 mg/kg PO q12h for more rapid onset of activity and greater efficacy; give 1 hour before a meal; pantoprazole 0.7–1.0 mg/kg IV q12–24h, lansoprazole and esomeprazole 1 mg/kg PO q24h have also been recommended.
- GI prokinetic agents—increase LES pressure and gastric emptying.
 - Cisapride 0.5–0.75 mg/kg PO q8h; more effective prokinetic than metoclopramide, must be obtained from a compounding pharmacy, must be administered enterally.
 - Metoclopramide 0.2–1.0 mg/kg PO, SC q8h or 1.0–3.0 mg/kg/day CRI; the higher

end of the dose range may be necessary depending on the response.

- Sucralfate 0.5–1 g PO q8h as a suspension or tablets mixed into a slurry with water. Sucralfate is a mucosal protectant that binds to inflamed tissue creating a protective barrier, stimulates growth factors, mucus and bicarbonate; efficacy for esophagitis has been questioned as drug activity requires an acidic environment and the esophageal environment is not expected to be acidic.
- Antibiotics—indicated with aspiration pneumonia, severe esophageal ulceration or esophageal perforation.
- Analgesics to manage esophageal pain.
 - Lidocaine solution (2.0 mg/kg PO q4–6h) for local analgesia.
 - Tramadol 2–4 mg/kg PO q8–12h.
- Anti-inflammatory dosage of corticosteroids (e.g., prednisone 0.5–1 mg/kg PO per day or divided q12h) may decrease fibrosis and esophageal stricture formation in severe cases; controversial and efficacy has not been supported by the literature. Should not be given when there is evidence of aspiration pneumonia.

CONTRAINDICATIONS

None

PRECAUTIONS

None

POSSIBLE INTERACTIONS

Sucralfate may interfere with gastrointestinal absorption of other drugs and it is best to separate dosing by 2 hours from other drugs; may not be clinically important.

ALTERNATIVE DRUG(S)

- Fentanyl analgesic patches—may be useful in severe cases of painful esophagitis.
- Ranitidine 2.0 mg/kg PO q12h, nizatidine 2.5–5.0 mg/kg PO q24h and erythromycin 0.5–1.0 mg/kg PO, IV have GI prokinetic effects and may be alternate or additive drugs.

**FOLLOW-UP****PATIENT MONITORING**

- Patients with mild esophagitis do not necessarily require follow-up endoscopy; tracking of clinical signs may be sufficient.
- Consider follow-up endoscopy in patients with ulcerative esophagitis and those at risk for esophageal stricture.

PREVENTION/AVOIDANCE

- Consider omeprazole 1 mg/kg PO to reduce gastric acidity 4 hours prior to anesthesia and cisapride 1 mg/kg 12–18 hours prior to anesthesia to reduce GER during anesthesia and surgery.
- Maropitant citrate has been recently shown to reduce nausea and vomiting post hydromorphone administration; may be useful to prevent vomiting and regurgitation

ESOPHAGITIS

(CONTINUED)

associated with the use of anesthesia and opioid premedications.

- If gastroesophageal reflux is the cause of esophagitis, owners should avoid late-night feedings; this tends to diminish gastroesophageal sphincter pressure during sleep.
- Proper patient preanesthesia fasting decreases the risk of GER; general recommendations are 0–2 hours preanesthesia removal of water and 6–8 hour preanesthesia removal of food.
- Follow oral administration of capsules and tablets with 5–10 mL bolus of water (especially for doxycycline), a meal or give with a treat such as a Pill Pocket to hasten transit time of pills to stomach. For cats coating pills with butter or applying Nutrical to the nose to stimulate licking after administration of tablets may also be effective.

POSSIBLE COMPLICATIONS

- Esophageal stricture formation.
- Esophageal perforation (rare).
- Aspiration pneumonia.
- Permanent esophageal dysmotility.
- Chronic reflux esophagitis.
- Barrett's esophagus (rare complication of chronic reflux esophagitis in cats).

EXPECTED COURSE AND PROGNOSIS

- Best results when patients are treated with a gastric acid suppressant (e.g., famotidine or omeprazole), a GI prokinetic (e.g., cisapride or metoclopramide), and a mucosal protectant (e.g., sucralfate).
- Mild esophagitis—generally favorable prognosis.
- Severe or ulcerative esophagitis—greater potential for complications and guarded prognosis.

- Complete recovery is possible if the disorder is recognized and treated before serious complications develop.



MISCELLANEOUS ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

H_2 RAs, PPIs, and glucocorticoids should all be used with caution during pregnancy.

SYNONYMS

Esophageal inflammation

SEE ALSO

- Dysphagia
- Esophageal Diverticula
- Esophageal Foreign Bodies
- Esophageal Stricture
- Gastroesophageal Reflux
- Hiatal Hernia
- Megaesophagus
- Regurgitation

ABBREVIATIONS

- GER = gastroesophageal reflux
- GERD = gastroesophageal reflux disease
- GI = gastrointestinal
- H_2 RA = H_2 receptor antagonist
- LES = lower esophageal sphincter
- NSAID = nonsteroidal anti-inflammatory drug
- PEG = percutaneous endoscopic gastrostomy
- PPI = proton pump inhibitor

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- Author** Steve Hill
Consulting Editor Stanley L. Marks
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Client Education Handout
available online

ETHANOL TOXICOSIS



BASICS

OVERVIEW

- Ethanol (CH_3OH)—short-chain alcohol; highly miscible with water; less volatile than comparable hydrocarbons (e.g., ethane); solvent for medications; component of alcoholic beverages; metabolized to acetaldehyde.
- Used intravenously to treat ethylene glycol poisoning.
- Denatured forms may contain other toxic fractions (e.g., acetone, benzene, camphor, castor oil, phthalates, kerosene, sulfuric acid, terpinols); may complicate effects.
- Alcohol concentration—expressed as proof (twice the percentage concentration).
- Acute oral lowest toxic dosage—5–8 mL/kg as pure alcohol; consider % alcohol in specific product consumed.
- Other alcohols (isopropanol, methanol) cause signs similar to ethanol. Toxicity of methanol is similar to ethanol; isopropanol is about half the toxicity of ethanol.
- Cell membrane damage; impaired sodium and potassium nerve conduction.
- May inhibit glutamate receptors in brain with reduction of cyclic guanosine monophosphate (GMP).

SIGNALMENT

- Most common in dogs.
- No breed or sex predilections.
- Young animals more susceptible.
- Exposure to beverages, dyes, ink, disinfectants, gasoline, mouthwashes, paint, varnishes, perfume, pharmaceuticals.
- Fermenting bread dough causes intoxication with gastric dilatation.

SIGNS

- CNS—predominant; develop within 15–30 minutes after ingestion on an empty stomach or 1–2 hours on a full stomach.
- High dosages—ataxia; reduced reflexes; behavioral changes; excitement or depression; hypothermia.
- Flatulence if source is bread dough.
- Polyuria and/or incontinence.
- Advanced—depression or narcosis; slowed respiratory rate; metabolic acidosis; cardiac arrest; death.

CAUSES & RISK FACTORS

- Alcoholic beverages, either accidental or intentional, most common source
- Spilled beverages, commercial products, or medications containing alcohol
- Intentional—by owners or others; dogs may readily consume beer if offered
- Fermented products—bread dough, rotten apples
- Dermal exposure—alcohol-containing products



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other alcohols—methanol; isopropanol; butanol
- Abused drugs—marijuana, barbiturates, benzodiazepines
- Early stages of ethylene glycol (antifreeze) toxicosis
- Halogenated or aliphatic hydrocarbon solvents
- Pesticides—amitraz; macrolide antiparasiticides

CBC/BIOCHEMISTRY/URINALYSIS

- Packed cell volume, total solids.
- Monitor for hypoglycemia; blood glucose < 60 mg/dL considered serious.
- Metabolic acidosis is likely from ethanol-induced lactic acidemia.

OTHER LABORATORY TESTS

- Blood ethanol—clinical signs in puppies at > 0.6 mg/mL and in adults at > 1–4 mg/mL; available at human and some veterinary laboratories.
- Blood gases and increased anion gap—evaluate potential acidosis.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Activated charcoal—not effective.
- Emesis or gastric lavage—only with caution in depressed animals and protection of airway to prevent aspiration.
- Respiratory depression—provide artificial ventilation.
- IV isotonic crystalloid fluids—correct dehydration.
- Acidosis—sodium bicarbonate carefully according to severity of acidosis.
- Cardiac arrest—cardiac therapy (see Cardiopulmonary Arrest).
- CNS depression reported improved with yohimbine.



MEDICATIONS

DRUG(S)

- Fomepizole (4-methyl pyrazole)—possible inhibition of alcohol metabolism (see Ethylene Glycol Toxicosis) but not specifically cleared for use against ethanol.

- Epinephrine and bicarbonate—cardiac arrest (see Cardiopulmonary Arrest).

- Treatment for acidosis may include administration of sodium bicarbonate.
 - Use if cause is not readily reversible, arterial pH is < 7.2, and ventilator procedures have not reduced acidemia.
 - mEq of bicarbonate required = $0.5 \times \text{bw}$ in kg \times (desired total CO_2 mEq/L – measured CO_2 mEq/L).
 - Give half the total calculated dose slowly over 3–4 hours.
 - Recheck blood gases and clinical status of the animal.
- Yohimbine for CNS depression—0.1–0.2 mg/kg IV. Start with lower dosage. IV half-life is short (< 2 hours) so repeat therapy may be needed. Not specifically approved for this use but reported effective.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Do not administer other CNS depressive drugs.



FOLLOW-UP

- Monitor blood pH, blood gases, urine pH, anion gap—evidence of acidosis.
- Recovery from clinical signs—usually within 8–12 hours.



MISCELLANEOUS

ABBREVIATIONS

- CNS = central nervous system
- GMP = guanosine monophosphate

Suggested Reading

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Author Gary D. Osweiler

Consulting Editor Lynn R. Hovda

ETHYLENE GLYCOL TOXICOSIS



BASICS

DEFINITION

Results primarily from ingesting substances containing ethylene glycol (e.g., antifreeze). Rarely from other products.

E

PATHOPHYSIOLOGY

- Ethylene glycol—rapidly absorbed from the gastrointestinal tract; food in the stomach delays absorption.
- Toxicity—initially causes CNS depression, ataxia, gastrointestinal irritation, and polyuria or polydipsia; rapidly metabolized in the liver by alcohol dehydrogenase to glycoaldehyde, glycolic acid; glyoxalic acid, and oxalic acid; leads to severe metabolic acidosis and renal epithelial damage.
- Minimum lethal dosage—cats, 1.4 mL/kg; dogs, 6.6 mL/kg.

SYSTEMS AFFECTED

- Gastrointestinal—irritated mucosa.
- Nervous—inebriation from ethylene glycol and glycoaldehyde owing to inhibition of respiration, glucose metabolism, and serotonin metabolism and alteration of amine concentrations.
- Renal/Urologic—initially, osmotic diuresis; later, metabolites, especially calcium oxalate monohydrate crystals, are directly cytotoxic to renal tubular epithelium, resulting in renal failure. The mechanism of toxicity is now thought to involve attachment of oxalate to cell plasma membrane, activation of enzyme activity, and production of free radicals and lipid peroxidation, leading to cell necrosis.

INCIDENCE/PREVALENCE

- Common in small animals.
- Highest fatality rate of all poisons; fatality rates higher for cats than dogs.
- Incidence similar in cats and dogs.

GEOGRAPHIC DISTRIBUTION

Higher incidence in colder areas where antifreeze is more commonly used.

SIGNALMENT

Species

Dogs, cats, and many other species, including birds

Mean Age and Range

- Any age susceptible (3 months–13 years)
- Mean, 3 years

SIGNS

General Comments

- Dose-dependent.
- Almost always acute.
- Caused by unmetabolized ethylene glycol and its toxic metabolites (frequently fatal).

Physical Examination Findings

- Early—from 30 minutes to 12 hours post-ingestion in dogs; nausea and vomiting; mild to severe depression; ataxia and knuckling; muscle fasciculations; nystagmus; head tremors; decreased withdrawal reflexes

and righting ability; polyuria and polydipsia.

- Dogs—with increasing depression, patient drinks less but polyuria continues, resulting in dehydration; CNS signs abate transiently after approximately 12 hours, but recur later.
- Cats—usually remain markedly depressed; do not exhibit polydipsia.
- Oliguria (dogs, 36–72 hours; cats, 12–24 hours) and anuria (72–96 hours post-ingestion)—often develop if untreated.
- May note severe hypothermia.
- Severe lethargy or coma.
- Seizures.
- Anorexia.
- Vomiting.
- Oral ulcers.
- Salivation.
- Kidneys—often swollen and painful, particularly in cats.

CAUSES

Ingestion of ethylene glycol, the principal component (95%) of most antifreeze solutions.

RISK FACTORS

Access to ethylene glycol—widespread availability; somewhat pleasant taste; small minimum lethal dose; lack of public awareness of toxicity.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute (30 minutes–12 hours post-ingestion)—ethanol, methanol, and marijuana toxicosis; ketoacidotic diabetes mellitus; pancreatitis; gastroenteritis.
- Renal stage—acute renal failure by nephrotoxins (e.g., aminoglycoside antibiotics, amphotericin B, cancer chemotherapeutic drugs, ibuprofen, oxalate-containing plants such as philodendrons, plants of the lily family [cats], cyclosporin, grape and raisin toxicosis [causes hypercalcemia, unlike ethylene glycol toxicosis], and heavy metals); leptospirosis, tubulointerstitial nephritis; glomerular and vascular disease; renal ischemia (hypoperfusion).

CBC/BIOCHEMISTRY/URINALYSIS

- PCV and total protein—often high owing to dehydration.
- Stress leukogram—common.
- High BUN and creatinine—dog, 36–48 hours post-ingestion; cat, 12 hours post-ingestion.
- Hyperphosphatemia may occur transiently 3–6 hours post-ingestion, owing to phosphate rust inhibitors in the antifreeze; hyperphosphatemia is also seen with azotemia owing to decreased glomerular filtration.
- Hyperkalemia if oliguric or anuric.
- Hypocalcemia—occurs in approximately half of patients, owing to chelation of calcium by oxalic acid; clinical signs infrequently observed because of acidosis.
- Hyperglycemia—occurs in approximately half of patients, owing to inhibition of glucose metabolism by aldehydes, increased epinephrine and endogenous corticosteroids, and uremia.
- Isosthenuria—by 3 hours post-ingestion,

owing to osmotic diuresis and serum hyperosmolality-induced polydipsia; continues in the later stages of toxicosis because of renal dysfunction.

- Calcium oxalate crystalluria—consistent finding; as early as 3 hours post-ingestion in cats and 6 hours in dogs; monohydrate form is more common.
- Urine—pH consistently decreases; inconsistent findings—hematuria; proteinuria; glucosuria; may note granular and cellular casts, WBCs, RBCs, and renal epithelial cells.

OTHER LABORATORY TESTS

Blood Gases

- Metabolites cause severe metabolic acidosis.
- Total CO₂, plasma bicarbonate concentration, and blood pH—low by 3 hours post-ingestion; markedly low by 12 hours.
- PCO₂—decreases, owing to partial respiratory compensation.
- Anion gap—increased by 3 hours post-ingestion; peaks at 6 hours post-ingestion; remains increased for approximately 48 hours (ethylene glycol metabolites are unmeasured anions). Glycolate, a metabolite of EG, can result in a false increase in plasma lactate, which could lead to the assumption that acidosis is due to increased lactate, rather than EG toxicosis.

Other

- Serum osmolality and osmole gap—high by 1 hour post-ingestion, in parallel with serum ethylene glycol concentrations; dose-related; usually remain high for approximately 18 hours post-ingestion; ethylene glycol toxicosis most common cause of a high osmolal gap.
- EG serum concentration—peaks 1–6 hours post-ingestion; usually not detectable in the serum or urine by 72 hours.
- Commercial kits: PRN Pharmacol REACT EG measures concentrations at > 50 mg/dL; estimate by multiplying the osmole gap by 6.2.
- Test does not detect metabolites so must be used within the first few hours post-ingestion.
- Results are available in 6 minutes but should not be read over 10 minutes.
- Labeled for dogs and cats.
- Some cats may have toxicosis at levels below 50 mg/dL.
- False-positive test results can be seen with propylene glycol, glycerol, mannitol, and sorbitol. Ethanol may combine with propylene glycol or glycerol to give a false positive.
- Woods lamp examination of urine, face, paws, or vomitus may detect fluorescein that is sometimes added to antifreeze. This method is non-specific and may be unreliable.

IMAGING

Ultrasonography—renal cortices may be hyperechoic as a result of crystals.

DIAGNOSTIC PROCEDURES

- Kidney biopsy—with anuria; confirm diagnosis.
- Cytologic examination of kidney imprints—often diagnostic; numerous calcium oxalate crystals.

(CONTINUED)

ETHYLENE GLYCOL TOXICOSIS

E

PATHOLOGIC FINDINGS

- Kidneys often swollen.
- Post-mortem examination of kidney reveals the presence of calcium oxalate crystals in the tubules.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Cats—usually inpatient.
- Dogs—usually outpatient if < 5 hours post-ingestion and treated with fomepizole; inpatient if > 5 hours for intravenous fluids to correct dehydration, increase tissue perfusion, and promote diuresis.

NURSING CARE

- Goals—prevent absorption; increase excretion; prevent metabolism.
- Induction of vomiting and gastric lavage with activated charcoal not recommended unless can be performed in first 30 minutes following ingestion due to the rapid absorption of ethylene glycol.
- Intravenous fluids—correct dehydration, increase tissue perfusion, and promote diuresis; accompanied by bicarbonate given slowly intravenously to correct metabolic acidosis.
- Monitor serial plasma bicarbonate concentrations— $0.5 \times$ body weight (kg) \times (24 – plasma bicarbonate) = sodium bicarbonate needed (mEq).
- Monitor urine pH in response to therapy.
- Azotemia and oliguric renal failure (dogs)—most of the ethylene glycol has been metabolized; little benefit from inhibition of ADH; correct fluid, electrolyte, and acid-base disorders; establish diuresis; diuretics (particularly mannitol) may help; hemodialysis or peritoneal dialysis may be useful; may need extended treatment (several weeks) before renal function is re-established.

SURGICAL CONSIDERATIONS

Kidney transplantation—successfully employed in cats with ethylene glycol-induced renal failure.

**MEDICATIONS****DRUG(S) OF CHOICE****Dogs**

Fomepizole (4-methyl pyrazole; Antizol-Vet)—effective and non-toxic liver ADH inhibitor; more expensive than ethanol but less intensive care required; 5% (50 mg/mL) at 20 mg/kg IV initially; then 15 mg/kg IV at 12 and 24 hours; then 5 mg/kg IV at 36 hours.

Cats

• Fomepizole—cats must be given a higher dose of fomepizole than dogs; 125 mg/kg IV

initially, then 31.25 mg/kg at 12, 24, and 36 hours.

- Ethanol—use if fomepizole not available; 20% at 5 mL/kg diluted in fluids and given in an IV drip over 6 hours for 5 treatments; then over 8 hours for 4 more treatments.

CONTRAINDICATIONS

Avoid drugs that cause CNS depression, including ethanol.

PRECAUTIONS

- Competitive substrates (alcohols, such as ethanol) contribute to CNS depression; monitor respiration.
- Cats may become hypothermic; require heat.
- Other pyrazoles—may be toxic to the marrow and liver; do not substitute for fomepizole.

POSSIBLE INTERACTIONS

- Fomepizole—contributes slightly to CNS depression in cats; none in dogs.
- Ethanol—contributes to CNS depression; further increases serum osmolality.

ALTERNATIVE DRUG(S)

- Ethanol, propylene glycol, and 1,3-butanediol have—higher affinity for ADH than does ethylene glycol; effectively inhibit ethylene glycol metabolism; may cause CNS depression and increase serum osmolality; constant serum ethanol concentrations of 100 mg/dL will inhibit most ethylene glycol metabolism.
- Ethanol treatment requires hospitalization, constant intravenous infusion (ethanol and fluids); continuous monitoring for respiratory and acid-base status.

**FOLLOW-UP****PATIENT MONITORING**

BUN, creatinine, acid-base status, and urine output—monitored daily.

PREVENTION/AVOIDANCE

- Increasing client awareness of the toxicity helps prevent exposure; earlier treatment of patients.
- Use of antifreeze products (e.g., Sierra, Prestone LowTox) that contain propylene glycol, which is much less toxic.

POSSIBLE COMPLICATIONS

- Without azotemia—usually no complications.
- Urine concentrating ability—may be impaired with azotemia; may recover.

EXPECTED COURSE AND PROGNOSIS

- Untreated—oliguric renal failure (dogs, 36–72 hours; cats, 12–24 hours); anuria by 72–96 hours post-ingestion.
- Dogs treated < 5 hours post-ingestion—prognosis excellent

with fomepizole treatment.

- Dogs treated up to 8 hours post-ingestion—most recover.

- Dogs treated up to 36 hours post-ingestion—may be of benefit to prevent metabolism of any remaining ethylene glycol.

- Cats treated within 3 hours post-ingestion—prognosis good.
- If a large quantity of EG is ingested, prognosis is poor, unless treated within 4 hours of ingestion.
- Patients with azotemia and oliguric renal failure—prognosis poor; almost all of the ethylene glycol will have been metabolized.

**MISCELLANEOUS****AGE-RELATED FACTORS**

Patients < 6 months of age with oliguric renal failure sometimes fully recover.

SYNOMYMS

Antifreeze poisoning

SEE ALSO

- Hyperosmolarity • Renal Failure, Acute

ABBREVIATIONS

- ADH = alcohol dehydrogenase
- BUN = blood urea nitrogen
- CNS = central nervous system
- EG = ethylene glycol
- PCV = packed cell volume
- RBC = red blood cell
- WBC = white blood cell

Suggested Reading

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Authors Mary Anna Thrall, Gary D. Osweiler, Gregory F. Grauer, Heather E. Connally, and Sharon M. Dial

Consulting Editor Lynn R. Hovda



Client Education Handout
available online

EXCESSIVE VOCALIZATION AND WAKING AT NIGHTS



BASICS

DEFINITION

- Vocalization that is uncontrollable, excessive, at inappropriate times of day or night or that disrupts owners, neighbors or other animals.
- In night-time waking, the pet wakes during the night, does not fall asleep at bedtime, or awakens early leading to disruption of owner's sleep.

PATHOPHYSIOLOGY

- Varies with cause.
- Barking may be normal canine communication (social, threat, warning, care-soliciting) but unacceptable to owners.
- Owner responses may reinforce or increase anxiety (punishment).
- Cats are crepuscular, so early morning waking may be normal.
- May be due to medical conditions that cause anxiety, discomfort, irritability, or altered sleep-wake cycles.
- Hearing decline may be associated with increased vocalization.
- CDS can lead to sleep disturbances, anxiety and excessive vocalization.
- Night waking may be due to a change in schedule, environment, or activity, especially in senior pets that are more sensitive to change.

SYSTEMS AFFECTED

- Behavioral
- Diseases of other systems may cause or contribute to signs

GENETICS

N/A

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Asian breeds of cats may be prone to excess vocalization.
- Working and hunting breeds may be more prone to barking.

Mean Age and Range

- Puppies may not be able to sleep through the night without waking to eliminate.
- Senior pets may be more prone to vocalization and night waking due to underlying medical conditions.

Predominant Sex

Intact females during estrus and mating

SIGNS

Historical Findings

- Vocalization at times or in intensity that disturbs owners or neighbors.
- Sleeping pattern altered—does not fall asleep at bedtime, awakens during the night, or sleeps more during the day.
- Signs reported vary with how disruptive they are to the family, neighbors, and the pet's quality of life.
- Pets with CDS may pace, wander aimlessly, have decreased interest in social interactions, less responsive to stimuli and increasingly anxious.
- Additional signs related to medical causes.

Physical Examination Findings

Signs associated with underlying medical issues.

CAUSES

- Vocalization and night waking:
Medical—gastrointestinal, metabolic (renal, hepatic), urogenital, CNS disorders, CDS, hyperadrenocorticism or hypothyroidism (dog), hyperthyroidism (cat), pain, sensory decline
- Night waking
 - Anxiety or conflict
 - Normal for individual or breed
 - Alarm barking—response to novel stimuli
 - Territorial—warning or guarding
 - Owner inadvertently reinforces
 - Also reinforced each time stimulus retreats
 - Distress vocalization, e.g., howl or whine may be related to separation from social group
 - Growl—associated with agonistic displays
 - Stereotypic behaviors—dogs
 - Mating/Sexual (cats)

RISK FACTORS

- Increasing age
- Changes in schedule or environment



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Sleep disorders

CBC/BIOCHEMISTRY/URINALYSIS

To determine if underlying medical cause

OTHER LABORATORY TESTS

- T₄—senior cats
- Rule out hypothyroidism and hyperadrenocorticism in dogs

IMAGING

To rule out medical/neurologic if indicated

DIAGNOSTIC PROCEDURES

- Behavioral diagnosis based on history; observation of pet, owner, and their interactions; video if available.
- BAER if indicated to rule out auditory decline.
- Endoscopy and biopsy if GI suspected.

PATHOLOGIC FINDINGS

N/A



TREATMENT

APPROPRIATE HEALTH CARE

If any medical issues

NURSING CARE

If any medical issues

ACTIVITY

Insure behavioral needs are adequately met including sufficient daytime enrichment and programming.

DIET

- Feed from toys (work for food)
- Timed feeders to schedule feedings

CLIENT EDUCATION

Individualize for the pet, home, and problem

BEHAVIOR MODIFICATION

- Identify and minimize or avoid exposure to inciting stimuli.
- Provide a quiet and calm environment for security, rest and sleep.
- Structure all interactions (i.e., calm sit or down for all rewards).
- Reward-based training to teach calm/settle on cue ("Sit," "Down," "Mat").
- Response substitution—Use settle commands to train alternative acceptable behaviour.
- Head halter may provide more immediate control to quiet and calm.
- Eliminate any owner reinforcement.
- Owner anxiety, verbal reprimands, and punishment may increase anxiety and potentiate barking.
- Desensitize and counter-condition—expose the pet to the inciting stimulus at a low level (under the response threshold) and pair a favored reward (e.g., food treat) with each exposure to change the emotional response. Gradually progress to more intense stimulus.
- Devices that disrupt or inhibit vocalization may help to achieve quiet, which can then be reinforced; however, aversive techniques may increase anxiety.

ENVIRONMENTAL MODIFICATION

Modify environment to avoid or minimize exposure to stimuli that incite vocalization or wake the pet, e.g., covered crate, quiet room, thunder cap, classical music, white noise.

(CONTINUED)

EXCESSIVE VOCALIZATION AND WAKING AT NIGHTS**SURGICAL CONSIDERATIONS**

N/A

**MEDICATIONS****DRUG(S) OF CHOICE**

- Short-term or as-needed for situations of anxiety or for inducing sleep
- Benzodiazepines: dog, alprazolam 0.02–0.1 mg/kg; clonazepam 0.05–0.25 mg/kg; diazepam 0.5–2.2 mg/kg; cat, oxazepam 0.2–0.5 mg/kg; alprazolam 0.125–0.25 mg per cat; clonazepam 0.02–0.2 mg/kg
- Trazodone: dog, 3–12 mg/kg
- Melatonin: dog and cat, 3–6 mg (1.5–12 mg)
- For ongoing therapy for chronic anxiety or compulsive disorders: clomipramine (TCA): dog, 1–3 mg/kg PO q12h, cat, 0.5 mg/kg PO q24h; fluoxetine or paroxetine (SSRIs): dog, 1–2 mg/kg PO q24h, cat, 0.5 mg/kg PO q24h.
- Natural products that might be used adjunctively for anxiety: Adaptil, Feliway, l-theanine, alpha-casozepine, HarmonEase, SAMe or aromatherapy (lavender).
- For CDS: selegiline and cognitive supplements (see Cognitive Dysfunction Syndrome).

CONTRAINDICATIONS

Review contraindications and side effects for each drug used.

PRECAUTIONS

- Caution with drugs that might sedate in elderly pets.
- Monitor for undesirable behavioral effects.
- Avoid anticholinergic drugs in pets with CDS.

POSSIBLE INTERACTIONS

Do not use SSRIs and TCAs together with MAOIs such as selegiline and amitraz and use cautiously or avoid with buspirone and tramadol.

ALTERNATIVE DRUGS

- Concurrent sedation with acepromazine 0.5–2.2 mg/kg might be considered but it is not anxiolytic and may increase noise sensitivity and vocalization.
- For a less sedating anxiolytic consider buspirone at 0.5–1 mg/kg (q8–12h in dogs and q12h in cats).
- Analgesics for pain control.
- Gabapentin dog 10–30 mg/kg q8–12h, cat 5–20 mg/kg q8–24h.

**FOLLOW-UP****PATIENT MONITORING**

Modify the program based on response to therapy.

PREVENTION/AVOIDANCE

- Train calm and settle on cue (sit, down, go to mat).
- Predictable interactions, e.g., insure calm sit or down before any reward given.
- Reward desirable, do not punish undesirable behavior.
- Socialize and habituate pet when young to a wide range of people, pets, stimuli, and environments.
- Provide enrichment and scheduling to meet needs.

POSSIBLE COMPLICATIONS

- Night-time waking can lead to fatigue, increased irritability, and possibly aggression.
- Both night waking and vocalization can be particularly distressing to the pet owner's health and well-being and greatly weaken the bond.

EXPECTED COURSE AND PROGNOSIS

- Variable—based on diagnosis, environment, pet, and owner expectations.
- Most can be improved over time but might not eliminated.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

CDS

AGE-RELATED FACTORS

Increased anxiety and night waking more common in senior pets.

E

ZOONOTIC POTENTIAL

None but sleep disruption and anxiety in pets can contribute to sleep disruption and anxiety in the owners.

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

Sleep disturbances

SEE ALSO

- Cognitive Dysfunction Syndrome
- Compulsive Disorders—Cats
- Compulsive Disorders—Dogs
- Separation Distress Syndrome

ABBREVIATIONS

- BAER = brainstem auditory evoked response
- CDS = cognitive dysfunction syndrome
- CNS = central nervous system
- MAOI = monoamine oxide inhibitors
- SAMe = S-adenosyl-L-methionine-tosylate disulfate
- SSRI = selective serotonin reuptake inhibitor
- T₄ = thyroxine
- TCA = tricyclic antidepressant

Suggested Reading

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Authors Sagi Denenberg and Gary M.

Landsberg

Consulting Editor Gary M. Landsberg

EXERCISE-INDUCED WEAKNESS/COLLAPSE IN LABRADORS



BASICS

OVERVIEW

Inherited disorder causing weakness and collapse during intensive exercise in otherwise normal Labrador retrievers.

E

SIGNALMENT

- Labrador retrievers—nearly 10% of all pet, show, and field Labrador retrievers are affected.
- Also seen in Chesapeake Bay retrievers, curly-coated retrievers, Boykin spaniels and rarely in Old English sheepdogs, German wirehaired pointers, Bouvier des Flandres, Pembroke Welsh corgis, and cocker spaniels.
- Signs typically become apparent between 5 months and 3 years of age (average 12 months).
- No sex or color predilection.

SIGNS

General Comments

- No systemic signs.
- Collapse episodes are typically infrequent and occur only with extremes of exercise and excitement.
- Dogs can engage normally in hiking, swimming, jogging, and other activities that are not associated with a high level of excitement or stress.
- Symptomatic dogs are commonly reported to have an excitable temperament.

Physical Examination Findings

Between weakness/collapse episodes, physical and neurologic examinations are normal.

Features of Weakness/Collapse Episodes

- Weakness occurs after 5–20 minutes of intense exercise with excitement or stress.
- First abnormality noticed is a rocking or forced gait.
- The rear limbs become weak and unable to support weight.
- Many dogs will continue to run, dragging their rear limbs in a crouched posture.
- During a severe episode, all four limbs can be affected and rarely the dog may become recumbent and unable to move its limbs or raise its head.
- Some dogs are uncoordinated with a wide-based stance, and falling to the side during recovery from an episode.
- Dogs remain conscious and fully alert during the episodes.
- Rear limb muscles are flaccid during collapse and there is a loss of patellar reflexes.
- There may be increased extensor tone in the forelimbs of some collapsed dogs when they are lying in lateral recumbency.
- There is no apparent pain or discomfort on palpation or manipulation of the muscles, joints, or spine during or after collapse.

- Complete recovery occurs within 5–30 minutes.
- Rectal temperature is elevated (mean $> 107^{\circ}\text{F}$; $> 41.6^{\circ}\text{C}$) but not different from Labradors without exercise-induced collapse doing similar exercise.
- A few dogs with EIC have died during collapse—death is usually preceded by a short generalized seizure. The cause of death is uncertain but weakness of the respiratory muscles and extreme hyperthermia are suspected.

CAUSES

- Genetic disorder— inherited as an autosomal recessive trait.
- Symptomatic dogs—homozygous for a mutation in the dynamin 1 gene. Dynamin 1 (*DNM1*) is a protein important in neurotransmission in the brain and spinal cord during high-level neuronal activity. Evidence that the *DNM1* mutation associated with EIC has its most profound effect on DNM1 function when body temperature is elevated, as normally occurs with exercise.

RISK FACTORS

- Genetically affected dogs are at risk for collapse when participating in high-intensity exercise with concurrent excitement or stress.
- Affected dogs with a sedentary lifestyle or calm temperament may never exhibit weakness or collapse but most genetically affected dogs (> 80%) will have at least one episode of collapse before they reach 3 years of age.
- Collapse only occurs during specific trigger activities associated with a high level of excitement or anxiety.
- Trigger activities most likely to induce collapse include repetitive fun or training retrieves, upland bird hunting, intense play with other dogs, and running alongside an all-terrain vehicle.
- Increased ambient temperature and humidity seem to increase the risk of collapse in affected dogs.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- The episodic nature of the collapse, association with exercise and excitement, typical features of collapse including rear limb weakness and normal mentation, progression of weakness during an episode, and rapid complete recovery should lead to a presumptive diagnosis of EIC in an otherwise healthy Labrador retriever. Physical and neurologic examinations are normal; further evaluation is required to eliminate other causes of weakness and collapse and to confirm genetic susceptibility to collapse caused by EIC.
- Dogs with metabolic myopathies, polymyositis, and myasthenia gravis are typically much more exercise intolerant than dogs with EIC and they will collapse with mild exercise of short duration.
- Centronuclear myopathy (previously called hereditary Labrador retriever myopathy or Type II myofiber deficiency)—inherited muscle disorder in Labrador retrievers that causes generalized muscle atrophy, constant weakness that worsens with exercise, and absent patellar reflexes at rest. Diagnosis of this disorder is by muscle biopsy or DNA testing (www.labradorcnm.com).
- Cardiac arrhythmia—as a cause of exercise intolerance can be ruled-out by cardiac auscultation, palpation of femoral pulses and performing an ECG at rest and during collapse. Holter monitor or an ECG event recorder may be required to rule out intermittent cardiac arrhythmia as a cause of collapse.
- Pulmonary hypertension—can cause exercise intolerance and syncopal episodes as exercise and excitement increase systolic pressure in an already overloaded right ventricle and pulmonary arteries, resulting in reflex bradycardia, vasodilation, and hypotension.
- Hypoglycemia—ruled out by measuring blood glucose during an episode.
- Hypo- or hyperkalemia—ruled out by measuring potassium during collapse.
- Hypoadrenocorticism (Addison's disease)—can cause exercise induced hypoglycemic collapse or seizures; should be ruled-out with ACTH stimulation test.
- Seizures—abrupt in onset and usually associated with altered or loss of consciousness, convulsive activity, rapid recovery and postictal signs.
- Atypical epilepsy/paroxysmal dyskinesia—brief episodes of abnormal crouched gait, disequilibrium, head-bobbing, or incoordination can be seen in Labrador retrievers as a seizure or movement disorder. Episodes may be induced by exercise/excitement in some dogs, leading to confusion with EIC. The onset of signs is peracute, the episodes are short (usually less than 5 minutes), all limbs are involved, and recovery is immediate, helping to distinguish this disorder from the more progressive gait disturbance caused by EIC. Diagnosis can only be made by ruling out other disorders (including EIC) with testing.
- Cataplexy—peracute, non-progressive, brief episodes of flaccid paralysis.
- Heat stroke—collapse due to heat stroke is usually associated with bleeding, shock, and abnormal mentation. Acute renal failure, DIC, and death are common. Recovery, if it does occur, is prolonged.
- Malignant hyperthermia—hypermetabolic state triggered by certain anesthetics, extreme

(CONTINUED) EXERCISE-INDUCED WEAKNESS/COLLAPSE IN LABRADORS

E

heat, intense activity, or psychological stress in genetically susceptible dogs. Hyperthermia, generalized skeletal muscle contraction, rhabdomyolysis, and DIC occur and many dogs die. Recovery, if it does occur, is prolonged. In vitro contracture tests on muscle biopsies or identification of the causative genetic mutation of the ryanodine receptor (*RYR1*) is required for diagnosis.

CBC/BIOCHEMISTRY/URINALYSIS

Normal at rest and during collapse

OTHER LABORATORY TESTS

- Arterial blood gas—normal at rest, extreme respiratory alkalosis and mild metabolic acidosis during collapse identical to intensively exercising Labradors without EIC.
- Lactate and pyruvate—normal at rest, not consistently different during collapse from exercising Labradors without EIC.
- Thyroid evaluation—normal.
- ACTH stimulation test—normal.
- Analysis for mutation in the ryanodine receptor (*RYR1*) causing malignant hyperthermia—negative.
- Testing for acetylcholine receptor antibodies causing acquired myasthenia gravis—negative.

IMAGING

Thoracic and abdominal radiographs, abdominal ultrasound, echocardiography—normal.

DIAGNOSTIC PROCEDURES

ECG findings at rest and during collapse—normal.

DNA Testing

- Definitive diagnosis requires demonstration that a dog has two copies of the *DNM1* mutation.
- Testing can be performed on blood, cheek swabs, puppy dewclaws, or semen.
- Approximately 10% of all tested Labrador retrievers have two copies of the *DNM1* mutation (affected); > 30% of all tested Labrador retrievers have one copy of the *DNM1* mutation (carrier).
- Finding two copies of the *DNM1* mutation confirms that a dog is EIC affected but does not necessarily rule out other causes of exercise intolerance or collapse. It is important to do the necessary tests to rule out other causes of collapse that may be potentially more treatable.

PATHOLOGIC FINDINGS

- Muscle histology—normal.
- Complete post-mortem examinations of dogs dying during collapse due to EIC—normal.

**TREATMENT****ACTIVITY**

Most affected dogs can live normal active lives if specific trigger activities are avoided or done in moderation.

CLIENT EDUCATION

- Signs commonly worsen in the 3–5 minutes after exercise is terminated; some (< 5%) affected dogs die during collapse.
- All activity should be halted at the first sign of weakness or incoordination.
- Consider offering cool water orally, spraying with water, or immersing in water to lower body temperature.

SURGICAL CONSIDERATIONS

Some male dogs have experienced fewer episodes of collapse following neutering.

**MEDICATIONS****DRUG(S)**

There is no recommended drug therapy for this disorder. Treatment with phenobarbital or sedatives may decrease the excitement level in affected dogs, making them less likely to collapse, but this response is not consistent. Owners are advised to limit participation in trigger activities rather than chronically medicating their dogs.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS**FOLLOW-UP**

Most affected dogs can be managed effectively by avoiding trigger activities and carefully observing for the first signs of weakness.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Dogs with EIC do not develop other associated medical conditions as they age.

AGE-RELATED FACTORS

Episodes of collapse may become less frequent as dogs age, perhaps because of less excitement associated with trigger activities.

PREGNANCY/FERTILITY/BREEDING

- Animals should be tested to establish their EIC status prior to breeding.
- Affected dogs (with two copies of the *DNM1* mutation) should not be bred or should be bred only to known non-carriers to avoid producing affected offspring.
- Carrier dogs (with one copy of the *DNM1* mutation) should only be bred to known non-carriers to avoid producing affected offspring.

ABBREVIATIONS

- ACTH = adrenocorticotropin hormone
- DIC = disseminated intravascular coagulation
- *DNM1* = dynamin 1
- ECG = electrocardiogram
- EIC = exercise-induced collapse
- *RYR1* = ryanodine receptor

INTERNET RESOURCES

Answers to frequently asked questions and instructions for sample submission for DNA testing—website University of Minnesota Veterinary Diagnostic Laboratory: <http://www.cvm.umn.edu/vdl/ourservices/canine neuromuscular/home.html>.

Suggested Reading

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EXOCRINE PANCREATIC INSUFFICIENCY



BASICS

DEFINITION

Syndrome that is caused by inadequate amounts of pancreatic digestive enzymes in the small intestinal lumen.

E

PATHOPHYSIOLOGY

- Most commonly caused by insufficient synthesis and secretion of pancreatic enzymes from the exocrine pancreas.
- In rare cases can be caused by an obstruction of the pancreatic duct.
- Insufficient synthesis of pancreatic digestive enzymes can be due to destruction of acinar cells resulting from chronic pancreatitis (approximately 50% of cases in dogs and almost all cases in cats) or can be due to idiopathic pancreatic acinar atrophy (PAA; most common cause of exocrine pancreatic insufficiency in German shepherd dogs).
- Deficient exocrine pancreatic secretion results in maldigestion and nutrient malabsorption, leading to weight loss and loose stools with steatorrhea.
- Malabsorption contributes to small intestinal dysbiosis.

SYSTEMS AFFECTED

Nutritional—protein-calorie malnourishment.

GENETICS

Assumed to be hereditary in the German shepherd dog and probably transmitted by a complex trait (early studies have suggested an autosomal recessive trait, but this has not been substantiated).

INCIDENCE/PREVALENCE

- PAA is very commonly seen in the German shepherd dog. PAA is less commonly seen in rough-coated collies and Eurasians.
- Other causes of EPI may be seen in all dog and cat breeds.
- Less common in cats than in dogs.

GEOGRAPHIC DISTRIBUTION

SIGNALMENT

Species

Dog and cat

Breed Predilections

German shepherd dogs, rough-coated collies, and Eurasians

Mean Age and Range

- Pancreatic acinar atrophy in young adult dogs.
- Chronic pancreatitis in dogs and cats of any age.

SIGNS

General Comments

- Consider in young adult (age range approximately 1–4 years) German shepherd dogs with weight loss and loose stools.
- Severity—varies depending on the time until diagnosis and therapy.

Historical Findings

- Weight loss with a normal to increased appetite.
- Chronically loose stools or

diarrhea.

- Diarrhea often resembles cow feces and may be continuous or intermittent.
- Fecal volumes are larger than normal and may be associated with steatorrhea.
- Flatulence and borborygmus are common, especially in dogs.
- May show coprophagia and/or pica.
- May be accompanied by polyuria/polydipsia with diabetes mellitus as a sequel to chronic pancreatitis.

Physical Examination Findings

- Thin body.
- Decreased muscle mass.
- Poor-quality hair coat.
- Cats with steatorrhea may have greasy “soiling” of the hair coat in the perineal area, but this is seen in the minority of cases.

CAUSES

- Pancreatic acinar atrophy
- Chronic pancreatitis
- Pancreatic adenocarcinoma leading to pancreatic duct obstruction

RISK FACTORS

- Breed—German shepherd dogs, rough-coated collies, and Eurasians
- Any condition predisposing dogs or cats to chronic pancreatitis



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Secondary causes of chronic diarrhea and weight loss (e.g., hepatic failure, renal failure, hypoadrenocorticism, and hypothyroidism in dogs or hyperthyroidism in cats).
- Primary gastrointestinal disease (i.e., infectious, inflammatory, neoplastic, mechanical, or toxic).

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

Direct/Indirect Fecal Examinations

Negative for parasites

Exocrine Pancreatic Function Tests—Trypsin-Like Immunoreactivity

- Diagnostic test of choice in both dogs and cats.
- Principle of test—serum TLI can be measured by an assay that detects trypsinogen and trypsin that is directly released into the blood from pancreatic acinar tissue; serum TLI is detected in the serum of all normal dogs and cats with a functional exocrine pancreatic mass.
- Serum TLI concentrations are dramatically reduced with EPI.
- In dogs—cTLI $\leq 2.5 \mu\text{g/L}$.
- In cats—fTLI $< 8.0 \mu\text{g/L}$.
- Canine and feline TLI tests are species-specific.
- Advantages—simple; quick; single serum specimen (fasted); highly sensitive and specific for EPI in both species.

Other Exocrine Pancreatic Function Tests

- Assays of fecal proteolytic activity using casein-based substrates have been used to diagnose EPI in both dogs and cats. However,

fecal proteolytic activity is associated with false-positive and false-negative test results and should only be used in exotic species for which a serum TLI test is not available.

- An assay for the measurement of fecal elastase has recently been validated for the dog. However, this test is associated with high rate of false-positive test results and can not be recommended at this point. A positive test result, suggesting EPI, must be verified by measurement of a serum cTLI concentration.

Screening Tests for Malassimilation

Microscopic examination of feces for undigested food, assessment of fecal proteolytic activity and the plasma turbidity test are unreliable and *not* recommended.

Cobalamin and Folate

- Often run as a panel with TLI.
- Used to assess for concurrent dysbiosis or concurrent small intestinal disease (such as IBD).
- Cobalamin (vitamin B₁₂) is frequently deficient in both dogs and cats with EPI and can lead to treatment failure or complications if not addressed.

IMAGING

Abdominal radiography and ultrasonography are unremarkable unless the patient has additional conditions.

PATHOLOGIC FINDINGS

- Chronic pancreatitis—microscopically, acini and possibly islets are depleted and replaced by fibrous tissue. There may also be an active infiltrative infiltration.
- Pancreatic acinar atrophy—marked atrophy/absence of pancreatic acinar tissue on gross and histopathologic inspection in dogs with PAA.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient medical management.
- Patients with concurrent diabetes mellitus may initially require hospitalization for insulin regulation of hyperglycemia.

DIET

- Supplementation of the diet with pancreatic enzyme replacement is the mainstay of therapy.
- The type of diet does not play a role in the management of EPI in dogs and cats.
- However, low-fat and high-fiber diets should be avoided.
- Approximately 80% of all dogs with EPI and virtually all cats with EPI are cobalamin deficient and require cobalamin supplementation (pure injectable cobalamin at 250 µg/injection in cats and 250–1,500 µg/injection in dogs; once a week for 6 weeks, one more dose a month after that, and a recheck of serum cobalamin concentration a month after the last dose).
- Severely malnourished dogs may also require supplementation with tocopherol.

(CONTINUED)

EXOCRINE PANCREATIC INSUFFICIENCY

E

Body stores of other fat-soluble vitamins are probably also decreased in dogs and cats with EPI, but supplementation does not appear to be crucial.

CLIENT EDUCATION

- Discuss hereditary nature in German shepherd dogs.
- Discuss expense of pancreatic enzyme supplementation and need for life-long therapy.
- Discuss the possibility of diabetes mellitus in patients with chronic pancreatitis.

SURGICAL CONSIDERATIONS

Mesenteric torsion has been reported in German shepherd dogs with EPI in Finland but not North America.



MEDICATIONS

DRUG(S) OF CHOICE

- Powdered, pancreatic enzymes are the treatment of choice.
- Initially—mix enzyme powder in food at a dosage of 1 teaspoon/10 kg body weight with each meal; feed at least two meals daily to promote weight gain.
- Preincubation of enzymes with food does *not* improve the effectiveness of oral enzyme therapy.
- Cobalamin supplementation is crucial if the patient is cobalamin deficient.
- Administration of a proton pump inhibitor (e.g., omeprazole at 0.7–1.0 mg/kg q12h) may improve the condition in non-responsive patients.
- Most dogs and cats respond to therapy within 5–7 days. After a complete response has been achieved the amount of the pancreatic enzyme supplement may be gradually reduced to a dose that prevents return of clinical signs.
- Oral antibiotic therapy (tylosin, 25 mg/kg PO q12h) may be required for 4–6 weeks in patients with concurrent dysbiosis, but in most patients dysbiosis resolves spontaneously upon commencement of enzyme replacement therapy.

CONTRAINDICATIONS

Avoid tablets and capsules as mixing of enzymes and chyme is unpredictable.

ALTERNATIVE DRUG(S)

- The cost of pancreatic enzyme replacement is very high. Also, some cats refuse to consume the pancreatic enzyme supplement. These patients can often be successfully managed by administration of raw beef, pork, or game pancreas.
- Each teaspoon of

pancreatic enzyme supplement needs to be replaced with 1–3 ounces (approximately 30–90 g) of raw chopped pancreas.

- Raw pancreas can be kept frozen for months without losing enzymatic activity.



FOLLOW-UP

PATIENT MONITORING

- Weekly for first month of therapy.
- Diarrhea improves markedly—fecal consistency typically normalizes within 1 week.
- Gain in body weight.
- Patients that fail to respond after 2 weeks of enzyme therapy and cobalamin supplementation if indicated should be placed on antibiotics for concurrent dysbiosis.
- Once body weight and conditioning normalize, gradually reduce the daily dosage of enzyme supplements to a level that maintains normal body weight.

PREVENTION/AVOIDANCE

Do not breed patients that belong to a breed predisposed to pancreatic acinar atrophy.

POSSIBLE COMPLICATIONS

- Approximately 20% of dogs fail to respond to pancreatic enzymes and need further evaluation and therapy.
- Most patients with EPI have cobalamin deficiency and need to be managed accordingly.
- Some dogs treated with pancreatic enzyme supplements develop oral ulcerations. In most of these dogs the dose of pancreatic enzyme supplements can be decreased, while maintaining therapeutic response. In a few patients, the dose of the pancreatic enzyme supplement needs to be adjusted frequently to avoid treatment failure and oral ulceration.

EXPECTED COURSE AND PROGNOSIS

- Most causes are irreversible, and life-long therapy is required.
- Patients with EPI alone have a good prognosis with appropriate enzyme supplementation and supportive management.
- Prognosis is more guarded in patients with EPI and concurrent diabetes mellitus.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Dysbiosis.
- Inflammatory bowel disease.

- Diabetes mellitus.
- Associated vitamin K-responsive coagulopathy has been reported in two cats.

AGE-RELATED FACTORS

Consider EPI in young adult dogs with weight loss and loose stools.

PREGNANCY/FERTILITY/BREEDING

Do not breed animals with EPI suspected to be due to PAA.

SYNONYMS

- None

SEE ALSO

- Diarrhea, Chronic—Cats
- Diarrhea, Chronic—Dogs
- Pancreatitis—Canine
- Pancreatitis—Feline

ABBREVIATIONS

- cTLI = canine trypsin-like immunoreactivity
- EPI = exocrine pancreatic insufficiency
- fTLI = feline trypsin-like immunoreactivity
- IBD = inflammatory bowel disease
- PAA = pancreatic acinar atrophy

INTERNET RESOURCES

www.vetmed.tamu.edu/gilab

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Client Education Handout
available online

EYELASH DISORDERS (TRICHIASIS/DISTICHIASIS/ECTOPIC CILIA)



BASICS

OVERVIEW

- Trichiasis—when hair arising from normal skin contacts the corneal or conjunctival surfaces.
- Distichiasis—when extra lashes emerge from or near the meibomian gland orifices on the lid margin; these hairs may or may not contact the cornea.
- Ectopic cilia—single or multiple hairs that arise from the palpebral conjunctival surface several millimeters from the lid margin, most commonly near the middle of the superior lid. Occasionally ectopic cilia can arise on the back of the third eyelid.

SIGNALMENT

- Common in dog; rare in cat.
- Most common in young dogs.
- Any breed may be affected.
- Trichiasis: (a) facial fold trichiasis—common in brachycephalic breeds with prominent facial folds (e.g. Pekingese, pug and bulldog); (b) eyelid agenesis—sporadic. Usually bilateral at lateral aspect of upper lids in cats. Often associated with concurrent intraocular abnormalities;
- (c) entropion—conformational entropion is common in young dogs in predisposed breeds (Shar Pei, retriever, Chow Chow, among many others). Can be associated with blepharospasm (spastic entropion), scarring (cicatricial entropion), or enophthalmos; occasionally seen in cats.
- Distichiasis—predisposed breeds include cocker spaniel, American water spaniel, English bulldog, beagle, flat-coated retriever and dachshund. Dogs with distichiasis are also prone to have ectopic cilia. Rare in cats.
- Ectopic cilia—predisposed breeds include Pekingese, shih tzu and English bulldog.

SIGNS

Facial-Fold Trichiasis

- Epiphora.
- Pigmentary keratitis (especially nasally).
- Often associated with lagophthalmos.
- Occasional blepharospasm, especially if ulcerative keratitis is present.

Eyelid Agenesis

- Keratitis, including ulcerative keratitis
- Lagophthalmos
- Blepharospasm

Entropion

- Blepharospasm
- Epiphora
- Keratitis, including ulcerative keratitis

Distichiasis

- Usually asymptomatic.
- Stiff, stout cilia contacting the cornea—may note blepharospasm, epiphora, pigmentary and ulcerative keratitis.

Ectopic Cilia

- Severe blepharospasm.
- Epiphora.
- Superficial corneal ulcers with a rounded appearance (corresponding to lid movement) on the superior cornea; resistant to healing or

recurrent until the underlying problem is corrected.

CAUSES & RISK FACTORS

Usually related to facial conformation or breed predisposition, or is idiopathic.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Secondary to other adnexal abnormalities (e.g., entropion, eyelid agenesis).
- Keratoconjunctivitis sicca.
- Conjunctival foreign body.
- Infectious conjunctivitis.
- Diagnosis based on direct observation of abnormal cilia and lid conformation.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

TRICHIASIS

- May be managed conservatively in some patients by protecting the cornea with topical lubricating ointments.
- Clipping the hair on facial folds may cause these hairs to become stiffer and more irritating.
- Surgical correction of adnexal abnormalities.
- May resect facial folds.
- Medial canthoplasty—often an effective procedure for nasal trichiasis; also eliminates lagophthalmos and medial entropion.
- Entropion repair.
- Repair of eyelid agenesis or treat distichiasis as noted below.
- Treat underlying cause (e.g., spastic entropion, enophthalmia).

DISTICHIASIS

- Usually asymptomatic and requires no treatment.
- Symptomatic—may treat surgically by cryoepilation, electroepilation, transconjunctival electrocautery and periodic manual epilation.
- Lid-splitting and partial tarsal plate excision techniques—avoid; postoperative scarring may predispose patient to cicatricial entropion and impaired lid function.

ECTOPIC CILIA

- May be treated surgically—en-bloc resection of the cilia and associated meibomian gland.
- Cryotherapy—may be used as the sole treatment or as an adjunct after surgical resection.
- May develop ectopic cilia at other locations.
- Recheck patient if clinical signs recur.



MEDICATIONS

DRUG(S)

- Rarely indicated.
- Lubricant ointments—sometimes valuable to soften cilia and lessen irritation before surgical correction.
- Soft contact lens—sometimes can use temporarily to relieve clinical signs before surgical correction.
- Topical antibiotics—perioperative; recommended for patients undergoing surgery to minimize conjunctival flora in the surgical sites.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- Trichiasis—good prognosis when treated appropriately. Some corneal changes may be permanent (i.e., scarring, pigmentary keratitis).
- Distichiasis—regrowth can occur because destructive procedures must be done conservatively to minimize lid damage.
- Ectopic cilia—good prognosis. Occasionally adjacent hair follicles may not be visible at the first treatment session, or the germinal bud may not be destroyed and the hair shaft may regrow. Affected animals should not be used for breeding, especially breeds with low numbers of affected dogs.



MISCELLANEOUS

Suggested Reading

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FACIAL NERVE PARESIS AND PARALYSIS



BASICS

DEFINITION

Dysfunction of the facial nerve (CN VII) causing paresis (weakness) or paralysis of the muscles of facial expression, which include the ears, eyelids, lips, and nostrils.

PATHOPHYSIOLOGY

- Central—impairment of the facial nucleus within the rostral medulla (brainstem).
- Peripheral—impairment of the facial nerve anywhere along its length or at the neuromuscular junction.

SYSTEMS AFFECTED

- Nervous—facial nerve peripherally or its nucleus centrally.
- Ophthalmic—if parasympathetic preganglionic neurons that supply the lacrimal gland and gland of the third eyelid that course with the facial nerve proximally are affected, keratoconjunctivitis sicca develops due to lack of tear secretion.

GENETICS

N/A

INCIDENCE/PREVALENCE

More common in dog than cat

SIGNALMENT

Species

Dog and cat

Breed Predilections

Idiopathic paralysis—cocker spaniel, beagle, Pembroke Welsh corgi, boxer, English setter, golden retriever, and domestic longhair cats

Mean Age and Range

Adults

Predominant Sex

N/A

SIGNS

General Comments

- Assess strength of palpebral closure—there should be full eyelid closure when a finger is gently passed over the eyelids.
- Idiopathic—unaffected side may become affected within a few weeks to months; may rarely occur bilaterally at first presentation.
- Most patients with bilateral nerve involvement have polyneuropathy-associated systemic disease—look for other nerve deficits.
- May accompany other clinical signs and/or neurologic deficits—always perform a full neurologic examination.
- Ear droop is not always evident in cats and dogs with erect ears.

Historical Findings

- Messy eating; food left around mouth
- Excessive drooling on the affected side
- Facial asymmetry
- Eye—inability to close eyelids, rubbing, ocular discharge, ulceration

Physical Examination Findings

- Facial asymmetry—lip and ear droop, wide palpebral fissure, collapse of nostril.
- Decreased or absent palpebral reflex.
- Decreased or absent menace response (may see eye retraction rather than lid closure).
- Inability to close the eyelids.
- Excessive drooling or food falling from mouth on the affected side.
- Chronically, patients may have facial muscle contraction toward the affected side due to muscle fibrosis subsequent to paralysis and denervation.
- Decreased Schirmer tear test, mucopurulent discharge from the affected eye and exposure conjunctivitis or keratitis with concurrent keratoconjunctivitis sicca.
- Altered mentation (e.g., somnolence or stupor) and/or other cranial nerve abnormalities and gait disturbances may be noted when secondary to intracranial (brainstem) disease.
- Hemifacial spasms (facial nerve tetanus) may be infrequently observed in lesions affecting the facial nerve such as neuritis or otitis media. These patients have sustained contraction of the facial muscles giving a “grinning” appearance to the affected side of the face. This is a dynamic process and at times the face will appear normal, only to begin the “grinning” appearance once again. If one notices this clinical presentation, middle ear disease should be investigated thoroughly.
- Intermittent facial paresis can be observed in patients with a contralateral thalamocortical lesion when the patient is relaxed—due to “release” of the upper motor neuron influence on the lower motor neuron (CN VII).

CAUSES

Unilateral Peripheral

- Idiopathic
- Metabolic—hypothyroidism
- Infectious—otitis media-interna (dogs and cats)
- Inflammatory—nasopharyngeal polyps (cats), neuritis
- Iatrogenic—secondary to surgical ablation of external ear canal or bulla osteotomy; secondary to exuberant ear cleaning; idiosyncratic reaction to potentiated sulfonamides (dogs)
- Neoplastic—aural cholesteatoma, squamous cell carcinoma
- Trauma—fracture of the petrous temporal bone, direct injury to the facial nerve by laceration or compression by hematoma or other mass
- Toxic—tick bite paralysis (*Dermacentor* spp. (humans), *Ixodes holocyclus*)

Bilateral Peripheral

- Idiopathic—polyradiculoneuritis (coonhound paralysis)
- Immune-mediated—polyradiculoneuritis, polyneuropathy, myasthenia gravis

- Metabolic—paraneoplastic polyneuropathy (e.g., insulinoma)
- Toxic—botulism

CNS

- Most unilateral
- Infectious—viral, bacterial, fungal, rickettsial, protozoal encephalitis
- Inflammatory—granulomatous granulomatous meningoencephalitis (GME)
- Neoplastic—primary such as meningioma, choroid plexus tumor; metastatic tumor such as hemangiosarcoma, carcinoma, lymphoma

RISK FACTORS

Chronic otitis externa and otitis media



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Differentiate unilateral from bilateral involvement.
- Look for other neurologic deficits—behavior change, gait disturbance, other CN deficits.
- Idiopathic—diagnosis of exclusion; no historical or physical signs of ear disease and no other neurologic deficits.
- Hypothyroidism—with clinical evidence (e.g., lethargy, poor hair coat, weight gain, anemia, hypercholesterolemia, etc.).
- Otitis media-interna—Horner’s syndrome, head tilt, and KCS may be simultaneously present.
- CNS disease—if there is somnolence, gait disturbances or other CN deficits.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal in idiopathic facial paralysis.
- Fasting hypercholesterolemia, normocytic/normochromic non-regenerative anemia may be observed with hypothyroidism-associated facial paralysis.
- Hypoglycemia with insulinoma.

OTHER LABORATORY TESTS

- Indicated for patients with suspected underlying disease
- Insulin:glucose ratio to detect insulinoma
- Acetylcholine receptor antibodies to diagnose myasthenia gravis
- Total T4 and canine TSH to diagnose hypothyroidism

IMAGING

- CT—sensitive to evaluate middle-inner ear diseases, preferred modality to evaluate bony structures in middle ear.
- MRI—superior to CT for intracranial imaging, preferable for CNS disease; contrast enhancement of facial nerve in dogs with idiopathic facial nerve paralysis; the greater the extent of enhancement, the poorer the prognosis for return to function.
- Bulla radiographs—(four views; two obliques, 30° open mouth, dorso-ventral) not sensitive for middle-inner ear diseases.

FACIAL NERVE PARESIS AND PARALYSIS

(CONTINUED)

DIAGNOSTIC PROCEDURES

- Schirmer test—evaluate tear production (normal > 15 mm in 60 seconds), should always be performed when evaluating a patient with facial paresis/paralysis.
- Fluorescein test—evaluate for presence of corneal ulceration secondary to KCS.
- Otoscopic examination—evaluate integrity of tympanic membrane and for evidence of otitis media.
- CSF—evaluate for evidence of intracranial disease; not sensitive if used alone, should be combined with diagnostic imaging (e.g., MRI).
- Facial muscle electromyography—evaluate for denervation and neuromuscular disease.
- Facial and trigeminal nerve reflex electrodiagnostic testing—evaluate peripheral nerve integrity, distinguish between peripheral and central lesions.

PATHOLOGIC FINDINGS

Idiopathic—may see degeneration of large and small myelinated fibers without evidence of inflammation.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—idiopathic facial paralysis
- Inpatient—initial medical workup and management of systemic or CNS disease if present

NURSING CARE

N/A

ACTIVITY

N/A

DIET

No change required

CLIENT EDUCATION

- Clinical signs may be permanent; however, as muscle fibrosis develops, there is a natural “tuck up” of the affected side that reduces asymmetry; drooling usually stops within 2–4 weeks.
- Inform client that the other side can become affected.
- Discuss eye care—the cornea on the affected side may need lubrication, extra care may be needed if the animal is a breed with natural exophthalmia, client must regularly check eyes for redness, discharge or pain.
- Inform client that most animals tolerate this nerve deficit well; there is no significant impact on quality of life.

SURGICAL CONSIDERATIONS

Bulla osteotomy may be indicated for patients with disorders of the middle ear.



MEDICATIONS

DRUG(S) OF CHOICE

- Treat specific disease if possible (e.g., thyroxine for hypothyroidism).
- Idiopathic disease—no treatment required; efficacy of corticosteroids unknown although used commonly in humans to treat Bell's palsy.
- Tear replacement if Schirmer test value low (< 15 mm), in patients with KCS or with exophthalmic globes.

CONTRAINdications

If middle ear disease is suspected, and the tympanic membrane may be ruptured, do not use topical ear cleaning solutions due to risk of ototoxicity.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Reevaluate early for evidence of corneal ulcers.
- Reassess monthly (for 2–3 months) for menace responses, palpebral reflexes, and lip and ear movements to evaluate return of function, condition of affected eye and development of other neurologic deficits that would indicate progressive disease.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- KCS
- Corneal ulcers
- Severe contracture on side of lesion
- Permanent facial asymmetry (aesthetic only)

EXPECTED COURSE AND PROGNOSIS

- Depends on underlying cause if one is present.
- Idiopathic disease—prognosis guarded for full recovery.
- Improvement may take weeks or months or may never occur.
- Lip contracture sometimes develops.
- Corneal ulcers may perforate and require enucleation.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Facial neuritis
- Facial palsy
- Idiopathic facial neuropathy

SEE ALSO

- Hypothyroidism
- Keratitis, Ulcerative
- Keratoconjunctivitis Sicca
- Otitis Media and Interna

ABBREVIATIONS

- CN = cranial nerve
- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- GME = granulomatous meningoencephalitis
- KCS = keratoconjunctivitis sicca
- MRI = magnetic resonance imaging

Suggested Reading

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Client Education Handout
available online

FALSE PREGNANCY



BASICS

DEFINITION

- Physical and behavioral changes resulting from normal hormonal changes during diestrus and early anestrus in the non-pregnant bitch. The term false pregnancy is a misnomer, since the pattern of hormonal changes is normal.
- Physical, hormonal, and behavioral changes following a non-fertile mating or spontaneous ovulation in the queen.

PATHOPHYSIOLOGY

- Hormone profile of pregnant and non-pregnant bitch very similar following ovulation.
- All cycling bitches undergo a lengthy (2+ months) diestrus following ovulation.
- Mammary development and behavioral changes occur under the influence of progesterone and prolactin in late diestrus.
- Galactorrhea (excessive production and inappropriate excretion of milk) is seen following a rise in serum prolactin at the end of diestrus; with severe hypothyroidism—due to resulting hyperprolactinemia.
- False pregnancies in the bitch are thought to occur as a holdover from a period in evolution when females of a pack would cycle at the same time but only dominant individuals would become pregnant. Non-pregnant pack members were available to nurse puppies of the more dominant females.
- Any event that results in an abrupt drop in serum progesterone and rise in prolactin can lead to a clinically overt false pregnancy. Signs are frequently created iatrogenically when ovariectomy or ovariohysterectomy is performed during mid to late diestrus.
- Queens that ovulate spontaneously or ovulate following mating but do not become pregnant experience a 6-7-week period of diestrus due to elevated progesterone concentrations; some queens develop a clinically overt false pregnancy during this time.

SYSTEMS AFFECTED

- Reproductive
- Behavioral
- Endocrine

GENETICS

N/A

INCIDENCE/PREVALENCE

- False pregnancies occur in 100% of bitches following ovulation.
- >60% of cycling bitches exhibit signs of false pregnancy.
- Spontaneous ovulation occurs frequently in the queen (35–85%) depending on presence of other queens and tom. False pregnancy occurs after every non-pregnant ovulation in the queen; overt symptoms are uncommon.

SIGNALMENT

Species

Dog and cat

Breed Predilections

None

Mean Age and Range

Any age

Predominant Sex

Female only

SIGNS

General Comments

- Although all cycling bitches have similar progesterone and prolactin hormone profiles during late diestrus and early anestrus, they vary in the magnitude of clinical symptoms associated with the false pregnancy. This may be due in part to individual sensitivities to prolactin.
- Some bitches experience repeated overt false pregnancies while others have covert false pregnancies.
- The magnitude of symptoms can vary during each false pregnancy for the same bitch.
- Overt symptoms are uncommon in queens.

Historical Findings

- Estrus ~ 6–12 weeks ago (bitch).
- Estrus ~ 40 days ago (queen).
- OHE or OVE 3–14 days ago.
- Mammary gland development.
- Galactorrhea.
- Weight gain.
- Behavior change including nesting, maternal behavior, aggression, lethargy.
- Inappetance.
- Abdominal distension (rare).

Physical Examination Findings

- Mammary gland hypertrophy.
- Galactorrhea—fluid can be clear to milky to brown in color.

CAUSES

- Decline in serum progesterone concentration and rise in serum prolactin concentration.
- Decline in serum progesterone concentrations due to OVE or OHE during diestrus.
- Hyperprolactinemia—can be due to severe hypothyroidism.

RISK FACTORS

- OHE or OVE during diestrus
- Does not impact future fertility



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pregnancy
- Mastitis
- Mammary neoplasia.
- Mammary hyperplasia (queens)

• Pyometra

- Other causes of abdominal distension (organomegaly, ascites)
- Hypothyroidism
- Pituitary tumor causing hyperprolactinemia (rare)

CBC/BIOCHEMISTRY/URINALYSIS

- Normocytic, normochromic anemia—17–21% decrease in PCV during late diestrus.
- Hypercholesterolemia—75–94% increase during diestrus.

F

OTHER LABORATORY TESTS

Serum progesterone concentrations elevated if tested during diestrus.

IMAGING

- Ultrasonographic findings—uterine enlargement; performed after 25 days from mating; can be used to evaluate pregnancy status and uterine fluid accumulation.
- Radiographic findings—normal; performed after 54 days from mating; can be used to evaluate presence of fetal skeletons and uterine fluid accumulation.

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

N/A



TREATMENT

APPROPRIATE HEALTH CARE

- Usually no treatment needed.
- Outpatient treatment for medical management of clinical signs of false pregnancy.

NURSING CARE

- Prevent mammary gland stimulation from self-nursing with Elizabethan collar.
- Owners can cold pack mammary glands to reduce mammary gland activity.

ACTIVITY

Increase activity in sedentary dogs and cats to increase caloric expenditure and decrease calories available for lactation.

DIET

Decrease caloric intake for several days to reduce energy available for lactation.

CLIENT EDUCATION

- False pregnancies are normal in bitches and do not impact future fertility.
- Advise cat owners that pyometra can develop following spontaneous ovulations.

SURGICAL CONSIDERATIONS

- OVE or OHE if bitch or queen is not intended for use in a breeding program.
- Perform OVE or OHE during anestrus or early diestrus when possible.

FALSE PREGNANCY

(CONTINUED)



MEDICATIONS

DRUG(S) OF CHOICE

- Dopamine agonists—reduce milk production and some maternal behaviors by inhibiting prolactin release.
- Cabergoline 5 µg/kg PO q24h for 5–7 days
- Bromocriptine 10 µg/kg PO q8h for 5–7 days.

F

CONTRAINDICATIONS

Dopamine agonists can cause abortion if given to a pregnant bitch or queen as prolactin is luteotrophic. Drugs that suppress prolactin will terminate pregnancy by reducing progesterone and can cause premature parturition (abortion).

PRECAUTIONS

- Incidence of vomiting with bromocriptine administration reduced if given with food; cabergoline has fewer side effects and higher efficacy, but is more costly.
- Coat color changes in dogs possible with prolonged dopamine agonist treatment (uncommon).

POSSIBLE INTERACTIONS

Avoid acepromazine and metoclopramide; both can promote lactation and reduce the efficacy of dopamine agonists.

ALTERNATIVE DRUG(S)

- Short-term therapy with diazepam can be useful for bitches with extreme behavioral signs.
- Mibolerone 16 µg/kg PO q24h for 5–7 days to reduce symptoms of false pregnancy. Can also be used at 2.6 µg/kg/day starting at least 1 month prior to the next heat cycle to suppress estrus in bitches, which will prevent recurrence. Side effect and risks of treatment should be explained and owners should give informed consent prior to treatment. Do not give to cats.



FOLLOW-UP

PATIENT MONITORING

Have owners monitor mammary glands for inflammation and discoloration that could indicate mastitis.

PREVENTION/AVOIDANCE

- Perform OVE or OHE during anestrus or early diestrus when possible.
- Estrus suppression.

POSSIBLE COMPLICATIONS

Mastitis with significant mammary gland hypertrophy, galactostasis, and ascending infection.

EXPECTED COURSE AND PROGNOSIS

- Typically resolves in 2–4 weeks without treatment.
- Resolution in 5–7 days with dopamine agonist or mibolerone.
- May recur after any ovulation.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

- The tendency to display overt false pregnancies has no impact on fertility.
- Bitches and queens should be evaluated for possible pregnancy before treating for false pregnancy.

SYNOMYS

- Pseudopregnancy
- Pseudocyesis
- Pseudo-gestation
- False-whelping

ABBREVIATIONS

- OHE = ovariohysterectomy
- OVE = ovariectomy
- PCV = packed cell volume

INTERNET RESOURCES

- Gobello C, Concannon PW, Verstegen J. Canine pseudopregnancy: A review. In: Concannon PW, England G, Verstegen III J, Linde-Forsberg C, eds., Recent Advances in Small Animal Reproduction. International Veterinary Information Service, Ithaca NY, www.ivis.org; A1215.0801.
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Client Education Handout
available online

FAMILIAL SHAR-PEI FEVER

F



BASICS

DEFINITION

A familial autoinflammatory disorder in the Chinese Shar-Pei dog characterized by episodic fever and swollen hocks, and associated with progressive systemic amyloidosis.

PATOPHYSIOLOGY

• Shar-Pei dogs have a predisposition to reactive systemic amyloid deposition. The exact mechanism is multifactorial; however, it is now known that a genetic defect affecting the innate immune system plays a role. Environment and other gene modifiers play a role. The greater number of mutations in "meatmouth" (or heavily wrinkled/thick-skinned Shar-Peis) greatly increases the risk for clinical symptoms of FSF. Genetic alterations increase the levels of low molecular weight hyaluronan (LMW-HA). LMW-HA activates the release of pro-inflammatory cytokines. Interleukin-1 β is a key inflammatory mediator. Sequential production of inflammatory cytokines including TNF- α and IL-6 can induce increased levels of serum amyloid A (an acute-phase reactant). Excessive production of serum amyloid A results in the extracellular deposition of amyloid. Amyloid is deposited throughout the tissues; however, the most clinically important sites are the kidneys and liver. • Hepatic amyloidosis can lead to a friable liver susceptible to rupture and secondary hemoabdomen. • Renal amyloidosis and secondary nephrotic syndrome predispose Shar-Peis to states of hypercoagulability. • Similar to familial Mediterranean fever in people, these inflammatory mediators cause fever and serosal inflammation, affecting the pleura, peritoneum, and synovial membranes.

SYSTEMS AFFECTED

- Cardiovascular—venous thrombosis (e.g., PTE); systemic hypertension.
- Gastrointestinal—abdominal pain; vomiting; diarrhea; hemoabdomen; ascites.
- Hemic/Lymphatic/Immune—anemia; leukocytosis, with or without left shift; coagulation defects; hypercoagulable states; decreased immunoglobulin levels.
- Hepatobiliary—hepatomegaly; hepatic rupture; elevated liver enzymes; impaired hepatic function. • Musculoskeletal—joint effusion, especially of the tibiotarsi; lameness; stiffness; "walking on eggshells"; roach back; unwillingness to move. • Nervous—vascular accident; acute-onset neurologic signs (e.g., head tilt, vestibular ataxia, seizures).
- Ophthalmic—retinal detachment.
- Renal/Urologic—proteinuria; low specific gravity; polyuria; polydipsia.

- Respiratory—tachypnea or dyspnea.
- Skin—periarticular edematous soft tissue swelling, especially involving the tibiotarsal joint region; swollen muzzle; icterus; skin sloughing.

GENETICS

An autosomal recessive inherited disorder

INCIDENCE/PREVALENCE

- An estimated 23–28% of Shar-Peis are affected by this disorder. • An estimated 53% of Shar-Peis with fever have Shar-Pei fever.

SIGNALMENT

- Mean age—4 years • Range—19 weeks–9 years • Sex predisposition—female

SIGNS

General Comments

• Historical and physical examination findings vary depending on the organ affected and the severity of amyloidosis. • Some cases may have only a few of the following findings.

Historical Findings

- Episodic anorexia, lethargy, stiffness, swollen hocks and/or muzzle—self-limiting (24–36 hours) or responsive to NSAIDs.
- Intermittent bouts of abdominal pain, vomiting, and/or diarrhea. • Polyuria and polydipsia. • Weight loss.

Physical Examination Findings

- Marked fever 39.4–41.7°C (103–107°F) of 24- to 36-hour duration. • Lethargy and dehydration. • Edematous periarticular soft tissue swellings involving one or more joints. • Joint effusion. • Swollen muzzle.
- Abdominal pain. • Reluctance to move and hunched posture. • Tachypnea.
- Hepatomegaly, ascites, and icterus. • Pale mucous membranes secondary to chronic renal failure induced anemia or, in rare cases, hemoabdomen.

CAUSES

- Dysregulation of inflammatory processes in the Shar-Pei are thought to predispose the breed to development of secondary/reactive amyloidosis. • Any chronic infection, inflammation, immune-mediated disease, or neoplasia can cause reactive or secondary amyloidosis.

RISK FACTORS

Stress may trigger a fever episode.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infectious or immune-mediated causes of polyarthritis—e.g., *Ehrlichia*, Lyme disease, systemic lupus erythematosus, idiopathic polyarthritis. • Icterus (see chapter).
- Chronic renal failure (see Renal Failure, Chronic). • Polyuria and polydipsia (see chapter). • Fever of unknown origin.

CBC/BIOCHEMISTRY/URINALYSIS

- Nonregenerative anemia—secondary to chronic renal failure or acute hemoabdomen.
- Leukocytosis with or without left shift.
- Changes compatible with renal failure—e.g., elevated urea, creatinine, and phosphorus levels, and metabolic acidosis.
- Hypoalbuminemia—secondary to proteinuria or hepatic failure.
- Hypercholesterolemia—consistent with nephrotic syndrome (hypoalbuminemia, proteinuria, ascites, and elevated cholesterol).
- Elevations in ALP and ALT activity; elevated bilirubin level. • Proteinuria—in cases where the amyloid is deposited in the renal cortex; note: proteinuria may be absent as the majority of dogs have medullary amyloid deposition • Isosthenuria—with renal involvement or hepatic failure. Bilirubinuria—secondary to cholestasis.

OTHER LABORATORY TESTS

- *Ehrlichia*, *Anaplasma*, and *Borrelia* serology/Snap 4Dx/or PCR. • Heartworm tests—to rule out glomerulonephritis secondary to heartworm-induced antigen-antibody complexes. • Coombs' test, ANA, and rheumatoid factor—to identify concurrent, underlying immune-mediated disease. • PT and PTT—factors IX and X may be lost through the glomerulus and prolong PTT; liver failure can cause prolongation of both PT and PTT; organ thrombosis may cause DIC and concurrent prolongation of PT and PTT and increased D-dimers. • Antithrombin III level—may be low secondary to loss through the glomerulus.
- Thromboelastography—may demonstrate hypercoagulability. • IgA or IgG levels—may be low in some cases; low level thought to lead to increased risk of inflammation or infection.
- UPC ratio—elevated with deposition of amyloid in the glomeruli; typically > 13 with amyloidosis (normal: ≤ 0.5).

IMAGING

- Abdominal radiography—abnormalities may include hepatomegaly or decreased detail secondary to peritoneal effusion; abdominal effusion may be secondary to hypoalbuminemia, portal hypertension, or hemorrhage. • Thoracic radiography—abnormalities may include pleural effusion secondary to severe hypoalbuminemia or pleural inflammation. • Joint radiography—typically shows periarticular swelling of the soft tissues without bony involvement.
- Abdominal ultrasonography—may reveal a diffuse homogeneous hypoechoic hepatic parenchyma and rounded liver edges; the kidneys may appear hyperechoic along with loss of corticomedullary distinction.

DIAGNOSTIC PROCEDURES

- Synovial fluid analysis—may or may not reveal evidence of acute synovitis (i.e., the presence of PMNs and decreased joint fluid

FAMILIAL SHAR-PEI FEVER

(CONTINUED)

viscosity); inflammation may be limited to the lower supporting structures of the synovium.

- Kidney (cortex) and/or liver fine-needle aspiration or biopsy (pending normal PT, PTT, platelet number, and buccal mucosal bleeding time)—amyloid deposition. Biopsy preferred; however Congo red staining and polarized light has been used to confirm amyloid on cytology samples.

PATHOLOGIC FINDINGS

- Systemic deposition of amyloid in multiple organs, e.g., the kidneys, liver, gastrointestinal tract, spleen, lymph node, adrenal glands, heart, lungs, thyroid gland, prostate gland, intestinal vessels, and pancreas. • Amyloid deposition may be associated primarily with vessels or within the parenchyma.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—during minor episodes of pain and fever that respond to NSAIDs.
- Inpatient—required during periods of anorexia, fever, dehydration, marked lameness or nonspecific pain, vomiting or diarrhea, ascites, or episodes of cholestasis. • Intensive care management—required during organ failure or thromboembolic events.
- Emergency stabilization—indicated for hemoabdomen or if splenic, portal, or renal vein thrombosis is suspected.

NURSING CARE

- Balanced polyionic fluids—if patient is dehydrated or anorexic, or if vomiting and/or diarrhea are present. • Oxygen—in suspected cases of pulmonary thromboembolism.
- Abdominocentesis—may be required if ascites is causing respiratory compromise.
- Blood transfusions—may be indicated if anemia is severe. • Fresh frozen plasma—may be considered for DIC or other coagulopathies.
- Antibiotics—if sepsis is suspected or concurrent infection is diagnosed; broad spectrum should be used if sepsis is suspected; otherwise, antibiotic choice should be guided by a sensitivity panel.
- Analgesics for fever and pain; NSAIDs are contraindicated in cases with concurrent renal disease or gastrointestinal signs.
- Gastroprotectants—if gastric ulcer secondary to renal or hepatic disease is suspected.

ACTIVITY

Limit during febrile episodes.

DIET

- Protein restriction and phosphorus restriction in accordance with IRIS renal staging (see www.iris-kidney.com). • Dogs showing evidence of hepatic encephalopathy should be fed a protein-restricted diet once they are stable. • Omega-3 fatty acids—may be beneficial for glomerular disease.

CLIENT EDUCATION

- There is no cure for familial Shar-Pei amyloidosis; therapy is palliative. • Early therapy may decrease further deposition of amyloid. • Diagnostics should be performed to ensure that there is no underlying or concurrent problem that may be treatable.
- Affected dogs should not be bred.



MEDICATIONS

DRUG(S)

- Colchicine 0.03 mg/kg PO q12–24h; advised early in course of disease to delay amyloid deposition; unknown if colchicine has any beneficial effect once amyloid has been deposited
- DMSO 80 mg/kg SC 3 times/week or 125 mg/kg PO q12h; controversial, generally doubted to have significant clinical effect.
- Steroids—only if a concurrent immune-mediated disease is present.
- Low-dose aspirin therapy—0.5–1 mg/kg PO q12–24h if concerned about hypercoagulability.
- ACEi and/or ARB for significant proteinuria. ACEi 0.25–0.5 mg/kg PO q12–24h.
- Address hypertension with additional therapy as indicated.

CONTRAINdications

- NSAIDs are contraindicated in renal disease and gastrointestinal ulcers. • Aspirin is contraindicated with concurrent NSAID use.
- Colchicine is contraindicated with concurrent cyclosporine use. • ACEi are contraindicated in dehydrated or hypovolemic patients.

PRECAUTIONS

- Steroid use may accelerate amyloid deposition. • Colchicine can cause gastrointestinal upset; chronic use can be associated with bone marrow suppression.
- DMSO has a very strong odor.



FOLLOW-UP

PATIENT MONITORING

- Urine specific gravity—monitor for isosthenuria. • Urine protein:creatinine ratios—to monitor glomerular disease.
- Biochemistry panel—to monitor renal and hepatic parameters, including hypoalbuminemia. • CBC monitoring—for anemia/inflammatory leukon. • Blood pressure monitoring and fundic examination—for hypertensive patients.

PREVENTION/AVOIDANCE

Avoid puppies from lines that have a history of Shar-Pei fever.

POSSIBLE COMPLICATIONS

- Death—due to hepatic rupture or pulmonary thromboembolism.

- Neutrophilic vasculitis causing severe skin sloughing, STSS causing localized necrotizing fasciitis and/or concurrent shock and multiorgan failure.

EXPECTED COURSE AND PROGNOSIS

- Waxing and waning, progressive disorder with a fair to poor prognosis, depending on the time of diagnosis. • Inevitably fatal due to CKD or hepatic failure. • Time course may be weeks to more than 10 years.



MISCELLANEOUS

AGE-RELATED FACTORS

Tends to be more severe in cases diagnosed at an early age.

PREGNANCY/FERTILITY/BREEDING

Do not breed affected dogs.

SYNONYMS

- Swollen hock syndrome • Shar-Pei autoinflammatory disorder

ABBREVIATIONS

- ACEi = angiotensin converting enzyme inhibitor • ALP = alkaline phosphatase
- ALT = alanine aminotransferase • ANA = antinuclear antibody • ARB = angiotensin receptor blocker • CKD = chronic kidney disease • DIC = disseminated intravascular coagulation • DMSO = dimethyl sulfoxide
- FSF = familial Shar-Pei fever • IL-6 = interleukin-6 • NSAID = nonsteroidal anti-inflammatory drug • PCR = polymerase chain reaction • PMN = polymorphonuclear neutrophil • PT = prothrombin time
- PTE = pulmonary thromboembolism
- PTT = partial thromboplastin time
- STSS = streptococcal toxic shock syndrome
- UPC = urine protein creatinine ratio

INTERNET RESOURCES

- www.drjwv.com • www.wvc.vetsuite.com

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FANCONI SYNDROME

F



BASICS

OVERVIEW

A constellation of abnormalities caused by defective proximal renal tubular reabsorption of glucose, electrolytes, and amino acids.

SIGNALMENT

Species

Dog

Breed Predilections

Although sporadically reported in several breeds, idiopathic Fanconi syndrome primarily affects the basenji breed (approximately 75% of cases). In North America, 10–30% of basenjis are affected. It is presumed to be inherited in this breed, but the mode of inheritance is unknown.

Mean Age and Range

Age at diagnosis: 10 weeks–11 years. Affected basenjis usually are > 2 years of age; most develop clinical signs from 4 to 7 years.

Predominant Sex

No sex predilection

SIGNS

- Vary depending on the severity of specific solute losses and whether or not renal failure has developed.
- Loss of amino acids and glucose—usually not associated with clinical signs other than polyuria and polydipsia (most common clinical signs).
- Weight loss, often despite a normal appetite.
- Variable lethargy.
- May have decreased appetite.
- Poor body condition.
- Abnormal growth (rickets) may occur in young animals.

CAUSES & RISK FACTORS

- Inherited in basenjis.
- Acquired Fanconi syndrome has been reported in dogs given gentamicin, streptozotocin, maleic acid (experimental), amoxicillin, and chicken jerky treats from China; also reported secondary to primary hypoparathyroidism. Chicken jerky treat ingestion has become an important cause of Fanconi syndrome in the past 5 years. The causative toxin still has not been identified.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Primary renal glucosuria also causes glucosuria in the absence of hyperglycemia; documentation of aminoaciduria, mild proteinuria, or a hyperchloremic (normal anion gap) metabolic acidosis suggests Fanconi syndrome.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC usually normal.
- Hypokalemia in about one-third of cases.
- Hyperchloremic

metabolic acidosis.

- Azotemia if renal failure develops.
- Hypophosphatemia and hypocalcemia may occur in affected young, growing animals.
- Urine specific gravity usually low (1.005–1.018); mild proteinuria common; ketonuria may be present.

- Granular or lipid renal casts and bacteria were seen in 27–40% of dogs that developed proximal renal tubulopathy after eating chicken jerky treats.

OTHER LABORATORY TESTS

Hyperchloremic (i.e., normal anion gap) metabolic acidosis due to bicarbonaturia with urine pH < 5.5. Urine pH is > 6.0 in distal RTA (renal tubular acidosis), and this is a key diagnostic difference between proximal (Fanconi syndrome) and distal RTA. Bicarbonaturia does not occur unless a bicarbonate load is administered.

IMAGING

Radiography—young, growing dogs may have features of rickets and angular limb deformities; adult patients may exhibit decreased bone density.

DIAGNOSTIC PROCEDURES

Urinary clearance studies to document excessive excretion of solutes such as glucose, amino acids, and electrolytes are needed for confirmation. It is not recommended to test animals < 8 weeks of age because false-positive results may occur. A 24-hour urine sample can be sent to the Metabolic Genetic Disease Testing Center (University of Pennsylvania) to screen for aminoaciduria. Fractional reabsorption of amino acids in affected dogs ranges from 50% to 96% (normal range, 97–100%).

PATHOLOGIC FINDINGS

Renal papillary necrosis may occur as a late finding. Karyomegaly of the tubular cells has been reported.



TREATMENT

- Discontinue any drug that may cause Fanconi syndrome or treat for a specific intoxication.
- No treatment will reverse the transport defects in dogs with inherited or idiopathic disease.
- Because the number and severity of transport defects vary markedly among affected animals, treatment must be individualized.
- Treat for metabolic acidosis if blood bicarbonate concentration is < 12 mEq/L. Large doses of alkalinizing agents may be required because decreased proximal tubular resorptive capacity results in marked bicarbonaturia. The goal of alkali therapy is to maintain blood bicarbonate concentration at 12–18 mEq/L.
- Young, growing dogs may require vitamin D, calcium, and phosphorus supplementation.



MEDICATIONS

DRUG(S)

Use potassium citrate (1 mEq = 108 mg) at 50–500 mg/kg q12h (1 to > 10 mEq/kg/day; start with a low dosage) or sodium bicarbonate (1 mEq = 84 mg) at 80–300 mg/kg q8–12h (1 to > 10 mEq/kg/day; start with a low dosage) as dictated by blood gas and electrolyte data. These are much higher dosages than are necessary in distal RTA.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Avoid drugs that are nephrotoxic or have the potential to cause Fanconi syndrome (see “Causes & Risk Factors”).
- Avoid potassium chloride because affected patients are hyperchloremic.



FOLLOW-UP

- Monitor serum biochemistry at 14-day intervals to assess the effect of treatment; monitor serum potassium concentration regularly because bicarbonate therapy may aggravate renal potassium loss; once stable, monitor biochemistry at 3-month intervals.
- Clinical course varies; some dogs remain stable for years, others develop rapidly progressive renal failure over a few months; the cause of death usually is acute renal failure, often associated with severe metabolic acidosis.
- Some dogs (18% in one study) developed seizures or other neurologic signs several years after diagnosis.



MISCELLANEOUS

SEE ALSO

- Hypokalemia
- Renal Failure, Acute
- Renal Failure, Chronic

INTERNET RESOURCES

- Metabolic Genetic Disease Testing Center (University of Pennsylvania): <http://research.vet.upenn.edu/penngen/>
- Suggested treatment protocol for dogs with idiopathic Fanconi syndrome: <http://www.basenji.org/ClubDocs/fanconiprotocol2003.pdf>.

Suggested Reading

Thompson M, Fleeman L, et al. Acquired proximal renal tubulopathy in dogs exposed to a common dried chicken treat: retrospective study of 108 cases (2007–2009). Aust Vet J 2013, 91(9):368–373.

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FEAR AND AGGRESSION IN VETERINARY VISITS



BASICS

DEFINITION

- Fear—inevitable, negative emotional state caused by the anticipation/awareness of danger.
- Aggression—warning/intent to cause harm/increase distance in response to perceived threat.

F

PATOPHYSIOLOGY

See “Causes” and “Risk Factors”

SYSTEMS AFFECTED

- Behavioral—neurochemical input between the limbic system and forebrain allow for classically conditioned emotional (fear) memories, leads to defensive behavioral response.
- Sympathetic nervous system arousal.

GENETICS

Fearful/fractious temperaments are heritable.

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat

Breed Predilections

Any

Mean Age and Range

Any

Predominant Sex

Any

SIGNS

General Comments

- Displacement behaviors (yawns, lip licking, grooming, panting).
- Offensive and/or defensive threat displays.
- “4 F’s of behavior”: fight, flight, freeze, fidget.

CAUSES

- Previous/current frightening or painful veterinary visits create an involuntary fear response (“white coat effect”).
- Previous use of harsh/punitive tones of voice, physical manipulation.
- Additional exposure to individual patient’s triggers of fear (travel, dogs, strangers).
- Underlying fearful/anxious temperament; comorbid behavioral disorders.

RISK FACTORS

- Previous frightening/painful veterinary experiences.
- History of fearful/fractious behavior at previous visits or around any person.
- Harsh or punitive handling during puppy or kitten visits.
- Poor socialization during the sensitive socialization period (dog 3–12 wks; cat 2–7 wks).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pain • Irritability from illness—gastrointestinal discomfort, urogenital inflammation, visceral neoplasia
- Forebrain lesion • Cognitive dysfunction syndrome

CBC/BIOCHEMISTRY/URINALYSIS

Endogenous corticosteroid-induced (stress) leukogram possible (neutrophilia, lymphopenia, monocytosis); hyperglycemia; glucosuria (cats)

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

N/A



TREATMENT

APPROPRIATE HEALTH CARE

Prior to Handling

Assess the environment, patient and yourself. What patients see, smell, feel, taste, and hear affect emotional state. Utilize assessments to ameliorate stressors and create a successful handling plan.

Assess the Environment: make it comfortable for the patient

- Eliminate exposure to patient’s known triggers of fear or aggression.
- Reduce environmental stimuli (light, noise, movement, touch).
- Thermo-neutral comfort zone is 59–86°F, dogs; 86–100°F, cats.
- Ideal ambient sound level is 60 dB (stress at 85 dB).
- Provide pheromone support (Adaptil, Feliway).
- Mindfully manipulate owner presence; many do better with social support.
- Utilize highly palatable food for distraction and CC.
- Create a comfortable exam site (no slippery, shiny, cold surfaces).
- Provide a way for fearful patients to hide, feel covered, and protected.
- Ensure all supplies are readily available.

Assess the Animal

- Recognition of fear and impending aggression and interpretation of patient body language is critical.
- Anxiety, fear, and arousal are the motivations for aggression and other fractious behavior.
- Early recognition improves intervention efficacy and safety, and

decreases handling time.

- Track body language, willingness to approach, interaction with the environment and people.
- Identify displacement behaviors to flag patients that are not coping well.
- Monitor continually. Changes in location (lobby vs. radiology), interactions (social petting vs. exam), procedures (auscultation vs. nail trim), and personnel (female vs. male) affect patients.

Assess Yourself: Avoid Perceived Threats, Track your own Body Postures and Behavior

- Avoid direct eye contact, bending over, or putting your face near a fearful patient.
- Bend at the knee, turn your body to the side, and squat down (when safe).
- Avoid reaching out, petting on top of the head, sudden grabbing of the collar or body, or reaching into a carrier. Encourage patients to approach you, or have the handler they feel safe with bring them to you.
- Cat—encourage approach by patting the surface and using a soft voice. Remove carrier tops—do not pull or dump out patients.
- Allow time to sniff your hand. Gently scratch under the chin and pet the side of the head if postures indicate safety. Avoid petting beyond the shoulder as it is often arousing.
- Start exam at the head or middle and move back; save socially invasive or painful areas for last.
- Dog—hold your hand at your side, patting your leg gently, soft verbal encouragement, hold your palm open with valued treats if the dog approaches, and allow the dog to sniff and investigate.
- Gently pet under the chin and neck area; slowly move into the desired examination position.
- Start exam at the middle or rear and move towards the head.
- Lack of patient approach in response to a non-threatening invitation indicates the animal is maintaining social distance.
- Anticipate that your approach may lead to an aggressive response.
- If you must approach, do so from the side; work from the side and from behind the point of the shoulder.
- Avoid front-facing interactions unless the patient’s head is covered.
- Avoid loud talking and sudden movements.
- Work quietly, quickly, and effectively; often a narrow window of opportunity before fear and arousal escalate.
- Encourage handlers that are fearful of working with specific patients to stop and ask their team for help; reassess if and how to proceed.
- Fearful animals and fearful handlers are a dangerous combination, and often escalate each other’s fear, arousal, and aggressive responses.
- Ensure the culture supports this and the safety of each team member.
- Monitor handler frustration.
- Adversarial and punitive language and interactions must be avoided.
- Use language that is scientifically accurate and promotes

(CONTINUED)

FEAR AND AGGRESSION IN VETERINARY VISITS

patient empathy—fearful, painful, confused; and avoid choices that result in poor handling and may be offensive to clients—mean, bad, stupid, spiteful, evil, dominant. Handler language affects their actions as well as those of others. • Punishment (verbal, physical, leash corrections, “dominance maneuvers”) must be strictly avoided. Aversives increase fear, arousal, aggression, and are contraindicated. Behavioral signals of intent can also be blunted, making handling more dangerous. Negative experiences are likely to escalate fractious behavior during subsequent handling interactions at the hospital and possibly at home. • Create cultural norms that prohibit adversarial language and interactions.

Make a Handling Plan

Handling plans are unique to individual patients/working environment, and may require adjustments dependent on patient response. Initial planning may seem time consuming, but has a high payoff in staff safety, decreased future handling time, patient welfare, and client satisfaction. Chart information including what worked well and suggested changes to make the next visit even better.

Guidelines for a Patient Handling Plan

- Determine if and what the patient can eat; plan for CC that is appropriate and safe for the animal. • Select appropriate level of restraint for the individual patient and the procedures. • Select handling tools that increase safety and decrease patient fear and arousal. • Critically consider what needs to be performed—must the procedure be done today, or at all? Consider multiple visits of shorter duration with fewer procedures.
- Place the required procedures in order of most important to least important in the event the patient is unable to tolerate all of them. • Place those procedures in order of least aversive to most, so early difficult procedures do not inhibit ability to complete later ones. Trends among patients exist, individual differences also occur. • Consider pain, invasiveness, number of procedures, and how the patient is coping with minimal handling. Consider sending the patient home with a plan for return (oral sedation prior to travel, avoidance of known triggers and environmental management, DS/CC to specific handling or tools). Use chemical restraint immediately when unlikely the patient will be able to tolerate all procedures.
- Have chemical restraint prepared and waiting for at-risk patients; use before patient becomes aroused to promote efficacy, handler safety, and to reduce further advancement of patient fear.

Utilization of Counter-Conditioning

- A form of classical conditioning where an animal's reflexive negative emotional response (fear) to a stimulus (veterinary setting) is changed to a positive one (pleasure). Palatable

food is the easiest and most powerful means of establishing this association. • Prevents and/or treats established fear of handling and environment. • Most effective when food is first offered while the animal is relaxed and feels safe, then just before, during, and after the (aversive) procedure. Events may be aversive because they are painful (injections) or socially invasive (rectal temperature, nail trims). • Stressed animals may need to be fed the duration of handling to prevent escalation of fear and arousal. Utilize food that can be broken up into small pieces, or use sticky, smearable options. • Palatability must be high (meat baby food, liverwurst) to maximize the animal's interest in eating and increase the power of the positive emotional response. Petting and praise can be used additionally, but are far less powerful and may even be unpleasant for some pets. • Food serves as a “barometer” for patient stress; many won't eat even highly palatable food. Rejection should cue the handler to reassess patient comfort level, safety and handling plan.

Safe and Effective Restraint

Once the itinerary of procedures has been organized, a restraint plan should be coordinated for each procedure. Avoid the tendency to over-restrain animals. Stress often revolves around the restraint, rather than the procedure itself. When patients are CC with food, and stressors are mitigated through environmental management and non-threatening interactions with staff, less restraint is needed.

Guidelines for restraint

- Use the least restraint required to allow the specific procedure(s) to be performed properly (AVMA Restraint Policy). • When greater restraint is needed, provide firm, balanced pressure with global support around the patient. Prevent flailing by keeping control of head and rear end at all times. • Reserve lateral recumbency in dogs only for procedures that require it (ex. orthopedic exams). It is a threatening position for many. Most can be performed in a stand or sit position. Some dogs will assume this position when lured with a treat or asked to perform a “down.” If required, prevent flailing and hitting the head; move the patient slowly and steadily with full body support. • Reserve scruffing and/or stretching only for cats comfortable with this technique, and only when the procedure requires the cat to be in lateral recumbency. • Slide your hands along the patient's body, rather than releasing and grabbing when moving your hands or adjusting your position. • If the pet struggles longer than 3 sec., stop, reposition, and try again. Wait until relaxed, and preferably starts eating, before beginning the procedure. If after 2 or 3 attempts the patient does not relax and/or starts to get fractious, stop altogether and consider whether the procedure is

essential. • Essential: make a plan for chemical restraint. • Non-essential: send the animal home and create a plan for return.

Handling Tools

Designed to expedite veterinary procedures and increase safety. Handling tools also reduce the need for physical restraint and the stressful social interaction. The key is using them correctly, often, and early in the handling plan.

Pheromones

- An Adaptil diffuser for dogs and Feliway diffuser for cats in the reception area, examination rooms, and hospital wards may help to lower stress. • A pheromone spray or wipe can be used to reduce stress during travel, crating, on the examination table or in the clinic cages. Dogs might have the spray placed on a bandana around their neck prior to the visit, or can be fitted with an Adaptil collar at least one day in advance. • Never spray directly on the pet.

Muzzles

- Basket muzzle (plastic, metal):
 - Allows panting; safer for longer procedures and kennelled dogs. ◦ Food can easily be smeared along the inside of the muzzle, encouraging the dog to place its nose into the muzzle.
 - Increases safety so lightest restraint and CC can be used. ◦ Best if owner habituates and DS/CC to muzzle at home and have in place for arrival. ◦ If owner has not adapted pet to muzzle, first consider whether procedure can be postponed and client instructed to adapt to muzzle before the next visit. ◦ If staff must apply muzzle, safety is essential. Alternately, for short procedures or to facilitate an injection, a nylon slip-on muzzle might be easier to apply. [/sr1]
 - Feline muzzle (leather, plastic): Select a stiff leather or plastic option that covers both mouth and eyes. Provides handler safety and minimizes visual stimuli.

Elizabethan Collar

An alternative to the muzzle for conformation or intense fear of the muzzle this collar can be used to provide control of the head. For small dogs and cats a towel or blanket may be preferable.

Towels

- Towels or thick bedding can provide low-stress immobilization of cats and small dogs. • Provide head and body control, reduction of visual stimuli, and firm global pressure of handling; modifications can be made to gain access to the head. • Allow access for auscultation, abdominal palpation, and hind leg venipuncture. • Utilized to safely capture fleeing or fearful cats, remove from carrier or cage, and administer injections for chemical restraint; protect the cat from flailing and prevent bites and scratches.

Thunder Cap

- Limits visual stimuli; reduces anticipation of procedures, perception of handler posture, and known individual triggers (travel, dogs, strangers). • Utilize during travel, entering to

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(CONTINUED)

the building, procedures, hospitalization, and after chemical restraint (to keep the patient under the plane of sedation). • A muzzle or towel that covers the eyes/head may have the same effect on cats.

Thundershirt

Swaddles the dog or cat, providing firm, balanced pressure around the chest and torso, reducing arousal, anxiety, and fear.

Classical Music (Through a Dog's Ear/Through a Cat's Ear)

- Increases behaviors associated with relaxation in animals and people.
- Source of noise cancellation, masking potentially stressful external sounds.
- Relaxes clients, reminds staff to work quietly and slowly.

Squeeze Cage

- For essential procedures on dogs that are not safe to muzzle; protected contact used to administer injection of chemical restraint.
- Alternative created with a chain-link panel that swings out from the wall or an existing door. Hold panel open at $\leq 90^\circ$ while the dog is walked in; pull the lead through the crevice at the hinge for head control. Gently close the panel towards the wall, securing the dog; quickly inject through the panel.

Clipnosis (Cats only)

- Pinch-based inhibition ("trance-like" state, semi-immobile, relaxed, without activation of stress response) using Clipnosis Gentle Calming Clips or other tools, such as binder clips.
- Produces firm, even pressure when placed on the scruff, provides a hands-free option to hand-scruffing, typically with more behavioral calming.
- Place on cats when calm and relaxed. Cats that are averse to pressure on the scruff or are fractious are not candidates.
- Some have reservations regarding the tool and its effects on behavioral inhibition through freezing vs. calming.

Cat Carriers

- Select type that allows the cat to easily exit on its own or have a removable top that allows the cat to remain in the bottom portion during exam.
- Allows the cat to remain in a familiar area, prevents fleeing, and promotes hiding.
- Soft-sided carriers useful for fractious cats in need of chemical restraint. Cat remains in the familiar carrier while the mesh panel is pressed up against the body to allow IM injection.
- Allow hospitalized cats to have their carrier in their cage. Provides familiarity, stress relief, and has been shown to encourage a faster return to eating.
- Carrier is a more effective tool if cats are conditioned to enter and travel in it comfortably.

EZ Nabber

- Mesh netting tightly secured to rectangular metal enclosure; opens and closes manually to allow for capture and quick restraint.
- Valuable for fractious cats who are fleeing or housed in a wall unit cage; 2 ft. distance between the handler and the cat.
- Use to administer IM chemical restraint through the mesh.
- Cover with a towel once the cat is

inside to reduce visual exposure and protect handler.

- Alternately a fish net might be used to cover or wrap the cat.

NURSING CARE

N/A

ACTIVITY

N/A

DIET

N/A

CLIENT EDUCATION

- <http://www.catvets.com/public/PDFs/ClientBrochures/Cat-to-Vet-HandoutPrint.pdf>
- http://www.catalystscouncil.org/resources/health_welfare/cat_carrier_video/index.aspx
- <http://avsbonline.org/resources/position-statements>
- <http://indoorpet.osu.edu>
- www.zoomroomonline.com/dog-training-videos/dog-body-language.html

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

Chemical Restraint

- Allows safe effective handling, blocking further distress. Avoid allowing patients to become fractious/agitated before considering; reduces the efficacy, allows learning to occur, advances fear responses.
- Desired plane of sedation—animal requires little to no restraint to accomplish all desired interactions, is unaware.
- Injectable forms of sedation IM are the most effective means of safely handling a fractious or highly fearful patient; protocol selection based on age, temperament, degree of health/disease.
- Manage environment to achieve and maintain desired sedation (white noise, music, dim lights, owner support, avoid triggers, Thunder cap, cotton balls in ears).
- Muzzle sedated patients for added safety.
- Oral administration of sedative/anxiolytic medication prior to arrival so experience is less fear-provoking, safer, and requires lower doses to achieve effect.

Injectable Chemical Restraint—Dogs

- For young fractious dogs—dexmedetomidine (10–20 $\mu\text{g}/\text{kg}$) + opioid (butorphanol* 0.2–0.4 mg/kg) IM \pm ketamine (3 mg/kg) IM.
- Alternative option—Telazol (tiletamine/zolazepam) 5–10 mg/kg IM (not practical for dogs > 20 kg due to high volume injection).
- For geriatric fractious dogs—acepromazine (0.05 mg/kg) OR dexmedetomidine (5 $\mu\text{g}/\text{kg}$) + opioid (butorphanol* 0.2–0.4 mg/kg) IM.
- Reverse dexmedetomidine with equivolume of atipamezole to volume of

dexmedetomidine administered IM/SC; in ketamine protocols wait 30–60 min to reverse.

*A full Mu opioid agonist, ex. morphine (0.2 mg/kg), hydromorphone (0.05–0.1 mg/kg), or oxymorphone (0.1 mg/kg) superior for pain management

Oral transmucosal—Dogs

- For healthy fractious dogs—dexmedetomidine (40 $\mu\text{g}/\text{kg}$) + morphine (1 mg/kg) OTM; reverse dexmedetomidine with half volume of atipamezole to volume of total dexmedetomidine IM or SC.
- Select dogs that: are pain sensitive, allow handling of mouth by owners or staff, have been DS/CC to placement of a syringe in cheek pouch.
- 1 hour to full effect; increased contact time with mucosa improves efficacy (avoid swallowing, spilling); slow application is key, increased viscosity (add honey, commercial agents) helps.
- Often requires additional IM dose of dexmedetomidine (10 $\mu\text{g}/\text{kg}$) + morphine (0.1–0.2 mg/kg); 15 min. to effect.
- Caution: commonly see vomiting.

Injectable Chemical Restraint—Cats

- For young fractious cats—dexmedetomidine (10–20 $\mu\text{g}/\text{kg}$) OR acepromazine (0.1 mg/kg) + ketamine (3–5 mg/kg) + opioid (butorphanol* 0.2 mg/kg or morphine 0.2 mg/kg) IM.
- Alternative option—Telazol (tiletamine/zolazepam) 5–10 mg/kg IM.
- For geriatric fractious cats—acepromazine (0.05 mg/kg) OR dexmedetomidine (5–10 $\mu\text{g}/\text{kg}$) + ketamine (3–5 mg/kg) + opioid (butorphanol* 0.2 mg/kg) IM.
- Reverse dexmedetomidine with half volume of atipamezole to volume of dexmedetomidine administered IM; in ketamine protocols wait 30–60 min to reverse.

*Full Mu opioid agonist, ex. morphine (0.2 mg/kg), hydromorphone (0.05–0.1 mg/kg), or oxymorphone (0.1 mg/kg) is superior for pain management.

Oral Transmucosal—Cats

- For healthy fractious cats—dexmedetomidine (40 $\mu\text{g}/\text{kg}$) + buprenorphine (0.02 mg/kg) OTM. Reverse dexmedetomidine with fourth-half volume of atipamezole to volume of total dexmedetomidine administered IM or SC.
- Additional IM injection may be required.

Protocols courtesy R. Bednarski, DVM, MS, DACVA

Oral Sedative/Anxiolytics

Administer 90 min. prior to travel to relieve mild to moderate fearful/fractious behavior or help patient cope with injectable sedation. Doses should be repeated Q8-12hr PRN for inpatients.

Dogs

- Trazodone: 4.0–18.0 mg/kg PO; not exceeding 300 mg per dose.

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- Clonidine: 0.01–0.05 mg/kg PO; can be combined with trazodone and/or benzodiazepines.
- Acepromazine: 0.55–2.2 mg/kg PO; best in combination with trazodone, gabapentin, or benzodiazepine; avoid as sole agent, doesn't provide anxiolysis.
- Lorazepam: 0.05–0.5 mg/kg PO.
- Diazepam: 0.5–2.2 mg/kg PO.
- Gabapentin: 20–40 mg/kg PO; can combine with trazodone, acepromazine, benzodiazepines.

Cats

- Acepromazine: 1.1–2.2 mg/kg PO.
- Lorazepam: 0.05–0.25 mg/kg PO; can combine with acepromazine.
- Gabapentin: 10–20 mg/kg PO; can combine with acepromazine.
- Buprenorphine: 0.01–0.03 mg/kg OTM.

CONTRAINDICATIONS

Cats—avoid oral diazepam; acute hepatic necrosis reported.

PRECAUTIONS

• Agitation, gastrointestinal upset, heavy sedation, changes in appetite are potential side effects of all of above oral medications. Always have client perform drug trial at home to determine response and ideal dose.

• Benzodiazepines—caution in fractious patients; disinhibition of aggression possible. Avoid in patients with a history of aggression in the home environment.

POSSIBLE INTERACTIONS

Avoid combining oral acepromazine with clonidine due to potential for serious fluctuations in blood pressure.

ALTERNATIVE DRUGS

Neutraceuticals: Harmonese, Anxitane, Zylkene, Composure. Additional medications likely required.

**FOLLOW-UP****PATIENT MONITORING**

Evaluate physiologic and behavioral parameters for evidence of stress response activation, and maintenance of normal physiologic and behavioral parameters. Long-term efficacy evidenced by reduced fear and increased affiliative behavior at subsequent visits (i.e., behavior improves with each handling bout).

PREVENTION/AVOIDANCE

- Prevention is key. It is more effective, less expensive, faster, and easier to

avoid problematic behavior.

- Client education—proper socialization of puppies and kittens, acclimate to a travel, DS/CC to handling.
- Refer clients to science-based humane written, online, and direct referrals.
- Low-stress handling and CC during all puppy and kitten sequential vaccination visits and adult visits.
- “Happy visits” (DS/CC) for puppies and kittens between sequential vaccine visits, and for adults after intense or multiple sick visits or hospitalization.
- Offer well-managed, positive puppy and kitten classes at your hospital.

POSSIBLE COMPLICATIONS

Animals with fearful and/or aggressive behavior are not able to effectively receive routine wellness care, diagnostic testing, advanced treatments or hospitalization, jeopardizing overall physical wellness.

EXPECTED COURSE AND PROGNOSIS
N/A**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Pets displaying fearful or fractious behavior in a veterinary setting often have comorbid behavioral problems in the home environment, including aggression to owners or strangers, leash reactivity, resource guarding, and anxiety disorders. Opening a dialog with clients, screening for these behavioral issues, and effectively triaging them will promote the patient's overall behavioral wellness and handling.

AGE-RELATED FACTORS

- Socialization period—3–12 wks (dogs), 2–7 wks (cats); this is the period where early exposure can minimize fear. A few sessions of exposure to the veterinary setting, staff, and restraint during this time paired with a positive experience (food) can lead to less fear and improved acceptance of future handling.
- Fear period—8–10 wks. of age and between 4 and 11 mo. of age (dogs; unknown for cats). Susceptible to single-event learning, highly sensitive to negative experiences. Single frightening veterinary visit during this time frame can result in fear of setting, handling, or personnel.
- Social maturity—reached at 2–4 y of age (dogs), 1–2 y (cats); period where animals develop mature social behaviors. Dogs who are fearful as puppies or adolescents often may not show first signs of aggression until this time. Essential to recognize signs

of fear in juvenile and/or adolescent so a plan to CC a positive emotional response to the veterinary clinic, handling, and procedures can be established before aggression develops.

ZOONOTIC POTENTIAL

Bite wounds and associated infections are a zoonotic potential.

PREGNANCY/FERTILITY/BREEDING

Fearful and aggressive temperaments may be heritable and predispose to veterinary clinic fear.

SYNONYMS

Fear-related aggression, defensive aggression, pain related aggression, phobic behavior, fearful behavior

SEE ALSO

- Fears, Phobias and Anxieties—Dogs
- Fears, Phobias and Anxieties—Cats

ABBREVIATIONS

- CC = counterconditioning • DS = desensitization • OTM = oral transmucosal

INTERNET RESOURCES

- www.avsaponline.org
- www.drsophiayin.com
- <http://indoorpet.osu.edu/veterinarians>
- www.catalystcouncil.org
- www.doggonesafe.com/Signs_of_Anxiety
- <https://www.aspca.org/pet-care/virtual-pet-behaviorist/dog-behavior/canine-body-language> • www.catvets.com
- www.icatcare.org

Suggested Reading

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Yin S. Low stress handling, restraint, and behavior modification of dogs and cats. Davis, CA: Cattle Dog Publishing, 2009.

Authors Meghan E. Herron and Traci A. Shreyer

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**Client Education Handout
available online**

FEARS, PHOBIAS, AND ANXIETIES—CATS



BASICS

DEFINITION

• Fear is the feeling of apprehension resulting from the nearness of some situation or object presenting an external threat. The response of the autonomic nervous system prepares the body for “freeze, fight, or flight.” As such, it is a normal behavior, essential for adaptation and survival. • Anxiety is the anticipation of dangers from unknown or imagined origins that results in physiologic reactions associated with fear. Anxiety may occur in the aftermath of a fear-producing event or as a result of unrelated environmental changes that are unpredictable. • A phobia is a persistent and excessive fear of a specific stimulus, such as a thunderstorm or separation from an attachment figure.

PATHOPHYSIOLOGY

• Stress responses become problematic when the individual is not able to control the stressful situation by his or her actions or escape from it through appropriate behavioral responses. • Chronic anxiety or fear can lead to secondary behavior problems, such as overgrooming, spraying, or intercat aggression, or predispose the cat to health problems owing to a compromised immune system.

SYSTEMS AFFECTED

- Behavioral—hypervigilance, avoidance behaviors, possible aggression if handling or restraint attempted.
- Cardiovascular—increased heart rate and blood flow to internal organs during fear-evoking incidents.
- Endocrine/Metabolic—glucose release into the bloodstream, release of glucocorticoids.
- Gastrointestinal—decreased appetite.
- Hemic/Lymphatic/Immune—chronic stress effects on immune function.
- Musculoskeletal—weight loss over time as response to chronic stress effects on appetite, decreased food intake due to hiding behavior.
- Neuromuscular—may see a decrease in activity due to avoidance and hiding. Fearful/anxious reaction may also include pacing, trembling, repetitive activity.
- Ophthalmic—dilated pupils in response to autonomic nervous system stimulation.
- Respiratory—increased respiratory rate when anxious or frightened.
- Skin/Exocrine—may show signs of secondary problem behavior such as overgrooming.

GENETICS

- Genetic component unknown but possible.
- Breed/coat color and paternal personality have been linked to individual personality traits in cats.

SIGNALMENT

Any age, sex, or breed

SIGNS

General Comments

- Signs of fear or anxiety can vary between individuals and with different stimuli. • In mild cases of anxiety or fear, the cat may become tense and more reactive to environmental stimuli. Some individuals may retreat to perceived safe hiding places or show little movement. Cats in a panic can become very aggressive or destructive in their attempts to get away from the thing they fear.
- Stimuli triggering anxious or fearful responses may be very specific (a particular individual, noise, or situation) or more generalized.

Historical Findings

- Obtain a clear description of the cat's body language, behavior, and events or situations that consistently trigger anxiety or fear. Information about specific triggers associated with anxious or fearful behavior may be helpful in setting up a behavioral modification and environmental management program.
- Body postures associated with fearful behavior include ears flattened to the back or to the side of the head, crouched body posture when resting or moving, lowered head, tail tucked alongside the body or held low, piloerection, “Halloween cat” silhouette.
- Pupils are often dilated; cat may be panting, shaking, drooling, or shedding hair.
- If the fear is intense, cat may lose bladder and bowel control, express its anal sacs.
- Vocalizations are usually minimal, unless the cat is showing defensive behavior in response to a perceived threat.
- The cat may pace, vocalize, and solicit attention from the owner.
- Urine spraying, destructive scratching may be seen in anxious cats.
- Details of the cat's early life, if known, may indicate a history of poor socialization and environmental exposure or possible genetic influences, feral ancestry.

Physical Examination Findings

Usually unremarkable unless the cat has injured itself trying to escape or while seeking shelter during its fright. Cats in veterinary clinics often show behavior markedly different from what is seen at home.

CAUSES & RISK FACTORS

Fearful behavior in cats can be related to the following factors:

- Genetic influences on temperament.
- Lack of positive early experience and socialization, observational learning from fearful mother, other adult cats.
- Learning from negative experiences.
- Social stress, population pressure.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

A thorough medical history and physical examination will help differentiate physical causes from behavioral.

CBC/BIOCHEMISTRY/URINALYSIS

May be indicated by information obtained in the history and physical examination, or as premedication screen.

OTHER LABORATORY TESTS

As indicated if physical causes are suspected.

IMAGING

May be indicated if history, physical, and laboratory tests suggest an organic cause for the cat's behavior.



TREATMENT

ACTIVITY

Normal interactions with owners encouraged, but contact/outgoing behavior should not be forced.

DIET

- Normal dietary routine.
- Placement of food, water, and litter box may need to be altered if anxious or fearful behavior is limiting access.

CLIENT EDUCATION

General Comments

- Discuss behavioral expectations. Owner expectations in regards to social interactions with him- or herself and with other cats may be contributing to the problem and could affect prognosis.
- A reasonable treatment plan involving case-tailored behavioral modification and environmental adjustments, and ancillary information such as handouts or articles, will help the owner better understand the situation and implement treatment.

Behavioral Therapy

- Identify the specific stimulus that provokes the fearful or anxious behavior.
- Avoid exposure to the fear-producing stimuli, if possible. Provide ways for the cat to manage the situation, by noting its “hideout” preferences and creating a “safe place” for the cat to go to if the situation cannot be avoided.
- If the cat must be handled while fearful, caution and physical restraint aids (cat muzzles, cat bags, towel wraps etc.) should be used to prevent injury and decrease stress for both cat and handler.
- Desensitization and counter-conditioning to help decrease reactivity to the fear-producing stimulus. Systematic desensitization is a program of slowly increasing exposure to the object or situation the cat fears. Counter-conditioning consists of enhancing an internal and external environment counter to one of fear, usually accomplished with food rewards or other pleasurable stimuli such as playing with toys. See the suggested reading list for references that provide greater detail.
- Address secondary problems such as strained social interactions subsequent to defensive aggression directed toward humans or other cats, or elimination problems that may be the result of fears or anxieties.

(CONTINUED)

FEARS, PHOBIAS, AND ANXIETIES—CATS**MEDICATIONS****DRUG(S)**

- Medication can be a helpful adjunct to behavioral modification, if the animal's fearful or anxious behavior is so intense that it interferes with learning or other normal behavioral activities.
- No drug is approved by the FDA for use in cats for fearful behavior; therefore, clients must be advised that information concerning efficacy, contraindications, and side effects is limited and often extrapolated from the human literature.
- If there are questions or concerns about a specific patient or medication, a consultation with a veterinary behaviorist may be helpful.

Selective Serotonin Reuptake Inhibitors

- Fluoxetine (Prozac) 0.5–1.0 mg/kg PO q24h.
- Side effects: decreased appetite and irritability.
- Paroxetine (Paxil) 0.5–1.0 mg/kg PO q24h.
- Side effects: decreased appetite, irritability, constipation.

Tricyclic Antidepressants

- Clomipramine 0.5 mg/kg q24h, 2.5–5.0 mg/cat PO q24h.
- Side effects: sedation, anticholinergic effects, possible cardiac conduction disturbances in predisposed animals.
- Amitriptyline 0.5–1.0 mg/kg PO q12–24h.
- Side effects: sedation, anticholinergic effects, possible cardiac conduction disturbances in predisposed animals.

Azapirone

- Buspirone 0.5–1.0 mg/kg q12h, 2.5–7.5 mg/cat PO q12h.
- Side effects: GI upset, mild sedation, disinhibition of aggressive behavior.

Benzodiazepines

- Alprazolam 0.125–0.25 mg/cat q12h.
- Side effects: sedation, disinhibition of aggression, increased appetite.

CONTRAINDICATIONS

- Use of buspirone, TCAs, and SSRIs not recommended in animals with seizures. SSRIs and TCAs should not be used together nor combined with MAOIs such as amitraz and selegiline. • Diazepam (Valium) is not recommended for use in cats due to rare reported cases of fatal idiopathic hepatic necrosis.

PRECAUTIONS

- Basic laboratory tests are strongly suggested before placing an animal on a psychotropic medication, to ensure that liver and kidney

functions are sufficient to metabolize the medication and to check for any physical condition that may be a contraindication to specific drugs. • Medicating cats can prove stressful, especially when the medication is not palatable, as are many of the above medications. Compounding medications in a more palatable form can ease administration, increasing consumption and effectiveness of the drug.

POSSIBLE INTERACTIONS

Discuss any questions on possible drug interactions with a veterinary behaviorist or a pharmacist.

ALTERNATIVE DRUG(S)

Pheromone therapy (Feliway), initially developed for urine marking cases, has been used as an aerosol spray and/or room diffuser to calm anxious and fearful cats, at home, during travel, and during hospitalization or clinic visits. Alternative medications such as herbal or dietary preparations including L-theanine have been suggested for anxious and fearful behaviors in animals; some have scientific studies showing efficacy for these conditions in cats. Concomitant use of some herbal remedies and psychotropic medications may lead to serious drug interactions, so clients should be questioned about over-the-counter remedies they are currently giving the cat.

**FOLLOW-UP****PATIENT MONITORING**

Frequent follow-up either in person or by telephone is necessary, especially during the first few months of treatment, to motivate the client and monitor the effectiveness of any adjunct drug treatment.

PREVENTION/AVOIDANCE

- Calm interactions and positive associations with socialization from 2–7 weeks stimuli may keep fear-based reactions to a minimum.
- Early socialization to people, places and things up to 7 weeks, and ongoing positive exposure during the first year may help prevent some later problems with fearful behavior.

POSSIBLE COMPLICATIONS

Secondary behavior problems may arise or persist after the fearful or anxious behavior has diminished and will need specific treatment.

EXPECTED COURSE AND PROGNOSIS

- Animals with shy personalities or poor socialization histories may show a minimal

response to treatment. • A realistic “end point” depends on the animal's background (socialization history, genetic and individual differences in personality), the home situation, and other confounding factors such as the frequency of natural exposure to fear-producing stimuli. • Medication may help improve but not totally ameliorate signs.

**MISCELLANEOUS****F****ASSOCIATED CONDITIONS**

- Stereotypic or compulsive disorders. • Urine marking, inappropriate elimination.
- Defensive aggression directed toward humans, other animals: may also make cat a target for aggression from other cats.

ZOONOTIC POTENTIAL

Fear-related aggression may lead to defensive biting or scratching and subsequent infections.

PREGNANCY/FERTILITY/BREEDING

Avoid use in pregnant animals.

SEE ALSO

- Aggression, Overview—Cats • Fear and Aggression in Veterinary Visits • Compulsive Disorders—Cats • Fear and Aggression in Veterinary Visits • Housesoiling—Cats
- Marking, Roaming, and Mounting Behavior—Cats

ABBREVIATIONS

- FDA = US Food and Drug Administration
- GI = gastrointestinal • MAOI = monoamine oxidase inhibitor • SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant

INTERNET RESOURCES

For information on pheromone therapy see: www.feliway.com.

Suggested Reading

- Landsberg G, Hunthausen W, Ackerman L. Behavior Problems of the Dog and Cat, 3rd ed. Edinburgh: Saunders Elsevier, 2013.
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FEARS, PHOBIAS, AND ANXIETIES—DOGS



BASICS

DEFINITION

Fear

An emotion consisting of a psychological and a physiologic response (i.e., stress response) to the presence of a dangerous stimulus (e.g., person, animal, situation, sound, object) inducing an adaptive, avoidance reaction.

F

Phobias

- A marked, irrational, and excessive fear of a stimulus (e.g., animal, situation, person, sound, object) consisting of a physiologic and psychological response resulting in a maladaptive reaction.
- Most common—noises (e.g., thunderstorms or firecrackers).

Anxiety

Reaction consisting of a physiologic and psychological response triggered by the anticipation of future danger or memory of past dangers. The original fear-inducing stimulus does not have to be present to cause the response.

PATHOPHYSIOLOGY

- Information about a fear-inducing stimulus is conducted from sensory organs to the central nucleus (CN) of the amygdala. The CN sends output to the central grey matter (musculoskeletal response), the lateral hypothalamus (ANS response), and the stria terminalis (hormonal response), mounting a physiologic stress response.
- The physiologic stress response is graded based on the animal's perceived level of control, coping strategy, and perceived level of difficulty.
- Any neutral stimulus in the environment can be paired with physiologic stress response until the stimulus causes the physiologic response.
- Certain stress hormones enhance learning, memory consolidation, and retrieval.
- There is evidence that while frightening memories can be significantly reduced, they cannot be "erased."

SYSTEMS AFFECTED

- Behavioral—immobility, restlessness, pacing, circling, hyperattachment, escape, avoidance, defensiveness, destructiveness, vocalization, aggression.
- Cardiovascular—tachycardia.
- Endocrine/Metabolic—alterations in the HPA axis, increased blood glucose.
- Gastrointestinal—inappetence, hypersalivation, vomiting, diarrhea, defecation.
- Hemic/Lymphatic/Immune—stress leukogram.
- Musculoskeletal—self-injury.
- Neuromuscular—increased motor activity, trembling, decreased pain perception, catatonia.
- Ophthalmic—episcleral injection, mydriasis.
- Renal/Urologic—urination.
- Respiratory—tachypnea.
- Skin/Exocrine—traumatic injury, acral lick dermatitis (ALD).

GENETICS

Heredity influences the development of fears and phobias, although it is unclear at this

time to what extent specific fears (e.g., noise) are heritable.

INCIDENCE/PREVALENCE

Unknown for fears, anxieties, and phobias.

SIGNALMENT

No age, breed, or sex is overrepresented.

SIGNS

General Comments

Hypervigilance, ANS arousal, catatonia, increased motor activity, elimination, destruction, excessive vocalization, hypersalivation, panting, hiding, trembling, escape behaviors, fearful body language.

Historical Findings

Traumatic experience, inadequate socialization, fearful/anxious dam or sire, history of inability to escape stimulus (e.g., locked in crate), or exposure while alone.

Physical Examination Findings

Usually unremarkable; self-induced injuries possible.

CAUSES

- Inadequate socialization, traumatic event, hereditary, CDS, previous learning.
- Illnesses or painful physical conditions may increase anxiety and contribute to the development of fears, phobias, and anxieties.

RISK FACTORS

General—existing fears, anxieties, and phobias; inadequate socialization, rehoming, anxious/fearful/physically ill dam, traumatic event—especially when alone.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Behavioral—CDS, unruly behavior, incomplete housetraining, urine/fecal marking, attention-seeking behavior, lack of stimulation, territorial behavior.
- Medical—neoplasia (e.g., intracranial mass), endocrine disease (e.g., hepatomegaly, diabetes, hypothyroidism), cystitis, pyelonephritis, diabetes, gastrointestinal disease (e.g., colitis, parasites, food allergies, IBD, IBS), neurologic disease (e.g., seizures, neuritis), dermatologic (e.g., ALD, atopy, flea allergy dermatitis, food allergies), toxicity (e.g., lead, recreational drugs).

CBC/BIOCHEMISTRY/URINALYSIS

- Should be normal.
- Perform before initiating drug treatment.

OTHER LABORATORY TESTS

- Adrenal tests if indicated by history, signalment, physical examination, and laboratory tests.
- Assess thyroid status before initiating drug treatment.

IMAGING

CT or MRI to rule out structural brain disorder may be indicated. Other imaging as

necessary to diagnose and treat underlying medical disorders.

DIAGNOSTIC PROCEDURES

- Thorough behavioral history and observation of the patient (video of behavior is helpful).
- Screen patients for aggression.
- Exposure to stimulus if safe.
- Appropriate diagnostic procedures to evaluate any concurrent medical diseases.



TREATMENT

APPROPRIATE HEALTH CARE

- Typically outpatient.
- Inpatient (dayboarding/daycare)—fear-/anxiety-/phobia-inducing stimulus unavoidable, patient is causing self-injury, medication is not yet effective, owner is unable to complete treatment, hospitalization to stabilize patient on medication.
- Treatment includes owner education, safety, behavior modification to change emotional state of patient, environmental modification to facilitate avoidance and distract patient during episodes, and reduction of anxiety.
- Diagnose and treat any medical conditions that may cause pain, discomfort, or changes in mood as well as any injuries.

Safety

• Owner—should not physically manipulate the patient when frightened or hiding, as this can result in owner-directed aggression. Instead, attempt to move the dog with food or a toy.

• Patient—if intense escape attempts or self-injury is present, avoid crating and limit the dog's access to windows, doors, electrical wiring, and water lines. Consider dayboarding.

• Public—if the dog has shown aggression when fearful/anxious, owner should avoid provocative situations and use appropriate control devices (e.g., Head halter, basket muzzle).

Behavior Modification

- Avoid stimulus for 2–8 weeks depending on the severity of reaction while teaching coping skills to the patient (e.g., sit, watch, look at that, leave it, relaxation) and setting up a safe spot.
- Structured interactions with the owner (e.g., sit for all interactions).
- Independence exercises—down/stay with a food toy.
- Punishment (e.g., shock/choke collar correction, yelling, hitting) is contraindicated.
- Client should distract dog and redirect to play or a food toy when frightened or anxious.
- Desensitization and counter-conditioning—begin after coping tools have been taught. Should be attempted with supervision as it can sensitize the animal to the stimulus, causing the behavior disorder to progress.

Environmental Modification

- Create a safe spot where exposure to the fear-producing stimulus can be limited.
- Consider dayboarding/daycare.
- Limit use

(CONTINUED)

FEARS, PHOBIAS, AND ANXIETIES—DOGS

of a crate until the dog readily goes there, and does not panic when confined. • Rotate toys.

NURSING CARE

Behavior treatment appointments can be scheduled with veterinary technicians.

ACTIVITY

Increased exercise will act as environmental enrichment for the patient but will not by itself significantly lower anxiety/fear disorders.

CLIENT EDUCATION

- Advise owners that patient is not spiteful or guilty; may be a long course of treatment; will most likely be managed, not cured. • Help the client understand the subtlety of the signs involved and learn to recognize the signs associated with physiologic stress.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Should always be prescribed with a complete treatment plan in order to be compliant with the standard of care.
- Most treatment will be long-term, possibly years; minimum treatment is generally 6 months with concurrent behavior modification. If the dog has significantly improved in 6 months, try slow weaning by reducing the dose by 25–50% every 14 days.
- Situational, mild-PRN drug indicated (e.g., benzodiazepine, SARI) either alone if stimulus is occasional and predictable or more commonly concurrent with SSRI or TCA prior to event.

◦ Works best if administered before any signs of anxiety, fear, or panic; minimally 30–90 minutes before the anticipated provocative stimulus.

◦ Benzodiazepines: diazepam 0.50–2.2 mg/kg PO up to q4; clorazepate 0.50–2.2 mg/kg PO up to q4; alprazolam 0.01–0.1 mg/kg PO up to q4.

◦ SARI: trazodone 2.0–10.0 mg/kg PO up to q8h.

◦ Alpha2 agonist: clonidine 0.01–0.05 mg/kg PO up to q12h.

- Generalized, stimulus unavoidable or severe—daily administered drug indicated.

◦ Selective serotonin reuptake inhibitors, tricyclic antidepressants. Both TCAs and SSRIs can take up to 6 weeks to take effect. Patients should be started at the low end of the dosing range and then slowly increased in 2- to 4-week increments based on response to avoid side effects.

◦ TCA: clomipramine 1.0–3.0 mg/kg PO q12h.

◦ SSRI: sertraline 1.0–3.0 mg/kg PO q24; fluoxetine 0.5–2.0 mg/kg PO q24.

PRECAUTIONS

- All listed medications are extra-label except for clomipramine and fluoxetine for the treatment of separation anxiety in dogs in the

United States—follow Health and Human Services recommendations. • Cardiac conduction anomalies—use caution and monitoring when giving TCAs. • Use caution when prescribing drugs to geriatric patients or patients with hepatic or renal compromise—review metabolism and elimination of medication before prescribing. • Clients should receive drug information handouts with potential side effects listed.

• Mood-altering medications have the potential to increase agitation, fear, and aggression.

POSSIBLE INTERACTIONS

- Use caution when prescribing multiple medications concurrently that have the same mode of action. Review drug monographs for each drug before prescribing. • Do not use SARIs, SSRIs, or TCAs with MAOIs including but not limited to selegiline, Preventic collars, and Amitraz Dip. • Do not use SSRIs and TCAs together—possible risk of serotonin syndrome, which can be fatal.

ALTERNATIVE DRUGS**Supplements**

- Anxitane—as directed on label. Flavored—do not use in patients on elimination diets.
- Melatonin—< 5 kg → 1.0 mg; 5–12 kg → 1.5 mg; > 12 kg → 3.0–6.0 mg. All doses PO, up to q12h. • Zylkene—as directed on label. • SAMe—10–20 mg/kg PO q24h.
- Royal Canin Calm Diet (alpha-casozepine and tryptophan supplemented).

**FOLLOW-UP****PATIENT MONITORING**

- Clients should contact the veterinarian at 2-week intervals for the first 6–8 weeks of treatment. Typically the treatment plan will have to be altered possibly including medication dosing or medication changes.
- CBC, biochemistry, urinalysis, T₄, fT₄ q12 months for animals < 8 years on daily administered medications; senior dogs may require more frequent reassessment based on age and health.

PREVENTION/AVOIDANCE

- Proper socialization—8–12 weeks, including puppy classes starting at 8 weeks.
- Structured relationship with owner (sit for all interactions). • Basic obedience. • Treat traumatic experiences immediately.

POSSIBLE COMPLICATIONS

If left untreated or treated with medication only, progression is likely.

EXPECTED COURSE AND PROGNOSIS

- Course of treatment depends on response to medication, suitability of the environment, and client's ability to perform behavior modification. • Treatment duration varies from 2 to 12 months depending on severity

and number of problems. Only dogs who respond well to behavior modification and environmental management can be expected to be able to be weaned off medication.

- Typically, treatment will continue to some extent throughout the dog's life.

**MISCELLANEOUS****AGE-RELATED FACTORS**

CDS can present as non-specific fear.

PREGNANCY/FERTILITY/BREEDING

Most of the listed drugs are either not evaluated in or contraindicated in pregnant animals.

SYNONYMS

- Generalized anxiety • Neophobia • Specific anxiety

ABBREVIATIONS

- ALD = acral lick dermatitis • ANS = autonomic nervous system • CDS = cognitive dysfunction syndrome • CN = central nucleus • CT = computed tomography • HPA = hypothalamic-pituitary-adrenal • IBD = inflammatory bowel disease • IBS = irritable bowel syndrome • MAOI = monoamine oxidase inhibitor • MRI = magnetic resonance imaging • SARI = serotonin reuptake inhibitor/antagonist • SSRI = selective serotonin reuptake inhibitor • T₄ = thyroxine • TCA = tricyclic antidepressant

INTERNET RESOURCES

- American College of Veterinary Behaviorists: www.dacvb.org. • American Veterinary Society of Animal Behavior: www.avsonline.org.

Suggested Reading

- Horwitz D, Mills D, eds. BSAVA Manual of Canine and Feline Behavioural Medicine. 2nd ed. Gloucestershire, UK: BSAVA, 2002.
King J, Simpson B, Overall KL, et al. Treatment of separation anxiety in dogs with clomipramine: Results from a prospective, randomized, double-blinded, placebo-controlled clinical trial. *Appl Anim Beh Sci* 2000, 67:255–275.

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**Client Education Handout
available online**

FELINE CALICIVIRUS INFECTION



BASICS

DEFINITION

A common viral respiratory disease of domestic and exotic cats characterized by upper respiratory signs, oral ulceration, pneumonia, and occasionally arthritis, or a highly fatal systemic hemorrhagic disease.

F

PATHOPHYSIOLOGY

Rapid cytolysis of infected cells with resulting tissue pathology and clinical disease.

SYSTEMS AFFECTED

- Gastrointestinal—ulceration of the tongue common; occasional ulceration of the hard palate and lips; infection occurs in intestines; usually no clinical disease.
- Hemic/Lymphatic/Immune—hemorrhage.
- Musculoskeletal—acute arthritis.
- Ophthalmic—acute serous conjunctivitis without keratitis or corneal ulcers.
- Respiratory—rhinitis; interstitial pneumonia; ulceration of the tip of the nose.

GENETICS

None

INCIDENCE/PREVALENCE

- Persistent infection common.
- Clinical disease—common in multicat facilities, shelters, and breeding catteries.
- Routine vaccination—reduced incidence of clinical disease; has not decreased the prevalence of the virus.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Cat

Breed Predilections

None

Mean Age and Range

- Young kittens > 6 weeks old—most common.
- Cats of any age may show clinical disease.

Predominant Sex

None

SIGNS

General Comments

May present as an upper respiratory infection with eye and nose involvement, as an ulcerative disease primarily of the mouth, as pneumonia, as an acute arthritis, as a systemic hemorrhagic disease, or any combination of these.

Historical Findings

- Sudden onset.
- Anorexia.
- Ocular or nasal discharge, usually with little or no sneezing.
- Ulcers on the tongue, hard palate, lips, tip of nose, or around claws.
- Dyspnea from pneumonia.
- Acute, painful lameness.

Physical Examination Findings

- Generally alert and in good condition.
- Fever.
- Ulcers may occur without other signs.
- Systemic hemorrhage.

CAUSES

- A small, non-enveloped single-stranded RNA virus, feline calicivirus.
- Numerous strains exist in nature, with varying degrees of antigenic cross-reactivity.
- More than 1 serotype.
- Relatively stable and resistant to many disinfectants.

RISK FACTORS

- Lack of vaccination or improper vaccination
- Multi-cat facilities
- Concurrent infections with other pathogens (e.g., FHV-1 or FPV)
- Poor ventilation



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Feline viral rhinotracheitis
- Chlamydiosis
- *Bordetella bronchiseptica*

CBC/BIOCHEMISTRY/URINALYSIS

No characteristic or consistent findings

OTHER LABORATORY TESTS

Serologic testing on paired serum samples—detect a rise in neutralizing antibody titers against the virus.

IMAGING

Radiographs of the lungs—a consolidation of lung tissue in cats with pneumonia.

DIAGNOSTIC PROCEDURES

- Cell cultures to isolate the virus—oral pharynx; lung tissue; feces; blood; secretions from the nose and conjunctiva.
- PCR.
- Immunofluorescent assays of lung tissue—viral antigen.

PATHOLOGIC FINDINGS

- Gross—upper respiratory infection; ocular and nasal discharge; pneumonia with consolidation of large portions of individual lung lobes; possible ulcerations on the tongue, lips, and hard palate; systemic hemorrhages.
- Histopathologic—interstitial pneumonia of large portions of individual lung lobes; ulcerations on epithelium of the tongue, lips, and hard palate; mild inflammatory reactions in the nose and conjunctiva; systemic hemorrhages.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient, unless severe pneumonia or hemorrhages occur

NURSING CARE

- Clean eyes and nose as indicated
- Provide soft foods
- Oxygen—with severe pneumonia

ACTIVITY

Patients should be restricted from contact with other cats to prevent transmission of the causative virus.

DIET

- No restrictions.
- Special diets—perhaps to entice anorectic cats to resume eating.
- Soft foods—if ulcerations restrict eating.

CLIENT EDUCATION

Discuss the need for proper vaccination and the need to modify the vaccination protocol in breeding catteries to include kittens before they become infected (often at 6–8 weeks of age) from a carrier queen.

SURGICAL CONSIDERATIONS

None



MEDICATIONS

DRUG(S) OF CHOICE

- No specific antiviral drugs that are effective.
- Broad-spectrum antibiotics—usually indicated (e.g., amoxicillin at 22 mg/kg PO q12h).
- Secondary bacterial infections of affected cats are not nearly as important as with FHV-1 infections.
- Antibiotic eye ointments—to reduce secondary bacterial infections of the conjunctiva.
- Appropriate pain medication—for transient arthritis pain.

CONTRAINdicATIONS

None

PRECAUTIONS

None

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

- Monitor for sudden development of dyspnea associated with pneumonia.
- No specific laboratory tests.

PREVENTION/AVOIDANCE

- All cats should be vaccinated at the same time they are vaccinated against FHV-1 and FPV; routine vaccination with either MLV or inactivated vaccines should be done as early as 6 weeks of age and repeated every 3–4 weeks until at least 16 weeks of age.

(CONTINUED)

- Breeding catteries—respiratory disease is a problem; vaccinate kittens at an earlier age, either with an additional vaccination at 4–5 weeks of age or with an intranasal vaccine at 10–14 days of age; follow-up vaccinations every 3–4 weeks until 16 weeks of age.
- American Association of Feline Practitioners—classifies FHV, FPV, and calicivirus as core vaccines; vaccinate all cats with these three agents on the initial visit as early as 6 weeks of age, repeat every 3–4 weeks until 16 weeks of age, and 1 year after the last kitten vaccine; revaccinate for calicivirus every 3 years.
- Vaccination will not prevent virus infection in a subsequent exposure but will prevent serious clinical disease caused by most strains.

POSSIBLE COMPLICATIONS

- Interstitial pneumonia—most serious complication; can be life-threatening.
- Secondary bacterial infections of the lungs or upper airways.
- Oral ulcers and the acute arthritis usually heal without complications.
- Systemic hemorrhagic disease may be severe and fatal.

EXPECTED COURSE AND PROGNOSIS

- Clinical disease—usually appears 3–4 days after exposure.
- Once neutralizing antibodies appear, about 7 days after exposure, recovery is usually rapid.
- Prognosis excellent, unless severe pneumonia or systemic hemorrhagic disease develops.
- Recovered cats—persistently infected for long periods; will continuously shed small quantities of virus in oral secretions.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Affected cats may also be concurrently infected with FHV-1, especially in multi-cat and breeding facilities.

AGE-RELATED FACTORS

Usually occurs in young kittens whose maternally derived immunity has waned.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Generally no problem, because most cats have been exposed or vaccinated before becoming pregnant.

SYNONYMS

Feline picornavirus infection—FCV originally classified as a picornavirus; older literature refers to the infection by this name; no known picornavirus that infects cats.

SEE ALSO

Chlamydiosis—Cats

ABBREVIATIONS

- FCV = feline calicivirus
- FHV = feline herpesvirus
- FPV = feline parvovirus
- MLV = modified live virus
- PCR = polymerase chain reaction

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Client Education Handout available online

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FELINE FOAMY VIRUS INFECTION (FFV)



BASICS

OVERVIEW

- A complex retrovirus in the Spumaretrovirinae subfamily that infects cats, apparently with little or no pathogenic effect.
- Found worldwide; estimated prevalences, 10–70% or greater.
- Present in some non-domestic feline populations.
- Infection linked statistically with chronic progressive polyarthritis; disease has not been reproduced by experimental infection.
- Experimentally infected cats have subclinical glomerulonephritis and interstitial pneumonia.
- Some strains infect lymphoblastoid cells and induce apoptosis—suggests potential impact on immune function in cats.
- Research—disease potential low; nuisance when using feline-origin tissue culture cells; test cats and remove from study if FFV-positive.
- Potential for use as a gene therapy or vaccine vector is under investigation.

SIGNALMENT

- Cats—free-roaming more than multi-cat households or catteries.
- Prevalence of virus—low in kittens; increases with age.
- No clear sex predilection—some early studies found that males were more likely than females to be infected, but a study of Australian cats found no difference between rates of infection in males and females.
- Chronic progressive polyarthritis (possibly from immune complex formation) occurs predominantly in males aged 1.5–5 years.

SIGNS

- Most affected cats healthy.
- Statistical links with myeloproliferative disease and chronic progressive polyarthritis—may actually reflect co-infection with FIV, FeLV or other pathogens.
- Chronic progressive polyarthritis—swollen joints; abnormal gait; lymphadenomegaly.

CAUSES & RISK FACTORS

- Transmission—somewhat controversial; possibly through bites; free-roaming cats at greater risk of infection.
- Co-infections with FIV and FeLV—fairly common, possibly because of shared transmission modes and risk factors; FFV

co-infection does not enhance early pathogenesis of FIV infections.

- Transmitted efficiently from infected queens to their offspring, probably *in utero*.
- The high prevalence of infection in some cat populations suggests casual contact may play a role in transmission; this has not been demonstrated experimentally.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Signs of chronic progressive polyarthritis—test for FIV, FeLV, and septic joint disease.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

- Serologic testing—for FFV antibodies and virus isolation; not readily available; not particularly useful because correlation between FFV infection and disease is so tenuous.
- Qualitative real-time PCR—for detection of viral nucleic acids; available commercially; may be useful for establishing FFV-negative cat colonies and monitoring biologic products or vaccines.
- Virus isolation from peripheral blood lymphocytes or buffy coat cells.

DIAGNOSTIC PROCEDURES

- Joint fluid cytology—with chronic progressive polyarthritis; may reveal high numbers of neutrophils and large mononuclear cells.
- Histology—lymphocytic, plasmocytic infiltrates common with joint disease; osteoporosis with periarticular periosteal proliferation or periarticular erosions and joint deformities may be seen.



TREATMENT

None, except for treatment of chronic progressive polyarthritis.



MEDICATIONS

DRUG(S)

Chronic progressive polyarthritis—immunosuppressive doses of prednisone and

cyclophosphamide (see Immune-Mediated Polyarthritis for more information).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Immunosuppressive drugs—take care when using in patients co-infected with FIV or FeLV.



FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS

- Infection with FFV alone—adverse consequences unlikely.
- Chronic progressive polyarthritis—often difficult to control; poor prognosis for long-term recovery.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Chronic progressive polyarthritis
- Co-infections with FIV and FeLV

ZOONOTIC POTENTIAL

No evidence of zoonotic transmission, although studies are limited.

SYNOMYMS

- Feline syncytial virus
- Feline syncytium-forming virus

SEE ALSO

Immune-Mediated Polyarthritis

ABBREVIATIONS

- FeLV = feline leukemia virus
- FFV = feline foamy virus infection
- FIV = feline immunodeficiency virus
- PCR = polymerase chain reaction

Suggested Reading

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FELINE HERPESVIRUS INFECTION



BASICS

DEFINITION

Causes an acute disease in domestic and many exotic species of cats, which is characterized by sneezing, fever, rhinitis, conjunctivitis, and ulcerative keratitis.

PATHOPHYSIOLOGY

FHV-1—causes an acute cytopathic infection of respiratory or ocular epithelium after oral, intranasal, or conjunctival exposure. This intracellular virus travels from cell to cell and does not stimulate a strong immune response from the host.

SYSTEMS AFFECTED

- Integumentary—herpes dermatitis may occur near the nasal openings.
- Ophthalmic—often conjunctivitis with serous or purulent ocular discharge; ulcerative keratitis or panophthalmitis can occur.
- Reproductive—*in utero* infection owing to infection of pregnant queens may result in severe herpetic infections in neonates.
- Respiratory—rhinitis with sneezing and serous to purulent nasal discharge; tracheitis may occur; chronic sinusitis may be a sequela.
- Neurologic—latent virus found in optic nerve, ciliary ganglion, brainstem, cerebellum, and olfactory bulb.

GENETICS

N/A

INCIDENCE/PREVALENCE

- Common, especially in multi-cat households or other facilities housing large numbers of cats, due to ease of transmission. Catteries and shelters are the source of most infections.
- Perpetuated by latent carriers that harbor the virus in nerve ganglia, especially in the trigeminal ganglion.

GEOGRAPHIC DISTRIBUTION

Found worldwide

SIGNALMENT

Species

Affects all domestic and many exotic cats.

Breed Predilections

- None.
- Brachycephalic breeds have more severe corneal disease and are more likely to have corneal sequestra.

Mean Age and Range

- Cats of all ages
- Kittens most susceptible

Predominant Sex

N/A

SIGNS

Historical Findings

- Acute onset of paroxysmal sneezing.
- Blepharospasm and ocular discharge.
- Anorexia—from high fever, general malaise, or inability to smell.

- Recurrent signs—carriers.
- Abortion.

Physical Examination Findings

- Fever—up to 106°F (41°C).
- Rhinitis—serous, mucopurulent, or purulent nasal discharge.
- Conjunctivitis—serous, mucopurulent, or purulent ocular discharge.
- Chronic rhinitis/sinusitis—chronic purulent nasal discharge; presence of sinusitis cannot be determined without radiographs.
- Keratitis—ulceration, descemetocele, or panophthalmitis.

CAUSE

FHV-1, of which there is only 1 serotype.

RISK FACTORS

- Lack of vaccination for FHV-1 although vaccines do not bestow sterilizing immunity.
- Multiple cat facilities with overcrowding, poor ventilation, poor sanitation, poor nutrition, or physical or psychological stress.
- Pregnancy and lactation.
- Concomitant disease, especially owing to immunosuppressive organisms or other respiratory organisms.
- Kittens born to carrier queens—infected at about 5 weeks of age.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Feline calicivirus infection—less sneezing, conjunctivitis, ulcerative keratitis; may cause ulcerative stomatitis, pneumonia.
- Feline *Chlamydophila* infection—more chronic conjunctivitis, which may be unilateral; pneumonitis; intracytoplasmic inclusions in conjunctival scrapings; responds to tetracyclines or chloramphenicol.
- Bacterial infection (*Bordetella*, *Haemophilus*, or *Pasteurella*)—less nasal and ocular involvement; often respond to antibiotics.

CBC/BIOCHEMISTRY/URINALYSIS

- Not diagnostic.
- Transient leukopenia followed by leukocytosis may occur.

OTHER LABORATORY TESTS

- PCR testing from pharyngeal and conjunctival swabs will identify presence of the virus; more sensitive than other diagnostic modalities. May be transiently positive following MLV FHV-1 vaccination.
- Immunofluorescent assay—nasal or conjunctival scrapings; viral detection.
- Viral isolation—pharyngeal swab sample.
- Stained conjunctival smears—detect intranuclear inclusion bodies.

IMAGING

Radiography—open mouth ventrodorsal and rostrocaudal (skyline) views of the skull reveal presence of chronic disease in the nasal cavity

and frontal sinuses; infection cannot be reliably distinguished from neoplasia and inflammatory polyps; no abnormal radiographic findings with acute disease. CT provides a more accurate assessment of disease in the nasal cavity and frontal sinus when compared to radiographs. In many cats, it can differentiate neoplasia from inflammation based on the amount of bony destruction.

DIAGNOSTIC PROCEDURES

N/A

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PATHOLOGIC FINDINGS

- Gross—ocular and nasal discharge; mucosal edema of upper airway epithelium; tracheitis; sinusitis; ulcerative keratitis; panophthalmitis.
- Microscopic—submucosal edema; inflammatory cell infiltrates of upper respiratory and conjunctival tissues; chronic sinusitis; intranuclear inclusion bodies in epithelial cells.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient—nutritional and fluid support to anorectic cats; prevent contagion.

NURSING CARE

- Outpatient—keep patient indoors to prevent environmentally induced stress, which may lengthen the course of the disease.
- Fluids—intravenous or subcutaneous; to correct and prevent dehydration; to keep nasal secretions thin.

ACTIVITY

Isolate affected cats during the acute phase, because they are contagious.

DIET

- Outpatient—entice food consumption to avoid anorexia, which induces a cascade of negative consequences; offer foods with appealing tastes and smells.
- Inpatient—forced enteral feeding for anorectic cats; remove nasal secretions (so nasal breathing can occur) before starting orogastric tube feeding; avoid nasoesophageal tubes because of rhinitis.

CLIENT EDUCATION

- Inform client of the contagious nature of the disease.
- Discuss proper vaccination protocols and early vaccination of cats in multi-cat facilities and households.
- Inform client that early weaning and isolation from all other cats except littermates may prevent infections.

SURGICAL CONSIDERATIONS

Surgically implanted feeding tubes (esophagostomy tube, gastrostomy tube) may be needed when prolonged anorexia occurs.

FELINE HERPESVIRUS INFECTION

(CONTINUED)



MEDICATIONS

DRUG(S) OF CHOICE

- Broad-spectrum antibiotics—ampicillin (20–40 mg/kg PO q8h; 10–20 mg/kg IV, IM, SC q6–8h) or amoxicillin (10–40 mg/kg q8–12h PO, IM, SC) for secondary bacterial infections.
- Antibiotic combinations—ampicillin or amoxicillin and a fluoroquinolone (enrofloxacin [2.5 mg/kg PO, IM, IV q12h], orbifloxacin [2.5–7.5 mg/kg PO q24h], marbofloxacin [2.75–5.55 mg/kg PO q24h]), pradofloxacin [7.5 mg/kg] for secondary bacterial infections.
- Lysine-lactoferrin (500 mg PO q12h) more effective than lysine alone for treatment.
- Lysine (500 mg PO q12h) may have some virucidal effect.
- Ophthalmic antibiotics—for keratitis.
- Ophthalmic antivirals in order of efficacy—trifluridine, cidofovir, idoxuridine, ganciclovir, aciclovir; for herpetic ulcers; must be instilled q2h for significant effect except for cidofovir which can be given q12h.
- There is some evidence that administration of an intranasal vaccine 2–6 days prior to exposure will result in lessening of clinical signs. This may be helpful in an outbreak in a multi-cat setting.

CONTRAINDICATIONS

- Iodoxuridine ophthalmic may be painful in some cats; discontinue medication.
- Trifluridine, idoxuridine, acyclovir—toxic if given systemically.
- Systemic corticosteroids—may induce relapse in chronically infected cats.
- Ophthalmic corticosteroids—may predispose to ulcerative keratitis.
- Nasal decongestant drops—0.25% oxymetazoline HCl; decrease nasal discharge; contraindicated because some cats object and some experience rebound rhinorrhea.

PRECAUTIONS

Death is usually the result of inadequate nutritional and fluid support or immunosuppression due to FeLV or FIV.

ALTERNATIVE DRUG(S)

- Penciclovir—effectively inhibits FHV-1, doses unknown at this time.
- Famciclovir—early reports indicate efficacy at 15 mg/kg PO q8–12h.



FOLLOW-UP

PATIENT MONITORING

Monitor appetite closely; hospitalize for forced enteral feeding if anorexia develops.

PREVENTION/AVOIDANCE

Ammonia-based cleaners effectively kill the virus.

Vaccines

- Routine vaccination with an MLV or inactivated virus vaccine—prevents development of severe disease; does not prevent infection and local viral replication with mild clinical disease and virus shedding.
- Vaccinate at 8–10 weeks of age, at 12–14 weeks of age, and 16–18 weeks of age and with annual boosters for reasonable protection, especially in high-risk populations.
- Endemic multi-cat facilities or households—vaccinate kittens with a dose of an intranasal vaccine at 10–14 days of age, then parenterally at 6, 10, and 14 weeks of age; isolate the litter from all other cats at 3–5 weeks of age; then use kitten vaccination protocol to prevent early infections.

POSSIBLE COMPLICATIONS

- Chronic rhinitis or rhinosinusitis with long-term sneezing and nasal discharge.
- Herpetic ulcerative keratitis.
- Corneal sequestrum that must be removed surgically.
- Permanent closure of the nasolacrimal duct with chronic ocular discharge.

EXPECTED COURSE AND PROGNOSIS

- Usually 7–10 days before spontaneous remission, if secondary bacterial infections do not occur.
- Prognosis generally good, if fluid and nutritional therapy are adequate.
- Correlation between severity of acute signs and degree of latent infection.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Simultaneous viral or bacterial respiratory diseases.

AGE-RELATED FACTORS

More severe in young kittens

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Pregnant cats that develop disease may transmit FHV-1 to kittens *in utero*, resulting in abortion or neonatal disease.

SYNONYMS

- Coryza
- Feline Rhinotracheitis
- Rhino

SEE ALSO

Feline Calicivirus Infection

ABBREVIATIONS

- FeLV = feline leukemia virus
- FHV-1 = feline herpesvirus type 1
- FIV = feline immunodeficiency virus
- MLV = modified live virus
- PCR = polymerase chain reaction

Suggested Reading

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Client Education Handout
available online

FELINE HYPERESTHESIA SYNDROME



BASICS

OVERVIEW

- Idiopathic disorder of cats characterized by paroxysmal agitation, focal epaxial muscle spasms, vocalization, and intense biting or licking of the back, tail, and pelvic limbs.
- Also known as neurodermatitis, rolling skin disease, neuritis, psychomotor epilepsy, and pruritic dermatosis of Siamese.
- Pathophysiology is unknown. • Organ systems affected include: behavioral, nervous, neuromuscular, and skin/exocrine.

SIGNALMENT

Species

Cat

Breed Predilections

Can be seen in any breed, but Siamese, Abyssinian, Burmese, and Himalayan cats may be predisposed.

Mean Age and Range

- Signs can occur at any age • Most common at 1–5 years

SIGNS

- Episodes of twitching of the skin over the lumbar area, violent swishing of the tail, vocalizing, and biting or licking of the flank and pelvic region. • Pupils often dilate, and cats can become aggressive or appear agitated and run wildly about the environment.
- Episodes are several seconds to several minutes in length. Cats are typically normal between episodes but may be intolerant of being stroked along the back. • General physical examination often reveals no abnormalities aside from possible alopecia and broken hair over the lumbar area from self-mutilation. Many cats resent palpation of the thoracolumbar musculature, and manipulation of the area may elicit an episode. No neurologic deficits are present.

CAUSES & RISK FACTORS

- It is not known whether this syndrome is a manifestation of an underlying behavioral problem, a focal seizure disorder, or a localized sensory neuromyopathy causing hyperesthesia. It has been speculated that the cause is multifactorial, or that the syndrome is not a distinct entity with a single cause but rather can develop from a variety of different factors. • Cats that tend to be nervous or hyperexcitable have been described as having an increased risk; environmental stressors may serve as a trigger.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Dermatologic conditions causing pruritus—parasitic (e.g., flea, *Notoedres*,

Cheyletiella), fungal (e.g., dermatophytosis), or allergic (e.g., parasitic, inhalant, dietary); evaluate for underlying dermatitis; skin scrapings and fungal cultures can help confirm diagnosis. • Diseases of the vertebral column causing spinal pain—degenerative (intervertebral disc disease), inflammatory (discospondylitis, local meningitis), neoplastic, or traumatic; radiography of the vertebral column is helpful in evaluating for abnormalities; further diagnostics (e.g., spinal imaging, serologic testing for infectious agents, CSF analysis) may be necessary. • Forebrain disease causing behavioral changes and/or seizures—metabolic (hepatic encephalopathy), infectious/inflammatory (feline leukemia virus, feline immunodeficiency virus, feline infectious peritonitis, cryptococcosis, toxoplasmosis), neoplastic, vascular; complete diagnostic evaluation including bile acid tolerance, serologic testing for infectious causes, CSF analysis, and brain imaging may be indicated. • Behavioral condition—compulsive disorder; exclusion diagnosis.

CBC/BIOCHEMISTRY/URINALYSIS

- Frequently normal. • Increased globulin levels have been reported in some cats.

OTHER LABORATORY TESTS

None required

IMAGING

None required aside from that necessary to exclude differential diagnoses.

DIAGNOSTIC PROCEDURES

- Diagnosis is based on characteristic history and clinical findings, and by excluding other diseases that can cause similar signs. • There is no test or group of tests that support a definitive diagnosis. • EMG—evidence of abnormal spontaneous activity in the thoracolumbar epaxial muscles in one study of affected cats. • Muscle biopsy—if EMG changes; may reveal vacuoles within the epaxial muscles, with antibody labelling characteristics similar to those described with inclusion body myositis/myopathy in humans.



TREATMENT

- Outpatient. • Eliminate environmental changes that can precipitate episodes.
- Behavioral modification has been successful in reducing clinical manifestations in some cats. • In severe cases of self-mutilation, an Elizabethan collar or tail bandaging may be necessary.



MEDICATIONS

DRUG(S)

- Several pharmacologic agents

recommended, based on suspected underlying cause.

- Prednisolone is indicated if pruritic dermatitis is suspected.
- Antiepileptic drugs are often utilized. Phenobarbital (1–2 mg/kg PO q12h) is most effective but does not successfully control the episodes in all cats. Gabapentin (5–10 mg/kg PO q12h) can be used for both its antiepileptic properties as well as its analgesic effect in neuropathic pain.
- Selective serotonin reuptake inhibitors (fluoxetine 0.5–2.0 mg/kg PO q24h), tricyclic antidepressants (clomipramine 0.5–1.0 mg/kg PO q24h), or benzodiazepines (lorazepam 0.125–0.50 mg PO q8–24h) are recommended when a primary behavioral disorder is suspected.
- Carnitine and coenzyme Q10—if underlying myopathy.
- Treatment response is variable. In cats that respond, therapy is often life-long as episodes tend to resume after medication is discontinued.

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CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Fluoxetine inhibits the cytochrome P450 system and should be used cautiously with other drugs that undergo extensive hepatic metabolism including phenobarbital, benzodiazepines, and tricyclic antidepressants.



FOLLOW-UP

PATIENT MONITORING

Cats placed on phenobarbital—check serum drug concentrations in 2–3 weeks and adjust dosage as needed to maintain levels of 20–30 µg/mL (85–130 µmol/L); CBC and biochemistry profile at 6- to 12-month intervals to monitor for adverse effects.

PREVENTION/AVOIDANCE

Avoid any known environmental stressors.

EXPECTED COURSE AND PROGNOSIS

Prognosis depends on whether underlying cause is identified, response to medication, and frequency and severity of episodes.



MISCELLANEOUS

ABBREVIATIONS

- CSF = cerebrospinal fluid • EMG = electromyography

Suggested Reading

Ciribassi J. Feline hyperesthesia syndrome. Compend Contin Educ Pract Vet 2009, 31:116–132.

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FELINE IDIOPATHIC LOWER URINARY TRACT DISEASE



BASICS

DEFINITION

The terms "feline urologic syndrome" and "FUS" have been misused by the veterinary profession as diagnostic terms to describe disorders of domestic cats characterized by hematuria, dysuria, pollakiuria, perioria, and partial or complete urethral obstruction, because varying combinations of these signs may be associated with any cause of feline lower urinary tract disease. The similarity of clinical signs with diverse causes is not surprising since the feline urinary tract responds to various diseases in a limited and predictable fashion. Fortunately, with improved understanding of the causes and consequences of feline lower urinary tract disorders, these terms have been abandoned. At the time of this writing, the names idiopathic lower urinary tract disease (iLUTD) and feline idiopathic cystitis (FIC) have come into common use. However, these terms represent exclusionary diagnoses established only after known causes have been eliminated.

PATOPHYSIOLOGY

- Refer to specific chapters describing diseases listed in the "Differential Diagnosis" section.
- Initial episodes of idiopathic lower urinary tract diseases usually occur in the absence of significant numbers of detectable bacteria and pyuria. Prospective diagnostic studies of male and female obstructed and non-obstructed cats identified bacterial urinary tract infections in < 3% of young to middle-age adults and ~ 10% of geriatric adults. • The etiopathogenesis of iLUTD is uncertain. Proposed mechanisms include dysfunction of the urothelial barrier, neurogenic cystitis, mast-cell-induced neuroimmune disease, and systemic psychoneuroendocrine dysfunction.
- Experimental and clinical studies have implicated viruses, especially caliciviruses, as potential etiologic agents in some cats. • Some cats with lower urinary tract diseases exhibit findings similar to those observed in humans with interstitial cystitis, a non-malignant neuro-inflammatory disorder characterized by decreased urine concentrations of glycosaminoglycans and increased urinary bladder permeability, which is associated with damage to the glycosaminoglycan layer that covers the luminal surface of the urinary tract. These similarities prompted the hypothesis that some lower urinary tract diseases are analogous to human interstitial cystitis.
- Clinical observations suggest that stress may play a role in precipitating or exacerbating signs associated with idiopathic cystitis.

SYSTEMS AFFECTED

- Renal/Urologic—lower urinary tract.
- Persistent urethral outflow obstruction results in post-renal azotemia.

INCIDENCE/PREVALENCE

- The incidence of hematuria, dysuria, and/or urethral obstruction in domestic cats in the United States and Great Britain has been previously reported to be ~ 0.5–1% per year.
- The hospital proportional morbidity rate for iLUTD in cats with lower urinary tract signs is ~ 65%.

SIGNALMENT

Species

Cat

Mean Age and Range

- May occur at any age, but is most commonly recognized in young to middle-aged adults (mean 3.5 years).
- Uncommon in cats < 1 and > 10 years old.

SIGNS

Historical Findings

- Dysuria • Hematuria • Pollakiuria
- Perioria—urinating in inappropriate locations • Outflow obstruction

Physical Examination Findings

Thickened, firm, contracted bladder wall

CAUSES

- See "Pathophysiology" • Non-infectious diseases, including idiopathic cystitis
- Viruses implicated

RISK FACTORS

Stress—may play a role in precipitating or exacerbating signs; an unlikely primary cause.

DIFFERENTIAL DIAGNOSIS

- Metabolic disorders including various types of uroliths/urethral plugs. • Infectious agents including bacteria, mycoplasma/ureaplasma, fungal agents, and parasites. • Trauma.
- Neurogenic disorders including reflex dyssynergia, urethral spasm, and hypotonic or atonic bladder (primary or secondary).
- Iatrogenic disease including reverse flushing solutions, indwelling and post-surgical urethral catheters (especially open systems), and urethrostomy complications. • Anatomic abnormalities including urachal anomalies and acquired urethral strictures. • Neoplasia (benign and malignant). • Clinical signs may be confused with constipation.

CBC/BIOCHEMISTRY/URINALYSIS

- Hematuria and proteinuria without significant pyuria or bacteriuria—usually present. • If urethral obstruction persists, serum chemistry profiles reveal azotemia, hyperphosphatemia, hyperkalemia, and reduced TCO₂.

OTHER LABORATORY TESTS

- Absence of bacteriuria—verify by quantitative urine culture; collect urine specimens by cystocentesis to avoid contamination with bacteriuria that normally inhabit the distal urinary tract.
- Transmission electron microscopy has revealed calicivirus-like particles in some urethral plugs.

IMAGING

- Survey radiography—may exclude radiopaque uroliths or urethral plugs.
- Positive-contrast retrograde urethrocystography or antegrade cystography—may exclude urethral strictures, vesicourachal diverticula, and neoplasia.
- Double-contrast cystography—may exclude small or radiolucent uroliths, blood clots, and thickening of the bladder wall due to inflammation or neoplasia.
- Ultrasonography—may exclude uroliths.

DIAGNOSTIC PROCEDURES

- Cystoscopy—may exclude uroliths and diverticula. • Biopsies obtained with urinary catheters, cystoscopes, or via surgery—may permit morphologic characterization of inflammatory or neoplastic lesions; not routinely needed.

PATHOLOGIC FINDINGS

- Cystoscopy may reveal petechial hemorrhages (also called glomerulations) of the mucosal surface of the urinary bladder.
- Mucosal ulceration, congestion, submucosal edema, hemorrhage, and fibrosis; inflammatory cells may not be prominent, unless secondary bacterial urinary tract infections have resulted from catheterization or perineal urethrostomy.



TREATMENT

APPROPRIATE HEALTH CARE

- Patients with non-obstructive lower urinary tract diseases—typically managed as outpatients; diagnostic evaluation may require brief hospitalization. • Patients with obstructive lower urinary tract diseases—usually hospitalized for diagnosis and management.

DIET

- Appropriate dietary management recommended for persistent crystalluria associated with matrix-crystalline urethral plugs. • Empirical observations suggest that recurrence of signs may be minimized by feeding moist rather than dry foods. The goal is to promote the flushing action of increased urine volume, and increased dilution of toxins, chemical irritants, inflammatory mediators, and urolith-promoting constituents.

CLIENT EDUCATION

- Hematuria, dysuria, and pollakiuria—often self-limiting; subside within 4–7 days, but signs often recur unpredictably. • A lack of controlled studies demonstrate efficacy of most drugs used to treat this disorder symptomatically. • Males should be monitored for signs of urethral obstruction.
- Reduce environmental stress by minimizing impact of changes in the home, and maintaining a constant diet. Environmental

(CONTINUED)

FELINE IDIOPATHIC LOWER URINARY TRACT DISEASE

enrichment for indoor-housed cats consists of provision of necessary resources (food, water, litter boxes, space, play), providing a safe place to hide, refinement of cat-owner interactions, and management of conflict.

- Provide proper litter box hygiene.

SURGICAL CONSIDERATIONS

- We do not recommend cystotomy to lavage and debride the bladder mucosa as a form of treatment.
- Do not perform perineal urethrostomies to minimize recurrent urethral obstruction without localizing obstructive disease to the penile urethra by contrast urethrography.



MEDICATIONS

DRUG(S) OF CHOICE

- Tolteridine may be considered as an anticholinergic and antispasmodic to minimize hyperactivity of the bladder detrusor muscle and urge incontinence; suggested empirical dose is 0.05 mg/kg PO q12h. However, there have been no reports of controlled studies to evaluate its safety or efficacy.
- Amitriptyline, a tricyclic antidepressant and anxiolytic drug (with anticholinergic, antihistaminic, anti- α -adrenergic, anti-inflammatory, and analgesic properties)—empirically advocated to treat cats with severe recurrent or persistent signs; suggested empirical dosage is 5–10 mg/cat q24h given at night. We do not recommend amitriptyline for treatment of acute, self-limiting episodes of iLUTD.
- Butorphanol, buprenorphine, and fentanyl—have been empirically recommended for short-term analgesia in cats with idiopathic cystitis. However, there have been no reports of controlled studies to evaluate their safety or efficacy.
- Phenoxybenzamine—may be used to minimize reflex dyssynergia and functional urethral outflow obstruction; suggested empirical dosage is 0.5 mg/kg PO q12h.
- Prazosin—may be used to minimize reflex dyssynergia and functional urethral outflow obstruction; suggested empirical dosage is 0.25–0.5 mg/cat PO q12–24h.
- Pentosan polysulfate sodium, a semisynthetic glycosaminoglycan—empirically recommended to help repair the glycosaminoglycan coating of the mucosa of the urinary tract. Results of controlled clinical studies have not demonstrated any beneficial effects of pentosan polysulfate on reducing the severity or frequency of clinical signs in cats with iLUTD.
- Oral glucosamine alone or in combination with oral chondroitin sulfate has been

empirically recommended to help repair the damaged GAG layer coating the urothelium. Results of controlled clinical studies have not demonstrated any beneficial effects of glucosamine on reducing the severity or frequency of clinical signs in cats with iLUTD.

- Corticosteroids—no detectable effect on remission of acute clinical signs demonstrated; predispose to bacterial urinary tract infections, especially in cats with indwelling transurethral catheters.
- Nonsteroidal anti-inflammatory drugs—empirically recommended by some because of their anti-inflammatory and analgesic properties. However, the safety of NSAIDs in the treatment of idiopathic cystitis has not been evaluated by controlled clinical trials.
- Dimethylsulfoxide (DMSO)—no detectable effect on remission of clinical signs demonstrated.
- Antibiotics and methenamine—no detectable effect on remission of clinical signs in cats demonstrated.

CONTRAINdications

- Phenazopyridine—a urinary tract analgesic used alone or in combination with sulfa drugs; may result in methemoglobinemia and irreversible oxidative changes in hemoglobin resulting in formation of Heinz bodies and anemia.
- Methylene blue—a weak antiseptic agent; may cause Heinz bodies and severe anemia.
- Bethanechol—a cholinergic drug used to manage hypotonic urinary bladders; do not use in patients with urethral obstruction.

PRECAUTIONS

- Cats with urethral obstruction and post-renal azotemia are at increased risk for adverse drug events, especially with drugs and anesthetics that depend on renal elimination or metabolism.
- Indwelling transurethral catheters, especially when associated with fluid-induced diuresis, predispose patients to bacterial urinary tract infections.



FOLLOW-UP

PATIENT MONITORING

Monitor hematuria by urinalysis; cystocentesis may cause iatrogenic hematuria, so naturally voided samples are preferred.

PREVENTION/AVOIDANCE

- Empirical observations suggest that recurrence of signs may be minimized by feeding moist foods.
- Reduce environmental stress.

POSSIBLE COMPLICATIONS

- Indwelling transurethral catheters—cause trauma; predispose to ascending bacterial

urinary tract infections.

- Perineal urethrostomies—predispose to bacterial urinary tract infections and urethral strictures.

EXPECTED COURSE AND PROGNOSIS

Hematuria, dysuria, and pollakiuria often are self-limiting in patients with most idiopathic lower urinary tract diseases, subsiding within 4–7 days. These signs often recur unpredictably; the frequency of recurrence appears to decline with advancing age.

F



MISCELLANEOUS

AGE-RELATED FACTORS

Frequency of recurrence appears to decline with advancing age.

SYNONYMS

- Feline idiopathic cystitis
- Feline interstitial cystitis
- Feline urinary tract inflammation
- FUS • Feline urologic disease (see definition).

SEE ALSO

- Dysuria and Pollakiuria
- Hematuria
- Lower Urinary Tract Infection, Bacterial
- Lower Urinary Tract Infection, Fungal
- Urolithiasis, Struvite—Cats and Ferrets

ABBREVIATIONS

- DMSO dimethylsulfoxide
- FUS = feline urologic syndrome
- GAG = glycosaminoglycan
- iLUTD = idiopathic lower urinary tract disease
- NSAID = nonsteroidal anti-inflammatory drug

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Client Education Handout
available online

FELINE IMMUNODEFICIENCY VIRUS INFECTION (FIV)



BASICS

DEFINITION

A complex retrovirus that causes an immunodeficiency disease in domestic cats; same genus (*Lentivirus*) as HIV, the causative agent of AIDS in humans.

PATHOPHYSIOLOGY

- Infection disrupts immune system function; immune dysfunction occurs due to cytokine alterations, non-specific hyperactivation of B- and T-lymphocytes, immunologic anergy, and apoptosis of T-cells.
- Pathogenicity can be strain or subtype dependent; subtypes A and B are most common in the United States.
- Acute infection—virus spreads from the site of entry to the lymph tissues and thymus via dendritic cells, first infecting T-lymphocytes, then macrophages.
- Primary receptor is feline CD134; uses chemokine receptor CXCR4 as co-receptor.
- CD4⁺ and CD8⁺ cells—both can be infected lytically in culture; virus selectively and progressively decreases CD4⁺ (T-helper) cells; inversion of the CD4⁺:CD8⁺ ratio (from ~2:1 to <1:1) develops slowly; an absolute decrease of CD4⁺ T-cells is seen after several months of infection.
- Early infection and activation of CD4⁺ CD25⁺ regulatory T-cells may limit effective immune response to FIV infection.
- Patients are clinically asymptomatic until cell-mediated immunity is disrupted—decline is associated with decreased Th1 cytokines; humoral immune function—perturbed in advanced stages of infection.
- Macrophages—main reservoir of virus in affected cats; transport virus to tissues throughout the body; defects in function (e.g., increased production of TNF).
- Astrocyte and microglial cells in the brain and megakaryocytes and mononuclear bone marrow cells may be infected; neuronal loss may occur.
- Co-infection with FeLV may increase the expression of FIV in many tissues, including kidney, brain, and liver.

SYSTEMS AFFECTED

- Gastrointestinal—panleukopenia-like syndrome.
- Hemic/Lymphatic/Immune—loss of CD4⁺ T-cells; lymphocytic/plasmacytic infiltrates in tissues (especially gingiva, lymphoid tissues); lymphomas, mast cell tumors.
- Nervous—alterations in astrocyte function and neurotransmitter expression.
- Ophthalmic—anterior uveitis.
- Renal/Urologic—nephropathy.
- Reproductive—fetal death or perinatal infections.
- Other body systems—secondary infections.

GENETICS

- No predisposition for infection.
- May play a role in progression and severity.

INCIDENCE/PREVALENCE

United States and Canada—1.5–3% in the healthy cat population; 9–15% in cats with signs of clinical illness.

GEOGRAPHIC DISTRIBUTION

Worldwide; seroprevalence rates vary greatly.

SIGNALMENT

Species

Cat

Mean Age and Range

- Prevalence of infection increases with age.
- Mean age—5 years at time of diagnosis.

Predominant Sex

Male—more aggressive; roaming

SIGNS

General Comments

- Diverse owing to immunosuppressive nature of infection.
- Associated disease cannot be clinically distinguished from FeLV-associated immunodeficiencies.

Historical Findings

Recurrent minor illnesses, especially with upper respiratory and gastrointestinal signs.

Physical Examination Findings

- Depend on occurrence of opportunistic infections.
- Lymphadenomegaly—mild to moderate.
- Gingivitis, stomatitis, periodontitis (25–50% of cases).
- Upper respiratory tract—rhinitis; conjunctivitis; keratitis (30% of cases); often associated with feline herpesvirus and calicivirus infections.
- Chronic renal insufficiency—immune-mediated glomerulonephritis.
- Persistent diarrhea (10–20% of cases); bacterial or fungal overgrowth, parasite-induced inflammation; direct effect of FIV infection on the gastrointestinal epithelium.
- Chronic, non-responsive, or recurrent infections of the external ear and skin—from bacterial infections or dermatophytosis.
- Fever and wasting—especially in later stage; possibly from high levels of TNF.
- Ocular disease—anterior uveitis; pars planitis; glaucoma.
- Lymphoma or other neoplasia.
- Neurologic abnormalities—disruption of normal sleep patterns; behavioral changes (pacing and aggression); motor and neurocognitive deficits; peripheral neuropathies.

CAUSES

- Cat-to-cat transmission; usually by bite wounds.
- Occasional perinatal transmission.
- Sexual transmission uncommon, although FIV has been detected in semen.

RISK FACTORS

- Male
- Free-roaming



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Primary bacterial, parasitic, viral, or fungal

infections.

- Toxoplasmosis—neurologic and ocular manifestations may be the result of *Toxoplasma* infection, FIV infection, or both.
- Non-viral neoplastic diseases.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram may be normal.
- Anemia, lymphopenia or neutropenia—may be seen; neutrophilia may occur in response to secondary infections.
- Urinalysis and serum chemistry profile—high serum protein from hypergammaglobulinemia.

OTHER LABORATORY TESTS

Serologic Testing

- Detects antibodies to FIV.
- ELISA—routine screening test; kits for in-house use to microtiter plates for diagnostic laboratory use; confirm positive results with additional testing, especially in healthy, low-risk cats or when diagnosis would result in euthanasia.
- Western blot (immunoblot)—confirmatory testing of ELISA-positive samples.
- Kittens—when <6 months old may test positive owing to passive transfer of antibodies from an FIV-positive queen; a positive test does not indicate infection; retest at 8–12 months to determine infection.
- Vaccinated cats will test positive for FIV antibodies.

Others

- Virus isolation or detection—other methods occasionally available on an experimental basis.
- RT-PCR—useful in vaccinated cats or kittens with maternal antibody; use is hampered by inconsistent results between laboratories.
- CD4⁺:CD8⁺ evaluation—helps determine extent of immunosuppression.

PATHOLOGIC FINDINGS

- Lymphadenopathy—associated with follicular hyperplasia and massive paracortical infiltration of plasmacytes; later, may see a mixture of follicular hyperplasia and follicular depletion or involution; in terminal stages, lymphoid depletion is predominant finding.
- Lymphocytic and plasmacytic infiltrates—gingiva, lymph nodes and other lymphoid tissues, spleen, kidney, liver, and brain.
- Perivascular cuffing, gliosis, neuronal loss, white matter vacuolization, and occasional giant cells in the brain.
- Intestinal lesions similar to those seen with feline parvovirus infection (feline panleukopenia-like syndrome).



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient sufficient for most patients.
- Inpatient—with severe secondary infections until condition is stable.

(CONTINUED)

FELINE IMMUNODEFICIENCY VIRUS INFECTION (FIV)

F**NURSING CARE**

- Primary consideration—manage secondary and opportunistic infections.
- Supportive therapy—parenteral fluids and nutritional supplements, as required.

ACTIVITY

Normal

DIET

- Normal.
- Diarrhea, kidney disease, or chronic wasting—special diet, as needed.

CLIENT EDUCATION

- Inform client that the infection is slowly progressive and healthy antibody-positive cats may remain healthy for years.
- Advise client that cats with clinical signs will have recurrent or chronic health problems that require medical attention.
- Discuss the importance of keeping cats indoors to protect them from exposure to secondary pathogens and to prevent spread of FIV.

SURGICAL CONSIDERATIONS

- Oral treatment or surgery—frequently required; dental cleaning, tooth extraction, gingival biopsy.
- Biopsy or removal of neoplastic lesions.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Zidovudine (Retrovir) 5–15 mg/kg PO q12h: direct antiviral agent; most effective against acute infection; monitor for bone marrow toxicity.
- Immunomodulatory drugs—may alleviate some clinical signs; hr α -interferon (Roferon A) diluted in saline at 30 units/day PO for 7 days every other week; may increase survival rates and improve clinical status; high-dose recombinant feline omega-interferon (Virbagen Omega) at 1 million units/kg/day SC daily for 5 days at 3 intervals (d0–4, d14–18, d60–64) or lower-dose oral protocols may be effective; also try *Propionibacterium acnes* (Immunoregulin) at 0.5 mL/cat IV, once or twice weekly, or acemannan (Carrisyn) at 100 mg/cat PO daily.
- Gingivitis and stomatitis—may be refractory to treatment.
- Antibacterial or antimycotic drugs—useful for overgrowth of bacteria or fungi; prolonged therapy or high dosages may be required; for anaerobic bacterial infections use metronidazole at 7–15 mg/kg PO q8–12h or clindamycin at 11 mg/kg PO q12h.
- Corticosteroids or gold salts—judicious but aggressive use may help control immune-mediated inflammation.
- Anorexia—short-term appetite stimulation: diazepam at 0.2 mg/kg IV or oxazepam at 2.5 mg/cat PO.
- Topical corticosteroids—for anterior uveitis; long-term response may be incomplete or

poor; pars planitis often regresses spontaneously and may recur.

- Glaucoma—standard treatment.
- Yearly vaccination for respiratory and enteric viruses with inactivated vaccines is recommended.

CONTRAINdications

- Griseofulvin—avoid or use with extreme caution in FIV-positive cats; may induce severe neutropenia; neutropenia is reversible if the drug is withdrawn early enough but secondary infections associated with the condition can be life threatening.
- MLV vaccines—although unlikely, potential to cause disease in immunosuppressed cats.

PRECAUTIONS

Systemic corticosteroids—use with caution; may lead to further immunosuppression.

POSSIBLE INTERACTIONS

See "Contraindications"

**FOLLOW-UP****PATIENT MONITORING**

Varies according to secondary infections and other manifestations of disease.

PREVENTION/AVOIDANCE

- Prevent contact with FIV-positive cats.
- Quarantine and test incoming cats before introducing into multi-cat households.

Vaccine

- Dual subtype (A and D), inactivated whole virus plus infected cells vaccine (Fel-O-Vax FIV, Fort Dodge Animal Health).
- 0–100% efficacy after 3 doses, depending on study design and strain of challenge virus.
- Cannot distinguish between vaccinated and FIV-infected cats with antibody assays; virus detection by PCR is inconsistent.

EXPECTED COURSE AND PROGNOSIS

- Within the first 2 years after diagnosis or 4.5–6 years after the estimated time of infection, about 20% of cats die but > 50% remain asymptomatic.
- In late stages of disease (wasting and frequent or severe opportunistic infections), life expectancy is \leq 1 year.
- Overall survival time and quality of life for many FIV-positive cats will be similar to uninfected cats.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Secondary bacterial, viral, fungal, and parasitic disease
- Lymphoid tumors
- Immune-mediated disease

AGE-RELATED FACTORS

Kittens (up to 4–6 months old) may test positive because of passive antibody transfer.

ZOONOTIC POTENTIAL

- None known; evidence against FIV transmission to humans is compelling but cannot be considered conclusive owing to the relatively short time the virus has been studied.
- Macaques susceptible to experimental infection; evidence of CD4⁺ T-cell decline.
- Potential transmission of secondary pathogens (e.g., *Toxoplasma gondii*) to immunocompromised humans.

PREGNANCY/FERTILITY/BREEDING

FIV-positive queens—reported abortions and stillbirths; transmission to kittens is infrequent if the queen is antibody-positive before conception; rate of transmission may be subtype or strain-dependent (> 90% for experimental infections with some strains).

SYNONYMS

Feline immunodeficiency syndrome

SEE ALSO

Individual chapters on secondary infectious diseases, ocular disease, gingivitis, and stomatitis.

ABBREVIATIONS

- AIDS = acquired immune deficiency syndrome
- ELISA = enzyme-linked immunosorbent assay
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- HIV = human immunodeficiency virus
- hr α -interferon = human recombinant α -interferon
- MLV = modified live virus
- PCR = polymerase chain reaction
- RT-PCR = reverse transcriptase polymerase chain reaction
- TNF = tumor necrosis factor

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Client Education Handout
available online

FELINE INFECTIOUS PERITONITIS (FIP)



BASICS

DEFINITION

A systemic, immune-mediated, viral disease of domestic and exotic cats characterized by insidious onset, persistent non-responsive fever, pyogranulomatous tissue reaction, accumulation of exudative effusions in body cavities, and high mortality.

F

PATHOPHYSIOLOGY

- FIP virus replicates locally in epithelial cells of the upper respiratory tract, oropharynx, and intestinal tract.
- Immune-mediated disease—antiviral antibodies are produced, and the virus/antibody complex is taken up by macrophages.
- The virus is transported within monocytes/macrophages throughout the body; localizes at various vein wall and perivascular sites.
- Local perivascular viral replication and subsequent pyogranulomatous tissue reaction produce the classic lesion.

SYSTEMS AFFECTED

- Multisystemic—pyogranulomatous or granulomatous lesions in the omentum, on the serosal surface of abdominal organs (e.g., liver, kidney, and intestines), within abdominal lymph nodes, and in the submucosa of the intestinal tract.
- Nervous—vascular lesions can occur throughout the CNS, especially in the meninges.
- Ophthalmic—lesions may include uveitis and chorioretinitis.
- Respiratory—lesions on lung surfaces; pleural effusion in the wet form.

INCIDENCE/PREVALENCE

- Prevalence of antibodies against FCoV—high in most populations, especially in multi-cat facilities.
- Incidence of clinical disease—low in most populations, especially in single-cat households.
- Because of the difficulty in diagnosis, control, and prevention, outbreaks within breeding catteries may be catastrophic; in endemic catteries, the risk of an FCoV antibody-positive cat eventually developing FIP is usually < 10%.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Cats—domestic and exotic

Breed Predilections

Some families or lines of cats appear more susceptible. Cheetahs are particularly susceptible.

Mean Age and Range

- Highest incidence—in kittens 3 months to 2 years of age.
- Incidence decreases sharply after cats reach 2 years of age.
- Geriatric cats may have slightly increased incidence.

SIGNS

General Comments

- A wide range, depending on the virulence of the strain, effectiveness of the host immune response, and organ system affected.
- Two classic forms—wet or effusive form, targets the body cavities; dry or non-effusive form, targets a variety of organs.

Historical Findings

- Insidious onset.
- Gradual weight loss and decrease in appetite.
- Stunting in kittens.
- Gradual increase in the size of the abdomen, giving a potbellied appearance.
- Persistent fever—fluctuating; antibiotic unresponsive.

Physical Examination Findings

- Depression.
- Poor condition.
- Stunted growth.
- Weight loss.
- Dull, rough hair coat.
- Icterus.
- Abdominal and/or pleural effusion.
- Palpation of the abdomen—abdominal masses (granulomas or pyogranulomas) within the omentum, on the surface of viscera (especially the kidney), and within the intestinal wall; mesenteric lymph nodes may be enlarged.
- Ocular—anterior uveitis; keratic precipitates; color change to the iris; and irregularly shaped pupil.
- Neurologic—brain stem, cerebrocortical, or spinal cord.

CAUSES

- Feline coronavirus—two genomic types.
- FCoV-1 (causes perhaps 85% of infections).
- FCoV-2 (similar to canine coronavirus).
- Distinguishing between forms—there has been great effort to distinguish between the low virulent or avirulent enteric strains (FECV) and the virulent strains (FIPV), but FECV and FIPV occur in both type 1 and type 2 forms; within each type is a spectrum from avirulent viruses that produce asymptomatic infections to those that produce fatal FIP.

RISK FACTORS

- Contact with an FCoV antibody-positive cat
- Breeding catteries or multi-cat facilities
- Less than 2 years of age
- FeLV infection



DIAGNOSIS

- Wet form—relatively easy to diagnose clinically.
- Dry form—difficult to diagnose accurately.
- No single diagnostic laboratory Test.

DIFFERENTIAL DIAGNOSIS

- Fever of unknown origin—when other causes of fever are ruled out.
- Cardiac disease causing pleural effusion—effusion has low specific gravity and cell count.
- Lesions of lymphoma, especially in the kidney, on palpation.
- CNS tumors—most cats test positive for FeLV; for FeLV-negative cats, biopsy the lesion (if accessible) for

histopathology and immunohistochemistry for FCoV.

- Respiratory disease—FCV, FHV, chlamydiosis, or various bacteria.

- Pansteatitis (yellow fat disease)—classic feel and appearance of fat within the abdominal cavity; pain on abdominal palpation; often a fish-only diet.
- Panleukopenia producing enteritis—leukopenia; positive fecal canine parvovirus antigen assay.

CBC/BIOCHEMISTRY/URINALYSIS

- Leukopenia—common early in the infection; later leukocytosis with neutrophilia and lymphopenia.
- Mild to moderate anemia may occur.
- High total plasma globulin common.
- Often hyperbilirubinemia and hyperbilirubinuria.

OTHER LABORATORY TESTS

- Serum antibody tests—immunoassays, viral neutralization assays; detect antibodies against FCoV; positive tests not diagnostic, indicate only previous infection; correlation between height of titer and eventual confirmation of infection not high.
- PCR assays—detect viral antigen; accuracy of positive tests correlating with clinical disease is still being evaluated.

- Immunohistochemistry (immunoperoxidase) assays detect FCoV within specific cells of biopsy samples or histopathologic sections of tissues from cats with fatal diseases; excellent for confirming cause of specific lesions, especially inflammatory abdominal disease, which often is not diagnosed as FIP.

IMAGING

- Generally not required.
- May confirm abdominal and pleural effusions.
- May detect granulomatous lesions.

DIAGNOSTIC PROCEDURES

- Fluid obtained via thoracocentesis and abdominocentesis—pale to straw colored; viscous; flecks of white fibrin often seen; will clot upon standing; specific gravity usually high (1.030–1.040).
- Laparoscopy—to observe specific lesions of the peritoneal cavity; to obtain a biopsy sample for histopathology or immunohistochemistry confirmation.
- Exploratory laparotomy—may be indicated for difficult-to-diagnose patients if laparoscopy is not available.

PATHOLOGIC FINDINGS

Gross

- Vary depending on the organs or tissues involved.
- Patient will be emaciated, with a rough hair coat.

Wet Form

- Abdomen and/or thoracic cavity—may contain thick, viscous exudates.
- White, rough, pyogranulomatous plaques—may be on serosal surface of abdominal organs and the omentum.
- Granulomatous lumps—may protrude from the surface of the kidney.
- Granulomas—may be in the intestinal wall.

(CONTINUED)

FELINE INFECTIOUS PERITONITIS (FIP)

- Fibrous strands—may extend between organs.
- Liver—may have focal, pale lesions.
 - Iris—may be discolored.
 - Cornea—may see keratic precipitates.
 - CNS—may see lesions in the brain and/or the spinal cord.

Histopathologic

- Granulomas or pyogranulomas in any affected tissue.
- Lesions—start around veins; increase in size, involving large portions of tissue; microscopic appearance suggests the diagnosis.

**TREATMENT****APPROPRIATE HEALTH CARE**

Inpatient or outpatient, depending on stage and severity of disease and owner's willingness and ability to provide good supportive care.

NURSING CARE

- Therapeutic paracentesis—to relieve pressure from excessive ascites or pleural effusions.
- Important to encourage the affected cat to eat.

ACTIVITY

Restrict to prevent exposure of other cats, although greatest degree of virus shed occurs before the patient shows signs.

DIET

Any food that will entice the patient to eat.

CLIENT EDUCATION

- Discuss the various aspects of disease, including the grave prognosis; once clinical FIP is confirmed, nearly 100% of cats will eventually die of the disease.
- Inform client of the high prevalence of FCoV infection but low incidence of actual clinical disease; < 10% of FCoV antibody-positive cats < 2 years of age eventually develop clinical disease.

SURGICAL CONSIDERATIONS

- Generally none.
- Rarely, inflammatory abdominal disease from FCoV may present with intestinal obstruction; abdominal surgery may be required.

**MEDICATIONS****DRUG(S) OF CHOICE**

- No treatment routinely effective.
- Patients with generalized and typical signs almost invariably die.
- Most FCoV-positive cats have subclinical infection or mild, localized granulomatous disease that is not diagnosed as FIP.
- Immunosuppressive drugs (e.g., prednisolone and cyclophosphamide)—limited success.
- Corticosteroids (subconjunctival injection)—may help ocular involvement.

- Interferons—effective in vitro; limited success in vivo; a recombinant interferon reported to have some success in Japan.
- Antibiotics—ineffective because generally not associated with secondary bacterial infections.

ALTERNATIVE DRUG(S)

No antiviral drugs proven to be efficacious.

**FOLLOW-UP****PATIENT MONITORING**

Monitor for development of large quantities of pleural effusion.

PREVENTION/AVOIDANCE

- MLV intranasal vaccine—available against FIPV; efficacy low; cannot rely on vaccination alone for control; will produce antibody-positive cats, complicating monitoring in catteries or colonies; FIP vaccine is not generally recommended by the American Association of Feline Practitioners vaccine guidelines.
- Mother/offspring—main method of transmission appears to be from asymptomatic carrier queens to their kittens at 5–7 weeks of age, after maternally derived immunity wanes; break cycle of transmission by early weaning at 4–5 weeks of age and isolating litter from direct contact with other cats, including the queen.
- Routine disinfection—premises, cages, and water/food dishes; readily inactivates virus; reduces transmission.
- Introduce only FCoV antibody-negative cats to catteries or colonies that are free of virus.
- Restrict household cats to indoor environments.

POSSIBLE COMPLICATIONS

- Pleural effusion may require thoracocentesis.
- Intestinal obstruction from inflammatory abdominal disease.
- Neurologic disease from CNS lesions.

EXPECTED COURSE AND PROGNOSIS

- Clinical course—a few days to several months.
- Prognosis grave once typical signs occur; mortality nearly 100%.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

FeLV-positive cats—more prone to develop clinical disease.

PREGNANCY/FERTILITY/BREEDING

FIP virus can infect fetuses, resulting in fetal death or neonatal disease.

SYNOMYS

- Feline coronaviral polyserositis
- Feline coronaviral vasculitis
- Feline coronavirus infection

ABBREVIATIONS

- CNS = central nervous system
- FCoV = feline coronavirus
- FCV = feline calicivirus
- FECV = feline enteric coronavirus
- FeLV = feline leukemia virus
- FHV = feline herpesvirus
- FIP = feline infectious peritonitis
- FIPV = feline infectious peritonitis virus
- MLV = modified live virus
- PCR = polymerase chain reaction

INTERNET RESOURCES

- Addie D. Catvirus.com. Feline infectious peritonitis and coronavirus website. <http://www.dr-addie.com/>
- Cornell Feline Health Center; Client Information Brochure. Feline Infectious Peritonitis. <http://www.vet.cornell.edu/fhc/brochures/fip.html>

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Client Education Handout available online

FELINE ISCHEMIC ENCEPHALOPATHY



BASICS

DEFINITION

- Seasonal neurologic disease that occurs in outdoor cats or those with access to the outdoors in North America during late spring, summer, and early fall; usually results in sudden onset of seizures, circling, altered mentation, and/or blindness.
- Aberrant migration of a *Cuterebra* larva in the brain of a cat that often causes thrombosis or vasospasm of the middle cerebral artery with ensuing ischemic necrosis; degeneration of the superficial layers of the cerebral cortex and parenchymal destruction associated with the physical migration of the larva in the brain parenchyma.
- Must be differentiated from other causes of vascular diseases affecting the brains of cats as well as other neurologic diseases of cats.

PATOPHYSIOLOGY

- In FIE, the *Cuterebra* larva enters the nasal passage of the cat, migrates through the cribriform plate into the olfactory bulb of the brain, then along the olfactory peduncle and sometimes continues in the parenchyma of the brain or alternatively in the subarachnoid space; the parasite then, if still alive, migrates caudally, where it may compromise the MCA physically through the spines on the larvae's body, or possibly via a chemical agent secreted by the parasite causing vasospasm to the vessel; or the vasospasm may be secondary to the hemorrhage caused by the parasite; the parasite may then die in the SAS or within the parenchyma.
- The adult botfly lays eggs by the entrance of a rodent's den. The eggs hatch into the L1 stage of the larva, which attaches to the hair of the mouse or rabbit and enters the body through a normal orifice (mouth, nose, eye, or anus) and migrates into the associated tissues (nasopharynx, trachea, thoracic cavity, diaphragm, abdominal cavity). Then the larva continues its migration to reach a subcutaneous site in the inguinal or thoracic region where it matures first to the L2 stage and then within the warble to the L3 larval stage, emerges through the skin, drops off the host, pupates in the soil over the winter, and then emerges in the spring as the adult botfly; when the cat hunts near the rodent's den, the L1 larva attaches to the cat's hair and gains access to the nasal passage of the cat and begins the catastrophic pathway of feline ischemic encephalopathy.
- Occasionally the larva does not migrate through the cribriform plate but embeds in the nasal passage or respiratory tract of the cat, causing focal respiratory signs. The larva has also been found in the eye and oropharyngeal region.

SYSTEMS AFFECTED

- Brain and less commonly spinal cord.
- Larvae can also be found in the skin, nasal passage, pharynx, larynx, eye, trachea, and thorax of cats.

GENETICS

None

INCIDENCE/PREVALENCE

Not known

GEOGRAPHIC DISTRIBUTION

- North America only.
- Same distribution as the *Cuterebra* botfly.
- Disease is not recognized in locations that do not have the *Cuterebra* botfly, such as Australia and Japan.

SIGNALMENT

Breed Predilections

None

Mean Age and Range

- Median age—2 years old
- Range—1–7 years old

Predominant Sex

None

SIGNS

- Sudden onset of neurologic signs.
- Often preceded by upper respiratory signs 1–3 weeks prior to the neurologic signs (due to the migration of the parasite in the nasal passage).
- Often prosencephalic signs.
- Most commonly—seizures, circling, altered mentation, blindness.
- Sometimes multifocal neurologic signs.
- Rarely spinal cord signs.

CAUSES

Cuterebra larvae

RISK FACTORS

- Outdoor cats; access to outdoors
- July, August, and September in the northeast United States and southeast Canada. Can be found in May and June, in the southeast United States
- Hunting cats



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of vascular accidents in the brain such as renal disease with hypertension.
- External trauma.
- Tumors—progressive rather than sudden in onset.
- Infectious/inflammatory diseases—such as those caused by *Cryptococcus* sp., *Toxoplasma gondii*, feline infectious peritonitis virus, and feline immunodeficiency virus.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal
- CBC—occasionally neutrophilia, leukocytosis, or eosinophilia

- Chemistry—occasionally elevated globulins or hyperglycemia

OTHER LABORATORY TESTS

- Serology for FeLV, FIV, FIP—negative
- Cryptococcal antigen titers—negative
- Toxoplasma IgG and IgM—negative

IMAGING

- MRI—diagnostic modality of choice; detect track lesion extending from the cribriform plate into the olfactory bulb and frontal, parietal, and temporal lobes best recognized on dorsal sequences; may also see area of ischemic infarction; if performed soon after onset of signs, increased signal intensity on T2-WI, PD-WI, and FLAIR images associated with ischemia of the superficial layers of the cerebral cortex, or the area supplied by the MCA; scant parenchymal enhancement in the area of infarction after administration of contrast. If MRI is done more than 2–3 weeks after onset of signs, may find loss of overlying gray matter in the region supplied by the MCA and associated hydrocephalus ex vacuo. MRA (time of flight or post-contrast) may be of some utility in some cases.
- CT—limited value.

DIAGNOSTIC PROCEDURES

Cerebrospinal fluid—normal or non-suppurative inflammation with macrophages, lymphocytes, or eosinophils.

PATHOLOGIC FINDINGS

- Local areas of malacia and hemorrhage involving the olfactory bulbs and peduncles and brain transverse sections. Thorough examination of the cribriform plate, olfactory bulbs, and peduncles, as well as the remaining parenchyma, meninges, and overlying calvaria, may reveal the larva, which is approximately 5–10 mm in length (stage 2 larva), tan and with concentric rings of spines along the length of the body.
- Histopathologic features may include necrosis and hemorrhage of the parasitic track or less specific findings such as superficial laminar cerebrocortical necrosis, cerebral infarction, subependymal rarefaction, and astrogliosis and subpial astroglioses.



TREATMENT

APPROPRIATE HEALTH CARE

N/A

NURSING CARE

- Padded cage may be necessary if the cat is having seizures.
- Swivel IV line can be used if the patient exhibits propulsive circling or loss of balance.

ACTIVITY

N/A

DIET

N/A

(CONTINUED)

FELINE ISCHEMIC ENCEPHALOPATHY

F

CLIENT EDUCATION

- Only occurs in outdoor cats and those with access to the outdoors; strictly indoor cats do not develop FIE.
- Only occurs in summer months with the majority of patients seen during July, August, and September in the northeast United States and southeast Canada.
- May not occur in major metropolitan areas that do not have the normal appropriate hosts such as the cottontail rabbit.

SURGICAL CONSIDERATIONS

Successful removal of the parasite from the brain/spinal cord has not been reported in cats but may be possible if neuroimaging is available early after onset of clinical signs.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Supportive care including antiepileptic drugs and appropriate fluid supplementation, which may include thiamine administration and additional potassium intravenously depending on the nutritional status of the patient; typically phenobarbital is used at a maintenance dose of 7.5–15 mg PO, IM, or IV q12h/cat; in addition phenobarbital can be loaded at a total loading dose of 16 mg/kg IV, PO, or IM; this dose is usually divided over 24–48 hours (e.g., 4 mg/kg q12h for 2 days); then maintenance dose is started; diazepam can be used at 2.5–5 mg IV to stop cluster seizures or status epilepticus. Other anticonvulsants, such as levetiracetam, may also be utilized.
- A cocktail treatment has been proposed for recently affected cats—diphenhydramine IM at 4 mg/kg, 1–2 hours before giving ivermectin SC at 200–500 µg/kg and prednisolone sodium succinate at 30 mg/kg IV; treatment is repeated 24 and 48 hours after the first injection of ivermectin; in addition patients receive prednisone at 5 mg/cat q12h PO for 14 days and enrofloxacin at 22.7 mg PO q12h for 14 days; ivermectin is not approved for use against *Cuterebra* larva so appropriate client permission must be obtained prior to administration; the above cocktail treatment is not for patients with clinical signs > 1 week as the parasite is likely already dead.

CONTRAINDICATIONS

Do not use ivermectin in cats with known sensitivity.

PRECAUTIONS

No adverse effects from ivermectin have been noted; however, an anaphylactic or allergic reaction could occur if the *Cuterebra* larva suddenly dies and releases possible foreign antigens.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Can use dexamethasone instead of prednisone.

**FOLLOW-UP****PATIENT MONITORING**

Sequential neurologic evaluations

PREVENTION/AVOIDANCE

- Keep cat indoors.
- Use of monthly fipronil, imidacloprid, selamectin or ivermectin has been suggested to prevent infections with the parasite.

POSSIBLE COMPLICATIONS

- May continue to have uncontrolled seizures.
- May continue to circle compulsively.
- May have behavioral changes such as aggression.

EXPECTED COURSE AND PROGNOSIS

After initial onset, many patients improve and become acceptable pets; there may be persistent deficits, seizures, circling, and undesirable behavior such as aggression; persistent clinical signs depend on damage caused by the infarction and parasitic migration.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

None

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

None; however, aberrant *Cuterebra* larva migration has been reported in humans, most commonly as an ocular form in children.

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

CNS cuterebriasis

ABBREVIATIONS

- CT = computed tomography
- FeLV = feline leukemia virus
- FIE = feline ischemic encephalopathy
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- FLAIR = fluid attenuated inversion recovery
- MCA = middle cerebral artery
- MRA = magnetic resonance angiography
- MRI = magnetic resonance imaging
- PD-WI = proton density weighted images
- SAS = subarachnoid space
- T2-WI = T2-weighted images

INTERNET RESOURCES

- <http://Botfly.ifas.ufl.edu/links1.htm>.
- <http://Cal.vet.upenn.edu/dxendopar/>
- parasitepages/unknown/cutebra.html.
- <http://web.vet.cornell.edu/public/oed/neuropathology>.
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Client Education Handout
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FELINE LEUKEMIA VIRUS INFECTION (FELV)



BASICS

DEFINITION

A simple retrovirus (*Gammaretrovirus* genus) that causes immunodeficiency and neoplastic disease in domestic cats.

PATHOPHYSIOLOGY

- Four subgroups of FeLV—A, B, C, and T; FeLV-A is most transmissible and is present in all isolates; FeLV-B arises from recombination of FeLV-A *env* gene with endogenous retroviral sequences (50% of isolates); FeLV-C (1% of isolates) arises from a mutation in *env* gene sequences; FeLV T infects only T-cells.
- Early infection consists of five stages—(1) viral replication in tonsils and pharyngeal lymph nodes; (2) infection of a few circulating B-lymphocytes and macrophages that disseminate the virus; (3) replication in lymphoid tissues, intestinal crypt epithelial cells, and bone marrow precursor cells; (4) release of infected neutrophils and platelets from the bone marrow into the circulatory system; and (5) infection of epithelial and glandular tissues, with subsequent shedding of virus into the saliva and urine.
- If virus replication is terminated at stage 1, with no detectable viremia, the infection is considered to be *abortive*.
- If an adequate immune response stops progression at stage 2 or 3 (4–8 weeks after exposure) and forces the virus into latency after a transient viremia, it is called a *regressive* or nonproductive infection.
- If the immune response is not effective, persistent viremia (stages 4 and 5) usually develops 4–6 weeks after infection but may take 12 weeks, and the cat has a *progressive* or productive infection.
- Tumor induction—occurs when the DNA provirus integrates into cat chromosomal DNA in critical regions (oncogenes).
- Virus integration near the cellular gene *c-myc* or near genes influencing the expression of *c-myc*—often results in thymic lymphosarcoma.
- Feline sarcoma viruses—mutants of FeLV; arise by recombination between the genes of FeLV and host; virus-host fusion proteins are responsible for the efficient induction of fibrosarcomas.

SYSTEMS AFFECTED

- Hemic/Lymphatic/Immune—anemia; blood cell dyscrasias; bone marrow neoplasias; neuroendocrine dysfunction and immunosuppression; absolute decrease in CD4⁺ and CD8⁺ subsets of T-cells; decreased CD4⁺: CD8⁺ ratio.
- Nervous—degenerative myopathy, neoplasias.
- All other body systems—immunosuppression with secondary infections or development of neoplastic disease.

GENETICS

No genetic predisposition

INCIDENCE/PREVALENCE

- Prevalence in United States—2–3% in the healthy cat population; worldwide infection rate of 1–8% in healthy cats; 3–4 times greater in cats exhibiting signs of clinical illness.
- Decline in US prevalence since 1980s—attributed to test and removal programs, possibly vaccination programs.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Cat

Mean Age and Range

- Prevalence highest between 1 and 6 years of age
- Mean—3 years

Predominant Sex

Male:female ratio—1.7:1

SIGNS

General Comments

- Onset of FeLV-associated disease—usually occurs over a period of months to years after infection.
- Associated diseases—non-neoplastic or neoplastic; most of the non-neoplastic or degenerative diseases result from immunosuppression.
- Regressive infections may be associated with conditions such as cardiomyopathies, lymphomas and leukemias, anemia, other infectious diseases.
- Clinical signs of FeLV-induced immunodeficiency cannot be distinguished from those of FIV-induced immunodeficiency.

Historical Findings

- Patient allowed outdoors
- Member of a multi-cat household

Physical Examination Findings

- Depend on the type of disease (neoplastic or non-neoplastic) and occurrence of secondary infections.
- Lymphadenomegaly—mild to severe.
- Fever and wasting.
- Upper respiratory tract—rhinitis, conjunctivitis, and keratitis.
- Persistent diarrhea—bacterial or fungal overgrowth; parasite-induced inflammation; direct effect of infection on crypt cells.
- Gingivitis; stomatitis; periodontitis.
- Chronic, non-responsive, or recurrent infections of the external ear and skin; abscesses.
- Lymphoma—most common associated neoplastic disease (risk increased by 62-fold in FeLV-infected cats); thymic and multicentric lymphomas highly associated; miscellaneous lymphomas (extranodal origin) most frequently involve the eye and nervous system.
- Erythroid and myelomonocytic leukemias—predominant non-lymphoid leukemias.
- Fibrosarcomas—in patients co-infected with mutated sarcoma virus; most frequently in young cats.
- Peripheral neuropathies; progressive ataxia.

CAUSES

- Cat-to-cat transmission—close casual contact (grooming); shared dishes or litter

pans; bites.

- Perinatal transmission—fetal and neonatal death of kittens from 80% of affected queens; transplacental and transmammary transmission in at least 20% of surviving kittens from infected queens.

RISK FACTORS

- Age—kittens much more susceptible to infection than adults.
- Male—result of behavior.
- Free-roaming.
- Multi-cat household.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- FIV
- Other infections—bacterial, parasitic, viral, or fungal
- Non-viral neoplastic diseases

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia—often severe; most often nonregenerative; regenerative anemias usually associated with *Mycoplasma haemofelis* or *M. haemominutum* co-infections.
- Lymphopenia or lymphocytosis.
- Neutropenia—sometimes cyclic; may be in response to secondary infections or immune-mediated disease.
- Thrombocytopenia and immune-mediated hemolytic anemia—may occur secondary to immune complex formation.
- Urinalysis and serum chemistry profile findings—depend on system affected and type of disease.

OTHER LABORATORY TESTS

- IFA—identify FeLV p27 antigen in leukocytes and platelets in fixed smears of whole blood or buffy coat preparations; positive result indicates a productive infection in bone marrow cells; 97% of IFA-positive cats remain persistently infected and viremic for life; p27 antigen usually detected by 4 weeks after infection but may take up to 12 weeks for positive test; for leukopenic cats, use buffy coat smears rather than whole blood smears.
- ELISA—detect soluble FeLV p27 antigen in whole blood, serum, plasma, saliva, or tears; more sensitive than IFA at detecting early or transient infections; a single positive test cannot predict which cats will be persistently viremic; retest in 12 weeks; false-positive results more common when whole blood rather than serum or plasma is used; positive tests with saliva or tears should be checked with whole blood (IFA) or serum (ELISA).
- A few cats have persistently discordant ELISA-positive and IFA-negative tests or test positive only sporadically; this may be due to atypical local viral replication in tissues such as bladder or eyes (*focal* infection); demonstrates infection despite no detectable cell-associated viremia.
- FeLV vaccination does not interfere with testing—tests detect antigen, not antibody.

IMAGING

Thymic atrophy (fading kittens)

(CONTINUED)

FELINE LEUKEMIA VIRUS INFECTION (FeLV)

DIAGNOSTIC PROCEDURES

Bone marrow aspiration or biopsy—with erythroblastopenia (nonregenerative anemia), bone marrow often hypercellular owing to an arrest in differentiation of erythroid cells; true aplastic anemia with hypocellular bone marrow may be seen; some cases of anemia result from myeloproliferative disease.

PATHOLOGIC FINDINGS

- Lesions—depend on type of disease; bone marrow hypercellularity often accompanies neoplastic disease.
- Lymphocytic and plasmacytic infiltrates of gingiva, lymph nodes, other lymphoid tissues, spleen, kidney, and liver.
- Intestinal lesions similar to those seen with feline parvovirus infection (feline panleukopenia-like syndrome).



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient for most cats.
- Inpatient—may be required with severe secondary infections, anemia, or cachexia until condition stable.
- Blood transfusions—emergency support; multiple transfusions may be necessary; passive antibody transfer reduces level of FeLV antigenemia in some cats; thus, immunization of blood donor cats with FeLV vaccines is useful.

NURSING CARE

- Management of secondary and opportunistic infections—primary consideration.
- Supportive therapy (e.g., parenteral fluids and nutritional supplements) may be useful.

ACTIVITY

Normal

DIET

- Normal.
- Diarrhea, kidney disease, or chronic wasting—may require special diet.

CLIENT EDUCATION

- Discuss importance of keeping cats indoors and separated from FeLV-negative cats to protect them from exposure to secondary pathogens and to prevent spread of FeLV.
- Discuss good nutrition and routine husbandry for control of secondary bacterial, viral, and parasitic infections.

SURGICAL CONSIDERATIONS

- Biopsy or removal of tumors.
- Oral treatment or surgery—dental cleaning, tooth extraction, gingival biopsy.



MEDICATIONS

DRUG(S) OF CHOICE

- Zidovudine (Retrovir, 5–15 mg/kg PO q12h)—clinical improvement but does not clear virus.

- Immunomodulatory drugs—may alleviate some clinical signs; hr α -interferon (Roferon A, diluted in saline, 30 U/day PO for 7 days every other week) may increase survival rates and improve clinical status; *Propionibacterium acnes* (Immunoregulin, 0.5 mL/cat IV once or twice weekly); acemannan (Carrisyn, 100 mg/cat/day PO).

- *Mycoplasma haemofelis* infection—suspect in all cats with regenerative hemolytic anemia (see chapter, Hemotropic Mycoplasmosis (also Hemoplasmosis or Haemobartonellosis)).

- Lymphoma—management with standard combination chemotherapy protocols; periods of remission average 3–4 months; some cats may remain in remission for much longer.

- Myeloproliferative disease and leukemias—more refractory to treatment; for anemia, try erythropoietin (EpoGen, 35–100 IU/kg SC q48h); for neutropenia, try rhG-CSF (Neupogen, 5 μ g/kg SC q24h).

- Yearly vaccination for respiratory and enteric viruses with inactivated vaccines recommended.

CONTRAINdications

MLV vaccines—potential for disease in immunosuppressed cats.

PRECAUTIONS

Systemic corticosteroids—use with caution because of the potential for further immunosuppression.



FOLLOW-UP

PATIENT MONITORING

Varies according to the secondary infections and other manifestations of disease.

PREVENTION/AVOIDANCE

- Prevent contact with FeLV-positive cats.
- Quarantine and test incoming cats before introduction into multiple-cat households.

Vaccines

- Most commercial vaccines induce virus-neutralizing antibodies specific for gp70; reported efficacy ranges from < 20% to almost 100%, depending on the trial and challenge system; inactivated whole virus vaccines tend to be best (canarypox-FeLV recombinant vaccine has similar efficacy without adjuvant).
- Test cats for FeLV before initial vaccination; if prevaccination testing is not done, advise clients that the cat may already be infected.
- Vaccinate kittens at 8–9 weeks and 12 weeks of age; boost at 1 year of age; revaccinate every 2–3 years.

EXPECTED COURSE AND PROGNOSIS

Persistently viremic cats—> 50% succumb to related diseases within 2–3 years after infection.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Secondary bacterial, viral, fungal, and parasitic disease
- Lymphoid tumors
- Fibrosarcomas
- Immune-mediated disease

AGE-RELATED FACTORS

- Neonatal kittens—most (70–100%) susceptible to progressive infection.
- Older kittens—< 30% susceptible to progressive infection by 16 weeks of age but may develop regressive infections.

ZOONOTIC POTENTIAL

Probably low, but controversial—studies report conflicting results of antibodies to FeLV in humans and of correlation between certain human leukemias and exposure to cats.

PREGNANCY/FERTILITY/BREEDING

- Abortions, stillbirths, and fetal resorptions common in FeLV-positive queens.
- Transmission from queen to kittens—in at least 20% of live births.

SYNONYMS

FeLV-AIDS—a mutated FeLV that causes immunodeficiency disease to develop rapidly.

SEE ALSO

Individual chapters on neoplasia, secondary infectious diseases, ocular disease, and gingivitis/stomatitis.

ABBREVIATIONS

- AIDS = acquired immune deficiency syndrome
- ELISA = enzyme-linked immunosorbent assay
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- hr α -interferon = human recombinant α -interferon
- IFA = immunofluorescent antibody
- MLV = modified live virus
- rhG-CSF = recombinant human granulocyte colony-stimulating factor

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Client Education Handout
available online

FELINE PANLEUKOPENIA



BASICS

DEFINITION

An acute, enteric, viral infection of cats characterized by sudden onset, depression, vomiting and diarrhea, severe dehydration, and a high mortality.

PATHOPHYSIOLOGY

The causative virus, feline parvovirus, infects only mitotic cells, causing acute cell cytolysis of rapidly dividing cells.

SYSTEMS AFFECTED

- Gastrointestinal—intestinal crypt cells of the jejunum and ileum destroyed; acute enteritis with vomiting and diarrhea; shortened blunt villi with poor absorption of nutrients, dehydration, and secondary bacteremia.
- Hemic/Lymphatic/Immune—severe panleukopenia; atrophy of the thymus.
- Nervous and Ophthalmic—in neonatal kittens rapidly dividing granular cells of the cerebellum and retinal cells of the eye destroyed; cerebellar hypoplasia with ataxia and retinal dysplasia.
- Reproductive—*in utero* infection in non-immune queens leading to fetal death, fetal resorption, abortion, stillbirth, or fetal mummification.

GENETICS

N/A

INCIDENCE/PREVALENCE

- Unvaccinated populations—the most severe and important feline infectious disease.
- Routine vaccination—almost total control of this disease.
- Extremely contagious.
- Extremely stable virus, surviving for years on contaminated premises.

GEOGRAPHIC DISTRIBUTION

Worldwide in unvaccinated populations

SIGNALMENT

Species

- Felidae—all, domestic and exotic.
- Canidae—susceptible to the closely related canine parvovirus; some exotic canids may be susceptible to FPV infection.
- Mustelidae—especially mink; may be susceptible.
- Procyonidae—raccoon and coatiundi; susceptible.

Breed Predilections

None

Mean Age and Range

- Unvaccinated and previously unexposed cats of any age can become infected once passively transferred maternal immunity has been lost.
- Kittens 2–6 months of age—most

susceptible to develop severe disease.

- Adults—often mild or subclinical infection.

Predominant Sex

N/A

SIGNS

Historical Findings

- History of recent exposure (e.g., adoption shelter).
- Newly acquired kitten.
- Kitten 2–4 months old from a premises with a history of FP.
- No vaccination history or last vaccinated when < 16 weeks of age.
- Sudden onset, with vomiting, diarrhea, depression, and complete anorexia.
- Owner may suspect poisoning.
- Cat may have disappeared or hid for 1 day or more before being found.
- Owner may report cat hangs head over water bowl or food dish but does not eat or drink.

Physical Examination Findings

- Depression—may be mild to severe.
- Typical “panleukopenia posture”—sternum and chin resting on floor, feet tucked under body, and top of scapulae elevated above the back.
- Dehydration—appears rapidly; may be severe.
- Vomiting and diarrhea may occur.
- Body temperature—usually mild to moderately elevated or depressed in the early stages of disease; becomes severely subnormal as affected cat becomes moribund.
- Abdominal pain—may be elicited on palpation.
- Small intestine—either turgid and hose-like or flaccid.
- Subclinical or mild infections with few or no clinical signs common, especially in adults.
- Ataxia from cerebellar hypoplasia—kittens infected *in utero* or neonatally; signs evident at 10–14 days of age and persist for life: hypermetria; dysmetria; incoordination with a base-wide stance and an elevated “rudder” tail; alert, afebrile, and otherwise normal; retinal dysplasia sometimes seen.

CAUSES

Feline Parvovirus

- Small, single-stranded DNA virus.
- Single antigenic serotype.
- Considerable antigenic cross-reactivity with canine parvovirus Type 2 and mink enteritis virus.
- Extremely stable against environmental factors, temperature, and most disinfectants.
- Requires a mitotic cell for replication.

Canine Parvovirus Types 2a, 2b, and 2c

- CPV-2a, CPV-2b, and CPV-2c can produce FP in domestic and/or exotic cats.
- Properties of CPV like those for FPV.

RISK FACTORS

- Anything that increases the mitotic activity of the small intestinal crypt cells—intestinal

parasites; pathogenic bacteria. • Secondary or co-infections—viral upper respiratory infections. • Age—kittens 2–6 months of age tend to be more severely affected.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Panleukopenia-like syndrome of FeLV infection—chronic infection; chronic enteritis; chronic panleukopenia; often anemia; patient positive for FeLV antigen in the blood and/or saliva.
- Salmonellosis—usually subclinical infection; severe gastroenteritis; total WBC counts usually high.
- Acute poisoning—similar to acute or fulminating disease; severe depression; subnormal temperature; total WBC count not severely depressed.
- Many diseases of cats can cause mild clinical signs that are hard to differentiate from mild FP; total WBC count is always low during the acute infection with FP, even in subclinical infections.

CBC/BIOCHEMISTRY/URINALYSIS

- Panleukopenia—most consistent finding; leukocyte counts usually between 500 and 3,000 cells/dL during the acute disease.
- Biochemical findings usually non-specific.

OTHER LABORATORY TESTS

- CPV antigen fecal immunoassay (Cite Canine Parvovirus Test Kit, IDEXX Labs)—not licensed for feline panleukopenia; detects FPV antigen in feces.
- Chromatographic test strip—feces for FPV and CPV.
- Serologic testing—paired serum samples (acute and convalescent); detects rising antibody titer.

DIAGNOSTIC PROCEDURES

- Viral isolation from feces or affected tissues (e.g., thymus, small intestine, spleen).
- Electron microscopy of feces—detects parvovirus particles, presumably FPV.

PATHOLOGIC FINDINGS

Gross

- Rough hair coat.
- Severe dehydration.
- Evidence of vomiting and diarrhea.
- Weight loss.
- Edematous and turgid small intestine.
- Petechial or ecchymotic hemorrhages on the serosal and/or mucosal surfaces of the jejunum and ileum.
- Thymic atrophy.
- Gelatinous or liquid bone marrow.
- In utero* or neonatal infection—gross hypoplasia of the cerebellum.

Microscopic

- Dilated small intestinal crypts with sloughing of epithelial cells.
- Shortened and

(CONTINUED)

blunt intestinal villi. • Absence of lymphocytic infiltrates in all tissues. • Lymphocytic depletion of follicles of lymph nodes, Peyer's patches, and spleen. • Neonatal and fetal infection—disorientation and depletion of the granular and Purkinje cells of the cerebellum. • Eosinophilic intranuclear inclusions in affected tissues during early stages of infection; not usually observed on routine histopathologic examination of formalin-fixed tissues.



TREATMENT

APPROPRIATE HEALTH CARE

- Main principles of treatment—rehydration; reestablishment of electrolyte balance; supportive care until the patient's immune system produces antiviral antibodies that neutralize the virus. • Inpatient—severe cases; hydration and replacement electrolyte therapy. • Outpatient—mild cases.

NURSING CARE

- Fluid therapy—essential in severe cases; with electrolyte replacement and intravenous nutrient support may well make the difference between survival and death. • Whole blood transfusions—if plasma protein falls < 4 g/dL or if total WBC counts fall < 2,000 cells/dL.

ACTIVITY

Keep patient indoors during the acute disease—prevent contamination of the environment; prevent the cat from going into hiding.

DIET

Temporarily withhold food until the acute gastroenteritis is controlled.

CLIENT EDUCATION

- Inform client that all current and future cats in the household must be vaccinated against FPV before exposure. • Inform client that the virus will remain infectious on the premise for years unless environment can be adequately disinfected with household bleach.

SURGICAL CONSIDERATIONS

None



MEDICATIONS

DRUG(S) OF CHOICE

Broad-spectrum antibiotics—counter secondary bacteremia from intestinal bacteria.

CONTRAINDICATIONS

Oral medications until gastroenteritis has been controlled.

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

- Monitor hydration and electrolyte balance closely. • Monitor CBC daily or at least every 2 days until recovery. • Recovered cats are immune against FPV infection for life and do not require further vaccination.

PREVENTION/AVOIDANCE

- Contaminated environments (e.g., cages, floors, food and water dishes) should be disinfected with a 1:32 dilution of household bleach. • FPV resistant to most commercial disinfectants.

Vaccines

- FP vaccines are core vaccines—to be given to all cats. • FP completely preventable by routine vaccination of kittens. • MLV or inactivated parenteral vaccines. • MLV intranasal vaccine. • Immunity—long duration, perhaps even for life. • Kittens—vaccinate as early as 6 weeks of age, then every 3–4 weeks until 16 weeks of age; Recent American Association of Feline Practitioners vaccine guideline recommendations have changed the last kitten vaccine to be given when kitten is at least 16 weeks of age, instead of 12 weeks of age; maternally derived immunity in some kittens may not have waned until 16 weeks of age. • Boosters—1 year after last kitten vaccine; then repeat not more frequently than every 3 years. • Do not use MLV vaccines in pregnant cats.

POSSIBLE COMPLICATIONS

- Chronic enteritis—fungal or other cause. • Teratogenic effects (cerebellar hypoplasia resulting in ataxia for life)—virus infection of fetus. • Shock and other complications—severe dehydration and electrolyte imbalance.

EXPECTED COURSE AND PROGNOSIS

- Most cases acute, lasting only 5–7 days. • If death does not occur during the acute disease, recovery is usually rapid and uncomplicated; it may take several weeks for the patient to regain weight and body condition.
- Prognosis is guarded during the acute disease, especially if the total WBC count is < 2,000 cells/dL.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Viral upper respiratory diseases, including feline viral rhinotracheitis and feline calicivirus infection.

AGE-RELATED FACTORS

- Clinical—generally a disease of kittens
- Subclinical—usually adults

FELINE PANLEUKOPENIA

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

- Unvaccinated pregnant cats are at great risk of infection. • Fetuses almost always become infected with fatal or teratogenic effects, even when the dam has a subclinical infection.
- Fetal resorption, abortion, fetal mummification, stillbirth, or birth of weak, fading kittens. • Kittens may show ataxia from cerebellar hypoplasia when they become ambulatory.

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SYNOMYNS

- Feline distemper • Feline parvovirus infection • Feline viral enteritis

ABBREVIATIONS

- CPV = canine parvovirus • FeLV = feline leukemia virus • FP = feline panleukopenia
- FPV = feline parvovirus • MLV = modified live virus • WBC = white blood cell

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Client Education Handout
available online

FELINE PARANEOPLASTIC ALOPECIA



BASICS

OVERVIEW

- Rare condition characterized by cutaneous lesions which serve as markers of internal neoplasia.
- Most affected cats have pancreatic adenocarcinoma with metastases to liver, lungs, pleura, and/or peritoneum; also reports of bile duct and hepatocellular carcinoma.
- The link between internal malignancies and cutaneous lesions is unknown; may involve cytokines producing atrophy of the hair follicles.

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SIGNALMENT

- Domestic shorthair cats only reported cases
- Median age—13 years; range of 7–16 years

SIGNS

- Decrease in appetite followed by rapid weight loss and excessive shedding.
- Pruritus—variable; sometimes with excessive grooming.
- Hair loss—rapidly progressive.
- Some affected cats may be reluctant to walk, owing to painful fissuring of the footpads.
- Hairs epilate easily.
- Severe alopecia—ventral neck, abdomen, and medial thighs.
- Stratum corneum may “peel,” leading to a glistening appearance to the skin.
- Alopecic skin is shiny, inelastic, and thin, but not fragile.
- Gray lentigines may develop in alopecic areas.
- Footpads may be fissured and/or scaly; often painful.

CAUSES & RISK FACTORS

- Majority of cases are associated with underlying pancreatic adenocarcinoma.
- Internal carcinomas, such as bile duct and hepatocellular, possible causes.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hyperadrenocorticism—polyuria, polydipsia, and skin fragility.
- Hyperthyroidism—polyphagia.
- Hypothyroidism—spontaneous condition rare in cats; not associated with glistening skin.
- Feline symmetrical alopecia—hair loss self-induced; not associated with easy epilation.
- Thymoma—skin is thick, scaly and fissured, lymphocytic interface dermatitis; radiographs reveal thoracic mass.

- Demodicosis—mites not associated with paraneoplastic alopecia.
- Dermatophytosis—hair loss often associated with breakage, not spontaneous shedding; inappetence and weightloss rare.
- Alopecia areata—rarely involves the entire ventral surface; inappetence and weight loss rare.
- Telogen effluvium—not associated with miniaturization of hair follicles.
- Skin fragility syndrome—fragile skin not associated with paraneoplastic alopecia.
- Superficial necrolytic dermatitis—not associated with marked exfoliation and miniaturization of hair follicles.

CBC/BIOCHEMISTRY/URINALYSIS

No consistent abnormalities; may be helpful in ruling out other differentials.

OTHER LABORATORY TESTS

- Endocrine (thyroid profiles and a dexamethasone suppression test)—rule out endocrine disease.
- Skin scrapings—rule out demodicosis.
- KOH examination of hairs and/or fungal culture—rule out dermatophytosis.
- Skin cytology—possible secondary *Malassezia* infection (causing pruritus).

IMAGING

- Ultrasonography—pancreatic mass and/or nodular lesions in the liver or peritoneal cavity; failure to demonstrate nodules does not exclude the diagnosis, neoplasia may be too small for detection.
- Thoracic radiographs—metastatic lesions in the lungs or pleural cavity.

DIAGNOSTIC PROCEDURES

- Skin biopsy.
- Laparoscopy or exploratory laparotomy—identify primary and metastatic tumors.

PATHOLOGIC FINDINGS

- Histopathologic examination of the skin*—non-scarring alopecia; severe atrophy of hair follicles and adnexa; miniaturization of hair bulbs; mild to severe acanthosis; variable absence of stratum corneum; variable mixed superficial perivascular infiltrates of neutrophils, eosinophils, and mononuclear cells; some have secondary *Malassezia* infections.
- Primary tumor—usually pancreatic adenocarcinoma, rarely primary bile duct or hepatocellular carcinomas.
- Metastatic nodules—common in the liver, lungs, pleura, and peritoneum.



TREATMENT

- Removal of tumor via partial pancreatectomy may be curative; however,

prognosis is guarded, as majority of cases have metastatic disease.

- Chemotherapy or other medications—no reported response.
- Affected animals rapidly deteriorate; euthanasia should be suggested as a humane intervention.
- Supportive care—only if owners refuse to consider euthanasia; feed highly palatable, nutrient-dense foods and/or tube feed.



MEDICATIONS

DRUG(S)

N/A

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS

- Progressive deterioration.
- Supportive care—ultrasonography and thoracic radiographs may demonstrate progression of metastatic disease.
- Death most often occurs within 2–20 weeks after onset of skin lesions.



MISCELLANEOUS

SEE ALSO

Adenocarcinoma, Pancreas

ABBREVIATION

- KOH = potassium hydroxide

Suggested Reading

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FELINE SYMMETRICAL ALOPECIA



BASICS

OVERVIEW

- Alopecia in a symmetrical pattern with no gross changes in the skin.
- Common clinical presentation in cats.
- Manifestation of several underlying disorders.

SIGNALMENT

No age, breed, or sex predilection reported

SIGNS

- Total to partial hair loss; most often symmetrical but can occur in a patchy distribution.
- Areas of the body commonly affected: ventrum, caudal dorsum, and lateral and caudal thighs.
- Patchy areas of hair loss (unsymmetrical) on the distal extremities or body.

CAUSES & RISK FACTORS

- Cutaneous hypersensitivity—flea allergic dermatitis, food, atopy.
- Ectoparasites—flea bite dermatitis, Cheyletiellosis, *Otodectes cynotis*.
- Infection—dermatophytosis.
- Neurologic or behavioral—"psychogenic alopecia." (uncommon as primary cause of symptoms.)
- Stress or metabolic—telogen effluvium.
- Neoplasia—pancreatic neoplasia (paraneoplastic alopecia).
- Hyperadrenocorticism.
- Alopecia areata.
- Hyperthyroidism (early sign).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

See "Causes & Risk Factors"

CBC/BIOCHEMISTRY/URINALYSIS

Eosinophilia in some allergic cats

OTHER LABORATORY TESTS

Serum thyroxine—hyperthyroidism

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Flea combing—identify fleas, flea excrement, or both.
- Microscopic examination of hair—self-induced hair loss results in broken blunt shafts; endogenous hair loss results in tapered ends (telogen hairs).
- Fecal examination—excess hair, mites, and ova (*Cheyletiella*), tapeworm, or fleas.
- Food elimination diet trial—adverse reactions to food.
- Intradermal tests—atopy.
- Skin biopsy—confirm presence of underlying cause (e.g., hypersensitivity dermatitis, psychogenic, or rarely, systemic disease).
- Cytology of papules or crusts, if present, may have large numbers of eosinophils.
- Microscopic examination of skin scrapings—ectoparasites.
- Hair plucks—dermatophyte arthrospores or *Demodex* mites adjacent to hair shafts.

PATHOLOGIC FINDINGS

- Histopathologic findings—vary depending on the cause.
- Feline psychogenic alopecia—hair follicles and skin normal.
- High numbers of mast cells, eosinophils, lymphocytes, or macrophages suggest allergic dermatitis.
- Alopecia areata—lymphocytic inflammation that encircles the bulb portions of the hair follicles; rare.



TREATMENT

- Management of the underlying cause.
- Inform the owner of the diagnostic plan and the time it could take to see a response (hair coat regrowth).



MEDICATIONS

DRUG(S)

- Antihistamines—e.g., chlorpheniramine 0.5 mg/kg PO q8h
- Glucocorticosteroids: Prednisolone 0.5 mg/kg PO, alternate-day therapy
- Amitriptyline 1–2 mg/kg PO daily

- Clomipramine hydrochloride 0.5 mg/kg q24h
- Cyclosporine, modified (Atopica) 5–7 mg/kg PO daily

CONTRAINdications/POSSible INTERACTIONS

- Glucocorticosteroids—can cause alopecia, diabetes mellitus, polydipsia, polyuria, polyphagia, and weight gain; can suppress pruritus, making it difficult to determine the underlying cause.
- Withdraw antipruritic medications (including glucocorticosteroids) as the diagnostic tests near completion (e.g., restricted-ingredient food trials).



FOLLOW-UP

- Frequent examinations are essential in confirming the differential diagnoses.
- Successful identification of the underlying cause offers the best prognosis, if the cause can be controlled (e.g., flea bites or food hypersensitivity).



MISCELLANEOUS

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Author David Duclos

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FEVER



BASICS

DEFINITION

Higher than normal body temperature because of a changed thermoregulatory set point in the anterior hypothalamus; normal body temperature in dogs and cats is 100.2–102.8°F (37.8–39.3°C). Fever of unknown origin (FUO)—at least 103.5°F (39.7°C) on at least four occasions over a 14-day period and illness of 14 days in duration without an obvious cause.

PATHOPHYSIOLOGY

Exogenous or endogenous pyrogens cause release of endogenous substances that reset the hypothalamic thermoregulatory center to a higher temperature, activating a physiologic responses to raise the body temperature to this new set point. Physiologic consequences include increased metabolic demands, muscle catabolism, bone marrow suppression, heightened fluid and caloric requirements, and possibly DIC and shock.

SYSTEMS AFFECTED

- Cardiovascular—tachycardia
- Hemic/Lymphatic/Immune—bone marrow depression and DIC
- Nervous—cerebral edema, depression

GEOGRAPHIC DISTRIBUTION

Incidence of infections varies significantly.

SIGNALMENT

Species

Dog and cat

Breed Predilections

Some breed-associated conditions may result in FUO (e.g., shar-pei fever).

Mean Age and Range

Any age

Predominant Sex

Any sex

SIGNS

General Comments

- Fever lowers bacterial division and increases immune competence.
- Prolonged fever > 105°F (> 40.5°C) leads to dehydration and anorexia.
- Fever > 106°F (> 41.1°C) may lead to cerebral edema, bone marrow depression, heart arrhythmia, electrolyte disorders, multiorgan damage, and DIC.

Historical Findings

- Clinical history (e.g., contact with infectious agents, lifestyle, travel, recent vaccination, drug administration, insect bites, previous illness, allergies) and physical examination (including retinal examination) may help identify an underlying disease condition.
- Fever patterns of fever (e.g., sustained, intermittent) is rarely helpful.

Physical Examination Findings

- Hyperthermia
- Lethargy
- Inappetence

- Tachycardia
- Tachypnea
- Hyperemic mucous membranes
- Dehydration
- Shock

CAUSES

Infectious Agents (Most Common)

- Viruses—FeLV, FIV, parvovirus, distemper, herpes, calicivirus
- Bacteria—Gram-positive and Gram-negative endotoxins, *Mycoplasma*, *Bartonella*
- Systemic fungi—*Histoplasma*, *Blastomyces*, *Coccidioidomycetes*, *Cryptococcus*
- Rickettsiaceae—*Rickettsia rickettsii* (Rocky Mountain spotted fever)
- Anaplasmataceae*—*Ehrlichia canis*, *Anaplasma phagocytophila*, *Neorickettsia helminthoeca*
- Parasites and protozoa—*Babesia*, *Toxoplasma*, aberrant larva migrans, *Dirofilaria* thromboemboli, *Leishmania*, *Cytauxzoon*, *Hepatozoon*, *Neospora*
- Leptospira* spp
- Borrelia burgdorferi* (Lyme disease)

Immune-Mediated Processes

Systemic lupus erythematosus, immune-mediated hemolytic anemia, immune-mediated thrombocytopenia, pemphigus, polyarthritis, polymyositis, rheumatoid arthritis, vasculitis, hypersensitivity reactions, transfusion reaction, and infection secondary to inherited or acquired immune defects.

Endocrine and Metabolic

Hyperthyroidism, hypoadrenocorticism (rare), pheochromocytoma, hyperlipidemia, and hypernatremia

Neoplasia

Lymphoma, myeloproliferative disease, plasma cell neoplasm, mast cell tumor, malignant histiocytosis, metastatic disease, necrotic tumor, and solid tumor, particularly in liver, kidney, bone, lung, and lymph nodes.

Other Inflammatory Conditions

Cholangiohepatitis, hepatic lipidosis, toxic hepatopathy, cirrhosis, inflammatory bowel disease, pancreatitis, peritonitis, pleuritis, granulomatous diseases, portosystemic shunting, thrombophlebitis, infarctions, pansteatitis, panosteitis panniculitis, hypertrophic osteodystrophy, blunt trauma, cyclic neutropenia, intracranial lesions, and pulmonary thromboembolism.

Drugs and Toxins

Tetracycline, sulfonamide, penicillins, nitrofurantoin, amphotericin B, barbiturates, iodine, atropine, cimetidine, salicylates (high dosages), antihistamines, procainamide, and heavy metals.

FUO—Dogs

- Infection (28%)—discospondylitis, blastomycosis, and other fungal infections, valvular endocarditis, soft tissue or parenchymal abscesses, bacteremia, septic arthritis, septic meningitis, pyothorax, pulmonary foreign body/abscess, stump pyometra, bronchopneumonia, osteomyelitis, peritonitis, prostatitis, pancreatitis, pyelonephritis, osteomyelitis, sepsis secondary to immunodeficiency, leptospirosis, leishmaniasis, toxoplasmosis, Lyme disease,

infection with *Ehrlichia*, *Anaplasma*, *Bartonella* • Immune-mediated disease (27%)—immune-mediated polyarthritis, meningitis, vasculitis, others • Bone marrow disease, including neoplasia (16%)

- Neoplasia (7%) • Miscellaneous (10%)—hypertrophic osteodystrophy, meningitis, lymphadenitis, panosteitis, portosystemic shunting, drug reaction, toxin, shar-pei fever • Undiagnosed (12%)

FUO—Cats

- Most are virally mediated (e.g., FeLV, FIV, FIP, less commonly parvovirus, herpes, and calicivirus).
- Persistent occult bacterial infection with atypical bacteria, sometimes secondary to bite wounds (e.g., *Yersinia*, *Mycobacteria*, *Nocardia*, *Actinomycetes*, and *Brucella*).
- Pyothorax common.
- Additional causes—pyelonephritis, blunt trauma, penetrating intestinal lesion, dental abscess, systemic mycoses (e.g., *Histoplasma*, *Blastomyces*, *Coccidioides*), lymphoma, and solid tumors.
- Immune disorders are rare, as are endometritis, discospondylitis, pneumonia, and endocarditis.

RISK FACTORS

- Recent travel
- Exposure to biologic agents
- Immunosuppression
- Very young or old animals



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

True fever must be differentiated from hyperthermia. Stress in the hospital may cause a mild temperature rise. Temperatures up to 103°F (39.4°C) may be caused by stress or illness. Temperatures > 104°F (> 40°C) are almost always important. Temperatures > 107°F (> 41.7°C) are usually not fever, more likely to be primary hyperthermia.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC and blood smear—leukopenia or leukocytosis, left shift, moncytosis, lymphocytosis, thrombocytopenia, or thrombocytosis, spherocytes, organisms.
- Biochemistry profile and urinalysis vary with the organ system involved.

OTHER LABORATORY TESTS

- If infectious disease is suspected, attempt to culture an organism—urine culture, blood cultures (i.e., three anaerobic and three aerobic cultures, taken during a rise in temperature or 20 minutes apart; try to use as much volume as possible to increase diagnostic yield; consider using resin vials that bind antibiotics), fungal and CSF cultures, synovial and prostatic fluid, and biopsy specimens.
- FeLV and FIV test, Snap 4DX test, serologic tests or PCR for *Toxoplasma*, *Borrelia*, *Mycoplasma*, *Bartonella*, *Anaplasma*, *Ehrlichia*, *Rickettsia*, FIP, systemic mycoses.
- Fecal examination if gastrointestinal signs.

(CONTINUED)

FEVER**F**

- Tracheal wash or bronchoalveolar lavage if respiratory involvement.
- Occult heartworm test if pulmonary embolism suspected.
- If immune disorders suspected—cytologic examination of synovial fluid; Coombs' test, RF (anticanuclear antibody titer and rheumatoid factor test are often unrewarding).
- PLI level • T_4 to rule out hyperthyroidism in cats.

IMAGING**Radiography**

- Abdominal radiographs to scan for tumors and effusion.
- Thoracic radiographs to rule out pneumonia, neoplasia, and pyothorax.
- Survey skeletal radiographs for bone tumors, multiple myeloma, osteomyelitis, discospondylitis, panosteitis, hypertrophic osteopathy, and hypertrophic osteodystrophy.
- Dental and skull radiographs to look for tooth root abscess, sinus infections, foreign bodies, and neoplasia.
- Contrast radiography (e.g., gastrointestinal and excretory urography) to look for evidence of neoplasia or infection.

Ultrasonography

- Abdominal (plus directed aspirate or biopsy, if indicated) to look for abdominal neoplasia and abscess or other site of infection (e.g., pyelonephritis, pancreatitis, pyometra).
- Echocardiography if endocarditis suspected.

Nuclear Imaging

- Radionuclide scanning procedures to evaluate for bone tumors, osteomyelitis, and pulmonary embolism.
- Computed tomography or MRI if indicated.
- Image fusion (combination of positron emission tomography using radioactively labeled fluorodeoxyglucose and CT).

DIAGNOSTIC PROCEDURES

- Arthrocentesis (culture and cytology).
- Bone marrow aspirate and biopsy if malignancy or myelodysplasia suspected.
- Lymph node, skin, or muscle biopsy if clinically indicated.
- Examination of fine-needle aspirate or biopsy of any mass or abnormal organ.
- CSF tap if neurologic signs suggest brain tumor or meningitis.
- Endoscopy and biopsy if gastrointestinal signs.
- Exploratory laparotomy—last resort if all other diagnostic tests fail to determine the cause and the patient is not improving.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Goals of treatment:
 - Reset the thermoregulatory set point to a lower level
 - Remove the underlying cause.

NURSING CARE

- Fluid administration (IV) often lowers body temperature.
- If the patient is dehydrated, initiate isotonic crystalloids.
- Topical cooling

if fever is severe (convection cooling with fans, evaporative cooling with isopropyl alcohol on foot pads, axilla, and groin). • Only use antipyretic treatment when fever is prolonged and life-threatening ($> 106^\circ\text{F}$, $> 41.1^\circ\text{C}$) and topical cooling is unsuccessful. Impaired patients (e.g., those with heart failure, seizures, or respiratory disease) require antipyretic treatment earlier. Antipyretic treatment may preclude elucidation of the cause, delay correct treatment, and complicate patient monitoring (e.g., reduction of fever is an important indication of response to treatment).

DIET

Febrile patients are in a hypercatabolic state and require high caloric intake.

CLIENT EDUCATION

Work-up of patients with FUO often extensive, expensive, and invasive, and may not result in a definitive diagnosis.

SURGICAL CONSIDERATIONS

Surgery may be necessary in some animals with underlying infectious (e.g., pyometra, peritonitis, pyothorax, and liver abscess) or localized.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Selection depends on the diagnosis.
- Do not use broad-spectrum (i.e., "shotgun") treatment in place of a thorough diagnostic workup unless the patient's status is critical and deteriorating rapidly.

Antibiotics

- Based on results of bacterial culture or serology.
- In emergency situations, combination antibiotic therapy can be started after culture specimens have been obtained (e.g., cephalothin, 20 mg/kg IV q6–8h; combined with enrofloxacin 10 mg/kg IV q24h). Additional antimicrobials depend on the main clinical suspicion based on preliminary laboratory and clinical evidence.
- Do not give antibiotics longer than 1–2 weeks if ineffective.

Antipyretics

- Dipyrrone—dogs, 25 mg/kg IV
- Aspirin—dogs, 10 mg/kg PO q12h; cats, 6 mg/kg PO q48h
- Deracoxib—dogs, 1–2 mg/kg/day
- Meloxicam 0.1 mg/kg/d, flunixin meglumine—dogs, 0.25 mg/kg SC once (give IV fluids).

Glucocorticoids

- Block acute phase response. Do not use unless infectious causes have been ruled-out.
- May mask clinical signs, may lead to immunosuppression, and are not recommended for use as antipyretics; administration of corticosteroids to cats with intractable FUO after ruling out infectious diseases may promote a favorable response.

- Primarily indicated for fever associated with immune-mediated disease and certain steroid-responsive tumors (e.g., lymphoma).

Phenothiazines

Depress normal thermoregulation center and cause peripheral vasodilation. Use with caution due to sedative and hypotensive effects.

PRECAUTIONS

Side effects of antipyretics include emesis, diarrhea, gastrointestinal ulceration, renal damage, hemolysis, hepatotoxicity (acetaminophen, particularly dangerous in cats), and muscle stiffness (flunixin meglumine).

POSSIBLE INTERACTIONS

Combination of NSAIDs and steroids raises the risk of gastrointestinal hemorrhage.

**FOLLOW-UP****PATIENT MONITORING**

- Body temperature at least q12h.
- If the cause of the fever continues to elude the clinician, repeat the history and physical examination along with screening laboratory tests.
- If fever develops or worsens during hospitalization, consider nosocomial infection or superinfection.

EXPECTED COURSE AND PROGNOSIS

Vary with cause; in some patients (more commonly in cats), an underlying cause cannot be determined.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Young animals—infectious disease more common; prognosis better than in old animals.
- Old animals—common causes are neoplasia and intra-abdominal infection; signs tend to be more non-specific; prognosis often guarded.

SYNOMYMS

Pyrexia

SEE ALSO

Heat Stroke and Hyperthermia

ABBREVIATIONS

- CSF = cerebrospinal fluid
- DIC = disseminated intravascular coagulation
- FUO = fever of unknown origin
- NSAID = nonsteroidal anti-inflammatory drug
- PCR = polymerase chain reaction
- PLI = pancreatic lipase immunoreactivity
- RF = rheumatoid factor
- TNF = tumor necrosis factor

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FIBER-RESPONSIVE LARGE BOWEL DIARRHEA



BASICS

OVERVIEW

- A type of chronic idiopathic large bowel diarrhea that occurs in dogs that respond favorably to dietary fiber supplementation.
- Exclusion diagnosis that requires eliminating known causes of chronic large bowel diarrhea and clinical response to dietary fiber supplementation.
- No pathophysiologic studies have been performed.
- Only 3 reports in dogs comprising 83 cases.
- May overlap with a stress-associated poorly defined syndrome that has been called irritable bowel syndrome, also referred to as nervous colitis, spastic colon, or mucus colitis.

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SIGNALMENT

- Dogs of all ages (0.5–14 years); median 6 years.
- Many breeds, including mixed breeds; common breeds include German shepherd dog, miniature schnauzer, cocker spaniel, and miniature or toy poodle.

SIGNS

- Chronic diarrhea (soft to liquid) with classic large bowel characteristics; tenesmus, excess fecal mucus, hematochezia, increased frequency (median 3.5 times/day), and urgency.
- Diarrhea usually episodic alternating with periods of normal stool; diarrhea may be continuous in approximately 25% of dogs.
- Less common signs include occasional vomiting, decreased appetite during episodes of diarrhea, abdominal pain, and anal pruritus.
- Weight loss rare.
- Stress factors or abnormal personality traits in approximately 35% of dogs; visitation, travel, moving, construction, invisible fence, recent adoption or considered nervous, high-strung, sensitive, noise phobia, aggressive, anxiety or depressive disorders.
- Physical examination reveals no significant findings related to the gastrointestinal tract.

CAUSES AND RISK FACTORS

Unknown; stress or abnormal personality traits may play a role in some.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Chronic idiopathic large bowel diarrhea has been diagnosed in approximately 25% of dogs undergoing colonoscopy.
- Dietary indiscretion.
- Highly digestible diet-responsive diarrhea.
- Hypoallergenic diet-responsive diarrhea.
- Whipworms.
- *Clostridium perfringens*-associated diarrhea.
- Lymphocytic plasmacytic colitis.
- Eosinophilic colitis.
- Miscellaneous types of colitis.
- Irritable bowel syndrome.

- Colonic neoplasia (adenocarcinoma, lymphoma, and adenoma are most common).
- Cecal inversion.

CBC/BIOCHEMISTRY/URINALYSIS

No consistent or specific abnormalities, although can recognize peripheral eosinophilia occasionally in dogs with colonic whipworms, eosinophilic colitis, and food allergy.

OTHER LABORATORY TESTS

Multiple fecal floatations by zinc sulfate; negative for whipworms and other parasites.

IMAGING

- Abdominal radiographs within normal limits.
- Abdominal ultrasound within normal limits.

DIAGNOSTIC PROCEDURES

- Highly digestible diet trial for 2–4 weeks; no improvement in stool quality.
- Elimination or hypoallergenic diet trial for 2–4 weeks; no improvement in stool quality.
- *Clostridium perfringens* enterotoxin fecal ELISA negative.
- Therapeutic deworming for whipworms (fenbendazole 50 mg/kg PO q24h for 5 days; no improvement).
- Colonoscopy usually within normal limits or only mild nonspecific findings such as slight increases in granularity or friability.

PATHOLOGIC FINDINGS

- Histopathologic evaluation of colonic biopsy samples within normal limits.
- Multiple biopsy samples should be evaluated from throughout the colon from the cecum to the rectum.



TREATMENT

- Health care can be provided on an outpatient basis and consists of dietary fiber supplementation.
- Activity level does not have to be modified.
- A highly digestible "GI" diet should initially be supplemented with 1–3 tbsp daily of psyllium hydrophobic mucilloid (Metamucil 10.2 g psyllium/tbsp).
- Psyllium is a soluble fiber that adsorbs water, improving fecal consistency, promotes bacterial fermentation and production of volatile fatty acids, which act as an energy source for colonic epithelial cells.
- Median dose is 2 tbsp/day, or 0.13 tbsp/kg/day, or 1.3 g psyllium/kg/day.
- Initial response to lower amounts of fiber supplementation or the use of other types of fiber is not as successful.
- After 2–3 months without diarrhea, the amount of fiber can be slowly reduced successfully in approximately 50% of dogs.
- After resolution of diarrhea with psyllium supplementation, owners may attempt to switch to a commercial high fiber (insoluble fiber) diet that may be more convenient to feed; however diarrhea may

return in 50% of dogs.

- After resolution of diarrhea with psyllium supplementation, owners may be able to switch from the highly digestible "GI" diet to a high-quality maintenance dog food.
- Lack of initial response to fiber supplementation suggests that the chronic idiopathic large bowel diarrhea may be due to irritable bowel syndrome and pharmacologic management of that disorder should be instituted.



MEDICATIONS

None indicated

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

No known interactions of fiber supplementation with commonly used drugs.



FOLLOW-UP

- Patient monitoring requires periodic assessment of the stool quality, performed during recheck office examinations or via telephone interviews.
- If stresses were initially identified, stress reduction should be attempted.
- If abnormal personality traits were initially identified, they should be modified.
- Dietary soluble fiber supplementation can occasionally produce excessive flatulence, which can be managed by reduction in the fiber dosage.
- Prognosis is very favorable as approximately 85% of dogs have an excellent or very good long-term response to fiber supplementation.



MISCELLANEOUS

- There are no known associated conditions.
- Age does not play a role in diagnosis or treatment.
- There is no known zoonotic potential.
- There are no special considerations regarding pregnancy, fertility or breeding.

Suggested Reading

Lecoindre P, Gaschen FP. Chronic idiopathic large bowel diarrhea in the dog. *Vet Clin North Am* 2011; 41:447–456.

Leib M. Treatment of chronic idiopathic large bowel diarrhea in dogs with a highly digestible diet and soluble fiber: A retrospective review of 37 cases. *J Vet Int Med* 2000; 14:27–32.

Author Michael S. Leib

Consulting Editor Stanley L. Marks

FIBROCARTILAGINOUS EMBOLIC MYELOPATHY



BASICS

DEFINITION

Acute ischemic necrosis of the spinal cord caused by fibrocartilaginous emboli.

PATHOPHYSIOLOGY

- Emboli—found in spinal cord arteries, veins, or both; source is possibly intervertebral disc material or marrow of vertebral body.
- Exact mechanism of entry into the spinal vasculature unknown.

SYSTEMS AFFECTED

Nervous

GENETICS

N/A

INCIDENCE/PREVALENCE

- Common cause of spinal cord disease in non-chondrodystrophic breeds of dogs.
- Not reported in chondrodystrophic breeds.
- Rare in cats.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Giant- and large-breed dogs—highest prevalence.
- Miniature schnauzers and Shetland sheepdogs—overrepresented; hyperlipoproteinemia and resultant hyperviscosity common in these breeds; may contribute to spinal cord infarction without fibrocartilaginous emboli.

Mean Age and Range

- Most patients 3–5 years old
- Range 16 weeks–10 years

Predominant Sex

Slight male predominance

SIGNS

Historical Findings

- Mild trauma or vigorous exercise at the onset of signs common.
- Sudden onset.
- Affected dog typically cries in pain; pain subsides in minutes to hours (at most).
- Signs of paresis or paralysis develop over a matter of seconds, minutes, or hours.
- Condition stabilizes within 12–24 hours.

Physical Examination Findings

N/A

Neurologic Examination Findings

- Deficits—usually lateralized; unaffected side usually mildly affected or normal; symmetrically distributed in a few patients.
- Pain—at onset of signs and then generally absent; usually subsided by the time patient is

examined; may be felt for a few hours in severely affected patients.

- Any level of the spinal cord can be affected, depending on the distribution of the embolic material.
- Mild ataxia to paralysis.
- Upper or lower motor neuron deficits.
- Spinal cord injury—unilateral; or only the dorsal or ventral aspect of the spinal cord, causing an ipsilateral limb deficit with sensory loss but muscle tone and motor function preserved (or vice versa); other odd combinations possible in patients with focal quadrant injuries.
- If signs progress beyond 24 hours, consider other diseases.

CAUSES

Unknown

RISK FACTORS

- Vigorous exercise may trigger the incident
- Hyperlipoproteinemia



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute, non-progressive, asymmetric, and non-painful spinal cord disease—presence of these characteristics greatly helps in the diagnosis.
- Back and neck pain with symmetrical signs—intervertebral disc disease; discospondylitis; vertebral tumor; fracture and luxation; survey radiography, MRI, CT, and/or myelography help confirm the diagnosis.
- Parenchymal spinal cord hemorrhage secondary to bleeding diathesis (e.g., caused by anticoagulant rodenticide ingestion, thrombocytopenia, or disseminated intravascular coagulation)—rule out by examining for evidence of hemorrhage, performing platelet count, and determining blood clotting times.
- Focal myelitis—differentiate on progressive history and CSF analysis.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

N/A

IMAGING

- Survey spinal radiograph—usually normal.
- Myelography and CT myelography—in acute stage often demonstrates focal intramedullary swelling at the embolic site; later, often normal or shows an area of cord atrophy.
- MRI—ideal diagnostic technique; on T2-weighted images, at site of lesion, there may be decreased signal intensity of disc and increased signal intensity of spinal cord parenchyma.

DIAGNOSTIC PROCEDURES

CSF Analysis

- Results depend on location (e.g., lumbar vs. cerebello-medullary cistern) and time of collection in relation to onset of clinical signs.
- Acute stage—increased RBC and neutrophils may be seen; a few days later, may see only mild increase in protein.
- Sometimes normal.

PATHOLOGIC FINDINGS

- Gross—focal spinal cord swelling with hemorrhage.
- Microscopic—emboli of fibrocartilage in arteries and veins of spinal cord and meninges; hemorrhagic necrosis and malacia in gray and white matter.



TREATMENT

APPROPRIATE HEALTH CARE

In-patient—for immediate medical treatment and diagnostic procedures.

NURSING CARE

- Keep recumbent patients on padded surface; turn frequently to prevent pressure sores.
- Assist and encourage patients to ambulate as soon as possible.
- Assist bladder emptying several times a day if needed by expression or catheterization to prevent bladder over distension and detrusor muscle injury.
- Hydrotherapy in pool or underwater treadmill—very helpful in rehabilitation.
- The use of a light weight chest harness with a dorsally located handle designed for the use by search and rescue dogs such as a Ruff Wear Web Master Dog Harness (www.ruffwear.com) can be very helpful for managing nursing care at home during recovery.

ACTIVITY

- Restrict until diagnosis is made in case of vertebral column instability from other causes such as intervertebral disc herniation or fracture/luxation.
- Once fibrocartilaginous embolic myelopathy is confirmed, activity should be encouraged, not restricted.

DIET

Normal unless hyperlipidemia is present, then feed a low fat diet such as Hill's Prescription Diet r/d.

CLIENT EDUCATION

- Inform client that recovery from paresis or paralysis is slow and gradual, when it occurs.
- Inform client that most patients need considerable home care during recovery.

SURGICAL CONSIDERATIONS

N/A

FIBROCARTILAGINOUS EMBOLIC MYELOPATHY

(CONTINUED)



MEDICATIONS

DRUG(S) OF CHOICE

Methylprednisolone sodium succinate—may be beneficial only if given within the first 8 hours after the onset of signs according to studies of acute spinal cord injury caused by spinal cord impact; 30 mg/kg IV as first treatment; then 15 mg/kg at 2 and 6 hours and every 6 hours thereafter for a total treatment period of 24–48 hours; give each dose slowly over 10–15 minutes; too rapid injection can cause vomiting. Controversial and may not be effective.

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CONTRAINDICATIONS

Non-steroidal analgesics—do not administer with methylprednisolone sodium succinate; increases probability of gastrointestinal ulceration.

PRECAUTIONS

- Methylprednisolone sodium succinate—no benefit with longer treatment (> 24–48 hours) and dramatically increases adverse effects (e.g., gastrointestinal ulceration).
- High-fiber and low fat diet such as Hill's Prescription Diet r/d during and after steroid treatment reduces gastrointestinal ulceration.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Sequential neurologic evaluations—during the first 12–24 hours after the initial examination.
- Neurologic status—at 2, 3, and 4 weeks after onset of clinical signs.

- Urinary incontinence—urinalysis and culture and sensitivity to detect urinary tract infection.

PREVENTION/AVOIDANCE

- Recurrence highly unlikely but possible.
- No known method of prevention in most cases.
- If hyperlipidemia, feed a low fat diet (< 10%) and oral omega-3 fish oils 10–30 mg/kg q24h.

POSSIBLE COMPLICATIONS

- Fecal and urinary incontinence
- Urinary tract infection
- Urine scalding and pressure sores

EXPECTED COURSE AND PROGNOSIS

- Pain perception present and upper motor neuron signs—prognosis for marked improvement good.
- Loss of pain perception—prognosis poor.
- Areflexia of limbs or sphincters—almost no chance of recovery.
- Reduced purposeful movements and reflexes—functional recovery common; some degree of permanent deficit likely.
- Progression of clinical signs from upper to lower motor neuron and an enlarging area of sensory loss indicate ascending or descending myelomalacia and a hopeless prognosis; consider euthanasia.
- Neurologic status—little change in the first 14 days after onset; most improvement occurs between days 21 and 42; remyelination is complete in most patients within 6–12 weeks after onset; if no improvement after 21–30 days, recovery is unlikely.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Disorders that lead to a compromise in circulatory function may predispose or mimic fibrocartilaginous embolic

myelopathy—hyperadrenocorticism; hypothyroidism; high systemic blood pressure; hyperviscosity syndrome; hyperlipidemia; bleeding diathesis; bacterial endocarditis.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

High-dose corticosteroid administration—may cause premature delivery.

ABBREVIATIONS

- CSF = cerebrospinal fluid
- CT = computed tomography
- MRI = magnetic resonance imaging
- RBC = red blood cell

Suggested Reading

Gandini G, Cizinauska S, Lang J, et al. Fibrocartilaginous embolism in 75 dogs: Clinical findings and factors influencing the recovery rate. *J Small Anim Pract* 2003; 44:76–80.

Grunenfelder FI, Weishaert D, Green R, et al. Magnetic resonance imaging findings in spinal cord infarction in three small breeds dogs. *Vet Radiol Ultrasound* 2005; 46:91–96.

Hawthorne JC, Wallace LJ, Fenner WR, et al. Fibrocartilaginous embolic myelopathy in miniature schnauzers. *J Am Anim Hosp Assoc* 2001; 37:374–383.

Mikszewski JS, Van Winkle TJ, Troxel MT. Fibrocartilaginous embolic myelopathy in five cats. *J Am Anim Hosp Assoc* 2006; 42:226–233.

Summers BA, Cummings JF, de Lahunta A. *Veterinary Neuropathology*. St Louis, MO: Mosby, 1995, pp. 246–249.

Author Allen Franklin Sisson

Consulting Editor Joane M. Parent



Client Education Handout
available online

FIBROSARCOMA, BONE



BASICS

OVERVIEW

- Primary bone fibrosarcoma arises from stromal elements within the marrow cavity and is characterized by malignant spindle cells that produce varying amounts of collagen but not any osteoid or cartilage.
- In dogs, FSA accounts for <5% of all primary bone tumors with the metaphysis or diaphysis of long bones affected most commonly.
- In cats, FSA has been reported to be the second most common bone tumor in cats and can involve the maxilla, mandible, humerus, scapula, carpus, digits, ribs, and sacrum.

SIGNALMENT

- Dog and cat.
- No obvious breed or gender predilections in dog or cats.
- Reported age ranges 1.5–12 years in dogs and 9–13 years in cats.

SIGNS

Historical Findings

Appendicular FSA

- Lameness, usually progressive but occasionally acute if there is a pathologic fracture.
 - A palpable swelling may be present.
- Axial FSA**
- Localized swelling with or without pain is common.
 - Tumors arising from the mandible or maxilla can be associated with halitosis, dysphagia, pain on opening the mouth, or nasal discharge.
 - Vertebral tumors may induce neurologic deficits secondary to spinal cord compression.
 - Rib tumors are rarely associated with respiratory signs unless large and causing space-occupying effects.

Physical Examination Findings

Appendicular FSA

- Lameness of variable severity, ranging from minimal to non-weight-bearing.
- A palpable swelling may be present.

Axial FSA

- Variable physical examination findings.
- Depending on the size and location of the tumor, a mass may be visible or palpable.

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other primary bone tumors (osteosarcoma, chondrosarcoma, hemangiosarcoma).

- Metastatic bone tumors (transitional cell, prostatic, mammary, thyroid, apocrine gland anal sac carcinomas).

- Tumors that locally invade adjacent bone (nasal carcinoma; oral squamous cell carcinoma, melanoma, fibrosarcoma, ameloblastoma; synovial sarcoma; histiocytic sarcoma; digital squamous cell carcinoma, melanoma).
- Hematopoietic tumors (myeloma, lymphoma).
- Bacterial or fungal osteomyelitis.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

IMAGING

- Radiographs of the primary lesion show features of an aggressive bone lesion (bone lysis, cortical destruction, non-homogenous bone formation, ill-defined zone of transition).
- Thoracic radiographs are recommended to screen for pulmonary metastasis.
- CT is recommended for axial tumors to more accurately stage local disease and plan for surgery and/or radiation therapy.

DIAGNOSTIC PROCEDURES

- Histopathology is needed for a definitive diagnosis.
- Primary bone FSA has been reported to metastasize to a variety of locations: lungs, regional lymph nodes, other bones, skin, pericardium, and myocardium. Consider additional diagnostic evaluation as indicated to rule out metastasis to these or other locations.



TREATMENT

- Amputation is recommended for appendicular tumors.
- For axial tumors, wide surgical excision is recommended whenever possible. If surgical excision is incomplete, adjuvant radiation therapy might help improve local control.
- Stereotactic radiation therapy provides effective local control for canine osteosarcoma and might be an alternative to surgery for patients with FSA.
- Palliative analgesic therapy is recommended for patients with nonresectable local disease or gross metastasis, or when definitive therapy is declined.



MEDICATIONS

DRUG(S)

- Nonsteroidal anti-inflammatory drugs.
- Tramadol (2–5 mg/kg PO q6–12h).

- Gabapentin (3–10 mg/kg PO q8–24h).

- Intravenous aminobisphosphonates (pamidronate, zoledronate) might alleviate bone pain and attenuate bone resorption.
- Adjuvant chemotherapy has not been evaluated, but given the high metastatic risk, doxorubicin as a single agent or alternating with cisplatin or carboplatin might be reasonable; consult a veterinary oncologist for current recommendations.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

None

F



FOLLOW-UP

PATIENT MONITORING

Physical examination and thoracic radiographs every 2–3 months.

EXPECTED COURSE AND PROGNOSIS

- There is limited information regarding long-term prognosis.
- Complete excision of the primary tumor can potentially provide long-term control.
- Up to half of patients will develop metastasis. Metastasis has been identified as long as 19 months after amputation.



MISCELLANEOUS

SEE ALSO

- Chondrosarcoma, Bone
- Osteosarcoma

ABBREVIATIONS

- CT = computed tomography
- FSA = fibrosarcoma
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

Albin LW, Berg J, Schelling SH.

Fibrosarcoma of the canine appendicular skeleton. JAAHA 1991, 27:303–309.

Author Dennis B. Bailey

Consulting Editor Timothy M. Fan

FIBROSARCOMA, GINGIVA



BASICS

OVERVIEW

- Fibrosarcoma is a mesenchymal tumor characterized by malignant spindle cells that produce varying amounts of collagen.
- Oral FSA arises most commonly in the gingiva; it occasionally involves the lips and rarely the tongue.
- In dogs, FSA is the third most common oral malignancy (20% of all oral tumors).
- In cats, FSA is the second most common oral malignancy (5–15% of all oral tumors).

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SIGNALMENT

- Dogs: overall, large-breed dogs are predisposed. Golden retrievers are overrepresented specifically for the histologically low-grade but biologically high-grade FSA variant (see "Pathologic Findings"). Median age is 7 years (range, 1–16 years).
- Cats: no breed predilections. Median age 10 years (range 1–21 years).

SIGNS

Historical Findings

- Visible mass arising within the oral cavity.
- Halitosis, hypersalivation, dysphagia, and/or bloody oral discharge.
- Oral pain—head-shy behavior and/or decreased food intake despite showing interest in food.

Physical Examination Findings

- A firm, smooth mass is seen most commonly.
- The overlying mucosa usually is intact, although trauma and ulceration from the occlusal teeth is common with larger tumors.
- Halitosis, hypersalivation, and/or oral bleeding.
- Difficulty or pain when opening the mouth and/or facial deformity.
- Ipsilateral mandibular lymphadenopathy.
- Nasal discharge, epistaxis, or decreased air flow through the nares (maxillary tumors).

CAUSES & RISK FACTORS

None identified



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other oral tumors including melanoma, squamous cell carcinoma, and epulis (ameloblastoma or periodontoma)

- Tooth root abscess
- Osteomyelitis
- Dentigerous cyst
- Craniomandibular osteopathy

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

IMAGING

- Skull or dental radiographs recommended to evaluate for bone involvement (present in 60–70%).
- CT imaging can more accurately stage local disease and is useful for planning surgery and/or radiation therapy. It is especially helpful for maxillary tumors and large or caudal mandibular tumors.

DIAGNOSTIC PROCEDURES

- Histopathology is required to reach a definitive diagnosis.
- Cytology or histopathology of the ipsilateral mandibular lymph node recommended to screen for metastasis.

PATHOLOGIC FINDINGS

Histologically low-grade yet biologically high-grade tumors have been described, particularly in golden retrievers and other large-breed dogs. Initially, on histopathology these tumors were classified as benign lesions (nodular fasciitis, chronic inflammatory nodules, granulation tissue) or low-grade FSA. However, aggressive biologic behavior including bone destruction (75%), lymph node metastasis (20%), and pulmonary metastasis (12%) is present in affected dogs.



TREATMENT

- Surgical excision—removal of the mass and adjacent bone (maxillectomy or mandibulectomy) with a margin of at least 2–3 cm is recommended whenever possible.
- If excision is incomplete, adjuvant radiation therapy is recommended to improve local control.
- Radiation therapy can be considered as a sole local treatment modality when surgery is not possible or declined.
- Palliative care focuses on pain control.



MEDICATIONS

DRUG(S)

- Nonsteroidal anti-inflammatory drugs.
- Tramadol (2–5 mg/kg PO q6–12h).

- Gabapentin (3–10 mg/kg PO q8–24h).
- Empiric antibiotic therapy can be considered for secondary bacterial infections.

CONTRAINDICATIONS/POSSIBLE

INTERACTIONS

Use NSAIDs cautiously in all cats and in dogs with renal insufficiency.



FOLLOW-UP

PATIENT MONITORING

Physical examination every 2–3 months and thoracic radiographs every 3–4 months.

EXPECTED COURSE AND PROGNOSIS

- Most patients die or are euthanized due to local disease.
- Overall metastatic rate is 20–30% (regional lymph nodes and lungs).
- With surgery alone, individual prognosis depends on tumor size, tumor location, and surgical resectability, with reported median survival varying 9–24 months, and long-term control is possible with complete excision.
- Combining surgery (incomplete excision) with radiation therapy, median survival is 18 months.
- With radiation therapy alone, median progression-free survival is 45 months for tumors < 2 cm, 31 months for tumors 2–4 cm, and 7 months for tumors > 4 cm.
- There is limited information for cats, but prognosis likely is more guarded due to the difficulty of complete surgical excision.



MISCELLANEOUS

ABBREVIATIONS

- CT = computed tomography
- FSA = fibrosarcoma

Suggested Reading

Frazier SA, Johns SM, Ortega J, et al. Outcome in dogs with surgically resected oral fibrosarcoma (1997–2008). Vet Comp Oncol 2013, 10(1):33–43.

Author Dennis B. Bailey

Consulting Editor Timothy M. Fan

FIBROSARCOMA, NASAL AND PARANASAL SINUS



BASICS

OVERVIEW

- Fibrosarcoma is a malignant tumor of spindle cells that produce varying amount of collagenous (fibrous) stroma.
- In dogs, FSA accounts for up to 5% of all canine sinonasal tumors and is the second most common nasal sarcoma.
- Nasal FSA is uncommon in cats.

SIGNALMENT

- In dogs, no breed or gender predilections have been identified. Median age 9 years (range 1–16 years).
- Uncommon in cats—no obvious predilections.

SIGNS

Historical Findings

- Unilateral or bilateral epistaxis and/or mucopurulent discharge.
- Sneezing, stertorous breathing, and/or facial deformity.
- Decreased appetite and/or halitosis secondary to oral cavity invasion.
- Seizures, behavior changes, and/or obtundation secondary to cranial invasion.

Physical Examination Findings

- Epistaxis and/or nasal discharge (unilateral or bilateral).
- Decreased nasal air flow (unilateral or bilateral).
- Pain on nasal or paranasal sinus palpation or percussion.
- Facial deformity, decreased retropulsion of the eyes or exophthalmia, and epiphora.
- Visible mass effect protruding through the palate into the oral cavity.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other nasal tumors—adenocarcinoma, squamous cell carcinoma, chondrosarcoma, osteosarcoma, lymphoma, transmissible venereal tumor (dogs), nasopharyngeal polyp (cats).
- Fungal rhinitis—aspergillosis and penicilliosis (dogs), cryptococcosis (cats), sporotrichosis (both).
- Rhinosporidiosis (dogs).
- Viral rhinitis—herpesvirus and calicivirus (cats).
- Foreign body.
- Thrombocytopenia or other coagulopathy.
- Tooth root abscess and oronasal fistula.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal

OTHER LABORATORY TESTS

- Nasal flush for cytology and culture—rarely helpful
- Coagulation profile
- Buccal mucosal bleeding time
- Regional lymph node aspiration and cytology

IMAGING

- Skull radiographs—soft tissue opacity in the nasal cavity and/or frontal sinuses, as well as destruction of the turbinates, nasal septum, vomer, or surrounding palatine, maxillary, and/or frontal bones.
- Thoracic radiographs to screen for pulmonary metastasis.
- CT is superior to radiographs for detecting soft tissue opacity within the nasal cavity and surrounding sinuses, bony destruction, and extension through the cribriform plate into the brain.

DIAGNOSTIC PROCEDURES

- Blood pressure measurement and fundic examination.
- Mandibular lymph node cytology to screen for possible metastasis.
- Rhinoscopy can sometimes be helpful for visualizing a mass or fungal plaque and guiding a subsequent biopsy.
- Tissue biopsy and histopathology is needed for definitive diagnosis. The biopsy instrument should not pass the level of the medial canthus of the eye to avoid penetrating the cribriform plate.



TREATMENT

- Radiation therapy is the treatment of choice.
- Conventional linear accelerator is used most commonly. However, if available, stereotactic radiation therapy can reduce the number of radiation treatments and reduce adverse effects while maintaining treatment efficacy.
- Palliative radiation protocols (fewer treatments and lower total radiation dose) might be preferable for dogs with very advanced disease.
- Surgery alone is ineffective.



MEDICATIONS

DRUG(S)

- Prednisone (0.5–1 mg/kg PO q24h) to help relieve nasal congestion.

- Phenylephrine nasal spray can be used intermittently to help with epistaxis.
- Empiric antibiotic therapy can be considered for secondary bacterial infections.
- Consult a medical oncologist for current recommendations.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Physical examinations every 2–3 months and thoracic radiographs every 3–4 months.
- CT of the nasal cavity can be considered to monitor disease regression or if clinical signs recur or worsen.

EXPECTED COURSE AND PROGNOSIS

- Overall metastatic rate is < 20% (usually involve regional lymph nodes and/or lungs).
- Median survival with palliative care alone is 3 months.
- With definitive radiation therapy, 1-year relapse-free survival rate is around 50% and 2-year relapse-free survival rate is around 30%.
- For patients with nasal tumors in general, extension into the frontal sinuses and/or erosion through the bones of the nasal passage is associated with a three-fold increase in risk of local recurrence.
- Brain involvement is a poor prognostic factor.
- Unilateral versus bilateral involvement is not a significant prognostic factor.



MISCELLANEOUS

SEE ALSO

- Adenocarcinoma, Nasal
- Chondrosarcoma, Nasal and Paranasal Sinus
- Epistaxis

ABBREVIATIONS

- CT = computed tomography
- FSA = fibrosarcoma

Suggested Reading

Sones E, Smith A, Schleis S, et al. Survival times for canine intranasal sarcomas treated with radiation therapy: 86 cases (1996–2011). Vet Radiol Ultrasound 2013, 54(2):194–201.

Author Dennis B. Bailey

Consulting Editor Timothy M. Fan

FIPRONIL TOXICOSIS



BASICS

OVERVIEW

- Phenylpyrazole compound with selective toxicity against insects.
- Discovered in 1987, registered as a pesticide in the United States in 1996; used worldwide today.
- Uses:
 - Topical flea and tick spot-on products ("plus" versions include S-methoprene)
 - Roach and ant-bait stations
 - Flea and tick sprays for pets
 - Granular turf products
 - Soil treatment
 - Crop pest control

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SIGNALMENT

- Dogs:
 - Accidental ingestion and/or licking of topical spot-on products.
 - Chewing ant and roach-bait stations or licking gel products.
 - Ingesting liquid from bottles or granules from bags containing product.
- Cats:
 - Accidental ingestion of topical spot-on product from grooming.

SIGNS

- Dermal—skin irritation, alopecia, or dermal hypersensitivity reaction
- Oral—hypersalivation, nausea, vomiting, diarrhea
- Ingestion of large doses: CNS—hyperexcitability, tremors, convulsions, seizures, death

CAUSES & RISK FACTORS

- Ingestion by dogs, especially young dogs occurs more frequently due to behavioral factors. With chronic studies in dogs, severe neurotoxic signs were observed at a dose of 20 mg/kg.
- Wide availability and frequent access to products.
- Biggest concern is exposure to concentrated products frequently found on farms and ranches or used by pesticide control applicators.



DIAGNOSIS

- History of exposure.
- Detected in blood, tissue, hair with GC/MS.

- Differential diagnosis: dogs and cats—exposure to agents that can cause dermal hypersensitivity or CNS signs.



TREATMENT

- Baseline CBC, chemistry profile, and UA should be performed to rule out pre-existing organ dysfunction which could increase the risk for toxicosis.
- For dermal reaction, bathe with liquid dishwashing detergent and rinse thoroughly.
- Antihistamine or steroids for dermal hypersensitivity reaction.
- With ingestion of a large dose, one dose of activated charcoal with sorbitol may be beneficial.
- Methocarbamol for tremors.
- Anticonvulsants for seizures.
- IV fluids (balanced crystalloid) at twice maintenance if CNS signs occur.



MEDICATIONS

- Activated charcoal (0.5–1 mg/kg PO) and an osmotic cathartic (sorbitol or sodium sulfate, 125 mg/kg PO) × 1 dose for large ingestions.
- Methocarbamol for tremors—50–150 mg/kg IV. Max daily dose 330 mg/kg/day (cats and dogs).
- Anticonvulsants for seizures—diazepam 0.5–2 mg/kg IV (dogs and cats); phenobarbital 2–6 mg/kg IV (dogs and cats).
- Diphenhydramine 2–4 mg/kg q8–12h PO; 1 mg/kg q8–12h IM, SC, IV.
- Dexamebasone 0.5–1 mg/kg IV or IM (dogs); 0.125–0.5 mg/kg IV or IM (cats).



FOLLOW-UP

Patients usually recover well with symptomatic and supportive care; no long term organ damage is expected to occur.



MISCELLANEOUS

- Puppies/young dogs are less discriminate and more likely to chew up product containers.
- Young and geriatric animals may have lower detoxification capabilities.

PREGNANCY/FERTILITY/BREEDING

Fipronil was administered to rats (route of exposure not included) to determine reproductive effects. No reproductive effects were noted at 30 ppm (2.54 mg/kg/day in males and 2.74 mg/kg/day in females). The lowest dosage at which reproductive effects were observed was 300 ppm (26.0 mg/kg/day in males and 28.4 mg/kg/day in females) based on unspecified clinical signs in the offspring, reduced litter size, decreased body weights, decreased mating, reduced fertility, reduced post-implantation and offspring survival, and delay in physical development.

ABBREVIATIONS

- CNS = central nervous system
- GC/MS = gas chromatography/mass spectrometry
- PPM = parts per million
- UA = urinalysis

INTERNET RESOURCES

Fipronil Technical Fact Sheet, Nation Pesticide Telecommunications Network <http://npic.orst.edu/factsheets/fiptech.pdf>

Suggested Reading

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Hovda LR, Hooser SB. Toxicology of newer pesticides for use in dogs and cats. Vet Clin North Am Small Anim Pract 2002, 32:455–467.

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BASICS

DEFINITION

Excessive formation of gases in the stomach or intestinal tract. Eructation is the passage of gas from the stomach through the mouth, while flatus refers to the gas released through the anus.

PATHOPHYSIOLOGY

- Often results from a diet change or indiscretion but may herald a more serious gastrointestinal disease.
- Swallowed air (aerophagia) and the bacterial fermentation of nutrients are the main sources of gastrointestinal gas; less significant sources include the interaction of gastric acid and pancreatic/salivary bicarbonate and diffusion of gases from the blood.
- Poorly digestible diets that escape intestinal assimilation, and are therefore available for colonic fermentation, and diets that liberate odiferous gases are associated with flatulence; these include slowly absorbed or non-absorbable oligosaccharides (whole grains, soybeans, beans, and peas), spoiled food, high-fat diets, milk products, and spices.
- Fiber-containing foods contribute to flatus indirectly through reduced dry-matter digestibility and directly by fermentation of the fiber in the colon.
- Dogs and cats are lactose intolerant; a dietary concentration of 1.5 g/kg/day (11 g lactose in 1 cup of milk) may produce flatus and diarrhea.
- A rapid change in diet or an increase in the concentration of a dietary component, especially carbohydrate or fiber, may cause flatus during a period of intestinal adaptation.
- As much as 99% of flatus is composed of nitrogen, oxygen, hydrogen, carbon dioxide, and methane, all of which are odorless.
- Malodorous gases, including ammonia, hydrogen sulfide, indole, skatole, volatile amines, and short-chain fatty acids, compose the residual 1%. Protein maldigestion is often responsible for production of malodorous gases.
- Disease states causing malassimilation of nutrients (such as protein-losing enteropathies in dogs or inflammatory bowel disease), making them available for colonic fermentation, can cause flatus.

SYSTEMS AFFECTED

Gastrointestinal

GENETICS

No known genetic basis, although brachycephalic breeds are overrepresented.

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Common complaint in dog; rare in cat

Breed Predilections

Excessive aerophagia is seen in brachycephalic breeds, sporting dogs, and those with gluttonous/competitive eating behavior.

Mean Age and Range

Any age

Predominant Sex

None

SIGNS

Historical Findings

Increased frequency and possibly volume of flatus detected by the pet owner.

Physical Examination Findings

- Mild abdominal discomfort caused by gastrointestinal distention possible—mild discomfort can be difficult to recognize but may be reported by owner as a pet that has repeated swallowing efforts, restlessness, or lethargy.
- When flatus is due to gastrointestinal disease, concurrent gastrointestinal signs such as diarrhea, vomiting, borborygmus, changes in appetite, and weight loss may be present.

CAUSES

Increased Aerophagia

- Gluttony or competitive eating
- Respiratory disease or any cause of increased respiratory rate
- Feeding shortly after exercise
- Brachycephalic breeds

Diet-Related

- Diets high in non-absorbable oligosaccharides—soybeans, peas, beans.
- Diets high in fermentable fiber—lactose, pectin, inulin, psyllium, oat bran.
- Diets high in complex starches (e.g., whole grains) that are slowly digested.
- Spoiled diets.
- Milk products.
- Abrupt changes in diet.
- Spices and food additives/supplements.

Disease Conditions

- Acute and chronic intestinal disease—including protein-losing enteropathies, inflammatory bowel disease; intestinal dysbiosis; neoplasia; irritable bowel syndrome; parasitism; bacterial, protozoal, or viral enteritis; and food allergy or intolerance.
- Exocrine pancreatic insufficiency.

RISK FACTORS

- Nervous, gluttonous, or competitive eating.
- Eating soon after exercise.
- Brachycephalic breeds.
- Abrupt dietary changes.
- Inappropriate (feeding table food that is likely to be fermented) or spoiled foods.
- Sedentary lifestyle—a 1998 study reported that 43% of randomly chosen dog owners detected flatulence, most commonly in

sedentary pets, with no association to a particular diet.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Distinguish dietary and behavioral causes of flatus from gastrointestinal disease by thorough evaluation of the patient history; this allows the clinician to ascertain the type of diet, amount fed, frequency of feeding, frequency of dietary changes or additions, and the environment in which the patient is fed.
- Investigate feeding method—frequency, amount, relationship to exercise, how offered, and incidence of competitive eating. Observation of the patient while eating may be required to identify gluttony.
- Perform a complete physical examination with a focus on gastrointestinal evaluation. Palpate the abdomen for gassy bowel loops, pain, and distention, and auscultate the abdomen for bowel sounds, absence of which indicates ileus. Rectal examination for evaluation of rectal and pelvic anatomy.
- Assess body condition score; if low, this may indicate concurrent gastrointestinal disease or inadequate food intake. Obesity may be associated with a sedentary lifestyle that may be a risk factor.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal unless significant bowel disease is present (e.g., hypoalbuminemia in PLE).

OTHER LABORATORY TESTS

- Rectal cytology to evaluate presence of neoplasia, parasites, fungal organisms.
- Zinc sulfate flotation tests or fecal ELISA to evaluate giardiasis.
- Fecal PCR for *Tritrichomonas* in young cats or kittens.
- Fecal cultures to evaluate salmonellosis or campylobacteriosis.
- Serum trypsin-like immunoreactivity to evaluate exocrine pancreatic insufficiency.
- Serum cobalamin and folate concentrations to test for severe small intestinal mucosal disease.

IMAGING

- Abdominal ultrasonography to diagnose gastrointestinal masses or mural thickening.
- Contrast studies may be needed in some cases to detect an obstructive pattern.
- Assessment of gut motility is difficult at best, but scintigraphic markers can be used in some referral facilities. Upper GI series using barium can be used to detect delayed gastric or intestinal emptying; however, the study can be extremely variable secondary to stress.

DIAGNOSTIC PROCEDURES

Gastrointestinal biopsy specimens obtained at surgery or via endoscopy to detect infiltrative gastrointestinal disease.

FLATULENCE

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient—treat any underlying gastrointestinal disease.

NURSING CARE

None

ACTIVITY

Encourage an active lifestyle—exercise increases GI motility, which will help expel flatus and increase regularity of defecation.

DIET

- Feed smaller meals more frequently in an isolated, quiet environment.
- Change diet to one that is highly digestible, with low fiber and fat concentrations (e.g., intestinal or hypoallergenic diets formulated for prescription purposes are all reasonable choices), or feed homemade diets containing boiled chicken and white rice (dogs) or whole chicken with skin (fat) balanced with vitamins and minerals. (Note: cats should not be fed a carbohydrate source, to eliminate carbohydrate intolerance as part of this issue.)
- A change in the protein or carbohydrate source, or removing the additives, benefits some individuals.

CLIENT EDUCATION

Discourage dietary indiscretion (e.g., garbage ingestion or coprophagia).

SURGICAL CONSIDERATIONS

None



MEDICATIONS

DRUG(S) OF CHOICE

- Carminatives are medications that relieve flatulence—there are no studies to show safety or benefit of these drugs in dogs or cats.
- Zinc acetate binds sulfhydryl compounds.
- Yucca schidigera* binds ammonia and is added to pet foods as a flavoring agent.
- Dry activated charcoal absorbs virtually all odiferous gases when mixed directly with human feces and flatus; however, the number of flatus events, gas volume, or odor were not decreased in people.
- Inclusion of activated charcoal, *Y. schidigera*, and zinc acetate in a treat reduced the frequency of highly odiferous episodes in dogs.
- Bismuth subsalicylate (dogs, 1 mL/kg PO initially then 0.25 mL/kg q6h) adsorbs hydrogen sulfide and has antibacterial properties; however, long-term, multiple daily

dosing precludes its practicality. Not recommended for use in cats due to potential for salicylate toxicity.

- Simethicone is an antifoaming agent that reduces the surface tension of gas bubbles, allowing easier coalescence and release of intestinal gas; however, gas production is unaltered.
- Pancreatic enzyme supplements may reduce flatulence in some patients with reduced pancreatic enzyme production.

CONTRAINDICATIONS

Avoid bismuth subsalicylate in cats and in dogs with gastroduodenal ulceration and bleeding disorders.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

- More than 30 herbal and botanical preparations are available; however, the dosage, safety, and efficacy are unknown.
- Use of probiotics to normalize or stabilize the intestinal microenvironment has been advocated and would be safe to try; however, no studies of efficacy of this approach have been completed.



FOLLOW-UP

PATIENT MONITORING

Response to therapy

PREVENTION/AVOIDANCE

- Avoid diets high in non-absorbable oligosaccharides and high in fermentable or non-fermentable fibers.
- Avoid milk products, spoiled diets, and abrupt changes in diet.
- Do not feed shortly after exercise.
- Use of probiotics to improve the commensal bacterial flora may be beneficial if bacterial disruption is the primary cause of flatulence.

POSSIBLE COMPLICATIONS

None

EXPECTED COURSE AND PROGNOSIS

N/A



MISCELLANEOUS

ASSOCIATED CONDITIONS

Gastrointestinal disease

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYS

N/A

SEE ALSO

- Campylobacteriosis
- Exocrine Pancreatic Insufficiency
- Inflammatory Bowel Disease
- Irritable Bowel Syndrome
- Salmonellosis
- Small Intestinal Dysbiosis

ABBREVIATIONS

- ELISA = enzyme-linked immunosorbent assay
- GI = gastrointestinal
- PCR = polymerase chain reaction
- PLE = protein-losing enteropathy

INTERNET RESOURCES

Veterinary Information Network:
www.vin.com/VIN.plx.

Suggested Reading

Davenport DJ, Remillard RL, Simpson KW, et al. Gastrointestinal and exocrine pancreatic disease. In: Hand MS, Thatcher CD, Remillard RL, et al., eds. Small Animal Clinical Nutrition, 5th ed. Topeka, KS: Mark Morris Institute, 2010, pp. 725–810.
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Client Education Handout
available online

FLEA BITE HYPERSENSITIVITY AND FLEA CONTROL



BASICS

DEFINITION

- Flea infestation—large number of fleas and flea dirt.
- Flea bite dermatitis—non-hypersensitivity reaction to flea bites.
- Flea bite hypersensitivity (FBH)—allergic reaction to antigens in flea saliva.
- Biomass—population of immature stages (eggs, larvae, and pupae) and adult fleas.

FLEA LIFE CYCLE

- *Ctenocephalides felis* (cat flea) main cause: not host specific—parasitizes cats, dogs; has many wildlife hosts.
- Adult fleas mate on host and within 24 hours females lay up to 50 eggs per day.
- Eggs fall off pets in the environment and hatch.
- Larvae have negative phototropism and infest carpets, upholstery and under furniture.
- Eggs from wildlife and feral cats survive in moist, protected areas like sheds and covered spaces.
- Larvae undergo molts until they pupate; the cocoon enhances survival.
- Adults emerge when environmental conditions and host availability are favorable.
- Less than 5% of the total flea burden is found as adults on the pet.
- The majority of the biomass is found as immature stages in the home and in peridomestic areas that are shaded and moist.

PATOPHYSIOLOGY

- Flea bite hypersensitivity—caused by a low molecular weight hapten and two high molecular weight allergens.
- Increased binding to dermal collagen; form a complete antigen necessary for eliciting FBH.
- Flea saliva—contains histamine-like compounds that irritate skin.
- Intermittent exposure favors FBH; continuous exposure is less likely to result in hypersensitivity.
- Both IgE and IgG anti flea antibodies reported.
- Immediate and delayed hypersensitivity reactions reported.
- Late-phase IgE-mediated response; occurs 3–6 hours after exposure.
- Cutaneous basophil hypersensitivity; an infiltration of basophils into the dermis; mediated by either IgE or IgG; subsequent exposures cause the basophils to degranulate; manifests as immediate and delayed hypersensitivity.

SYSTEMS AFFECTED

Skin/Exocrine

GENETICS

FBH—unknown inheritance pattern; common in atopic breeds

INCIDENCE/PREVALENCE

Varies with climatic conditions and flea population. Microclimate in the home may allow year-round infestations.

GEOGRAPHIC DISTRIBUTION

FBH—may occur anywhere; non-seasonal in climates that are warm and humid, and year-round in animals housed indoors when flea infestations are not controlled.

SIGNALMENT

Species

Dogs and cats

Breed Predilections

FBH—any breed; common in atopic breeds

Mean Age and Range

FBH—rare < 6 months of age; average age range, 3–6 years, but may be seen at any age

Predominant Sex

N/A

SIGNS

Historical Findings

- Pruritus
- Chewing
- Licking
- Exposure to other animals
- Lack of consistent or effective flea control

Physical Examination Findings

- Determined by the severity of the reaction.
- Finding fleas and flea dirt is beneficial, although not essential, for the diagnosis of FBH. When appropriate signs are present flea parasitism should be suspected and flea control instituted.
- Sensitive animals require a low exposure and tend to over-groom, removing evidence of infestation.
- Dogs—lesions concentrated in the caudal-dorsal-lumbosacral region; caudal aspect of the thighs, lower abdomen, and inguinal region; primary lesions are papules; secondary lesions (e.g., hyperpigmentation, lichenification, alopecia, and scaling) and pyotraumatic dermatitis (“hotspots”) common in uncontrolled FBH.
- Cats—alopecia and crusting dermatitis in a wedge-shaped pattern over the caudal dorsal lumbosacral region and often around the head and neck; other presentations include “barbering” of the inguinal region, miliary dermatitis, and lesions of the eosinophilic granuloma complex.

CAUSES

See “Pathophysiology”

RISK FACTORS

FBH—intermittent exposure to fleas; incidence commonly seen in conjunction with atopy.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Food allergy
- Atopy
- Ectoparasitism
- Dermatophytosis
- Pyoderma
- Any pruritic skin disease

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal
- Cats—occasional eosinophilia

OTHER LABORATORY TESTS

- Skin scrapings—negative.
- Flea combings—fleas or flea dirt.
- RAST and ELISA—variable accuracy; both false-positive and false-negative results reported.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Diagnosis based on historical information and distribution of lesions and/or response to adequate flea control.
- Fleas or flea dirt is supportive but may be difficult to find, especially in cats.
- Identification of *Dipylidium caninum* segments in stool is supportive.
- Intradermal allergy testing with flea antigen—reveals positive immediate reactions in large numbers of flea-allergic animals; delayed reactions (24–48 hours) may sometimes be observed in allergic animals that show no immediate reaction.
- The most accurate test is response to appropriate treatment.

F

PATHOLOGIC FINDINGS

- Superficial perivascular dermatitis.
- Eosinophilic intraepidermal microabscesses.
- Eosinophils as a major cellular component of the dermis.
- Histopathologic evaluation—may not definitively differentiate FBH from atopy, food allergy, or other hypersensitivities.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient therapy

NURSING CARE

N/A

ACTIVITY

N/A

DIET

N/A

CLIENT EDUCATION

- Inform owners that there is no cure for FBH; flea-allergic animals often become more sensitive to flea bites as they age.
- Hypo sensitization is not considered effective.
- Medications that stop itching are meant to be a respite while flea control is instituted.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

TREATMENT STRATEGIES

- Itch relief
- Flea control
 - Pet-targeted
 - Insect-targeted
 - Premises-targeted
 - Environment-targeted

DRUG(S) OF CHOICE

Itch Relief

Corticosteroids

- Anti-inflammatory dosages for symptomatic relief to break itch-scratch cycle while instituting adequate flea control. Use only as much as is needed and for the shortest

FLEA BITE HYPERSENSITIVITY AND FLEA CONTROL

(CONTINUED)

duration to achieve the desired effect. Rapid relief from itching and the distress it causes both pets and owners is important, but does not replace counseling on methods to prevent reoccurrence. • Injectable—one dose is most often sufficient to stop itching while flea control is achieved. ◦ Triamcinolone acetonide injectable—dogs, 0.11–0.22 mg/kg IM/SC. ◦ Dexamethasone sodium phosphate injectable—dogs, 0.07–0.16 mg/kg IM/SC. • Methylprednisolone acetate injectable—cats, 5.5 mg/kg (20 mg per average-sized cat) IM/SC. • Oral: ◦ Prednisolone—cats, 0.5–1 mg/kg PO q12h for 5–7 days then taper; dogs, 0.5–1 mg/kg PO q24h for 7 days then taper.

Antihistamines

Little to no effect.

Flea Control

Goals are the immediate reduction or elimination of adult fleas on the host and to break the cycle of flea development in the home and in the immediate environment.

Pet-Targeted Flea Control

- Topical/Spot-On: ◦ Dinotefuran/pyriproxyfen—rapid-acting spot-on product for dogs and cats; a second canine product contains high-dose permethrin and should not be used on cats. ◦ Fipronil plus IGR (GABA antagonist)—spot-on treatment for cats and dogs (spray treatment for dogs). ◦ Imidacloprid plus IGR—monthly spot-on treatment for cats and dogs; a second canine product contains permethrin and should not be used on cats; also available as a collar. ◦ Etofenprox plus IGR—monthly spot-on for dogs and cats, non-carbamate sodium channel blocker, classified by EPA as a reduced risk pesticide. ◦ Indoxycarb—monthly spot-on, dogs only, sodium channel blocker, activated by flea digestive enzymes, contains permethrin, should not be used on cats. ◦ Selamectin—for dogs and cats, monthly spot-on, chloride channel blocker; also has IDI action. • Sprays: usually contain pyrethrins, and pyrethroids with IGR. When compared to cost of spot-on products the per-pet, per-application expense is much lower.

Insect Growth Regulators (IGRs)

S-methoprine and pyriproxyfen are analogs of insect juvenile hormone that bind to immature stages and prevent maturation.

Insect Development Inhibitors (IDIs)

- Lufenuron and selamectin inhibit chitin synthesis in egg shell, immature stages and adults. • Oral: ◦ Nitenpyram—neonicotinoid flea adulticide; orally administered; rapid onset, but short acting; for dogs and cats. ◦ Spinosad—monthly oral treatment for dogs and cats. ◦ Afoxolaner and Fluralaner—isoxazoline chloride channel blocker; oral product for dogs only.

Premises-targeted flea control

- Indoor treatment—"foggers/bombs" and premises sprays; contain organophosphates,

pyrethrins, and/or insect growth regulators. Etofenprox plus IGR and permethrin/pyrethrin plus IGR, available in inverted aerosol sprays; apply according to manufacturer's directions; treat all areas of the house; can be applied by the owner. Foggers/Bombs do not effectively penetrate all areas commonly inhabited by fleas such as under furniture; hand-held sprays are highly effective against biomass, may be directed where flea populations reside, and have long residual activity. • Professional exterminator—discuss products with representative.

Environment-targeted flea control

• Outdoor treatment—concentrate in shaded areas; sprays usually contain pyrethroids or organophosphates and an insect growth regulator; easy-to-use products applied by attaching dispensing container to garden hose; also available in premixed applicator containers; owners should be educated on areas of application based on likelihood of reinfestation from feral cats and wildlife. Nematode (*Steinerma carpocapsae*)—very safe and chemical-free but expensive and may not survive shipping.

CONTRAINDICATIONS

N/A

PRECAUTIONS

- Label instructions—must be strictly followed. • Spinosad can potentiate neurologic side effects of high-dose ivermectin—but is safe when combined with heartworm preventive dose. • Pyrethrin/pyrethroid-type flea products—adverse reactions include depression, hypersalivation, muscle tremors, vomiting, ataxia, dyspnea, and anorexia; do not use in cats.
- Organophosphates—use inappropriate given the current alternatives. • The animal should be bathed thoroughly to remove remaining chemicals and treated appropriately.

ALTERNATIVE DRUG(S)

- Powders and dips—adverse reactions and toxicity make their use inappropriate given the current alternatives. • Over-the-counter products often contain the same combinations or one active ingredient as veterinarian dispensed products but the absence of proper education concerning OTC product use and off-pet flea control often leads to failures in flea control as well as resolution of FBH.



FOLLOW-UP

PATIENT MONITORING

- Pruritus—a decrease means the FBH is being controlled. • Fleas and flea dirt—absence is not always a reliable indicator of successful treatment in very sensitive animals.

PREVENTION/AVOIDANCE

- Warm climates and infested premises require year-round flea control. • Seasonally warm climates—begin flea control in when temperatures consistently remain above freezing.

POSSIBLE COMPLICATIONS

- Secondary bacterial folliculitis • Acute moist dermatitis • Acral lick dermatitis

EXPECTED COURSE AND PROGNOSIS

Prognosis is good if strict flea control is instituted.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Approximately 80% of atopic dogs are also allergic to flea bites.

AGE-RELATED FACTORS

Package should be consulted for the minimum approved age for application.

ZOONOTIC POTENTIAL

In areas of moderate to severe flea infestation, people can be bitten by fleas; usually papular lesions are located on the wrists and ankles. Humans may also be infected with *Dipylidium caninum*, and fleas play a role in transmission of cat scratch disease (*Bartonella henselae*) among cats and humans.

PREGNANCY/FERTILITY/BREEDING

- Corticosteroids and organophosphates—do not use in pregnant bitches and queens.

SYNOMYS

Flea bite allergy

ABBREVIATIONS

- ELISA = enzyme-linked immunosorbent assay • FBH = flea bite hypersensitivity
- GABA = gamma-aminobutyric acid
- IDI = insect development inhibitor
- IGR = insect growth regulator • RAST = radioallergosorbent test

INTERNET RESOURCES

The Companion Animal Parasite Council: <http://capcvet.org/>

Suggested Reading

Sousa CA, Halliwell RE. The ACVD Task Force on canine atopic dermatitis (XI): The relationship between arthropod hypersensitivity and atopic dermatitis in the dog. *Vet Immunol Immunopathol* 2001, 81(3–4):233–237.

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**Client Education Handout
available online**

FOOD REACTIONS, DERMATOLOGIC



BASICS

DEFINITION

- Adverse reactions to food affecting the skin
- Associated with ingestion of one or more substances

PATHOPHYSIOLOGY

- Pathogenesis not completely understood.
- Immediate and delayed reactions to specific ingredients documented; immediate reactions presumed to be type I hypersensitivity reactions; delayed presumed to be type III or IV.
- Failure or prevention of the development of oral tolerance to food allergens may encourage sensitization.
- Food intolerance—non-immunologic, idiosyncratic reaction; involves metabolic, toxic, or pharmacologic effects of offending ingredients.
- Adverse food reaction is the most common term used, and does not distinguish between immunologic and idiosyncratic reactions.
- Adverse food reactions patients associated with an increased predisposition to atopy.
- Cutaneous adverse food reactions can trigger flares of atopic dermatitis.

SYSTEMS AFFECTED

- Skin/Exocrine
- Gastrointestinal
- Nervous

GENETICS

N/A

INCIDENCE/PREVALENCE

- Approximately 5% of all dermatitis and 10–15% of allergic dermatitis in dogs and cats is caused by adverse reactions to food.
- 13–30% of food allergic dogs have concurrent atopy or flea bite hypersensitivity.
- Third most common pruritic skin disease in the dog; second most common in the cat.
- Percentages vary greatly with clinicians and geographic location.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dogs and cats

Breed Predilections

- Dogs—none reported; breeds associated with Atopic dermatitis overrepresented.
- Cats—Siamese.

Mean Age and Range

- Any age: dogs—possibly increased development (over other allergic dermatoses) in patients < 12 months or > 7 years of age; cats—patients < 2 years or > 5 years of age.
- Most adult patients have been fed the offending allergen for over two years prior to becoming symptomatic.

Predominant Sex

None reported

SIGNS

General Comments

- Symptoms similar to other hypersensitivity reactions
- Pruritus is the main dermatological sign

Historical Findings

- Pruritus of any body location.
- Usually non-seasonal.
- Poor response to anti-inflammatory doses of glucocorticosteroids.
- Recurrent bacterial folliculitis with or without pruritus.
- Persistent otitis externa.
- Concurrent gastrointestinal symptoms in a minority of cases: vomiting and/or diarrhea, excessive borborygmus, flatulence, and frequent bowel movements.
- Very rare association of neurologic signs (seizures) with food hypersensitivity.
- Respiratory signs have been reported in dogs.

Physical Examination Findings

- Dogs—rump, perineum, axillae, groin, face, and interdigital areas frequently affected
- Cats—face, neck, and ears frequently affected
- Cats—lesions of the eosinophilic granuloma complex
- Otitis externa
- *Malassezia* dermatitis
- Secondary bacterial folliculitis
- Plaques
- Pustules
- Erythema
- Crusts
- Scale
- Self-induced alopecia
- “Psychogenic alopecia”
- Excoriation
- Lichenification
- Hyperpigmentation
- Urticaria
- Angioedema
- Pyotraumatic dermatitis
- Acral lick dermatitis

CAUSES

- Immune-mediated reactions (food hypersensitivity)—result from the ingestion and subsequent presentation to the immune system of one or more glycoproteins (allergens) either before or after digestion; sensitization may occur at the gastrointestinal mucosa, after the substance is absorbed, or both; cross-reactivity between various food allergens, and between food and pollen allergens, has been demonstrated.
- Non-immune-mediated reactions (food intolerance)—result of ingestion of foods with high levels of histamine or substances that induce histamine either directly or through histamine-releasing factors.

RISK FACTORS

- Unknown.
- Intestinal parasites or intestinal infections may damage the intestinal mucosa, resulting in the abnormal absorption of allergens and subsequent sensitization.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Flea bite hypersensitivity—usually confined to the caudal half of the body; often seasonal.
- Atopy—associated with pruritus of the face, feet, axilla, groin, and perineum; often seasonal; if pruritus first occurs at < 12 months or > 7 years of age in dogs, then food hypersensitivity should be investigated prior to work up for atopic dermatitis; 20–30% of dogs with adverse reactions to food also have atopic dermatitis.
- Drug reactions—history of drug administration before the development of signs and improvement after withdrawal of the suspected drug.
- Scabies mites—pruritus usually specific to the ears, elbows, and hocks (dogs) and head, ears, and neck (cats); mites in skin scrapings and/or response to specific therapy.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

In vitro (serum) allergy tests; poor correlation between test results and food exposure; poor correlation between diet trial and test results; not completely sensitive or specific; significant discrepancy between labs; currently no standard to enable comparisons between techniques; not recommended as a diagnostic test for food allergy or for choosing appropriate ingredients for food trials.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- There is no single laboratory test available to help the clinician to confirm or refute the presence of food sensitivity.
- Diagnosis is based on dietary exclusion in the form of restricted-ingredient food trials followed by challenge and redevelopment of symptoms.

Food Elimination Diet

- Definitive test for adverse food reactions.
- Tailored to the individual patient.
- Diet must be restricted to one novel protein and one novel carbohydrate.
- Most patients will improve within 6–8 weeks.
- Food trials should be continued up to 10 weeks unless improvement occurs earlier.
- Home-cooked food trials remove possible sources of antigen due to processing, storage,

FOOD REACTIONS, DERMATOLOGIC

(CONTINUED)

and cross-contamination from other ingredients.

Challenge and Provocation Diet Trials

- Used if the patient improves on the elimination diet.
- Challenge—feed the patient the original diet; a return of the signs confirms that the original diet contains an inciting ingredient; the challenge period should last until the signs return but no longer than 10 days.
- Provoke (provocation diet trial)—if the challenge confirmed the presence of an adverse food reaction, add single ingredients to the elimination diet; test ingredients include a full range of meats (beef, chicken, fish, pork, lamb), a full range of carbohydrates (corn, wheat, soybean, rice), eggs, and dairy products; the provocation period for each ingredient should last up to 10 days or less if signs develop sooner; results guide the selection of commercial foods that do not contain the offending substance(s).

PATHOLOGIC FINDINGS

- Skin biopsy—not diagnostic; help confirm or eliminate other differential diagnoses.
- Histopathologic findings—variable; common findings suggest hypersensitivity; secondary bacterial folliculitis or *Malassezia* dermatitis may be present.



TREATMENT

Avoidance of the offending food substance(s)

APPROPRIATE HEALTH CARE

Outpatient management

NURSING CARE

N/A

ACTIVITY

No change

DIET

Avoid any food substances that caused the clinical signs to return during the provocation phase of the diagnosis.

CLIENT EDUCATION

- Explain the principles involved in each phase of the diagnostic test diets.
- Instruct client to eliminate treats, chewable toys, vitamins, medication wraps, and flavored medications (e.g., heartworm preventive) as these may contain ingredients from the patient's previous diet.
- If a home-cooked diet is needed, the website www.balanceit.com is useful to create a diet with adequate supplementation.
- Outdoor pets must be confined to prevent foraging and hunting.
- Advise all family members to adhere to the restricted-ingredient diet trial protocol.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

- Systemic antipruritic drugs—may be useful during the first 2–3 weeks of diet trial to control self-mutilation.
- Antibiotics or antifungal medications—useful for secondary bacterial folliculitis or *Malassezia* dermatitis.

CONTRAINDICATIONS

- Antibiotics that are known to have anti-inflammatory effects (e.g., tetracycline, doxycycline, erythromycin, and trimethoprim-sulfamethoxazole) may confuse response to dietary trials.
- Glucocorticosteroids and antihistamines should be discontinued for at least 10–14 days while on the diet trial to allow correct assessment of the animal's response.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

Examine patient and evaluate and document the pruritus and clinical signs every 3–4 weeks.

PREVENTION/AVOIDANCE

- Avoid intake of any of the ingredients included in the previous diet including treats and chewable vitamins and toys.

POSSIBLE COMPLICATIONS

Other causes of pruritus must be eliminated or controlled to permit accurate assessment of the effect of dietary antigens on clinical signs.

EXPECTED COURSE AND PROGNOSIS

- Prognosis is good if food ingredients are the only cause of pruritus and offending ingredients are avoided.
- Rarely a dog or cat may develop hypersensitivity to new substances, requiring a new elimination diet trial.
- A partial response to a food elimination diet trial suggests a combined food reaction with atopy or with another cause of pruritus.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Superficial bacterial folliculitis
- *Malassezia* dermatitis
- Otitis externa
- Atopic dermatitis

AGE-RELATED FACTORS

None except age ranges during which symptoms of food allergy most often develop.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Adverse reactions to food
- Food allergy
- Food hypersensitivity
- Food intolerance

SEE ALSO

- Atopic Dermatitis
- Contact Dermatitis
- Flea Bite Hypersensitivity and Flea Control
- *Malassezia* Dermatitis
- Otitis Externa and Media
- Pyoderma

Suggested Reading

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Olivry T, DeBoer DJ, Préaud P, et al. International Task Force on Canine Atopic Dermatitis. *Vet Dermatol* 2006, 17:223–235.

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Author David Duclos

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**Client Education Handout
available online**

FOOD REACTIONS (GASTROINTESTINAL), ADVERSE



BASICS

DEFINITION

- Adverse food reactions encompass disorders with an immunologic basis (food allergy), non-immunologic reaction (food intolerance), and toxic reactions (food intoxication, uncommon).
- Adverse food reactions may be associated with gastrointestinal (GI) signs (vomiting and/or diarrhea) in dogs and cats. In a practical sense, food allergy and food intolerance may have similar signs, diagnostics, and treatments and may not be easily distinguishable.
- Food allergy is a common cause for cutaneous signs, such as pruritus, and may occasionally be associated with gastrointestinal signs. Food-allergic pets may uncommonly have both GI signs and cutaneous lesions.

PATOPHYSIOLOGY

- The pathogenesis of food allergy involves complex immunologic events: a leaky intestinal mucosal barrier, dysregulated immune responses, and loss of oral tolerance. Most food allergies are due to type 1 hypersensitivity reactions. Major food allergens include milk, eggs, beef, chicken, and plant proteins from corn, wheat, and soybeans.
- Food intolerance may be due to idiosyncratic reactions to dietary ingredients or additives, pharmacologic reactions to compounds in the diet, defects or deficiencies in the metabolic pathways needed to use the food, or a toxicity reaction to food ingredients or spoiled foodstuffs.
- Toxic reactions to food may occur when a foodstuff is ingested in large amounts (e.g., onion poisoning).
- Food that is spoiled or that contains microorganisms or their toxins can produce a wide range of clinical signs and severity.

SYSTEMS AFFECTED

- Dermatologic
- Endocrine/Metabolic
- Gastrointestinal

GENETICS

- Heritable food allergy is observed in soft-coated Wheaten terriers (suspect autosomal recessive trait).
- German shepherd dogs are at risk for immunologic-mediated intestinal inflammation (i.e., idiopathic IBD) associated with heritable defects in innate immunity. Dietary antigens may provoke adverse host responses in susceptible dogs which contribute to gut inflammation.
- Gluten-sensitive enteropathy has been seen primarily in Irish setters.
- Siamese and Siamese cross cats may be at increased risk.

- The specifics of a genetic basis are not well defined.

INCIDENCE/PREVALENCE

More common in cat than dog

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

- Cats and dogs of any age or breed and either sex can be affected.
- Irish setters are predisposed to gluten-sensitive enteropathy; they tend to display clinical signs by 4–7 months of age.
- Dogs with chronic enteropathies that are diet-responsive tend to be younger adult animals.

SIGNS

General Comments

- Food intolerance commonly produces diarrhea (small or large bowel), vomiting, flatulence, anorexia, and abdominal discomfort.
- Food allergy may cause cutaneous signs, such as pruritus and hair loss, which may be associated with GI signs.

Historical Findings

- Acute food intolerance may accompany feeding a novel foodstuff, a new food source, or dietary change.
- Clients may report cessation of clinical signs in the fasted state or within days of an elimination dietary trial.

Physical Examination Findings

The physical examination is generally nonspecific but may show abdominal discomfort, flatulence, bloating, or patchy areas of alopecia along the pinnae of the ears and periorbital regions, especially in cats.

CAUSES

- Idiosyncratic reactions to food additives—colorings, preservatives (BHA, monosodium glutamate, sodium nitrate, sulfur dioxide, etc.), spices, propylene glycol, etc.
- Pharmacologic reactions—vasoactive substances (i.e., histamine), psychoactive agents, stimulants (i.e., theobromine, caffeine), etc.
- Metabolic defects or deficiencies—brush border enzyme defects (i.e., lactase deficiency), inborn errors of metabolism, aminopeptidase N (in gluten-sensitive enteropathy).
- Toxic reactions to foods or spoiled foods—spices, oxalate toxicity, lectin toxicity, *N*-propyl disulfide aflatoxicosis, ergotism, botulism, dietary indiscretion, etc.
- Genetic mutations in innate immunity genes regulating host responses to dietary constituents.

RISK FACTORS

- Young Irish setters susceptible to gluten-sensitive enteropathy may be at greater

risk to develop the disease if exposed to gluten at an early age.

- Host genetic susceptibility is suspected in Wheaten terriers and German shepherd dogs.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Inflammatory bowel disease, parasitism, exocrine pancreatic insufficiency, and antibiotic responsive diarrhea can produce signs similar to those of adverse food reactions.
- A presumptive diagnosis of adverse food reaction is made upon resolution of GI signs while feeding an elimination diet containing protein hydrolysates or a novel intact protein source.
- Dietary trials using a home-made diet are sometimes used but are generally not intended for long-term administration.
- Gastrointestinal signs often improve within days, especially in cats.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal; animals with food allergy may occasionally have eosinophilia.

OTHER LABORATORY TESTS

- Few diagnostic tests are specific.
- Diagnostics are performed to rule out other differentials and to treat complicating factors.
- Fasting serum folate and cobalamin levels are useful in evaluating hypocabalaminemia and the distribution of small intestinal mucosal disease.
- Rule out exocrine pancreatic insufficiency by evaluating serum trypsin-like immunoreactivity.
- The detection of antigen-specific serum immunoglobulins is generally not recommended because they are considered unreliable in animals.

IMAGING

- Abdominal radiographs or ultrasound may be useful in eliminating differential diagnoses.
- Doppler evaluation (ultrasound) may detect alterations in blood flow through the celiac and cranial mesenteric arteries of dogs.

DIAGNOSTIC PROCEDURES

- Perform an elimination dietary trial of 2 weeks in cats and 3 weeks in dogs with GI signs.
- Following improvement on an exclusion diet, use challenge exposure to sequential single ingredients to specifically identify the incriminating dietary ingredient. While technically the gold standard this is generally impractical in a clinical setting.
- Exclusive feeding with a novel protein source indefinitely is generally required to prevent clinical relapse.
- Perform urinalysis and urine protein:creatinine ratio (if indicated) in diet-responsive Wheaten terriers to screen for

FOOD REACTIONS (GASTROINTESTINAL), ADVERSE

(CONTINUED)

concurrent glomerular injury with urinary protein loss.

PATHOLOGIC FINDINGS

- Villous atrophy and mild lymphoplasmacytic enteritis may be seen with food allergy.
- Endoscopic mucosal biopsy may confirm intestinal inflammation in food-allergic animals.

**TREATMENT****APPROPRIATE HEALTH CARE**

Generally treat on an outpatient basis

NURSING CARE

N/A

ACTIVITY

No restrictions

DIET

- Feed a hydrolysate or novel intact protein diet as previously described.
- Cats are generally sensitive to more than one dietary ingredient.
- Multiple high-quality commercial diets are available for use in dogs and cats with food-responsive enteropathy.
- If this approach is used, examination of the ingredients of the various diets is recommended to determine if any patterns exist that might help identify the offending ingredient(s).

CLIENT EDUCATION

Caution against feeding any scraps or varying from a set diet.

SURGICAL CONSIDERATIONS

N/A

**MEDICATIONS****DRUG(S) OF CHOICE**

- Generally no medications are used.
- Associated problems (e.g., ARD or IBD) may require medical therapy as suggested in the sections specific to these problems.

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

- Assess efficacy of elimination dietary trial by observing improvement in clinical (GI) signs.
- Consider repeating evaluation for primary mucosal disease (IBD) if animals are unresponsive to dietary therapy.

PREVENTION/AVOIDANCE

- Avoiding the offending food ingredient(s) is recommended.
- If no specific ingredient has been identified, adherence to a set exclusion diet is recommended.

POSSIBLE COMPLICATIONS

ARD and inflammatory bowel disease

EXPECTED COURSE AND PROGNOSIS

- Prognosis for a full recovery is excellent in most cases if dietary recommendations are strictly adhered to.
- Wheaten terriers with food allergy warrant a guarded prognosis for full recovery.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

ARD and inflammatory bowel disease may be associated with adverse food reactions.

AGE-RELATED FACTORS

The severity of gluten-sensitive enteropathy in susceptible Irish setter puppies may be reduced by avoiding gluten-containing cereals.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Food intolerance
- Food allergy
- Dietary sensitivity
- Food-responsive enteropathy

SEE ALSO

- Diarrhea, Acute
- Diarrhea, Antibiotic Responsive
- Diarrhea, Chronic—Cats
- Diarrhea, Chronic—Dogs
- Exocrine Pancreatic Insufficiency
- Gastroenteritis, Eosinophilic
- Gastroenteritis, Lymphocytic-Plasmacytic
- Gluten-Sensitive Enteropathy in Irish Setters
- Inflammatory Bowel Disease

ABBREVIATIONS

- ARD = antibiotic responsive diarrhea
- FRE = food-responsive enteropathy
- IBD = inflammatory bowel disease

INTERNET RESOURCES

Veterinary Information Network:
www.vin.com/VIN.plx.

Suggested Reading

Gaschen FP, Merchant SR. Adverse food reactions in dogs and cats. *Vet Clin North Am Small Anim Pract* 2011, 41(2):361–379.

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Author Albert E. Jergens

Consulting Editor Stanley L. Marks



**Client Education Handout
available online**

GALLBLADDER MUCOCELE

G



BASICS

OVERVIEW

- Accumulation of tenacious, thick, mucoid bile conglomerate in the gallbladder (GB), obstructing storage capacity and function.
- Inspissated biliary sludge expands the GB, leading to necrotizing cholecystitis. • A canine syndrome, rare in cats.

SIGNALMENT

- Dog • Shetland sheepdogs, miniature schnauzers, Cocker spaniels—overrepresented. • Middle-aged to older adults. • No sex predilection. • Associated with endocrinopathies.

SIGNS

General Comments

- Symptomatic or asymptomatic
- Asymptomatic discovered on abdominal ultrasonography for other health concerns

Historical Findings: symptomatic

- Episodic abdominal discomfort • Anorexia
- Vomiting • Polyuria/polydipsia • Lethargy
- Collapse: vasovagal or bile peritonitis

Physical Examination Findings

- May show no physical signs early in syndrome • Lethargy • Cranial abdominal discomfort • Jaundice late in syndrome
- Dehydration • Fever

CAUSES & RISK FACTORS

- Inborn errors of lipid metabolism may increase risk: miniature schnauzer, Shetland sheepdogs. • Medical conditions associated with hypercholesterolemia or promoting dyslipidemias: hypothyroidism, typical or atypical (sex hormone) adrenal hyperplasia, glucocorticoid therapy, diabetes mellitus, recurrent pancreatitis, feeding high fat diet to dog with a predisposing disorder. • GB dysmotility—may play a causal role. • Cystic hypertrophy of mucus-producing GB mucosa—common in older dogs; may play a causal or facilitatory role.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Conditions causing bile stasis—GB dysmotility; neoplasia; choleliths; pancreatitis

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Inflammatory leukogram—variable
- Non-regenerative anemia—if chronic inflammation or hypothyroidism

Biochemistry

- High liver enzymes—only sign of illness in some dogs or may be noted on acute presentation; ALP, GGT, ALT, ± AST. • High ALP: early in syndrome development may indicate an underlying glycogen-type vacuolar hepatopathy (VH) and endocrinopathy (adrenal related). • Variable hyperbilirubinemia. • Low albumin if ruptured biliary tree and bile peritonitis.
- Prerenal azotemia if ruptured GB, sepsis, or dehydration from postprandial vomiting.
- Electrolyte abnormalities with fluid and acid-base disturbances—reflecting bile peritonitis or extensive vomiting.

Urinalysis

No specific features

OTHER LABORATORY TESTS

- Triglyceride concentrations—high if inborn error of lipid metabolism: certain breeds, endocrinopathies, diabetes mellitus, hypothyroidism, or pancreatitis. • Coagulation tests—normal, unless chronic EHBDO, GB rupture, bile peritonitis, sepsis, or DIC.

IMAGING

- Abdominal radiography—normal or large liver; loss of detail in cranial abdomen if focal peritonitis (necrotizing cholecystitis, GB rupture); intrahepatic gas indicates septic inflammation with gas-producing bacteria (rare). • Abdominal ultrasonography—liver may be large, with rounded margins; diffuse to multifocal hyperechoic hepatic parenchyma common (associated with VH); typical US image is a GB lumen filled with amorphous echogenic debris appearing as a stellate or finely striated pattern, resembling a sliced kiwi fruit (“kiwi sign”); distended GB and sometimes distended common bile duct and cystic duct if EHBDO; fluid interface surrounding GB enhances wall image and suggests cholecystitis or GB rupture; diffusely thick GB wall with segmental hyperechogenicity and double-rimmed or laminated wall if necrotizing cholecystitis; edema may enhance GB wall imaging; may occur with hepatitis, cholangiohepatitis, or third-space fluid dispersals (hypoproteinemia, right heart failure, renal failure, pyelonephritis, abdominal effusion, iatrogenic fluid overload); GB rupture associated with discontinuous GB wall, or a difficult to image GB; GB mucocele (GBM) may be released into the abdominal cavity where a discrete free floating “mass” may be discovered; pericholecystic fluid or generalized effusion, and hyperechogenicity of surrounding tissues may indicate focal peritonitis and bile leakage; intrahepatic bile ducts may be difficult to

visualize or may appear prominent (ascending cholangitis) or distended (EHBDO). • GB motility study—indicated if impending GBM recognized serendipitously and GB volume ≥ 1.2 mL/kg body weight; sequential GB volume measurements after meal ingestion (100 g), may include 1 mg/kg erythromycin as motilin agonist provoking GB contraction. Normal GB contracts $\geq 25\%$ initial volume on one or more postprandial images: image GB at 0, 15, 30, 45, 60, 90, 120 minutes after feeding.

DIAGNOSTIC PROCEDURES

- Aspiration sampling—fluid adjacent to biliary structures or free in abdominal cavity; clarifies GB rupture and infection; **caution:** do not perform cholecystocentesis on a suspected GBM as this may cause bile peritonitis; GBM contents usually difficult to sample owing to their thick, tenacious character. • Laparotomy—for diagnosis, cholecystectomy and perhaps cholecystenterostomy. • Laparoscopy: only if technical excellence achieved for cholecystectomy by this method. • Liver biopsy—evaluates for coexistent or antecedent hepatobiliary disorders. Collect biopsy distant to the GB to avoid sampling perihepatic glands. • Bacterial culture /sensitivity—effusion, GB wall and contents, and liver; aerobic and anaerobic bacteria.
- Cytology—impression smears of GB, liver, and bile for immediate determination of suppurative septic inflammation and neoplasia. Make smears of bile particulates where bacteria are “tangled.”

PATHOLOGIC FINDINGS

- Gross—GB distended, wall may be erythematous or hemorrhagic with focal areas of necrosis; focal peritonitis may be evident; liver and extrahepatic biliary structures usually appear normal; GB contents: dark green-black, tenacious, firm, or organized solid yellow-green on cut surface with a rubbery texture. Proliferative lesions on GB mucosa usually represent cystic mucosal hyperplasia or papillary proliferations.
- Microscopic—variable mixed inflammatory infiltrate and fibrosis (chronic) in lamina propria of GB wall, focal areas of necrosis if necrotizing cholecystitis; GB mucosal hyperplasia—common; ascending cholangitis and cholangiohepatitis may develop as secondary complications; hepatocytes may demonstrate VH (glycogen and/or lipid inclusions) if underlying endocrinopathy (see associated conditions). Asymptomatic GB removed preemptively may only demonstrate cystic mucosal hyperplasia.

GALLBLADDER MUCOCELE

(CONTINUED)



TREATMENT

- Outpatient management with ursodeoxycholic acid and S-adenosylmethionine (SAMe) to induce cholerisis and provide hepatoprotection—medical therapy is not advised to resolve a GBM. Has resolved syndrome in some dogs but patients subject to GBM recurrence. Naïve treatment with choleretics may result in GB rupture.
- Inpatient—treatment depends on whether patient presents with severe acute necrotizing cholecystitis or syndrome determined incidentally on ultrasound examination.
- If patient is hyperlipidemic, investigate cause and restrict dietary fat (food, medications).
- Symptomatic patients require exploratory surgery for cholecystectomy and evaluation/treatment for potential bile peritonitis.
- Cholecystotomy and mucocele removal with GB retention may lead to GBM recurrence and bile peritonitis.
- Fluid therapy—balanced polyionic solutions to correct hydration and electrolytes.
- Be prepared for blood component therapy.
- Abdominal lavage—at surgery if bile peritonitis confirmed.

G

MEDICATIONS

DRUG(S)

Antimicrobials

Initiate broad-spectrum antimicrobials *before* surgery: enteric Gram-negative and anaerobic organisms most likely opportunists; continue treatment 4–8 weeks if septic complications; adjust drugs based on culture and sensitivity test reports.

Vitamin K₁

0.5–1.5 mg/kg IM or SC q12h for three doses—if jaundiced; oral route maybe ineffective if EHBDO: fat-soluble vitamin malabsorption.

Antiemetics/Antacids/Gastroprotectants

- Metoclopramide 0.2–0.5 mg/kg PO, IV, or SC q6–8h or 1–2 mg/kg/day by CRI.

- Ondasetron 0.5–1.0 mg/kg PO 30 min before feeding, maximum q8h or 0.1–0.2 mg/kg slow IV push q6–12h—if vomiting.
- H₂-receptor antagonists: famotidine 0.5 mg/kg PO, IV, SC q12–24h; may need to increase dose for efficacy.
- Omeprazole or pantoprazole may induce p450 cytochrome associated drug interactions; 24–48 h delay onset of action.
- Sucralfate 0.25–1.0 g PO q8–12h—for upper gastrointestinal bleeding.

Cholerisis

- Maintain hydration status.
- Ursodeoxycholic acid: choleretic, hepatoprotectant, anti-inflammatory, anti-endotoxic effects: (10–15 mg/kg PO divided BID daily with food), tablets provide best bioavailability; treat indefinitely
- S-adenosyl-methionine (SAMe) provides GSH-dependent choleretic effect, dose may be higher than used as an antioxidant (see below); choleresis with 40 mg/kg PO per day.

Antioxidants

- Vitamin E: α -tocopherol 10 IU/kg PO daily with food; antioxidant, anti-inflammatory, antifibrotic effects.
- S-adenosylmethionine (SAMe): 20 mg/kg PO daily 2h before feeding, use SAMe with proven bioavailability; give until liver enzymes normalize or indefinitely if chronic hepatitis.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Repeat sequential hematology, biochemistry, and imaging to monitor response.
- Persistent clinicopathologic features may implicate underlying endocrinopathy requiring documentation and treatment, or an intrahepatic cholangiopathy.

POSSIBLE COMPLICATIONS

- Cholangitis or cholangiohepatitis • Bile peritonitis • EHBDO

EXPECTED COURSE AND PROGNOSIS

- Good with successful surgery, chronic choleretic therapy, correction or management of comorbid conditions, diet modification.
- Anticipate a protracted clinical course with ruptured biliary tract or peritonitis.
- Recrudescence may occur even if mucocele removed and GB retained, with or without chronic medical therapy.



MISCELLANEOUS

SEE ALSO

- Bile Peritonitis • Cholecystitis
- Cholelithiasis • Hepatitis, Chronic
- Vacuolar Hepatopathy

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- BUN = blood urea nitrogen
- CRI = constant rate infusion
- DIC = disseminated intravascular coagulation
- EHBDO = extrahepatic bile duct obstruction
- GB = gallbladder
- GBM = gallbladder mucocele
- GGT = γ -glutamyltransferase
- GSH = glutathione
- VH = vacuolar hepatopathy

Suggested Reading

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- Worley DR, Hottinger HA, Lawrence HJ. Surgical management of gallbladder mucoceles in dogs: 22 cases (1999–2003). *J Am Vet Med Assoc* 2004, 225:1418–1422.
- Author** Sharon A. Center
Consulting Editor Sharon A. Center

GASTRIC DILATION AND VOLVULUS SYNDROME



BASICS

DEFINITION

- A disease in dogs in which the stomach dilates and subsequently rotates around its short axis. • Also known by the acronym GDV.

PATHOPHYSIOLOGY

- The exact mechanism involved in the development of GDV is poorly understood.
- The volvulus can occur in any direction, but the vast majority occurs in a clockwise rotation when the animal is in dorsal recumbency and the surgeon is viewing the patient from the caudal aspect.
- Factors thought to contribute include ingestion of a large amount of food or water, delayed gastric emptying, and excessive post-prandial activity. However, these factors do not occur with all cases of GDV.
- Subsequent to the gastric rotation, gas and fluid continue to become entrapped within the gastric lumen. Progressive distention of the stomach occurs.
- As the stomach becomes progressively distended, intra-abdominal pressure increases. This leads to compression of the compliant blood vessels of the abdomen including the caudal vena cava and portal vein. The reduction in blood flow through these major vessels leads to decreased cardiac return and hypovolemic shock.
- Decreased perfusion can lead to systemic effects including organ death, local and systemic inflammatory cascades, and disseminated intravascular coagulation.

SYSTEMS AFFECTED

- Gastrointestinal—decreased perfusion can lead to ischemic necrosis of the stomach. Due to the higher metabolic demand, the mucosa is predisposed to the effects of ischemia.
- Cardiovascular—significant decrease in the venous return to the heart results in a hypovolemic state. This leads to decreased cardiac output, which can lead to organ hypoxia and tissue damage/tissue death.
- Decreased myocardial perfusion, as well as the generation of inflammatory mediators, can lead to cardiac arrhythmias, particularly premature ventricular contractions.
- Hemic/Lymphatic/Immune—splenic insult is common, via avulsion of the short gastric vessels, splenic torsion, or splenic infarction.

GENETICS

No direct genetic predisposition confirmed; however, dogs with a first-order relative with a history of GDV are at an increased risk for development of GDV.

INCIDENCE/PREVALENCE

An incidence rate for large- and giant-breed dogs has been reported to be around 6%.

SIGNALMENT

Species

Dog

Breed Predilections

- Any large, deep-chested breed.
- Great Dane.
- German shepherd dog.
- Rarely reported in smaller, deep-chested breeds such as dachshund and Pekingese.

Mean Age and Range

Any age; risk increases with increasing age.

SIGNS

Historical Findings

- Vomiting, which often progresses to non-productive retching or “dry heaves”
- Anxious behavior
- Abdominal pain
- Abdominal distention
- Collapse
- Ptyalism
- Lethargy

Physical Examination Findings

- Possibly distended abdomen; however, distended stomach may be contained under ribs, in which case abdominal distention will not be seen.
- Tachycardia.
- Tachypnea or dyspnea.
- Weak pulses, pale mucus membranes with a prolonged capillary refill time are suggestive of hypovolemia.

CAUSES

- Unknown.
- Likely a multifactorial origin that includes anatomic, genetic, and environmental factors.

RISK FACTORS

- Classically has been linked to activity following a meal.
- Anatomic predisposition in deep-chested dogs, particularly large and giant breeds.
- It was also thought that a lowered food bowl encouraged aerophagia, which could lead to GDV. Recently eating from a RAISED food bowl has been identified as a risk factor for development of GDV.
- Having a first-degree relative with GDV and faster speed of eating have also been identified as being risk factors associated with the development of GDV.
- Possibly having gastrointestinal neoplasia, as it can cause motility disturbances as well as gastric retention of food and/or air.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other diseases that cause acute abdominal distention and potentially circulatory attenuation include septic peritonitis, hemoabdomen, intestinal volvulus, or acute gastroenteritis.
- “Food bloat” is the common name for gastric dilation without concurrent volvulus. This commonly occurs in dogs that engorge themselves with food.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—stress leukogram, hemoconcentration, thrombocytopenia possibly.
- Biochemistry—electrolyte abnormalities are commonly encountered.

May see azotemia due to hypovolemia (prerenal). • Urinalysis—may see increased specific gravity with dehydration.

OTHER LABORATORY TESTS

Plasma lactate concentration has been found to be useful in predicting underlying gastric necrosis as well as prognosis. Median plasma lactate levels in dogs with gastric necrosis were significantly higher (6.6 mmol/L) than in dogs without gastric necrosis (3.3 mmol/L). Survival of dogs with plasma lactate levels < 6.0 mmol/L was 99%, compared with the 58% survival experienced by dogs with lactate levels > 6.0 mmol/L.

G

IMAGING

- Adequate stabilization is often necessary before obtaining radiographs.
- Abdominal radiography—a right lateral abdominal radiograph is the imaging modality of choice. Classically reveals compartmentalization of the stomach, which is considered to be pathognomonic.
- Dorsoventral view—may be helpful in confirming the disease.

DIAGNOSTIC PROCEDURES

- Very rarely, uncertainty may persist subsequent to obtaining survey radiographs.
- A positive-contrast upper GI can be attempted with CAUTION, as these patients are at an increased risk for aspiration!

PATHOLOGIC FINDINGS

- Splenic torsion may also be a concurrent finding.
- The stomach itself becomes edematous and undergoes vascular congestion and infarction, which can lead to necrosis.



TREATMENT

APPROPRIATE HEALTH CARE

- **This disease syndrome represents an emergency!** • Patients should be hospitalized, thoroughly assessed, and aggressively treated for cardiovascular insufficiency.
- A myriad of fluid therapy approaches are employed predicated on patient situation and personal preference. Crystallloid therapy, colloid therapy, or a combination can be used. If crystallloid therapy is chosen a dose of 90 ml/kg of an isotonic solution is administered over 30–60 minutes. Administered through cephalic or jugular venous access sites.
- Subsequent to cardiovascular stabilization, gastric decompression should be performed.
- Orogastic intubation is the preferred method of obtaining gastric decompression. Cardiovascular-sparing medications may be administered to patients in an effort to facilitate orogastric intubation. Commonly, considerable resistance is encountered upon reaching the esophageal hiatus. The lubricated tube can be twisted or repositioned to facilitate passage. Differing patient positions (sitting, standing, etc.) can also be attempted to facilitate passage.
- In cases where

GASTRIC DILATION AND VOLVULUS SYNDROME

(CONTINUED)

orogastric intubation is unsuccessful, percutaneous gastrocentesis can be attempted. A point of maximal tympany is located that typically corresponds to an area of the stomach that is gas-filled. A large diameter needle or catheter is passed into the stomach at this area. Gas typically will elicit an audible noise when escaping. Considerable time is necessary to achieve gastric decompression using this technique. • Upon patient stabilization and gastric decompression, surgical intervention is indicated. In rare cases in which patient is unresponsive to stabilization attempts, immediate surgical intervention may be taken.

ACTIVITY

Restriction of activity for approximately 2 weeks postoperative is recommended.

DIET

- Oral intake of food is recommended as soon as adequate recovery has been achieved.
- The role of food bowl height in the occurrence and recurrence of this disease is unclear at this time.
- Consider fat-restricted diets to enhance gastric emptying.

CLIENT EDUCATION

Owners of large- and giant-breed dogs who are not aware of the clinical signs of gastric dilation and volvulus should be educated.

SURGICAL CONSIDERATIONS

- Surgical intervention should be performed as soon as possible in a stable patient or in a patient in which diligent stabilization efforts have proved ineffective.
- Surgical intervention has three main goals: (1) anatomical reposition of the stomach (and spleen if applicable); (2) assessment of organ viability; (3) prevention of recurrence.
- Once repositioned, the stomach and spleen should be assessed. If non-vital areas are present, removal should be performed via partial gastrectomy and/or splenectomy.
- Prevention of recurrence is achieved through a permanent gastropexy. Multiple techniques for performing gastropexy have been described and choice of technique is largely based on surgeon preference.



MEDICATIONS

DRUG(S) OF CHOICE

- Perioperative antibiotics are indicated. The surgery itself, depending on severity and progression of disease, may be a clean, clean-contaminated, contaminated, or dirty surgery. It is often next to impossible to ascertain this information before the surgery is performed.
- Antibiotic selection should be predicated upon potential pathogens that the patient may be exposed to. Moderate-to-severe disease may expose the host to enteric

pathogens due to visceral perforation or loss of normal mucosal barriers to hematogenous bacterial translocation from the gastrointestinal tract. For these patients cefoxitin sodium (30 mg/kg IV q6–8h) may be an appropriate choice. For patients in which no entry into the gastrointestinal tract has occurred, cefazolin sodium (22 mg/kg IV q2h intraoperatively) is sufficient.

- Gastric protectants may be implemented to minimize or prevent gastrointestinal ulcerations.

CONTRAINdications

- The use of some synthetic colloids (e.g., hydroxyethyl starch) has been linked to disruption in the formation of the primary clot and may not be appropriate to use in certain patients with GDV, such as those with an underlying coagulopathy like concurrent DIC.
- Drugs that significantly depress cardiovascular function should be avoided if possible (e.g., acetylpromazine).

PRECAUTIONS

Patients may acutely decompensate at any time, particularly under anesthetic intervention.

ALTERNATIVE DRUG(S)

Efficacy of the administration of corticosteroids in patients affected with GDV is currently lacking.



FOLLOW-UP

PATIENT MONITORING

- Nursing care—some patients may require recumbent care for several days before eventual recovery.
- Adequate pain control.
- Premature ventricular contractions commonly occur postoperatively. These result from myocardial hypoperfusion and resultant ischemic damage, or due to splenic insult or removal. The monitoring of heart rhythm is recommended.
- Monitor urine production and renal function postoperatively.

PREVENTION/AVOIDANCE

- Elevation of food bowl is argued.
- Avoid exercise after eating or drinking.
- Possibly slowing the rate of consumption of meals.
- Some soak dry food in water before feeding or feed multiple, smaller meals.

POSSIBLE COMPLICATIONS

- Gastric dilation may recur, even after a gastropexy is performed. Recurrence of volvulus with an appropriately performed gastropexy is exceedingly rare.
- Failure to remove necrotic gastric tissue may result in eventual stomach perforation and septic peritonitis.
- Cardiac arrhythmias (particularly premature ventricular complexes), DIC, and gastric ulceration may also occur.

EXPECTED COURSE AND PROGNOSIS

- A heightened awareness by dog owners combined with an increased understanding of the complex pathophysiologic events associated with GDV have significantly reduced the mortality rate associated with this disease over the past 30 years.
- Prognosis in dogs treated appropriately that do not have gastric necrosis is excellent, with a reported survival rate of 98%.
- Dogs with gastric necrosis have a more guarded prognosis, with a reported survival rate of 66%.
- One article reported an overall short-term survival rate of 83.8%. Negative prognostic indicators included hypotension, DIC, peritonitis, and the need to perform both a splenectomy as well as a partial gastrectomy.



MISCELLANEOUS

AGE-RELATED FACTORS

A higher rate of GDV is typically seen in middle-aged to older dogs.

SYNOMYS

- Bloat
- Gastric torsion

SEE ALSO

- Sepsis and Bacteremia
- Shock chapters

ABBREVIATIONS

- DIC = disseminated intravascular coagulation
- GDV = gastric dilation and volvulus syndrome
- GI = gastrointestinal

Suggested Reading

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Client Education Handout
available online

GASTRIC MOTILITY DISORDERS



BASICS

DEFINITION

Gastric motility disorders result from conditions that directly or indirectly disrupt normal gastric emptying, which in turn may cause abnormal gastric retention, gastric distention, and subsequent gastric signs associated with anorexia, nausea, and vomiting.

PATHOPHYSIOLOGY

The stomach has two distinct motor regions. The proximal stomach relaxes to accommodate food and regulates the expulsion of liquids. Intrinsic slow contractions of this region push liquids through the pylorus. The distal stomach mechanically breaks down and expels solids through strong peristaltic contractions. The gastric pacemaker, an area of intrinsic electrical activity, located in the greater curvature of the stomach regulates distal gastric motility and emptying. Gastric electrical activity, dietary composition, and extrinsic factors all influence emptying. During fasting, indigestible solids are expelled from the stomach by migrating myoelectric complexes (MMC). These complexes produce strong “digestive housekeeper” contractions that sweep through the stomach and small intestine to mid-jejunum every 2 hours in the fasted state preparing the GI tract for the next meal. MMC motility is under the regulation of the hormone motilin. Dysrhythmias in normal gastric electrical activity may be fundamental in the pathophysiology of disorders affecting gastric motility.

SYSTEMS AFFECTED

Gastrointestinal

INCIDENCE/PREVALENCE

Unknown. Many factors can alter gastric emptying although they may not result in clinical disease.

SIGNALMENT

Species

Dog and cat

Breed Predilections

Unknown

Mean Age and Range

Signs occur at any age though it is uncommon to observe primary motility disorders in young animals.

SIGNS

General Comments

Clinical signs are often secondary to the primary etiology causing the gastric motility disorder.

Historical Findings

- The major clinical sign is chronic post-prandial vomiting of food. The stomach should normally be empty after an

average-sized meal in approximately 6–8 hours in dogs and 4–6 hours in cats (note: normal emptying times vary greatly from animal to animal and are influenced by meal volume, caloric density, fiber content, and environmental factors). Vomiting of undigested food > 12 hours following the meal suggests abnormal gastric motility or possibly outflow obstruction. Vomiting can occur, however, any time following eating.

- Other signs include gastric distention, nausea, anorexia, belching, pica, and weight loss.
- The distal esophageal sphincter may also be incompetent with gastric hypomotility and signs associated with reflux esophagitis may be present.

Physical Examination Findings

- Normal or findings associated with the underlying cause of the disorder.
- Palpation of a large, distended stomach.
- Decreased gastric sounds on abdominal auscultation.

CAUSES

- Primary idiopathic gastric motility disorders may arise from defects in normal myoelectric activity. Most motility disorders occur secondary to other primary conditions.
- Metabolic disorders include hypokalemia, uremia, hepatic encephalopathy, and hypothyroidism.
- Nervous inhibition as the result of stress, fear, pain, or trauma.
- Drugs such as the anticholinergics, β -adrenergic agonists, narcotics, and chemotherapeutics.
- Primary gastric disease such as outflow obstructions, gastritis, gastric ulcers, parvovirus, and gastric surgery.
- Gastric dilatation volvulus (GDV) syndrome is suspected to be in part the result of abnormal gastric motility associated with changes in myoelectric and mechanical activity. Some dogs with GDV may also continue to have signs of gastric hypomotility following surgical gastropexy.
- Gastroesophageal reflux and enterogastric reflux (see Biliary Vomiting Syndrome) may result from primary gastric hypomotility.
- Dysautonomia is associated with abnormal esophageal, gastric and intestinal motility.

RISK FACTORS

Any potential gastric disease may result in secondary hypomotility.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

The differential diagnosis is extensive and should include any condition causing vomiting. Gastric outflow obstructions must always be ruled out.

CBC/BIOCHEMISTRY/URINALYSIS

Routine hemogram, serum chemistry profile, urinalysis, and fecal flotation must be performed to rule out the potential cause of gastric hypomotility. Continued vomiting

may result in dehydration, electrolyte abnormalities, or acid-base imbalance.

OTHER LABORATORY TESTS

Specialized testing may be required to determine a specific cause of gastric hypomotility, and is individualized for each patient.

IMAGING

Survey Radiographs

Abdominal radiographs may reveal a gas-, fluid-, or ingesta-distended stomach. (Note: it is important to determine when the patient was last fed in relationship to when radiographs were taken.)

G

Liquid Barium Contrast Study

May be evidence of delayed gastric emptying and decreased gastric contractions if evaluated using fluoroscopy. Some cases may have normal emptying of liquids but abnormal emptying of solids. (Note: the stress of radiographs may decrease gastric emptying even in the normal animal.)

Food Barium Contrast Study

Barium mixed with a standard meal may demonstrate delayed gastric emptying of solids. Normal dogs should empty their stomachs by approximately 6–8 hours. Abnormal gastric retention is associated with significantly longer gastric emptying times.

Food-Marker Contrast Study

Barium-impregnated small markers (BIPS) or other radiopaque markers mixed with a standard meal will have delayed passage similar to the food barium contrast study.

Radionuclide Emission IMAGING

Radionuclide markers mixed with a meal give the most clinically accurate measurement of emptying. Gastric emptying times (time for a standard meal to leave the stomach) range from 4 to 8 hours.

Ultrasonography

Ultrasound can be used to evaluate antral and pyloric motility.

Smartpill

This is a non-invasive wireless sensor capsule that is given orally and transmits data on pressures, transit time, luminal pH and temperature as it passes through the stomach and small and large bowel. It has been validated for use in the healthy dog but as yet there are limited reports evaluating clinical conditions.

DIAGNOSTIC PROCEDURES

Endoscopy

Endoscopic findings are frequently normal in idiopathic conditions. Food may be found in the stomach when it should be empty following a 12-hour pre-endoscopic fasting period. Endoscopy will detect obstructive or inflammatory diseases of the stomach.

Pathologic Findings

- Idiopathic conditions have normal gastric mucosa.
- Gastric histology may identify

GASTRIC MOTILITY DISORDERS

(CONTINUED)

inflammatory or neoplastic causes to explain the gastric hypomotility.



TREATMENT

APPROPRIATE HEALTH CARE

- Most patients are treated as outpatients.
- With severe vomiting or dehydration and electrolyte imbalance, hospitalization and specific therapy are required.

NURSING CARE

G Dehydration with fluid and electrolyte imbalance requires appropriate fluid replacement.

ACTIVITY

Restrictions are based on the underlying disease.

DIET

- Dietary manipulation is important in the management of primary gastric motility disorders.
- Diets should be formulated that are liquid or a semi-liquid consistency and low in fat and fiber content.
- Small-volume meals with frequent feeding should be given.
- Often dietary manipulation alone is successful in managing patients with delayed gastric emptying from a motility disorder.

CLIENT EDUCATION

Discuss possible underlying etiologies of altered gastric motility and that the response to therapy varies with individual cases.

SURGICAL CONSIDERATIONS

- Large-breed dogs with chronic GDV syndrome and gastric retention should have a prophylactic surgical gastropexy.
- Following any gastric surgery it generally takes several days but up to 14 days for motility to return to normal.
- Patients with mechanical gastric outflow obstructions require surgical correction.



MEDICATIONS

DRUG(S) OF CHOICE

Gastric Prokinetic Agents

- Metoclopramide increases the amplitude of antral contractions, inhibits fundic receptive relaxation, and coordinates duodenal and gastric motility. It is a dopamine receptor antagonist in the proximal GI tract resulting in increased release of acetylcholine from enteric neurons. At higher concentrations it has serotonin (5HT₄) agonist effects. It also has antiemetic effects, blocking the chemoreceptor trigger zone in the brainstem in dogs but not cats. Oral dosage is 0.2–0.5 mg/kg q8h given 30 minutes before meals (use lower dose in cats) or as a CRI at 1–2 mg/kg q24h. Metoclopramide is generally considered to be a weak prokinetic

agent in dogs and recent studies suggest it has little effect at increasing the lower esophageal sphincter pressure.

- Cisapride works directly by cholinergic neurotransmission (5HT₄ agonist) of gastrointestinal smooth muscle, stimulating motility. The proposed mechanism of action is that it enhances the release of acetylcholine at the myenteric plexus, but does not induce nicotinic or muscarinic receptor stimulation. Cisapride increases lower esophageal sphincter pressure, improves gastric emptying, and promotes increased motility of both the small and large intestine. A suggested dose is 0.2–0.5 mg/kg PO q8–12h given before meals. Cisapride is currently available through compounding pharmacies because the human product has been removed from the market because of associated cardiac arrhythmias not identified to occur in dogs or cats. Mosapride (0.5–2 mg/kg PO q12–24h) and Prucalopride (0.02–0.6 mg/kg PO q12–24h) are also serotonergic (5HT₄ agonist) prokinetic agents not yet available in the United States.

• Macrolide antibiotics, including erythromycin and clarithromycin, are motilin receptor agonists and increase gastrointestinal motility. Motilin is a GI hormone that promotes MMC associated motility. Erythromycin given at low (sub-microbiologic) doses binds on motilin receptors promoting acetylcholine release, which in turn promotes gastric emptying. The suggested dose of erythromycin for specific motility effects is 0.5–1 mg/kg PO q8–12h, given 30 minutes before meals.

- Other drugs: Domperidone is a peripheral dopamine receptor antagonist that has been marketed outside the United States. It regulates the motility of gastric and small-intestinal smooth muscle similar to that of metoclopramide. Mirtazapine is a noradrenergic and specific serotonergic antidepressant and has reported gastric prokinetic effects in dogs.
- The H₂ receptor antagonists ranitidine (1–2 mg/kg q8h) and nizatidine (2.5–5 mg/kg q24h) have reported prokinetic effects on gastric motility due to acetylcholinesterase inhibition. They are considered as poor prokinetic drugs and recent studies question ranitidine's prokinetic activity in dogs. Neither cimetidine nor famotidine affect gastric emptying.

CONTRAINDICATIONS

- Gastric prokinetic agents should not be administered in patients with a gastric outflow obstruction.
- Metoclopramide is contraindicated with concurrent phenothiazine and narcotic administration or in animals with epilepsy.

PRECAUTIONS

- Metoclopramide may cause nervousness, anxiety, or depression.
- Cisapride may cause depression, vomiting, diarrhea, or abdominal cramping.
- Erythromycin may cause vomiting.



FOLLOW-UP

PATIENT MONITORING

- Response to therapy varies according to the underlying cause.
- Failure to respond medically necessitates further investigation for mechanical obstruction.

EXPECTED COURSE AND PROGNOSIS

- The length of treatment depends on the ability to resolve the underlying disorder or on the response to therapy.
- It may take gastric surgery or parvovirus cases several days to up to 2 weeks to regain normal gastric function.
- Generalized dysautonomia has a grave prognosis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Gastric hypomotility may be associated with both reflux esophagitis and reflux gastritis (see biliary vomiting syndrome).

PREGNANCY/FERTILITY/BREEDING

Avoid gastric prokinetic agents in pregnant animals.

SYNOMYMS

- Gastric atony
- Gastric hypomotility

SEE ALSO

- Biliary Vomiting Syndrome
- Gastric Dilatation and Volvulus Syndrome
- Gastritis, Atrophic
- Gastritis, Chronic
- Gastroesophageal Reflux

ABBREVIATION

- GDV = gastric dilation and volvulus syndrome

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Client Education Handout
available online

GASTRITIS, ATROPHIC



BASICS

OVERVIEW

A type of chronic gastritis characterized histologically by a focal or diffuse reduction in size and depth of gastric glands with associated inflammatory cells.

SIGNALMENT

- Variable, uncommon in young patients. • A high prevalence in the Norwegian Lundehund (range 4–13 years old), males overrepresented.

SIGNS

- Chronic vomiting, most often intermittent, food or bile. • Anorexia, lethargy, weight loss, edema or ascites.

CAUSES & RISK FACTORS

- Idiopathic inflammatory gastroenteritis a potential risk factor. • May reflect chronic gastritis of any cause. • Suspect genetic predisposition in the Norwegian Lundehund.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other forms of chronic gastritis and chronic enteritis

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia with thrombocytopenia or thrombocytosis may be present if gastric ulceration is present. • Panhypoproteinemia with no proteinuria can be present with primary disease and in animals with concurrent protein-losing enteropathy.

OTHER LABORATORY TESTS

- Achlorhydria has been reported in dogs; may lead to intestinal dysbiosis. • Consider diagnostic testing for hepatobiliary and pancreatic disease, as well as for subnormal cobalamin concentration, in cats.
- Endoscopic biopsies of the small intestines should be performed to evaluate for infiltrative disease.

IMAGING

- Survey radiographs of the thorax and abdomen are typically unremarkable. Stomach may contain ingesta despite adequate fasting, suggesting delayed gastric emptying. • Ultrasonography of the abdomen may reveal a thickened or normal gastric wall, gastric masses, the presence or absence of mesenteric lymphadenopathy, thickened or normal intestinal walls, presence or absence of abdominal effusion. • Lymphadenopathy and masses may be present with gastric neoplasia.

DIAGNOSTIC PROCEDURES

Definitive diagnosis: gastroscopy with biopsy and histopathologic evaluation.

PATHOLOGIC FINDINGS

- Histopathologic examination of gastric biopsy specimens reveals glandular atrophy and inflammatory infiltrates (neutrophils or mononuclear cells). Majority of lesions are located in the fundic region. In non-Lundehunds, lymphocytic plasmacytic gastritis found with atrophy. Fibrosis may be present. • Mucin staining in Lundehunds gives abnormal mucus neck cells and pseudo-pyloric metaplasia. Neoplastic transformation may be associated with linear hyperplasia of neuroendocrine cells (requires special staining, request in suspected cases: chromagrin A, synaptophysin, Sevier-Munger method). • The role of *Helicobacter* infection is controversial. Cats developing atrophic gastritis have been found to have *H. pylori* infections, but active *Helicobacter* infections have not been documented in canine cases. Urease activity in gastric biopsies is not diagnostic and poorly correlated with actual infection. Clinical infection is supported by histological documentation of spiral bacteria in gastric mucosa and pits with associated inflammation.



TREATMENT

- Optimal therapy is unknown. Trial therapy for food-responsive gastropathy with an elimination diet can be tried. Tylosin can be administered in the event that the disorder has an antibiotic-responsive component. Treat any underlying etiology identified. • Enteral feeding tube may be indicated in cachexic patients. • If gastric emptying is delayed, low residue fat-restricted diets may aid in emptying; elimination diets containing novel, single protein sources may be helpful in select cases.



MEDICATIONS

DRUG(S)

- Histamine type-2 receptor antagonists (e.g., famotidine 0.5–1 mg/kg PO q12h) or proton pump inhibitors (e.g., omeprazole 0.7–1.5 mg/kg PO q12–24h) to inhibit gastric acid secretion and prevent esophagitis. Long-term use of omeprazole should be avoided if possible in light of potential adverse effects (hypocalcemia, osteoporosis, intestinal dysbiosis, hypocobalaminemia, increased risk of diarrhea). • If vomiting persists, antiemetics such as maropitant (1–2 mg/kg PO or SC q24h, for 5 days in dogs, 15 days in cats) or ondansetron (0.5 mg/kg PO or SC q24h for 5–7 days) or prokinetics such as metoclopramide (0.2–0.5 mg/kg PO q8h) or

cisapride (0.3–0.5 mg/kg PO q8–12h) may be indicated. • If infection with *Helicobacter* spp. is confirmed based upon histopathologic lesions in the stomach consistent with *Helicobacter* infection, consider triple therapy: amoxicillin at 11–22 mg/kg PO q12h, metronidazole 10–15 mg/kg PO q12h and famotidine 0.5–1.0 mg/kg PO q12h or omeprazole 0.7–1.5 mg/kg PO q24h for 2 weeks. This infection may recur.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Be cautious with medications known to exacerbate gastritis, such as corticosteroids and nonsteroidal anti-inflammatory drugs.



FOLLOW-UP

- Long-term intermittent antacid therapy may be required—long-term administration of omeprazole is discouraged. • Correlation with progression to gastric cancer (adenocarcinoma or neuroendocrine carcinoma) is suspected but not proven. However, this has been documented in the Norwegian Lundehund breed. If signs persist or recur, monitor for developing gastric tumors (chest radiographs, abdominal ultrasound).



MISCELLANEOUS

Hypergastrinemia and hypoacidity is suspected but not proven in veterinary patients.

ASSOCIATED CONDITIONS

- Chronic enteritis of inflammatory, autoimmune, or infectious causes.
- Protein-losing enteropathy in the Lundehund.

SEE ALSO

- Gastritis, Chronic • Vomiting, Chronic

Suggested Reading

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GASTRITIS, CHRONIC



BASICS

DEFINITION

- Intermittent vomiting of > 1–2 weeks in duration secondary to gastric inflammation.
- Presence of gastric erosions or ulcers dependent on the inciting cause and duration.

PATHOPHYSIOLOGY

- Chronic irritation of the gastric mucosa by chemical irritants, drugs, foreign bodies, infectious agents, or hyperacidity syndromes resulting in an inflammatory response in the mucosal surface that may extend to involve submucosal layers.
- Chronic allergen exposure or immune-mediated disease may also produce chronic inflammation.

SYSTEMS AFFECTED

- Gastrointestinal—esophagitis may result from chronic vomiting or gastroesophageal reflux.
- Respiratory—aspiration pneumonia is infrequently seen secondary to chronic vomiting; it is more likely if concurrent esophageal disease exists or if the patient is debilitated.

INCIDENCE/PREVALENCE

Relatively common

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Old, small-breed dogs (i.e., Lhasa apso, Shih Tzu, miniature poodle) are more commonly affected with antral mucosal hyperplasia and hypertrophy.
- Norwegian Lundehunds are predisposed to chronic atrophic gastritis.
- Basenjis and the Drentse patrijshond (aka Dutch partridge dog or Drent) breed can develop chronic hypertrophic gastritis.

Mean Age and Range

Varies with underlying cause

Predominant Sex

Varies with underlying cause

SIGNS

Historical Findings

- Vomitus is frequently bile-stained and may contain undigested food, flecks of blood, or digested blood ("coffee grounds").
- Frequency varies from daily to every few weeks and increases as gastritis progresses.
- Vomiting may be stimulated by eating or drinking.
- Early morning vomiting before eating may indicate bilious vomiting syndrome.
- May see weight loss with chronic anorexia.
- May see melena with ulceration (not common).
- Increased water intake.
- Diarrhea, if concurrent intestinal disease

Physical Examination Findings

- Generally within normal limits.
- May be thin with persistent anorexia.
- May have pale mucous membranes with anemia from

chronic blood loss.

- May find cranial abdominal pain (rarely noted).

CAUSES

- Inflammatory—immune-mediated, dietary allergy or intolerance, idiopathic.
- Dietary indiscretion—plant material, foreign objects, chemical irritants.
- Toxins—fertilizers, herbicides, cleaning agents, heavy metals.
- Metabolic/endocrine disease—azotemia, chronic liver disease, hypoadrenocorticism, pancreatitis.
- Neoplastic—common: gastrointestinal lymphoma, gastric adenocarcinoma, small cell lymphoma (especially cats, recent increase in dogs); infrequent: gastric polyps, gastrinoma, leiomyosarcoma, plasma cell tumor, mast cell tumor.
- Parasitism—*Physaloptera* spp. (dogs, cats), *Ollulanus tricuspis* and *Gnathostoma* spp. (cats).
- Drugs—NSAIDs, glucocorticoids.
- Infectious—*Helicobacter* spp., *Pythiosis*, viral (distemper in dogs, feline leukemia virus in cats).
- Miscellaneous—duodenogastric reflux (bilious vomiting syndrome), stress, achlorhydria.

RISK FACTORS

- Medications—NSAIDs, glucocorticoids.
- Environmental—unsupervised/free-roaming pets are more likely to ingest inappropriate foods or materials.
- Ingestion of a dietary antigen to which an allergy or intolerance has been acquired.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Although the causes listed above are included in the differential diagnosis of chronic gastritis, an identifiable cause is often not found for the gastric inflammation.
- Must differentiate chronic vomiting from chronic regurgitation (active vs. passive vomiting).
- Small intestinal inflammation and gastric or small intestinal neoplasia often present with signs and physical exam findings similar to those of gastric inflammation.
- Idiopathic gastritis—diagnosis of exclusion; often characterized by a predominantly lymphoplasmacytic infiltrate (superficial or diffuse).
- Eosinophilic gastritis, hypertrophic gastritis, granulomatous/histiocytic gastritis, and atrophic gastritis are less common; often overlap of histologic changes exists in the types of inflammatory infiltrates.
- Atrophic gastritis differs on endoscopic examination—resulting in visualization of the submucosal vessels secondary to thinning of the gastric mucosa.
- Hypertrophic gastritis—prominent mucosal folds that do not flatten with gastric insufflation.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram usually unremarkable unless systemic disease present.
- Hemoconcentration if severe dehydration.
- May see

- nonregenerative (anemia of chronic disease) or regenerative anemia (blood loss).
- With ulceration—microcytic, hypochromic anemia associated with iron deficiency if prolonged, severe blood loss.
- May see eosinophilia with eosinophilic gastroenteritis.
- Azotemia with low urine specific gravity in uremic gastritis.
- Increased serum hepatic enzyme activities, total bilirubin, or hypoalbuminemia with chronic hepatic disease.
- Hyperkalemia and hyponatremia suggest Addison's disease.
- Hyponatremia, hypokalemia, hypochloremia, and an elevated bicarbonate level with an acidotic urine suggest a gastric outflow obstruction (hypochloremic metabolic alkalosis).

OTHER LABORATORY TESTS

Elevated serum gastrin level without azotemia suggests a gastrinoma.

IMAGING

- Survey abdominal radiographs—usually normal, but may reveal radiodense foreign objects, a thickened gastric wall, or gastric outflow obstruction with persistent gastric distension.
- Contrast radiography—may detect foreign objects, gastric outflow obstruction, delayed gastric emptying, or gastric wall defects or thickening.
- Ultrasonography—may detect gastric wall thickening, ulceration, and gastric foreign objects.

DIAGNOSTIC PROCEDURES

- Gastroscopy—usually adequate for visualization of the gastric mucosa and for biopsy but in most cases one should also evaluate and biopsy the duodenum.
- Gastric biopsy and histopathology is required for diagnosis, even if gastric mucosa appears normal.
- Foreign objects can be identified and retrieved via endoscopy.
- Exploratory celiotomy is indicated if a perforated ulcer or submucosal lesion of the gastric wall is suspected and partial gastrectomy or full-thickness biopsy is required.
- Fecal flotation may reveal intestinal parasites.

PATHOLOGIC FINDINGS

- Idiopathic gastritis—inflammatory infiltrates vary; can be lymphocytes, plasma cells, neutrophils, eosinophils, and/or histiocytes.
- Mucosal changes can be degenerative, hyperplastic, or atrophic.
- May see varying degrees of edema and fibrous tissue; may see *Helicobacter* spp. Must be noted within gastric glands to be significant and should be accompanied by a lymphofollicular gastritis; special stains can be requested for fungal hyphae and *Helicobacter*.
- May see lymphoplasmacytic inflammation along with *Helicobacter* spp. Treatment for *Helicobacter* may result in resolution of clinical signs without immunosuppressive therapy.
- If hyperplastic changes are noted, a gastrin level should be obtained before institution or after discontinuation of antacids, H₂ blockers or proton pump blockers.

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

- Most patients are stable at presentation unless vomiting is severe enough to cause dehydration.
- Can typically manage as outpatient, pending diagnostic testing or undergoing clinical trials of special diets or medications.
- If patient is dehydrated or if vomiting becomes severe, hospitalize and institute appropriate intravenous crystalloid fluid therapy (see Vomiting, Acute).

DIET

- Soft, low-fat food ideally from a single carbohydrate and protein source.
- Non-fat cottage cheese, boiled skinless white meat chicken, boiled hamburger or tofu as a protein source, and rice, pasta, or potato as a carbohydrate source, in a ratio of 1:3.
- Frequent, small meals (q4–6h or more frequently).
- Can use novel protein source or hydrolyzed protein diet if dietary allergy is suspected.
- Feed diets for a minimum of 2–3 weeks to assess adequacy of response.
- Feed a late-night meal to help prevent bilious vomiting syndrome in the early morning hours.

CLIENT EDUCATION

- Gastritis has numerous causes.
- Diagnostic workup—may be extensive; usually requires a biopsy for a definitive diagnosis.

SURGICAL CONSIDERATIONS

- Surgical management if a granulomatous mass or hypertrophy is causing a gastric outflow obstruction.
- Gastrotomy for removal of foreign objects if endoscopic retrieval is unsuccessful or is not available.



MEDICATIONS

DRUG(S) OF CHOICE

- Treat any gastric erosions and ulcers (see Gastroesophageal Reflux Disease).
- Give glucocorticoids (prednisone 2–4 mg/kg PO q24h [rarely requires high end of dose to start]; taper by 25% every 2–3 weeks over 2–3 months) for chronic gastritis secondary to suspected immune-mediated mechanisms if no clinical response to dietary management. Never exceed a total dose of 60 mg of prednisone no matter how heavy the dog is.
- Treatment for *Helicobacter* gastritis—amoxicillin (22 mg/kg PO q12h), peptobismol (15 mg/kg PO q6–8h) and metronidazole (10 mg/kg PO q12h) for 3 weeks (see *Helicobacter* Infection).
- Antiemetics (maropitant 1 mg/kg PO/SC q24h) for fluid and electrolyte disorders caused by frequent or profuse vomiting (see Vomiting, Acute).
- Metoclopramide (0.2–0.4 mg/kg PO q6–8h), cisapride

(0.5–1 mg/kg PO q8h to q12h), or low-dose erythromycin (0.5–1 mg/kg PO q8h) to increase gastric emptying and normalize intestinal motility if gastric emptying is delayed or gastroduodenal reflux is present. Metoclopramide is most effective as a CRI administered at 1–2 mg/kg q24h.

CONTRAINDICATIONS

- Do not use prokinetics, metoclopramide, or cisapride if gastric outflow obstruction is present.
- Antacids are not indicated with atrophic gastritis and achlorhydria.

PRECAUTIONS

- Steroids are immunosuppressive, making close monitoring for secondary infections important.
- Steroids may also inhibit the normal gastric mucosal barrier, leading to ulceration.

ALTERNATIVE DRUG(S)

- Synthetic prostaglandin E1 (misoprostol 1–3 µg/kg PO q6–8h) to prevent gastric mucosal ulcers with NSAID toxicity.
- For additional immunosuppression when in need of an immediate response, add chlorambucil (0.1–0.2 mg/kg q24h for 7 days then q48h). Often used in place of azathioprine but can be used in addition. A recent study suggests that this addition may be superior to adding azathioprine.
- Immunosuppressive drugs such as azathioprine (2.2 mg/kg PO q24h, tapering to q48h after 2–3 weeks in dogs) if an immune-mediated mechanism is suspected and response to dietary management and glucocorticoid administration is inadequate. Expect response to occur in 2–3 weeks. Avoid use of azathioprine in cats because the drug is markedly myelosuppressive.



FOLLOW-UP

PATIENT MONITORING

- Resolution of clinical signs indicates a positive response.
- Recheck electrolytes and acid-base status if initially abnormal.
- Complete blood counts should be obtained weekly and then reduced to q4–6 weeks for patients on myelosuppressive drugs (i.e., azathioprine, chlorambucil). Additional chemistry monitoring q2–3 months as well.
- Repeat diagnostic workup and consider possible rebiopsy if signs decrease but do not resolve.
- Repeat diagnostic workup and consider rebiopsy if signs resolve and then recur several months to years later, especially in cats. IBD can progress to small cell lymphoma in the cat.

PREVENTION/AVOIDANCE

- Avoid medications (e.g., corticosteroids, NSAIDs) and foods that cause gastric irritation or allergic response in the patient.
- Prevent free-roaming and potential for dietary indiscretion.

GASTRITIS, CHRONIC

POSSIBLE COMPLICATIONS

- Progression of gastritis from superficial to atrophic gastritis.
- Gastric erosions and ulcers with progressive mucosal damage.
- Aspiration pneumonia.
- Electrolyte or acid-base imbalances.

EXPECTED COURSE AND PROGNOSIS

Varies with underlying cause



MISCELLANEOUS

AGE-RELATED FACTORS

Young animals are more likely to ingest foreign objects.

G

PREGNANCY/FERTILITY/BREEDING

- Prednisone has been used safely in pregnant women; corticosteroids have been associated with increased incidence of congenital defects, abortion, and fetal death.
- Azathioprine has been used safely in pregnant women and may be a good substitute for corticosteroids in pregnant animals.
- Do not administer misoprostol to pregnant animals.

SEE ALSO

- Gastritis, Atrophic
- Gastroduodenal Ulcer Disease
- Gastroenteritis, Eosinophilic
- Gastroenteritis, Lymphocytic-Plasmacytic
- *Helicobacter* Infection
- Hypertrophic Pyloric Gastropathy, Chronic
- Physalopterosis

ABBREVIATIONS

- IBD = inflammatory bowel disease
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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Client Education Handout
available online

GASTRODUODENAL ULCERATION/EROSION (GUE)



BASICS

DEFINITION

Ulcers are defects that extend completely through the mucosa; erosions only extend part way through the mucosa.

PATHOPHYSIOLOGY

- Gastroduodenal ulcers/erosions (GUE) result from various factors which damage or overwhelm normal gastric mucosal defense and repair mechanisms.
- Factors protecting the stomach from GUE include the mucus-bicarbonate layer, gastric epithelial cell turnover, gastric mucosal blood flow, and locally produced prostaglandins.

SYSTEMS AFFECTED

- Gastrointestinal—ulcers and/or erosion are most common in the stomach and then the proximal duodenum; however, neoplasia and some drugs (e.g., flunixin meglumine) can cause ulceration anywhere in GI tract.
- Cardiovascular—hemorrhage may cause anemia, tachycardia, systolic heart murmur, and/or hypotension.
- Peritoneal cavity—perforation may cause peritonitis/sepsis/SIRS.

INCIDENCE/PREVALENCE

- 40–60% in exercising Alaskan sled dogs.
- Relatively common in dogs receiving NSAIDs or dexamethasone.

SIGNALMENT

Species

- Primarily dog; cat uncommonly affected.

Breed Predilections

Chow chows, rough-coated collies, Staffordshire bull terriers, and Belgian shepherd dogs have increased incidence of gastric carcinoma.

Mean Age and Range

All ages

Predominant Sex

Male dogs are predisposed to gastric carcinoma.

SIGNS

General Comments

Patients can be asymptomatic, hyporexic, vomiting, and/or have GI bleeding. Severity of clinical signs is not necessarily proportional to size/number of GUE.

Historical Findings

- Some animals with GUE are asymptomatic (e.g., patients taking NSAIDs or dexamethasone, dogs working in extreme environments).
- Hyporexia is the most common clinical sign.
- Vomiting, hematemesis, and/or melena may be seen (in decreasing order of frequency).
- Cranial abdominal pain ("praying position") is rarely seen.
- Weakness, pallor, lethargy, and/or collapse if severe anemia or SIRS develops.

Physical Examination Findings

- Physical examination often normal.
- Melena is rare.
- Pale mucous membranes and weakness if severely anemic (infrequent).
- Tachycardia, hypotension, and prolonged capillary refill time if hypovolemic shock or perforation/SIRS occur.

CAUSES

Drugs

- NSAIDs—COX-2 selective NSAIDs are usually safer than non-selective NSAIDs, however, GUE and perforation can occur with all COX-2 selective NSAIDs.
- Coadministration of glucocorticoids (either systemic or local) enhances ulcerogenic potential of NSAIDs. Some NSAIDs are renowned for being extremely ulcerogenic (flunixin meglumine, naproxen, indomethacin).
- Glucocorticoids: dexamethasone is probably the most ulcerogenic. Prednisolone is much less likely to cause GUE unless there are additional stress factors (e.g., hypoxemia, hypoperfusion) affecting the GI mucosa.

Gastrointestinal Diseases

- Gastrointestinal neoplasia: carcinomas are most common cause of neoplastic ulceration, but leiomyomas/leiomyosarcomas are renowned for causing severe hemorrhage.
- Pythiosis can cause severe GUE. It is a regionally important disease and is becoming increasingly widespread in North America.
- Foreign bodies can be associated with GUE, but they are usually not an important cause in the stomach. Intestinal foreign bodies (especially linear foreign bodies) commonly cause intestinal ulceration/perforation.
- Gastric hyperacidity.

Infectious Diseases

Pythiosis

Metabolic Diseases

- Hepatic disease
- Hypoaldrenocorticism
- Pancreatitis

Toxicity

Heavy metal poisoning (arsenic, zinc, thallium, iron, or lead are rare causes)

Neoplasia

- GI neoplasia (carcinoma, lymphoma, leiomyoma, GI stromal tumor [GIST])
- Paraneoplastic hyperacidity (mastocytosis, gastrinoma)

Stress/Major Medical Illness

- Shock/severe hypotension (e.g., secondary to trauma or surgery)
- SIRS (heat stroke, sepsis)
- Burns
- Sustained strenuous exercise (especially in extreme environments, either cold or hot)

RISK FACTORS

- Ulcerogenic drugs (NSAIDs, dexamethasone)
- Hypovolemic shock/SIRS
- Extreme exercise



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Esophageal disease (neoplasia, esophagitis, foreign body) diagnose with radiography and/or esophagoscopy.
- Coagulopathies (thrombocytopenia, anticoagulant poisoning): diagnose with platelet count, coagulation testing.
- Bronchopulmonary disease causing hemoptysis: diagnose with radiography and/or bronchoscopy.
- Regurgitation or vomiting of blood (hematemesis) swallowed from respiratory tract or swallowed with food.
- Pepto-Bismol, sucralfate, or activated charcoal cause stool to resemble melena.

CBC/BIOCHEMISTRY/URINALYSIS

- Acute blood loss (i.e., 3–5 days): non-regenerative anemia/hypoalbuminemia.
- Blood loss > 7 days: regenerative anemia/hypoalbuminemia.
- Chronic blood loss: iron deficiency anemia (i.e., microcytic, hypochromic, variable reticulocytosis) and hypoalbuminemia.
- BUN:creatinine ratio may be elevated with acute, severe GI hemorrhage, but this is hard to evaluate without recent pre-bleed laboratory values.

OTHER LABORATORY TESTS

- Fecal flotation (parasitism)
- Bile acids (hepatic insufficiency)
- Resting serum cortisol (screen for hypoadrenocorticism)
- Serum gastrin concentrations (gastrinoma is rare)

IMAGING

- Abdominal radiography (GI foreign body, abdominal mass, pancreatitis, pneumoperitoneum, effusion, hepatic disease).
- Barium contrast radiography is very insensitive for GUE.
- Ultrasonography has high specificity but questionable sensitivity for GI lesions (e.g., infiltrates, altered layering, ulcer); cannot detect erosions.

DIAGNOSTIC PROCEDURES

- Endoscopy is most sensitive test for GUE. It also allows biopsy of lesions. Can try to biopsy margin including normal and abnormal tissue; however, it is optimal to biopsy normal appearing tissue around GUE plus the periphery of the ulcer. Be careful about biopsying center of ulcers as this occasionally causes perforation.
- Fine-needle aspirates or biopsies of infiltrative lesions in GI tract.
- Abdominocentesis may reveal septic peritonitis if ulcer perforates.
- Exploratory surgery can be done to look for GUE, but it can be hard to see GUE or other mucosal lesions from serosal surface. It is easy to look into stomach through gastrostomy incision and miss lesions.

PATHOLOGIC FINDINGS

- GUE are grossly visible.
- Gastric body and antrum are most common sites of GUE (especially from NSAIDs and

(CONTINUED)

GASTRODUODENAL ULCERATION/EROSION (GUE)

dexamethasone), but GUE can occur anywhere in stomach. • Proximal duodenal ulceration is classic but not diagnostic for excessive gastric acid secretion (mast cell tumor, gastrinoma). • Microscopically can see inflammation, neoplasia, or fungal organisms.

**TREATMENT****APPROPRIATE HEALTH CARE**

VERY IMPORTANT: Remove underlying cause if possible, especially drugs, toxins, and/or poor perfusion. Some GUE resolve spontaneously if cause is removed.

SUPPORTIVE CARE

- IV fluids if needed to maintain hydration, gastric mucosal perfusion, and/or treat shock.
- Transfusions if patient has severe GI hemorrhage.

ACTIVITY

Based upon patient's condition

DIET

- Discontinue oral intake if vomiting.
- When feeding is resumed, feed small amounts of low-fat/low-fiber diet.

CLIENT EDUCATION

- Dogs are especially prone to NSAID-induced GUE because these drugs usually have a longer half-life in dogs than in humans. • Never administer an NSAID (especially if sold for human use) unless specifically told to use it by a veterinarian. For example, a low dose of aspirin at 0.5 mg/kg q24h is frequently used to prevent thromboembolic disease in dogs at increased risk. • Hyporexia is often the first sign of GUE and may be the only evidence in patients receiving NSAIDs. • Adverse effects of NSAIDs reduced by giving drug with food.
- Proton pump inhibitors help prevent NSAID-induced GUE, but misoprostol is probably the most effective prophylactic drug.
- No drug is effective in preventing dexamethasone-induced GUE.

SURGICAL CONSIDERATIONS

- If GI blood loss is potentially life threatening, perform gastroduodenoscopy to identify sites of hemorrhage and then either surgically resect lesions or cauterize sites endoscopically (either electrically or chemically). • Surgical excision of ulcers is indicated if medical treatment shows no evidence of helping after 5–7 days. • Rarely need to do intraoperative endoscopy to locate lesions which cannot be found at surgery.
- Rarely may need to have surgeon telescope intestines over the tip of the endoscope to allow thorough examination of entire jejunal mucosa.

**MEDICATIONS****DRUG(S) OF CHOICE**

• Proton pump inhibitors (PPIs) are currently the most potent inhibitors of gastric acid secretion. They irreversibly block the parietal cell proton pump. They require 3–5 days to achieve maximum efficacy, but immediate effects are still superior to that of H₂ receptor antagonists. They can be used as first-line therapy for any GUE, but they are especially indicated for gastrinomas. Omeprazole (1–2 mg/kg PO q12–24h, dog), esomeprazole or lansoprazole (1 mg/kg PO q24h, dog) can be administered orally whereas pantoprazole (1 mg/kg IV q24h, dog) can be administered parenterally. • Histamine (H₂) receptor antagonists competitively inhibit gastric acid secretion. Ranitidine (1–2 mg/kg SC, PO, IV q8–12h, dog and cat); famotidine (0.5–1 mg/kg PO, IV q12–24h, dog and cat); nizatidine (5 mg/kg PO q24h, dog). Famotidine is most potent. Cimetidine should be avoided in light of its short half-life and relative ineffectiveness. Lafutidine is a new H₂ receptor antagonist that is supposed to be as effective as a PPI, but there is currently no experience with its use in veterinary medicine.

• Sucralfate (0.5–1 g PO q6–8h) protects ulcerated tissue by binding to ulcer sites and stimulating prostaglandin synthesis.

• Antiemetics if vomiting is frequent or nausea is severe. Maropitant (1 mg/kg SC q24h for 5 days, dog; 2 mg/kg PO q24h for 5 days, dog); ondansetron (0.5 mg/kg IV q12h, dog; 0.2 mg/kg IV q12h, cat). • Oral antacids (e.g., calcium carbonate) are poorly effective and not recommended.

POSSIBLE INTERACTIONS

- Sucralfate may slow absorption of other drugs. • Antacids may slow absorption of other drugs.

ALTERNATIVE DRUG(S)

Misoprostol, synthetic prostaglandin E1 analogue, (2–5 µg/kg PO q8–12h) used prophylactically to prevent NSAID-induced ulcers. Can be used to treat any existing ulcer. Do not use in pregnant patients (causes abortion).

**FOLLOW-UP****PATIENT MONITORING**

If medications are going to be effective, the patient should show evidence of clinical improvement within 5–7 days.

PREVENTION/AVOIDANCE

- Administer NSAIDs with food.
- Concurrent use of PPI when chronically

administering NSAIDs helps prevent GUE. If PPIs are inadequate, misoprostol is usually more effective. • COX-2 selective or dual LOX/COX inhibitors are less likely to cause GUE than non-selective NSAIDs, but they can still cause GUE and perforation/peritonitis.

POSSIBLE COMPLICATIONS

- Hemorrhage, ulcer perforation, and/or septic peritonitis

EXPECTED COURSE AND PROGNOSIS

• Varies with underlying causes. • GUE not due to local malignancy can usually (not always) be treated successfully medically (especially if one can remove the cause). However, if perforation has occurred, surgery is necessary.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Anemia

AGE-RELATED FACTORS

Neoplasia more common in older animals

ZOONOTIC POTENTIAL

None

SEE ALSO

- Hematemesis • Melena

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone
- COX = cyclooxygenase • DIC = disseminated intravascular coagulation • GI = gastrointestinal • GUE = gastric ulceration/erosion • IV = intravenous
- LOX = lipoxygenase • NSAID = nonsteroidal anti-inflammatory drug • PPI = proton pump inhibitor • SIRS = systemic inflammatory response syndrome

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**Client Education Handout
available online**

GASTROENTERITIS, EOSINOPHILIC



BASICS

DEFINITION

An inflammatory disease of the stomach and intestine, characterized by an infiltration of eosinophils, usually into the lamina propria, but occasionally involving the submucosa and muscularis.

PATOPHYSIOLOGY

- Antigens bind to IgE on the surface of mast cells, resulting in mast cell degranulation.
- Some of the products released are potent eosinophil chemotactants.
- Eosinophils contain granules with substances that directly damage the surrounding tissues.
- Eosinophils can also activate mast cells directly, setting up a vicious cycle of degranulation and tissue destruction.

SYSTEMS AFFECTED

- Gastrointestinal—generally stomach and small intestine; large intestine may be affected.
- In the cat, hypereosinophilic syndrome can involve the GI tract, liver, spleen, kidney, adrenal glands, and heart. There are also rare reports in the dog, particularly in rottweilers.

GENETICS

N/A

INCIDENCE/PREVALENCE

- Eosinophilic gastroenteritis is reportedly more common in dogs than in cats.
- Less common than lymphocytic-plasmacytic gastroenteritis.
- A mixed cellular infiltrate of eosinophils, lymphocytes, and plasma cells may be present occasionally.

SIGNALMENT

Species

Dog and cat

Breed Predilections

German shepherds, rottweilers, soft-coated Wheaten terrier, and Shar-Pei may be predisposed.

Mean Age and Range

- Dogs—most common in animals <5 years of age, although any age may be affected.
- Cats—median age, 8 years; range, 1.5–11 years reported.

Predominant Sex

None reported

SIGNS

Historical Findings

- Intermittent vomiting, small bowel diarrhea, anorexia/hyporexia, and/or weight loss are the most common findings, similar to other causes of gastroenteritis.
- One report states that 50% of cats with eosinophilic gastritis/enteritis had hematochezia or melena.

Physical Examination Findings

- Cats—thickened bowel loops may be palpated.
- Evidence of weight loss may be present.
- If hypereosinophilic syndrome is the cause of the GI disease, enlarged

peripheral lymph nodes, mesenteric lymphadenopathy, hepatomegaly, and splenomegaly may also be noted.

CAUSES

- Idiopathic eosinophilic gastroenteritis
- Parasitic • Immune-mediated—food allergy; adverse drug reaction; associated with other forms of inflammatory bowel disease
- Systemic mastocytosis • Hypereosinophilic syndrome • Eosinophilic leukemia
- Eosinophilic granuloma

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- All of the causes listed above are included in the differential diagnosis of eosinophilic infiltrates in the stomach and small intestine.
- Idiopathic eosinophilic gastroenteritis is a diagnosis of exclusion.
- Multiple fecal floatations and direct smears are imperative to rule in or rule out intestinal parasitism.
- Routine deworming with a broad-spectrum product is commonly indicated, even when all fecal examinations are negative.
- Intestinal biopsy differentiates the other causes of inflammatory bowel disease from eosinophilic gastroenteritis.
- Dietary trial should rule-in or rule-out food allergy or hypersensitivity.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram may reveal a peripheral eosinophilia—more common in cats than dogs, especially common and pronounced in hypereosinophilic syndrome.
- Panhypoproteinemia or hypoalbuminemia may be present if a protein-losing enteropathy is also present.
- Liver enzyme elevations and/or azotemia may be seen with hypereosinophilic syndrome.
- Urinalysis is usually normal.

OTHER LABORATORY TESTS

- Buffy-coat smear to help rule out systemic mastocytosis, when suspected.
- Serum cobalamin levels may be low suggesting ileal disease, folate levels may be increased suggesting small intestinal bacterial overgrowth.

IMAGING

- Plain abdominal radiographs provide little information but are useful to rule out other diseases that may present with similar clinical signs.
- Barium contrast radiography may demonstrate thick intestinal walls and mucosal irregularities but does not provide any information about etiology or the nature of the thickening.
- Ultrasonography—used to measure stomach and intestinal wall thickness and to rule out other diseases; used to examine the liver, spleen, and mesenteric lymph nodes in animals with

hypereosinophilic syndrome. When seen, aspirates of these organs are often indicated.

DIAGNOSTIC PROCEDURES

- Definitive diagnosis often requires histopathology of biopsy samples obtained via endoscopy or laparotomy.
- Bone marrow aspirates are recommended if systemic mastocytosis or significant peripheral eosinophilia is apparent.
- Exploratory laparotomy may be indicated if distal small intestine is involved, or abdominal organomegaly is present.

PATHOLOGIC FINDINGS

- Thickened rugal folds, erosions, ulcers, and increased mucosal friability may be present in the stomach, although grossly it can appear normal.
- Ulcerations and erosions may be seen in the intestine.
- Eosinophilic infiltrates can be patchy in the intestine; multiple biopsies may be necessary to obtain a diagnosis.
- Histopathology reveals a diffuse infiltrate of eosinophils into the lamina propria; the submucosa and muscularis can also be involved (more common in cats).



TREATMENT

APPROPRIATE HEALTH CARE

- Most treated on an outpatient basis.
- Patients with systemic mastocytosis, protein-losing enteropathies, or other concurrent illnesses may require hospitalization until they are stabilized.

NURSING CARE

- If the patient is dehydrated or must be NPO because of vomiting, any balanced crystalloid solution such as lactated Ringer's solution is adequate; otherwise, select fluids on the basis of secondary diseases.
- If severe hypoalbuminemia from protein-losing enteropathy, consider colloids such as hetastarch. Small dogs under 15 pounds (7 kg) may benefit from a plasma transfusion resulting in transient increase in albumin. This may result in improved stability during anesthesia, allowing for further diagnostics and biopsies.

ACTIVITY

No need to restrict unless severely debilitated.

DIET

- Dietary manipulation is usually a critical component of therapy and may take several forms.
- Highly digestible diets with limited macronutrient sources (elimination or hydrolyzed diets)—extremely useful for eliciting remission; can be used as maintenance diets once the patient is stabilized. Most cases are managed successfully long term in this way.
- Dogs—examples include: Hill's Prescription Diet d/d and Hill's z/d; Purina HA; Royal Canin Hypoallergenic diets; Iams Response Formula FP or KO; balanced homemade diets.
- Cats—examples

(CONTINUED)

include: Hill's Prescription Diet z/d and d/d; Purina HA; Royal Canin Hypoallergenic diets; Iams Response LB. • Monomeric diets (e.g., elemental diet)—have non-allergenic components; can be used in patients that are not vomiting but have moderate-to-severe GI inflammation; useful if a food allergy is suspected. However, treatment with monomeric diets is rarely necessary. • In patients with severe intestinal involvement and significant protein-losing enteropathy, total parenteral nutrition may be indicated until remission is obtained. TPN is rarely necessary. • Once the patient is stabilized, an elimination diet trial may be instituted if food allergy or intolerance is the suspected cause to determine the offending nutrient. This is generally not done.

CLIENT EDUCATION

Explain the waxing and waning nature of the disease, the necessity for lifelong vigilance regarding inciting factors, and the potential for long-term therapy.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

- Glucocorticoids: prednisone 2–4 mg/kg PO q24h (rarely requires high end of dose to start). Never exceed a total dose of 50 mg/day in a dog, no matter how heavy. • Gradually taper corticosteroids approximately 25% every 2–3 weeks until at 25% of original dose, then extend to 4- to 8-week intervals before discontinuing; relapses are more common in patients that are taken off corticosteroids too quickly. • Occasionally other immunosuppressive drugs can be used to allow a reduction in corticosteroid dose and avoid some of the adverse effects of steroid therapy. These medications are also added in refractory cases. • When in need of rapid immunosuppression, add chlorambucil (0.1–0.2 mg/kg q24h for 7 days then q48h). Often used in place of azathioprine but can be used in addition. A recent study suggests that this addition may be superior to adding azathioprine. Avoid the simultaneous implementation of 3 different immunosuppressive drugs at the same time.
- Immunosuppressive drugs such as azathioprine (2.2 mg/kg PO q24h, tapering to q48h after 2–3 weeks) if an immune-mediated mechanism is suspected and response to dietary management and glucocorticoid administration is inadequate. Expect response to occur in 2–3 weeks.
- Budesonide, an orally administered glucocorticoid with a high first-pass effect, has been used successfully to treat cats and dogs with inflammatory bowel disease; it appears to have more of a topical effect on the

intestinal tract. Reports have shown that some absorption and secondary effects on the adrenal pituitary axis occur. Current dose recommendations are 2–3 mg/m² q24h with a gradual taper over the course of 8–10 weeks (not based on scientific research) and often requires compounding for smaller dogs. The dose for cats and dogs weighing < 10 kg is 1 mg q24h with a gradual taper over the course of 8–10 weeks.

CONTRAINDICATIONS

If secondary problems are present, avoid medications that might be contraindicated for those conditions.

PRECAUTIONS

- Prednisone and budesonide (less commonly) can cause GI ulceration. Once evidence has been seen, the addition of gastric protectants is indicated. Use of gastric protectants has not been shown to prevent damage but is effective as a treatment.
- Azathioprine and chlorambucil can rarely cause bone marrow suppression in dogs; avoid the use of azathioprine in cats due to its myelosuppressive effects. All patients receiving azathioprine or chlorambucil should have a complete blood count 10–14 days after the start of treatment, with rechecks monthly and then bimonthly thereafter for the entire treatment period; bone marrow suppression can be seen at any time during treatment but is usually cumulative. It is generally reversible with drug discontinuation if caught early. A chemistry panel should also be regularly evaluated. • Pancreatitis, hepatic damage, and anorexia are other potential side effects of these drugs.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Initially frequent for severely affected patients; monitoring peripheral eosinophil counts may be helpful; the corticosteroid dosage is usually adjusted during these visits.
- Patients with less severe disease may be checked 2–5 weeks after the initial evaluation; monthly to bimonthly thereafter until corticosteroid therapy is completed. • Patients receiving azathioprine—monitor as mentioned above. • Patients usually do not require long-term follow-up unless the problem recurs.

PREVENTION/AVOIDANCE

If a food intolerance or allergy is suspected or documented, avoid that particular nutrient and adhere strictly to dietary restrictions.

GASTROENTERITIS, EOSINOPHILIC

POSSIBLE COMPLICATIONS

- Weight loss, debilitation in refractory cases.
- Adverse effects of corticosteroid therapy.
- Bone marrow suppression, pancreatitis, hepatitis, or anorexia caused by azathioprine and/or chlorambucil.

EXPECTED COURSE AND PROGNOSIS

- The vast majority of dogs with eosinophilic gastroenteritis respond to a combination of dietary manipulation and steroid therapy.
- Cats often have a more severe form of the disease, with a poorer prognosis than dogs.
- Cats often require higher doses of corticosteroids for longer periods of time to elicit remission.



MISCELLANEOUS

ZOONOTIC POTENTIAL

A consideration only when eosinophilic infiltrates are secondary to parasites (e.g., *Ancylostoma*, *Giardia*, and ascarids).

PREGNANCY/FERTILITY/BREEDING

- Prednisone has been used safely in pregnant women; corticosteroids have been associated with increased incidence of congenital defects, abortion, and fetal death. • Azathioprine has been used safely in pregnant women and may be a good substitute for corticosteroids in pregnant animals.

SEE ALSO

- Gastroenteritis, Lymphocytic-Plasmacytic
- Inflammatory Bowel Disease • Mast Cell Tumors

Suggested Reading

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GASTROENTERITIS, HEMORRHAGIC



BASICS

DEFINITION

A peracute hemorrhagic enteritis of dogs characterized by a sudden onset of severe bloody diarrhea that is often explosive, with vomiting, hypovolemia, and marked hemoconcentration due to a dramatic loss of water and electrolytes into the intestinal lumen.

PATHOPHYSIOLOGY

- Many conditions result in hemorrhagic diarrhea, but the acute hemorrhagic gastroenteritis (HGE) syndrome of dogs appears to have unique clinical features that distinguish it as a clinical entity separate from other conditions.
- HGE is characterized as a peracute loss of intestinal mucosal integrity with the rapid movement of blood, fluid, and electrolytes into the gut lumen. Dehydration and hypovolemic shock occur quickly. Translocation of bacteria or toxins through the damaged intestinal mucosa may result in septic or endotoxic shock.
- Histological examination of the intestinal tract shows superficial mucosal hemorrhagic necrosis without inflammation. Gastric mucosa is spared.

SYSTEMS AFFECTED

- Gastrointestinal
- Cardiovascular

GENETICS

Unknown; however, there appear to be specific small or toy breeds that may be overrepresented.

INCIDENCE/PREVALENCE

A common clinical condition

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog

Breed Predilections

- All breeds can be affected but the incidence is greater in small-breed and toy-breed dogs.
- Breeds most represented include miniature schnauzer, dachshund, Yorkshire terrier, and miniature poodle.

Mean Age and Range

Usually in adult dogs with a mean age of 5 years.

Predominant Sex

N/A

SIGNS

General Comments

- Clinical findings are variable in both the course and severity of the disease. The disease is usually peracute and associated with concurrent hypovolemic shock.

- Most animals affected were previously healthy with no historical environmental changes or concurrent gastrointestinal disease.

Historical Findings

- The signs usually begin with acute vomiting, anorexia, and lethargy that is followed by watery diarrhea quickly changing to bloody diarrhea.
- Signs progress rapidly and become severe within a period of hours (usually 8–12 hours) and are the result of hypovolemic shock and hemoconcentration.

Physical Examination Findings

- The patient is generally lethargic and weak and has prolonged capillary refill time and weak pulse pressure.
- Skin turgor as a reflection of dehydration may appear normal owing to the peracute nature of the disease and the lag time in compartmental fluid shifts.
- Abdominal palpation may be painful and fluid-filled bowel can be detected.
- Rectal examination identifies bloody diarrhea, and later in the course of disease a "raspberry jam" characteristic stool develops.
- Occasionally fever, but often the temperature is normal or even subnormal.

CAUSES

- The etiology is unknown; allergic, autoimmune and infectious causes have all been implicated.
- There is increasing evidence to suggest that *Clostridium perfringens* (CP) type A enterotoxin is involved in the disease and has been identified in necrotic mucosal surfaces.

RISK FACTORS

- Unknown.
- Most dogs are previously healthy with no major concurrent illness.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Parvovirus
- Circovirus
- Acute gastrointestinal ulceration
- Bacterial enteritis such as salmonellosis or *Campylobacter*
- Conditions resulting in endotoxic or hypovolemic shock
- Intestinal obstruction or intussusception
- Hypoadrenocorticism
- Heat stroke
- Pancreatitis
- Coagulopathy

CBC/BIOCHEMISTRY/URINALYSIS

- Hemoconcentration with the PCV generally > 60% and sometimes as high as 75% with discordant plasma proteins that are normal to decreased due to protein loss into the GI tract. Usually a stress leukogram.

- Biochemistry profile may reveal secondary hepatic enzyme elevations and high BUN due to prerenal causes.

OTHER LABORATORY TESTS

Fecal Tests

- The stool is negative for parasites.
- ELISA for parvovirus is negative.
- Fecal cytology shows many RBCs and occasional WBCs.
- Clostridium* may be cultured in high concentrations from healthy dogs and should not be used as a diagnostic test for dogs with HE. Fecal ELISA test for detection of *C. perfringens* enterotoxin is often positive. Culture for other enteric pathogens is negative. Fecal PCR for detection of *C. perfringens* alpha toxin gene alone is not sufficient to diagnose this disorder.

Coagulogram

Usually normal but rarely secondary DIC is a complication.

IMAGING

Abdominal radiographs or ultrasound show fluid- and gas-filled small and large intestine.

DIAGNOSTIC PROCEDURES

Electrocardiogram

Cardiac arrhythmias such as ventricular premature contractions and ventricular tachycardia may be noted.

Endoscopy

- Endoscopy is rarely indicated.
- Stomach may appear normal but small and large intestine will show diffuse mucosal hemorrhage, ulceration, and hyperemia.

PATHOLOGIC FINDINGS

Changes in the intestine include gross congestion and microscopic evidence of autolysis that is devoid of marked inflammation.



TREATMENT

APPROPRIATE HEALTH CARE

Patients suspected of having acute HGE should be hospitalized and treated aggressively because clinical deterioration is often rapid and can be fatal.

NURSING CARE

- Rapid volume replacement through a large-bore IV catheter is required in all cases.
- Balanced electrolyte solutions are given up to the rate of 40–60 mL/kg/hour IV until the PCV is < 50%.
- A moderate rate of maintenance fluids is given to maintain circulatory function and correct any potassium or other electrolyte deficits during the recovery period.
- Continued GI fluid losses should be estimated and that volume added to the fluid requirements.
- Hypoproteinemic animals may require colloids or plasma.

(CONTINUED)

GASTROENTERITIS, HEMORRHAGIC**ACTIVITY**

Restricted

DIET

- NPO during acute disease.
- During recovery period a bland, low-fat, low-fiber gastrointestinal diet should be fed for several days before returning to the normal diet.
- Consider increased dietary fiber to alter the intestinal microbiota to reduce the likelihood of recurrence of *C. perfringens*-associated diarrhea.

CLIENT EDUCATION

- Discuss the need for immediate and aggressive medical management. With appropriate therapy, mortality is usually low.
- Recurrence is reported in about 10% of the cases.

SURGICAL CONSIDERATIONS

N/A

**MEDICATIONS****DRUG(S) OF CHOICE**

- Parenteral antibiotics are generally recommended; however, their use in aseptic cases has been questioned. Antibiotics are used for potential septicemia. Amoxicillin/sulbactam (50 mg/kg q8h IV) is suggested prophylactically.
- An antiemetic such as maropitant (1 mg/kg q24h) is suggested to control nausea and vomiting.
- Antacids such as famotidine (0.5–1 mg/kg q12h) or pantoprazole (1 mg/kg q24h) given IV may be indicated.
- Excessive blood loss may require a blood transfusion (rare).

CONTRAINDICATIONS

N/A

PRECAUTIONS

Septic and or hypovolemic shock can occur quickly and consequently the animal should be monitored closely.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

- Oral antibiotics and intestinal protectants are of little benefit and generally not administered.

- Rectal administration of mucosal protectants such as sucralfate is of questionable value.
- Antidiarrheal drugs are contraindicated.
- Consider probiotics to alter the intestinal microbiota to reduce the likelihood of recurrence of *C. perfringens*-associated diarrhea.

**FOLLOW-UP****PATIENT MONITORING**

- Monitor the PCV and total solids frequently (at least every 4–6 hours).
- Modify the fluid replacement-based PCV, continued GI fluid losses, and circulatory function.
- If there is a failure of clinical improvement in 24–48 hours, re-evaluate the patient, as other causes of hemorrhagic diarrhea are probable.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Occasionally DIC may develop. Neurologic signs or even seizures secondary to the hemoconcentration may occur.
- Cardiac arrhythmias occur from suspected myocardial reperfusion injury.
- A hemolytic-uremic syndrome may occur (rare).
- Most dogs recover. Mortality rate can be high in untreated dogs. Fewer than 10% of treated dogs die, and 10–15% have repeated occurrences.

EXPECTED COURSE AND PROGNOSIS

- The course of the disease is generally short, lasting from 24 to 72 hours.
- The prognosis is good, and most patients recover with no complications.
- Sudden death is uncommon if adequately treated.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

Unknown

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYM

Acute hemorrhagic enterocolitis

SEE ALSO

- Diarrhea, Acute
- Vomiting, Acute

ABBREVIATIONS

- DIC = disseminated intravascular coagulation
- ELISA = enzyme-linked immunosorbent assay
- GI = gastrointestinal
- HGE = hemorrhagic gastroenteritis
- PCV = packed cell volume
- RBC = red blood cells
- WBC = white blood cells

Suggested Reading

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GASTROENTERITIS, LYMPHOCYTIC-PLASMACYTIC



BASICS

DEFINITION

- The most common form of inflammatory bowel disease characterized by lymphocyte and plasma cell infiltration into the lamina propria of the stomach and intestine; usually accompanied by other criteria of mucosal inflammation.
- Less commonly the infiltrates may extend into the submucosa and muscularis.

G

PATHOPHYSIOLOGY

- An aberrant immune response to environmental stimuli likely resulting in loss of mucosal homeostasis; alterations in intestinal microbiota (i.e., dysbiosis) maybe a trigger.
- Continued antigen exposure, coupled with dysregulated inflammation, results in disease, although the exact mechanisms and patient factors remain unknown.

SYSTEMS AFFECTED

- Gastrointestinal—typically small intestine and occasionally stomach; the colon can be independently or simultaneously affected.
- Extra-intestinal manifestations of inflammation are occasional seen (e.g., mild thrombocytopenia) although they are not well characterized.

GENETICS

Basenjis, Lundehunds, and soft-coated Wheaten terriers have familial forms of inflammatory bowel disease.

INCIDENCE/PREVALENCE

The most common form of IBD affecting dogs and cats.

SIGNALMENT

Breed Predilections

- Lundehunds and basenjis have unique forms of IBD; gluten-sensitive enteropathy affects Irish setters; protein-losing enteropathy and nephropathy affects soft-coated Wheaten terriers.
- German shepherds and Chinese Shar-Peis are predisposed to lymphocytic-plasmacytic gastroenteritis.
- Pure-breed cats (Asian breeds) may have a higher incidence.

Mean Age and Range

- Most common in middle-aged and older animals.
- Dogs as young as 8 months and cats as young as 5 months of age have been reported.

Predominant Sex

None reported

SIGNS

Historical Findings

- Signs associated with lymphocytic-plasmacytic gastritis with or without enteritis can vary in type, severity, and frequency.
- Generally have an intermittent or cyclical, chronic course over time. Flares are

characterized by spontaneous exacerbations and remissions.

- Cats—intermittent, chronic vomiting is the most common; chronic small bowel diarrhea is second.
- Dogs—chronic small bowel diarrhea is the most common; if only the stomach is involved, vomiting is the most common.
- Dogs and cats—anorexia and chronic weight loss are common; hematochezia, hematemesis, and melena are occasionally noted.

Physical Examination Findings

Varies from normal examination to a dehydrated, cachectic, and depressed patient depending on the disease severity and organ affected.

CAUSES

Pathogenesis is likely multifactorial and involves complex interactions between genetic, immunologic, and environmental (i.e., microbiota) factors.

Infectious Agents

- Giardia*, *Salmonella*, *Campylobacter*, and normal gastrointestinal microbiota have been implicated. Increased mucosally associated bacteria have been observed in dogs and cats with IBD compared to healthy animals.

Dietary Agents

- Meat proteins, food additives, artificial coloring, preservatives, milk proteins, and gluten (wheat) may contribute to the pathogenesis of chronic mucosal inflammation.

Genetic Factors

- Certain forms of IBD are more common in some breeds of dogs (see above).
- Certain major histocompatibility genes may render an individual susceptible to development of IBD.

RISK FACTORS

See "Causes"



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other infiltrative inflammatory bowel conditions (e.g., eosinophilic gastroenteritis, granulomatous IBD).
- Food hypersensitivity.
- Metabolic disorders.
- Neoplasia.
- Infectious diseases (e.g., histoplasmosis, toxoplasmosis, giardiasis, salmonellosis, *Campylobacter* enteritis, and bacterial overgrowth).
- Miscellaneous diseases (e.g., lymphangiectasia, gastrointestinal motility disorders, and exocrine pancreatic insufficiency).
- In the cat, consider hyperthyroidism, systemic viral infection (e.g., FeLV, FIV, FIP), and chronic pancreatitis.

CBC/BIOCHEMISTRY/URINALYSIS

- Often normal.
- Mild nonregenerative anemia and mild leukocytosis with or without a mild left shift.
- Hypoproteinemia is more common in dogs than cats with IBD.

OTHER LABORATORY TESTS

- Alterations in serum cobalamin and folate may serve to localize enteric regions of small intestinal inflammation.
- Serum pancreatic specific lipase to screen for pancreatic inflammation.
- Fecal alpha1-proteinase inhibitor to evaluate for protein-losing enteropathy.
- Trypsin-like immunoreactivity to evaluate for exocrine pancreatic insufficiency.
- Cats—T₄ and FeLV/FIV/toxoplasmosis serology are recommended to screen for infectious causes for gastrointestinal signs.

IMAGING

- Survey abdominal radiographs are usually normal.
- Barium contrast studies occasionally reveal mucosal abnormalities and thickened bowel loops but are typically not helpful in establishing a definitive diagnosis.

DIAGNOSTIC PROCEDURES

- Initiate a hypoallergenic dietary trial to rule out adverse food reactions; if signs resolve then additional diagnostics are not necessary.
- Always perform direct and indirect fecal examinations for parasites.
- Definitive diagnosis requires mucosal biopsy and histopathology, usually obtained via endoscopy.
- Exploratory laparotomy or laparoscopy may be indicated when portions of the GI tract, unapproachable by endoscopy, are involved or if abdominal organomegaly, lymphadenomegaly, or masses are present.
- Clinical assessment of disease severity using the canine IBD activity index (CIBDAI) is a useful tool.

PATHOLOGIC FINDINGS

- Grossly, stomach and intestinal appearance can range from normal to edematous, thickened, and ulcerated.
- The hallmark histopathologic finding is an infiltrate of lymphocytes and plasma cells in the lamina propria; architectural changes including villus atrophy, fusion, fibrosis, crypt abscessation and lymphangiectasia may be present to varying degrees.
- The distribution may be patchy, so numerous biopsy specimens are necessary to make the diagnosis.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient, unless the patient is debilitated from dehydration, hypoproteinemia, or cachexia.
- Monitor therapeutic responses using CIBDAI scores.

NURSING CARE

- If the patient is dehydrated or must be NPO because of severe vomiting, a balanced crystalloid such as lactated Ringer's solution is adequate; additional electrolyte supplementation may be necessary if alterations are present (e.g., potassium chloride).
- Colloids (dextrans or hetastarch)

(CONTINUED)

GASTROENTERITIS, LYMPHOCYTIC-PLASMACYTIC

should be given if severe hypoalbuminemia from protein losing enteropathy is present.

ACTIVITY

No restrictions

DIET

- Dietary therapy with an elimination or hydrolyzed diet is an essential component of patient management.
- Patients with severe intestinal involvement and protein-losing enteropathy may require total parenteral nutrition until stable.
- Highly digestible diets decrease the intestinal antigenic load, thus helping to reduce mucosal inflammation; appropriate diet therapy can contribute to clinical remission and can be used as a maintenance diet.
- Modification of the n3:n6 fatty acid ratio may also help to modulate the inflammatory response.
- Parenteral cobalamin supplementation is essential if serum levels are subnormal. Deficiencies in cobalamin can contribute to clinical signs and limit the effectiveness of dietary and medical therapy.
- Numerous commercial elimination diets that meet the above criteria are available for dogs and cats; home-cooked diets are also an excellent option but are more time-consuming for owners.
- Use fiber supplementation in dogs and cats with colitis.

CLIENT EDUCATION

- IBD is more likely to be controlled rather than cured, as relapses are common.
- Patience is required during the various food and medication trials that are often necessary.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Corticosteroids—the mainstay of treatment for idiopathic lymphocytic-plasmacytic enteritis; prednisone or prednisolone is used most frequently (1 mg/kg PO q12h) in dogs and cats; cats may require a higher dose to control their disease. Gradually taper the corticosteroid dose after 2–4 weeks of induction therapy when clinical signs are resolved; relapses are common if patients are tapered too quickly. Maintenance dosages q48–72h may be necessary in some patients. Cats may respond better to prednisolone than prednisone. Budesonide, a locally active steroid, may be used in patients that cannot tolerate the systemic side effects of prednisone. Parenteral steroids may be needed in severe cases in which oral absorption may be limited.
- Azathioprine (2 mg/kg q24–48h PO in dogs; not recommended in cats)—an immunosuppressive drug that can be used to allow a reduction in corticosteroid dose; delayed onset of activity (up to 3 weeks) limits effectiveness in acute cases.
- Chlorambucil (2 mg q48–72h PO in cats) is an effective alternative to azathioprine.

- Metronidazole—has antibacterial and antiprotozoal properties; some evidence that it also has immune-modulating effects in rodents; the dosage for IBD in dogs and cats is 10 mg/kg PO q12h.

ALTERNATIVE DRUG(S)

- Cyclosporine—may be useful in the therapy of refractory cases of lymphocytic-plasmacytic gastroenteritis; using Atopica, 2–5 mg/kg PO q12h for dogs, 1–4 mg/kg q12–24h for cats; dosage is very individualized so monitoring trough levels is recommended.
- Sulfasalazine—a sulfa analog that is broken down by luminal bacteria into sulfapyridine and mesalamine, the latter of which provides anti-inflammatory effects in the colon; dosage for dogs with colonic IBD is 10–30 mg/kg PO q8–12h. Use cautiously in cats and at reduced dosage due to the potential for salicylate toxicity.

PRECAUTIONS

- Azathioprine—causes bone marrow suppression, especially in cats; routine CBCs are recommended at 2 weeks, 1 month, and then bimonthly; bone marrow suppression is typically reversible if the drug is discontinued as soon as suppression is noted.
- Metronidazole—can cause reversible neurotoxicity at high dosages; discontinuation of the drug usually reverses the neurologic signs.
- Cyclosporine—can cause vomiting, gingival hyperplasia, and papillomatosis; associated with the development of lymphoma in humans.

POSSIBLE INTERACTIONS

- Cyclosporine can interfere with the metabolism of phenobarbital and phenytoin.
- Ketoconazole, erythromycin, and cimetidine can decrease hepatic metabolism of cyclosporine.
- Any drugs that are potentially nephrotoxic should be used with caution in conjunction with cyclosporine.

**FOLLOW-UP****PATIENT MONITORING**

- Severely affected patients on bone marrow suppressive medications require frequent monitoring (see above); adjust medications during these visits based on bloodwork and clinical signs.
- Check patients with less severe disease 2–3 weeks after their initial evaluation and then monthly to bimonthly until medications are tapered and clinical signs are resolved.

PREVENTION/AVOIDANCE

When a food intolerance or allergy is suspected or documented, avoid that particular item and adhere strictly to dietary restriction.

POSSIBLE COMPLICATIONS

- Weight loss and debilitation in refractory cases.
- Iatrogenic hyperadrenocorticism and steroid side effects.
- Bone marrow suppression, pancreatitis, hepatopathy, or anorexia can be caused by azathioprine.
- Vomiting, diarrhea, and anorexia with cyclosporine; decreasing the dosage temporarily typically will result in resolution of gastrointestinal signs.
- Keratoconjunctivitis sicca with sulfasalazine.

EXPECTED COURSE AND PROGNOSIS

- Dogs and cats with mild-to-moderate inflammation have a good-to-excellent prognosis for full recovery.
- Patients with severe infiltrates, particularly if other portions of the GI tract are involved, have a more guarded prognosis.
- Other prognostic indices associated with negative long-term outcome include severe mucosal lesions on endoscopy, hypocabalaminemia, and hypoalbuminemia.
- Often the initial response to therapy sets the tone for a given individual's ability to recover.

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**MISCELLANEOUS****PREGNANCY/FERTILITY/BREEDING**

- Corticosteroids have been associated with increased incidence of congenital defects, abortion, and fetal death.
- Azathioprine has been used safely in pregnant women, and may be a good substitute for corticosteroids in pregnant animals.
- Sulfasalazine should be used with extreme caution during pregnancy.

SEE ALSO

- Gastroenteritis, Eosinophilic
- Inflammatory Bowel Disease

ABBREVIATIONS

- CIBDAI = canine IBD activity index
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- GI = gastrointestinal
- IBD = inflammatory bowel disease

Suggested Reading

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Client Education Handout
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GASTROESOPHAGEAL REFLUX



BASICS

OVERVIEW

- Reflux of gastric or intestinal fluid into the esophageal lumen.
- Incidence unknown; probably more common than clinically recognized.
- Transient relaxation of the gastroesophageal sphincter or chronic vomiting may permit reflux of gastrointestinal juices into the esophageal lumen. Reflux is common in dogs with sliding hiatal hernias. A small amount of gastroesophageal reflux is a normal phenomenon in dogs and cats.
- Gastric acid, pepsin, trypsin, bicarbonate, and bile salts are all injurious to the esophageal mucosa with prolonged or repetitive contact.
- Esophagitis resulting from reflux may vary from mild inflammation of the superficial mucosa to severe ulceration involving the submucosa and muscularis.

SIGNALMENT

- Dog and cats; male or female.
- No breed predilections reported.
- May be associated with congenital hiatal hernia seen in Chinese Shar-Pei dogs and other brachycephalic breeds.
- Occurs at any age; younger animals may be at increased risk because of developmental immaturity of the gastroesophageal sphincter.
- Young animals with congenital hiatal hernia may also be at increased risk.

SIGNS

Historical Findings

- Regurgitation
- Hypersalivation
- Painful swallowing (odynophagia)
- Anorexia

Physical Examination Findings

- Often unremarkable.
- Changes consistent with brachycephalic syndrome that can increase the likelihood of reflux and hiatal herniation. Hypersalivation—with severe ulcerative esophagitis; possible pain on palpation of cervical esophagus.

CAUSES & RISK FACTORS

- Anesthesia with relaxation of lower esophageal sphincter tone.
- Retained gastric contents.
- Foreign body ingestion with esophagitis.
- Pill ingestion in cats especially associated with tetracyclines.
- Acquired or congenital hiatal hernia.
- Chronic vomiting with secondary esophagitis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Oral or pharyngeal disease
- Ingestion of caustic agent
- Esophageal foreign body

- Esophageal tumor
- Megaeosophagus—idiopathic; myasthenia gravis; vascular ring anomaly
- Hiatal hernia
- Gastroesophageal intussusception

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

N/A

IMAGING

- Survey thoracic radiography—usually unremarkable; may be air in the distal esophagus (nonspecific finding).
- Barium contrast radiography—reveals gastroesophageal reflux in some, but not all, animals; videofluoroscopy is superior to esophagram; aspiration pneumonia may be evident in the dependent portions of the lung.

DIAGNOSTIC PROCEDURES

- Esophagoscopy—the best means of confirming reflux esophagitis—irregular mucosal surface with hyperemia or active bleeding in the distal esophagus. Refluxed gastroduodenal secretions may be seen pooling in the distal esophagus near the LES which may or may not be open.
- Radiography is of little value in confirming mucosal lesions of GER.



TREATMENT

- Generally, managed as outpatient.
- Not necessary to restrict activity.
- Moderate-to-severe cases—may withhold food for 24 hours to promote esophageal rest and to minimize further reflux; thereafter, feed low-fat, low-protein meals in small, frequent feedings; dietary fat decreases gastroesophageal sphincter pressure and delays gastric emptying; protein stimulates gastric acid secretion and may precipitate GER.



MEDICATIONS

DRUG(S)

- Oral sucralfate suspension (0.5–1 g PO q8h).
- Gastric acid antisecretory agents—H2 blockers: ranitidine (1–2 mg/kg PO q12h); famotidine (0.5–1 mg/kg PO, SC, IV q12–24h); proton pump inhibitors: omeprazole (0.7–1.5 mg/kg PO q24h); pantoprazole (1 mg/kg IV q24h).
- Prokinetic agents—cisapride (0.3–0.5 mg/kg PO q8–12h); ranitidine (1–2 mg/kg PO, IV, SC q8–12h); metoclopramide (0.5 mg/kg, PO, q6–8h or 1–2 mg/kg q24h as CRI).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Sucralfate suspension may interfere with the absorption of other drugs (e.g., cimetidine, ranitidine, omeprazole, cisapride).



FOLLOW-UP

- Patients rarely require follow-up endoscopy.
- It may be appropriate in many patients to simply monitor clinical signs.
- Consider endoscopy for patients that do not respond to empirical medical therapies. Severe mucosal damage (esophagitis) may progress to stricture.
- Clients should avoid feeding high-fat foods; they promote gastric retention and might exacerbate reflux.
- Administer water (“wet” swallow) via syringe following pill administration in cats and dogs.
- The most important complications are esophagitis and stricture formation.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Hiatal hernia
- Administration of oral medications (pills) in cats and dogs

AGE-RELATED FACTORS

May be worse in younger animals because of developmental immaturity of the gastroesophageal sphincter mechanism.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

ABBREVIATIONS

- GER = gastroesophageal reflux
- LES = lower esophageal sphincter

Suggested Reading

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GASTROINTESTINAL OBSTRUCTION



BASICS

DEFINITION

The partial or complete physical impedance to the flow of ingesta and/or secretions aborally through the pylorus into the duodenum (gastric outlet obstruction) or through the small intestine. Obstructions in the pharynx, esophagus, large intestine, and rectum, and motility disorders are addressed in separate chapters (refer to "See Also").

PATHOPHYSIOLOGY

Gastric Outflow Obstruction

- Ingesta and fluids accumulate in the stomach.
- Vomiting results in loss of fluids rich in hydrochloric acid (from gastric secretions) with subsequent hypochloremic metabolic alkalosis.
- Varying degrees of dehydration, tissue compromise, malaise, and weight loss occur, depending on underlying etiology, severity, and chronicity.

Small Intestinal Obstruction

- Ingesta and fluids accumulate proximal to the obstruction.
- Vomiting may result in significant dehydration and electrolyte imbalances (particularly hypokalemia), depending on location (proximal vs. distal), partial or complete obstruction, and chronicity.
- Mucosal damage and bowel ischemia can result in endotoxemia and sepsis.

SYSTEMS AFFECTED

- Behavioral—associated with abdominal discomfort or pain (praying position, change in temperament).
- Cardiovascular—hypovolemic shock; tachycardia.
- Gastrointestinal—anorexia; vomiting; diarrhea; and malaise.
- Respiratory—aspiration pneumonia.

GENETICS

Unknown (see "Breed Predilections")

INCIDENCE/PREVALENCE

Common

SIGNALMENT

Species

- Dog and cat.
- Foreign bodies more common in dogs due to indiscriminate ingestion.

Breed Predilections

- Congenital pyloric stenosis—more common in brachycephalic breeds (e.g., boxers, Boston terriers) and Siamese cats.
- Acquired chronic hypertrophic gastropathy—more common in Lhasa apsos, Shih tzus, Pekingese, and poodles.
- Gastric dilation and volvulus—more common in large-breed dogs (e.g., German shepherds, Great Danes).

Mean Age and Range

- Foreign bodies—more common in young animals, but can occur at any age.
- Pyloric stenosis—occurs most often in young animals.
- CHG—more common in

middle-aged and older animals.

- Intussusceptions—most common in young animals.

SIGNS

Historical Findings

- Vomiting—hallmark sign; important to differentiate vomiting (forceful abdominal contractions) from regurgitation (passive); may occur soon after eating, especially with gastric outlet obstruction; vomiting food ingested > 8 hours after ingestion is consistent with delayed gastric emptying; usually more severe clinical signs with gastric and proximal small intestinal obstructions; may be characterized as projectile.
- Other variable clinical signs—anorexia; lethargy; malaise; ptalism; diarrhea; melena; and weight loss.
- Animals may continue to have bowel movements even with intestinal obstruction.
- Clients should be questioned about possible foreign body ingestion.

Physical Examination Findings

- The physical examination is often the most useful diagnostic procedure for intestinal obstruction.
- Findings can vary from normal to animal in life-threatening crisis—include dehydration, shock, palpable foreign body, abdominal discomfort or pain, and abdominal mass (intussusception or tumor).
- Linear foreign bodies—careful sublingual examination essential for detection; although more common in cats, linear foreign bodies also occur in dogs; sedation or anesthesia for oral examination and abdominal palpation is often very helpful in diagnosis.

CAUSES

Gastric Outflow Obstruction

- Foreign bodies
- Pyloric stenosis
- CHG
- Neoplasia
- GDV
- Granulomatous gastritis or gastroenteritis (e.g., pythiosis)

Small Intestinal Obstruction

- Foreign bodies
- Intussusception
- Hernias (with incarceration)
- Mesenteric torsion or volvulus
- Neoplasia
- Granulomatous enteritis
- Stricture

RISK FACTORS

- Exposure to and tendency to ingest foreign bodies.
- Intussusception—associated with intestinal parasitism and viral enteritis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Metabolic disease (e.g., renal failure, hepatic disease, diabetic ketoacidosis, hypoadrenocorticism).
- Infectious gastroenteritis (e.g., viral, bacterial, parasitic).
- Pancreatitis.
- Peritonitis.
- Toxicity.
- Gastroduodenal ulcer disease.
- Nonspecific gastroenteritis.
- CNS disease.

CBC/BIOCHEMISTRY/URINALYSIS

- These diagnostic tests are useful to rule out other causes for clinical signs (e.g., renal

failure, pancreatitis, liver disease, hypoadrenocorticism, diabetic ketoacidosis)

and to evaluate overall health status of the patient.

- Hemogram—may reveal anemia from gastrointestinal blood loss, stress leukocytosis, or a degenerative left-shifted leukocytosis or leukopenia due to severe mucosal injury or intestinal perforation with subsequent septic peritonitis.
- Chemistry profile and blood gas analysis—often reveal hypochloremic metabolic alkalosis with gastric outlet obstruction; hypokalemia and prerenal azotemia are variable findings.
- Hyperlactemia may be present due to hypoperfusion.

G

IMAGING

Survey Abdominal Radiography

- May reveal a radio opaque foreign body in the stomach or intestine, severe gastric distention, or obstructed loops of intestine with dilation due to fluid and/or gas.
- It is important to differentiate adynamic or functional ileus (usually diffuse) from obstruction (usually segmental).
- Radiographic interpretation must be done within the context of the history, physical examination, and other laboratory data to avoid misdiagnosis and unnecessary surgery.

Contrast Radiography

- Positive-contrast studies—may reveal delayed gastric emptying (> 4 hours with liquid contrast and > 8–10 hours with liquid contrast mixed with food), foreign bodies, complete obstruction, and masses.
- Pneumocolon—may be useful when ileocolic intussusception is suspected.

Abdominal Ultrasonography

May be useful in detecting foreign bodies, obstruction (especially intestinal intussusception), and marked disturbances in GI motility. Abdominal ultrasound can miss gastric foreign bodies and any animal suspected of having a GI foreign body should have abdominal radiographs performed if ultrasound is unremarkable.

Abdominal CT

Utilized when other imaging modalities have failed and as possible alternative to exploratory laparotomy.

DIAGNOSTIC PROCEDURES

- Gastrointestinal endoscopy—may be useful for confirming gastric and proximal intestinal obstruction and for obtaining biopsies of masses; particularly useful with some types of foreign bodies as retrieval may be possible. This may be performed in conjunction with exploratory laparotomy.
- Abdominal paracentesis or diagnostic peritoneal lavage and cytologic analysis—more sensitive than physical examination and radiography (i.e., can detect small amounts of abdominal effusion); may reveal non-septic inflammation associated with intestinal vascular compromise (prior to perforation) or septic

GASTROINTESTINAL OBSTRUCTION

(CONTINUED)

peritonitis; can indicate the need for exploratory laparotomy.

PATHOLOGIC FINDINGS

Histopathology of gastrointestinal masses causing obstruction—can reveal granulomatous inflammation, fungal infection (e.g., pythiosis), and neoplasia.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—for diagnosis, initial supportive medical care, and relief of the obstruction (usually with surgery).
- Surgery—acute intestinal obstructions are emergencies, and surgery should be performed as soon as possible after immediate supportive medical care; intestines do not tolerate vascular compromise well; intestinal resection and anastomosis frequently required (with associated increased morbidity and potential complications), but enterotomy may be successful if earlier diagnosis is made.
- Delay in diagnosis may result in intestinal necrosis, perforation, septic peritonitis, and increased likelihood of death.

NURSING CARE

- Intravenous crystalloid fluids—necessary for rehydration, circulatory support, and to correct acid-base and electrolyte abnormalities; for severe circulatory compromise (shock), administer isotonic crystalloid fluids at 90 mL/kg (dogs) or 45–60 mL/kg (cats) over 1 hour.
- Colloids (voluven or hetastarch)—may also be beneficial; frequent evaluation of hydration and electrolytes (with appropriate treatment adjustments) is necessary; for gastric outlet obstruction causing hypochloremic metabolic alkalosis, fluid of choice is 0.9% saline; otherwise, lactated Ringer's solution or other balanced electrolyte solution is adequate.
- Appropriate potassium supplementation—important.

ACTIVITY

Restricted

DIET

- Nothing by mouth until relief of obstruction and resolution of vomiting; then feed bland fat-restricted diet for 1–2 days, with gradual return to normal diet.
- Enteral tube feeding or parenteral feeding may be required postoperatively.

CLIENT EDUCATION

Warn that animals with the tendency to ingest foreign bodies are often repeat offenders; all reasonable efforts to prevent access to foreign bodies should be made.

SURGICAL CONSIDERATIONS

Gastric Outflow Obstruction

- Pyloroplasty or pyloromyotomy—for pyloric stenosis or CHG.
- Gastrotomy—for

foreign bodies not able to be removed with endoscopy.

- Resection (e.g., Billroth I gastroduodenostomy, Billroth II gastrojejunostomy)—for granulomatous or neoplastic masses.
- Gastropexy—for GDV.

Intestinal Obstruction

- Enterotomy
- Resection and anastomosis—with bowel ischemia and necrosis
- Open peritoneal lavage—with perforation and septic peritonitis
- Closed suction drainage—may be easier and as effective
- Prophylactic enteropexy—with intussusception



MEDICATIONS

DRUG(S)

- Broad-spectrum parenteral antibiotics—with significant mucosal injury or sepsis; ampicillin (20 mg/kg IV q8h) or ampicillin/clavulanate (50 mg/kg IV q8h) and an aminoglycoside (gentamicin 6.6 mg/kg IV q24h, amikacin 15 mg/kg IV q24h) or a fluoroquinolone (enrofloxacin 5–10 mg/kg IV q24h; for cats, ciprofloxacin 10 mg/kg IV q8h). Aminoglycoside antimicrobials should not be used until patient is well hydrated and adverse effects on kidney must be closely monitored via urinalysis (glycosuria, proteinuria, renal casts, decreased urine SG) and assessment of BUN, creatinine, and serum phosphorus values.
- Antiemetics—metoclopramide (0.2–0.5 mg/kg SC or IV q6–8h or 1–2 mg/kg q24h as a CRI); may be given *after* the obstruction has been relieved; cisapride is more potent than metoclopramide but is only available in an oral form (0.3–0.5 mg/kg q8–12h); maropitant may be used in dogs > 8 weeks and cats > 16 weeks at 1 mg/kg SC q24h.
- GI protectants-H₂-receptor antagonists (e.g., famotidine 0.5–1.0 mg/kg, SC, IM, IV q12h) and/or the gastric mucosal protectant sucralfate (250 mg/cat PO q8–12h or 250–1,000 mg/dog PO q8–12h)—may be used in patients with mucosal ulceration.
- Pantoprazole 0.7–1 mg/kg q12–24h.

CONTRAINDICATIONS

Prokinetic agents (e.g., metoclopramide and cisapride) must be avoided until obstruction is resolved.

PRECAUTIONS

Aminoglycoside antibiotics should be not used with shock, dehydration, or renal compromise because of their potential nephrotoxicity.



FOLLOW-UP

PATIENT MONITORING

- Monitor hydration, packed cell volume/total solids, and electrolyte status closely;

adjust fluid therapy accordingly.

- Monitor postoperatively for signs of peritonitis.

PREVENTION/AVOIDANCE

- Clients should be cautioned that some pets with tendencies to ingest foreign bodies may do so repeatedly.
- Efforts to prevent ingestion of foreign bodies are important.

POSSIBLE COMPLICATIONS

- Aspiration pneumonia
- Septic peritonitis (intestinal necrosis and perforation, dehiscence)
- Adynamic ileus and/or gastroparesis

EXPECTED COURSE AND PROGNOSIS

- Uncomplicated cases—prognosis good to excellent.
- Intestinal perforation and septic peritonitis—prognosis guarded initially.
- Obstructive granulomatous gastroenteritis—prognosis guarded to poor, especially with pythiosis.
- Mesenteric torsion or volvulus—prognosis poor to grave (most patients die despite surgery).



MISCELLANEOUS

AGE-RELATED FACTORS

See "Signalment"

SEE ALSO

- Acute Abdomen
- Constipation and Obstipation
- Dysphagia
- Esophageal Foreign Bodies
- Esophageal Stricture
- Gastric Dilation and Volvulus Syndrome
- Gastric Motility Disorders
- Hiatal Hernia
- Hypertrophic Pyloric Gastropathy, Chronic
- Intussusception
- Megacolon
- Megaesophagus
- Pythiosis
- Rectal Stricture
- Regurgitation
- Septic Peritonitis
- Vomiting, Acute
- Vomiting, Chronic

ABBREVIATIONS

- CHG = chronic hypertrophic gastropathy
- CNS = central nervous system
- GDV = gastric dilation and volvulus

Suggested Reading

Boag AK, Coe RJ et al. Acid-base and electrolyte abnormalities in dogs with gastrointestinal foreign bodies. *J Vet Intern Med* 2005; 19:816–821.

Hayes G. Gastrointestinal foreign bodies in dogs and cats: a retrospective study of 208 cases. *J Small Anim Pract* 2009; 50:576–583.

Authors Steven L. Marks and Albert E. Jergens

Consulting Editor Stanley L. Marks



Client Education Handout
available online

GIARDIASIS



BASICS

OVERVIEW

- Enteric infection of dogs and cats with lumen-dwelling protozoan parasite, *Giardia*.
- Direct transmission by ingestion of cysts that are immediately infective when shed in feces.
- Trophozoites, motile (flagellated) organisms released from ingested cysts, attach to surface of enterocytes in small intestine with ventral sucking disc; move from site to site.
- Can cause small bowel diarrhea, but infection often asymptomatic.

SIGNALMENT

- Dogs—up to 50% for pups, up to 100% in kennels.
- Cats—up to 11%.

SIGNS

- Clinical signs more common in young hosts; older dogs, cats usually asymptomatic.
- Signs can be acute, transient, intermittent, or chronic.
- Malabsorption syndrome with soft, frothy, greasy, voluminous feces (diarrhea), usually with rancid odor.

CAUSES & RISK FACTORS

- Transmitted by ingestion of cysts from feces in/on food, water, environment, or fur.
- Indirect water-borne transmission most common; cool, moist conditions favor cyst survival.
- Higher risk of infection in puppies and kittens, in high-density populations (kennels, catteries, animal shelters), and in dogs/cats with compromised immunity.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other infectious and non-infectious causes of small bowel diarrhea, maldigestion, and malabsorption syndromes, especially pancreatic exocrine insufficiency, inflammatory bowel disease.
- In cats, differentiate from infection with *Tritrichomonas blagburni*, a cause of large bowel diarrhea.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Detection of *Giardia* trophozoites, cysts, or antigen in feces.
- Trophozoites ($15 \times 8 \mu\text{m}$) detectable in fresh feces, especially diarrhea, and in duodenal aspirates obtained by endoscopy; identify in smear stained with Diff-Quik or Lugol's iodine by teardrop shape, with two prominent nuclei and in wet mount of aspirate or small amount of feces in saline by "falling leaf" motility; flotation media lyse trophozoites.
- Cysts, $\sim 12 \mu\text{m}$ long, oval with 2–4 nuclei, shed intermittently; centrifugal flotation of fresh feces in zinc sulfate (s.g. 1.18) preferred method; examination of three samples collected at 2- to 3-day intervals detects > 70% of infections; cysts distorted (crescent-shaped) in sugar or other flotation solution with s.g. > 1.25; formalin-ethyl acetate sedimentation useful in cases of steatorrhea.
- Commercial ELISA-based test kits available for in-house detection of *Giardia* antigen in feces; have variable sensitivity compared to zinc sulfate centrifugal flotation; can detect asymptomatic infection. False-negative or -positive results can occur with all methods. It is recommended that the ELISA kits are used to confirm suspicious cases rather than as a screening tool in healthy animals.



TREATMENT

- Treat as outpatients unless debilitated or dehydrated.
- Drug therapy should be combined with environmental cleaning and disinfection plus bathing of patient to prevent infection.
- Giardia* vaccines commercially available. Efficacy is poor and the vaccine is not widely used.



MEDICATIONS

DRUG(S)

- All drug use is extra-label.
- Fenbendazole 50 mg/kg PO q24h for 3 days (dogs) or 5 days (cats); second course of treatment may be necessary.
- Metronidazole 20–22 mg/kg q12h for 5 days in dogs.
- Metronidazole benzoate 22–25 mg/kg PO q12h for 5–7 days in cats.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Metronidazole only 67% effective in dogs; bitter taste; can cause anorexia; vomiting, CNS signs.
- Albendazole (25 mg/kg PO q12h for 2 days in dogs or 5 days in cats) is effective but is not recommended because it can be teratogenic and/or cause anorexia, depression, vomiting, ataxia, diarrhea, abortion, or myelosuppression.



FOLLOW-UP

- Repeat fecal examinations to confirm efficacy of treatment and to detect reinfection.
- Chronic infection can lead to debilitation.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- In North America, *Giardia* is the most common intestinal parasite in humans.
- Molecular data indicates that dog and cat isolates are host-specific and there is little data to demonstrate transmission from dogs or cats to humans.
- Most *Giardia* infections in humans are zoonotic or originate from livestock.
- Risk of zoonotic transmission from pets to immunocompetent humans appears to be low but is likely increased for humans with compromised immunity.

PREGNANCY/FERTILITY/BREEDING

Do not use albendazole in pregnant dogs or cats; it can be teratogenic.

ABBREVIATIONS

- CNS = central nervous system
- ELISA = enzyme-linked immunosorbent assay

INTERNET RESOURCES

- <http://www.capcvet.org>
- <http://www.cdc.gov>

Suggested Reading

Bowman DD. Georgis' Parasitology for Veterinarians, 9th ed. St. Louis, MO: (Saunders) Elsevier Science, 2009, pp. 89–91.

Author Matt Brewer

Consulting Editor Stephen C. Barr

Acknowledgment The author and editors acknowledge the previous contribution of Julie Ann Jarvinen.

GINGIVAL HYPERPLASIA/ENLARGEMENT



BASICS

OVERVIEW

- Enlargement of gingival tissue due to proliferation of its elements (abnormal multiplication or increase in the normal number of cells in normal arrangement).
- Probable familial tendency—boxers.

SIGNALMENT

- Dogs and rarely cats. • Breed predilections—boxers, Great Danes, collies, Doberman pinschers, Dalmatians.

G

SIGNS

- Thickening and increase in height of attached gingiva and gingival margin—sometimes completely covers tooth surface.
- Resultant formation of “pseudopockets”—increase in pocket depth due to increased gingival height; not due to loss of attachment, unless untreated and progresses to concurrent periodontal disease. • Gingival margin may be symmetrically enlarged, especially at incisors.
- Locally affected areas possible (shelves), but typically more generalized pattern found.
- Focally affected areas, other than the marginal gingiva, may develop hyperplastic areas due to chronic irritation, such as the “gum chewer’s lesion.” These areas should be evaluated for therapeutic need (excision).
- May form as protuberant masses (grape cluster) at gingival margins—biopsy necessary to rule out neoplasia.

CAUSES

Chronic inflammatory response to presence of bacteria in plaque associated with periodontal disease.

RISK FACTORS

- Breed predilection (see “Signalment”).
- Chronic drug administration—diphenylhydantoin, cyclosporine, nitrendipine, nifedipine.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Presumptive diagnosis based on clinical appearance, especially if generalized and found in breed with high predilection. • Oral neoplasia—e.g., peripheral odontogenic fibromas; usually not generalized; sometimes osseous changes present. • Oral papillomatosis—papilloma usually on mucosal surfaces. • Operculum—seen in young animals during eruption phase of teeth; incomplete loss and/or persistence of gingival tissue covering erupting tooth.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

Intraoral radiography—to rule out any underlying osseous changes (more common with epulides or tumors).

DIAGNOSTIC PROCEDURES

- Biopsy—focal area or areas that do not respond to standard therapy.
- Histopathology—to rule out neoplasia and other causes; histologic evaluation is only way to confirm.



TREATMENT

APPROPRIATE HEALTH CARE

Regular dental cleanings and homecare—to minimize effects of plaque and bacterial accumulation.

CLIENT EDUCATION

- Chronic, recurring problem that often needs repeated therapy. • Encourage the highest level of homecare and regular professional cleaning.

SURGICAL CONSIDERATIONS

Gingivectomy (Excising Excess Tissue) and Gingivoplasty (Recontouring)

- To remove excess gingival tissue and return pocket depths to normal. • Provide appropriate patient monitoring and support during anesthetic procedures. • Regional and local anesthetic injections or topical gels.
- Periodontal probe—to determine depth of pseudopocket; can mark pocket depth on outside of pocket with end of probe (“dots”).
- Excise excess tissue and reshape gingival margin. • Cold steel—sharp, stout scissors or scalpel blade. • Connect the dots made by probe with blade to approximate normal gingival margin or use scissors, following pocket depth to remove bulk tissue.
- Twelve-fluted bur on high-speed handpiece—contour margin to feather angle; assists in hemostasis. • Electrocautery or radiosurgery—use fully or partially rectified current; avoid damage to underlying bone or tissue. • Laser—use appropriately and avoid damage to tooth and bone. • Excessive thickness (incisor and canine region)—modified Widman technique; envelop flap to lift gingiva off tooth surfaces; excise tissue wedge to remove gingiva at the inside of the pocket to provide a more narrow width of attached gingiva; suture interdentally to secure gingiva; use digital pressure to reposition.
- Tincture of myrrh and benzoin—use dropper; coat cut margins and dry; 4–5 layers.
- Hemostatic solutions—to aid in hemorrhage control as needed.



MEDICATIONS

DRUG(S)

- Oral antimicrobials—chlorhexidine; zinc ascorbate gel.
- Postoperative pain management.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Patients on chronic administration of diphenylhydantoin or cyclosporine may be predisposed to hyperplastic changes.



FOLLOW-UP

PATIENT MONITORING

- Post-operative comfort—give pain medication as needed. • Regular examinations and professional cleaning and treatment—to avoid recurrence, which is common.

PREVENTION/AVOIDANCE

Regular professional cleaning, meticulous homecare.

POSSIBLE COMPLICATIONS

- Possible exacerbation of periodontal disease in pseudopockets if left untreated; deeper pockets are more susceptible to anaerobic bacterial infections. • Excessive heat with electrosurgical treatment may result in damaged teeth (pulpitis, pulpal death) and alveolar bone.

EXPECTED COURSE AND PROGNOSIS

- Good prognosis with regular care.
- Recurrence common.



MISCELLANEOUS

SEE ALSO

Oral Masses

INTERNET RESOURCES

<http://www.avdc.org/Nomenclature.html>

Suggested Reading

Lobprise HB. Blackwell's Five-Minute Veterinary Consult Clinical Companion—Small Animal Dentistry. Ames, IA: Blackwell, 2007 (for additional topics, including diagnostics and techniques).

Wiggs RB, Lobprise HB. Veterinary Dentistry: Principles and Practice. Philadelphia: Lippincott-Raven, 1997.

Author Heidi B. Lobprise

Consulting Editor Heidi B. Lobprise



BASICS

DEFINITION

• High IOP that causes characteristic degenerative changes in the globe, optic nerve, and retina with subsequent loss of vision. • Diagnosis—IOP > 25–30 mmHg (dogs) or > 31 mmHg (cats) as determined via applanation, rebound, or Schiotz tonometry (using the 1955 Friedenwald human conversion chart that accompanies the Schiotz instrument) with changes in vision or the appearance of the globe, optic nerve, and/or retina.

PATOPHYSIOLOGY

• Develops when the normal outflow of aqueous humor is impaired. • May be result of primary eye disease (narrow or closed filtration angles and goniodysgenesis, which have a genetic predisposition). • May be secondary to other eye diseases (primary lens luxation, anterior uveitis, intraocular tumor, or hyphema).

SYSTEMS AFFECTED

Ophthalmic system (uncontrolled, glaucoma is a painful, blinding disorder).

GENETICS

Dogs—predisposing anomalous configuration of the filtration angles is thought to be inherited; mode of inheritance uncertain.

INCIDENCE/PREVALENCE

Dogs—more common in some breeds; overall incidence of primary glaucoma is more than 0.8% of all hospital admissions listed with the North American Veterinary Medical Data Base. The prevalence of secondary glaucoma in any breed is approximately 0.8% as listed in the NAVMDB.

SIGNALMENT

Species

• Dog—primary and secondary. • Cat—primary rare; secondary seen in patients with signs of long-standing uveitis or with lens luxation.

Breed Predilections

• Goniodysgenesis—Arctic circle breeds (e.g., Norwegian elkhound, Siberian huskie, malamute, Akita, Samoyed); Bouvier des Flandres; Basset hound; chow chow; Shar-Pei; spaniels (e.g., American and English cocker, English and Welsh springer). • Narrow filtration angles—spaniel; chow chow; Shar-Pei; toy breeds (e.g., poodle, Maltese, and Shih Tzu). • Secondary to lens luxations—terriers (e.g., Boston, cairn, Manchester, Dandie Dinmont, Norfolk, Norwich, Yorkshire, Scottish, Sealyham, West Highland white, Parson Jack Russell, and fox) and Shar-Pei.

Mean Age and Range

• Primary (dogs)—any age; predominantly affects middle-aged (4–9 years of age).

- Secondary to primary lens luxations (dogs)—usually affects young (2–6 years of age).
- Secondary to chronic uveitis (cats)—usually affects older cats (> 6 years).

SIGNS

General Comments

• Cannot be accurately diagnosed without instrument tonometry. • All well-equipped small animal hospitals should have a tonometer.

Historical Findings

• Acute angle closure—apparent pain (blepharospasm, tenderness about the head, serous to seromucoid discharge); may note a cloudy or red eye; unless bilateral, vision loss usually not noticed. • Secondary—depends on primary disease. • Uveitis—may note pain (for many days), scleral injection, and corneal edema. • Anterior lens luxation—may note acute pain, scleral injection, and corneal edema; may see lens in the anterior chamber (if corneal edema is not severe). • Chronic uveitis (cats)—may note no signs of pain; enlarged, seemingly painless eye or a dilated pupil common. • Globe enlargement—may be noticed first by owners.

Physical Examination Findings

Acute Primary

• High IOP (often > 30 mmHg). • Blepharospasm. • Enophthalmos. • Episcleral injection. • Diffuse corneal cloudiness. • Dilated pupil. • Vision loss—may be detected by lack of a menace or dazzle response and/or lack of a direct or consensual pupillary light reflex. • Optic nerve may be normal in appearance or may be depressed or cupped.

Chronic (End Stage)

• Globe enlargement (buphthalmos). • Descemet's streaks ("Haab's striae"). • Subluxated lens with an aphakic crescent. • Optic nerve head atrophy. • Retinal necrosis—detected by peripapillary or generalized tapetal hyper-reflectivity.

Uveitis Induced

• Elevated IOP. • Episcleral injection. • Corneal edema. • Inflammatory debris in the anterior chamber. • Miotic pupil (±). • Posterior synechia (±). • Iris bombe (±).

CAUSES

- Primary—filtration angle anomalies.
- Secondary—impediment to aqueous humor outflow (e.g., uveitis: inflammatory cells or debris; lens luxation: lens or attached vitreous; hyphema: RBCs; ocular tumors: neoplastic cells).

RISK FACTORS

- Anterior uveitis. • Lens luxation.
- Hyphema. • Intraocular neoplasia.
- Topically applied mydriatics—may precipitate acute glaucoma in predisposed animals.
- Primary glaucoma (dogs)—consider all cases to be bilateral, even if one eye is normotensive; evaluation of the

unaffected eye by a veterinary ophthalmologist for filtration angle anomalies is indicated to determine the risk for future glaucoma in unaffected eye.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- See Red Eye. • Conjunctivitis—IOP not high; pupil not dilated; conjunctival hyperemia a more diffuse, red discolored instead of episcleral vessel engorgement.
- Uveitis—initially IOP is subnormal or hypotensive; usually results in a miotic pupil.
- Tonometry—usually differentiates glaucoma from other causes of a red eye.

CBC/BIOCHEMISTRY/URINALYSIS

- Primary—typically normal. • Secondary—abnormalities consistent with the primary systemic disease (e.g., thrombocytopenia with hyphema).

OTHER LABORATORY TESTS

Serologic testing for infectious diseases—may help diagnose cause of uveitis.

IMAGING

• Thoracic radiography or abdominal ultrasonography (secondary disease)—may demonstrate systemic lesions consistent with fungal or neoplastic dissemination to the eye as a cause of uveitis or hyphema. • Ocular ultrasound (secondary disease)—may facilitate evaluation of the eye if the ocular media is opaque.

DIAGNOSTIC PROCEDURES

- Instrument tonometry—essential. • Acute disease—refer to a veterinary ophthalmologist for a detailed ocular examination of both eyes, including evaluation of the filtration angles (gonioscopy). • ERG—may help determine if affected eye is capable of vision restoration with medical and/or surgical treatment; normal tracing does not necessarily indicate that the eye will be visual; decreased amplitude or flat tracing guarantees that vision will not return despite treatment.

PATHOLOGIC FINDINGS

- Histopathologic evaluation may reveal collapse of the filtration angle. • Loss of retinal ganglion cells. • Photoreceptor disruption. • Gliosis and "cupping" of the optic nerve head.



TREATMENT

APPROPRIATE HEALTH CARE

- Acute (dogs)—inpatient medical care.
- After discharge—reevaluate every 1–2 days for 1 week to monitor for return of increased IOP.

GLAUCOMA

(CONTINUED)

CLIENT EDUCATION

- Warn client that primary glaucoma is a bilateral disease; more than 50% of dogs develop glaucoma in the other eye within 8 months without prophylactic therapy.
- Warn client that up to 40% of dogs will be blind in the affected eye within the first year regardless of therapy.

SURGICAL CONSIDERATIONS

- Primary and lens luxation—induced cases are best treated surgically. • Primary (dogs)—many patients undergoing medical treatment alone will be non-visual at the end of the first year. • Procedures—enhance aqueous humor outflow (filtration devices); decrease production of aqueous humor (e.g., Nd:YAG or diode laser transcleral cyclophotocoagulation; endoscopic diode cyclophotocoagulation; or transcleral cyclocryosurgery to cause ciliary body ablation); possibly endoscopic diode laser cyclophotocoagulation more effective in maintaining normal IOP and vision. Removal of anteriorly luxated lens may result in visual eye as well as help lower IOP. • Blind, painful eyes—enucleate; evisceration and intraocular prosthesis implantation (if no intraocular infection or neoplasia); intravitreal gentamicin or cidofovir injection; all to minimize long-term medical therapy.



MEDICATIONS

DRUG(S) OF CHOICE

Use multiple agents to lower IOP into the normal range as quickly as possible in an attempt to salvage vision.

Acute Primary (Dogs)

- Emergency medical treatment may include one or more of the following: • If available, first try the prostaglandin/miotic agents latanoprost 0.005% (Xalatan; q12h), travoprost 0.004% (Travatan; q12h), or bimatoprost 0.03% (Lumigan; q12h).
- Apply one drop to affected eye, followed by another drop in 30 minutes. If IOP not normal 2 hours following first application (or prostaglandin/miotic agents not available), use: • Hyperosmotic agents—mannitol (1–2 g/kg IV over 20 minutes) or glycerin (1–2 mL/kg PO q8–12h); will dehydrate the vitreous humor to lower IOP. • Miotic agents—2% pilocarpine solution (q6–12h); 0.25% demecarium bromide (available only from compounding pharmacies such as Wedgewood Pharmacy, 800–331–8272; q12h); enhance aqueous outflow. • Oral carbonic anhydrase inhibitor—methazolamide (2–4 mg/kg q8–12h); reduce production of aqueous humor. • ± topical carbonic anhydrase inhibitors—dorzolamide 2% (Trusopt; q8h), brinzolamide 1% (Azopt; q8h); reduce aqueous humor production. • ± Topical beta-adrenergic

antagonists—timolol maleate 0.5% (q12h), levobunolol 0.5% (q12h), betaxolol 0.5% (q12h); reduce aqueous humor production.

Anterior Lens Luxation or Uveitis Induced (Dogs)

- Treated like primary disease. • Miotic agents—do not use. • Topical corticosteroids—used to reduce inflammation if no ulcerative keratitis.

Chronic Smoldering Uveitis (Cats)

- Topical corticosteroids. • Topical beta-blockers. • Topical carbonic anhydride inhibitors.

CONTRAINdications

- Topical atropine—do not use. • Miotic agents—do not use with primary anterior lens luxation or uveitis. • Use only one miotic agent. • Use only one beta-antagonist. • Use only one carbonic anhydride inhibitor (topical or systemic).

PRECAUTIONS

- Topical pilocarpine—irritating; may cause conjunctivitis and painful brow ache; may worsen uveitis. • Systemic absorption of topical beta-antagonists—may cause bronchoconstriction and bradycardia in small dogs and cats. • Systemic carbonic anhydride inhibitors—cause metabolic acidosis and electrolyte imbalances seen as panting, weakness, disorientation, and/or behavioral change. • Osmotic diuretics—may initiate acute pulmonary edema in patients with compromised cardiovascular-pulmonary disease. • Glycerin—do not use with diabetes mellitus; causes hyperglycemia.

POSSIBLE INTERACTIONS

Demecarium bromide—cholinesterase inhibitor; may lead to organophosphate poisoning if used in conjunction with organophosphate parasiticide products.

ALTERNATIVE DRUG(S)

Other diuretics (furosemide, thiazides, etc.) will *not* reduce IOP.



FOLLOW-UP

PATIENT MONITORING

- IOP—monitored often (initially daily followed by weekly) and regularly after starting initial therapy; if a hypotensive level is maintained for many weeks, slowly taper drug therapy. • Monitor for drug reactions.

PREVENTION/AVOIDANCE

- Primary—bilateral disease; recommend that a veterinary ophthalmologist examine the unaffected eye to determine its risk of developing glaucoma. • Prophylactic therapy for the predisposed, unaffected eye—0.25% demecarium bromide (q24h, at bedtime or q12h) or 0.005% latanoprost (q24h, at bedtime) or 0.5% timolol maleate (q12h) or

2% dorzolamide (q8–12h); delays onset of glaucoma in second predisposed eye.

POSSIBLE COMPLICATIONS

- Blindness • Chronic ocular pain

EXPECTED COURSE AND PROGNOSIS

- Chronic disease that requires constant medical treatment (even with surgical intervention). • With medical treatment only—most patients ultimately go blind.
- Surgical treatment—better chance of retaining vision longer; most patients do not remain visual for more than 2 years after initial diagnosis. • Secondary to lens luxation—may carry a fair prognosis with successful removal of the luxated lens and postoperative medical therapy. • Secondary to anterior uveitis—may carry a fair prognosis with control of uveitis.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

- All listed drugs may affect pregnancy.
- Primary and lens luxation cases—herited; do not breed affected animals.

SEE ALSO

- Anterior Uveitis—Cats • Anterior Uveitis—Dogs • Red Eye

ABBREVIATIONS

- ERG = electroretinography • IOP = intraocular pressure

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Client Education Handout
available online

GLOMERULONEPHRITIS



BASICS

DEFINITION

- Inflammation and progressive dysfunction of glomeruli. Commonly a consequence of intraglomerular immune complex deposition; with or without inflammatory cell infiltration.
- “Glomerulonephritis” (GN) should not be used as an umbrella term for all glomerular diseases, as glomerular injury may be initiated and progress without inflammation.
- Circulating antigen-antibody complexes may be deposited or trapped within glomeruli. Alternatively, immune complexes may form within the glomerular capillary wall when circulating antibodies react with “planted” antigens. Immune complexes activate complement and induce leukocyte infiltration, platelet aggregation, and fibrin deposition, all of which may contribute to glomerular damage; urinary loss of serum proteins and macromolecules also contribute to progressive tubular damage.
- Progressive cellular proliferation and glomerular basement thickening may progress to glomerular hyalinization and sclerosis, nephron loss, and azotemic CKD.

SYSTEMS AFFECTED

- Renal/Urologic—initial proteinuria with few or no white or red blood cells. With progressive disease, azotemia and uremic CKD occur.
- Cardiovascular—edema and ascites secondary to hypoalbuminemia and sodium retention may develop. Hypertension is common. Hypercholesterolemia and hypercoagulability may result in thromboembolic disease.

GENETICS

- Familial GN has been reported in Bernese mountain dogs, Brittany spaniels, bull terriers, bullmastiffs, French mastiffs, Dalmatians, Samoyeds, Doberman pinschers, cocker spaniels, Newfoundlands, rottweilers, Pembroke Welsh corgis, beagles, and soft-coated Wheaten terriers.

INCIDENCE/PREVALENCE

Subclinical glomerular disease is common in dogs. Up to 90% of random-source dogs have glomerular lesions noted on necropsy.

SIGNALMENT

Species

Dog; less commonly, cat

Breed Predilections

- See “Genetics.” • Labrador and golden retrievers may be predisposed to *Borrelia burgdorferi*-associated GN and rapidly progressive renal failure.

Mean Age and Range

- Dogs—mean age at diagnosis, 6.5–8.5 years. Hereditary nephritis may result in proteinuria prior to 6 months of age.
- Cats—mean age at diagnosis, 4 years.

Predominant Sex

- Dogs—no gender predilection
- Cats—75% are males

SIGNS

General Comments

- Proteinuria is often first noted on routine health screenings or during evaluation of urine for other medical problems.
- Clients may seek veterinary care for animals due to underlying infectious, inflammatory, or neoplastic diseases responsible for initiating immune complex formation.

Historical and Physical Examination Findings

- Mild-to-moderate protein loss—proteinuria does not itself result in clinical signs. Nonspecific signs noted by clients may include lethargy or weight loss.
- Severe protein loss (i.e., serum albumin concentration < 1–1.5 g/dL)—may result in transudative edema and/or ascites.
- Once nephron loss progresses to azotemic renal failure, polyuria/polydipsia, anorexia, nausea, and vomiting may occur.
- Dogs with pulmonary thromboembolism (uncommon) may be presented for acute dyspnea or unexplained panting.
- Acute blindness in dogs secondary to retinal hemorrhage or detachment may occur with severe systemic hypertension (uncommonly recognized).

CAUSES

- True auto-immune GN, in which antibodies target a native renal antigen, is rarely found in dogs and cats.
- Numerous infectious and inflammatory diseases associated with glomerular immune complex deposition or formation (see below). In many dogs and cats, however, no antigen source can be identified, and glomerular disease is considered idiopathic. Diseases associated with glomerulonephritis include:
 - Dogs—*infectious diseases* (anaplasmosis, babesiosis, brucellosis, dirofilariasis, ehrlichiosis, hepatozoonosis, infectious canine hepatitis, leishmaniasis, pyometra, borreliosis, chronic bacterial infections such as endocarditis and discospondylitis, trypanosomiasis); *neoplasia*; *inflammatory diseases* (e.g., systemic lupus erythematosus); *endocrinopathies* (hyperadrenocorticism, diabetes mellitus, long-term administration of corticosteroids); *hereditary nephritides*; *miscellaneous causes* (sulfonamides).
 - Cats—*infectious diseases* (e.g., FeLV, FIP, FIV, *Mycoplasma polyarthritis*); *neoplasia*.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Proteinuria—commonly due to inflammation of the post-glomerular urinary tract (e.g., bacterial cystitis/pyelonephritis, urolithiasis, tubular renal failure, neoplasia). Lower urinary tract inflammation is usually (but not always) associated with active urine sediment. Hyperglobulinemia may result in proteinuria, particularly when the sulfosalicylic acid turbidimetric test is used for protein detection. Like glomerulonephritis, renal amyloidosis often causes severe proteinuria with inactive urine sediment. Renal biopsy is the only accurate method for differentiating the various glomerular disease subtypes.
- Hypoalbuminemia—may result from decreased albumin production (liver disease) or gastrointestinal loss (protein-losing enteropathies).

G

CBC/BIOCHEMISTRY/URINALYSIS

- CBC usually unremarkable.
- Hypoalbuminemia and hypercholesterolemia occur in severe cases.
- Persistent proteinuria with inactive urine sediment (although hyaline casts may be noted).
- Microalbuminuria oftentimes precedes overt proteinuria, and may allow early detection of glomerular damage.
- With progressive glomerular disease, biochemical changes consistent with renal failure develop. Azotemia may precede complete loss of urine concentrating ability.

OTHER LABORATORY TESTS

Urine Protein:Creatinine Ratio

- Confirms increased loss of urine protein, and quantifies magnitude of proteinuria.
- The urine protein:creatinine ratio (UPC) can be used to assess therapeutic response and progression or remission of glomerular disease.
- The UPC ratio may also decrease once progressive glomerular sclerosis results in renal failure, the UPC ratio may decrease.

Protein Electrophoresis

- Urine and serum protein electrophoresis may identify monoclonal gammopathies or urinary immunoglobulin light chains (Bence-Jones proteins) in patients with lymphoid malignancy.

IMAGING

May be helpful when screening for initiating inflammatory, neoplastic, or infectious diseases. Mild renomegaly may be observed.

DIAGNOSTIC PROCEDURES

- Permits differentiation of the various histologic subtypes of glomerular disease.

GLOMERULONEPHRITIS

(CONTINUED)

Biopsy results may influence treatment recommendations, and provide prognostic information. Renal biopsies should be considered only once less invasive tests (e.g., CBC, serum biochemistry profile, urinalysis, and quantitation of proteinuria (UPC)) have been completed, and if coagulation testing is normal. • Relative contraindications: a solitary kidney, thrombocytopenia or other coagulopathies, renal lesions associated with fluid accumulation (e.g., hydronephrosis and renal cysts and abscesses). • Biopsy-related complications are more likely in dogs or cats weighing < 5 kg, or with severe azotemia.

G

PATHOLOGIC FINDINGS

- Varying severity of GBM thickening (membranous) and increased mesangial cellularity (proliferative); glomerular scarring may be noted (glomerulosclerosis).
- Biopsy tissue should be placed in special fixatives and preservatives at the time of collection rather than in formalin. Immunofluorescent and/or immunohistochemical staining and electron microscopy maximize the information gained from evaluation of renal biopsies.



TREATMENT

DIET

Sodium-reduced, high-quality, low-quantity protein diets are usually recommended. Most prescription "renal" diets meet these criteria.

CLIENT EDUCATION

Once azotemia and uremia occur, prognosis is guarded to poor due to rapidly progressive disease.



MEDICATIONS

DRUG(S) OF CHOICE

- The most specific and effective therapy is elimination of any source of antigenic stimulation. In most dogs the initiating disease or antigen source cannot be definitively identified, or may be impossible to eliminate (e.g., neoplasia).
- ACE inhibitors reduce proteinuria by altering glomerular filtration pressure. Enalapril (0.5 mg/kg q12–24h) has antihypertensive and antiproteinuric effects and slows renal disease progression in dogs with naturally-occurring idiopathic GN. Because proteinuria is directly toxic to renal tubules, ACE-inhibitor therapy should be initiated at the time of initial disease diagnosis unless severe azotemia is present.
- No controlled

veterinary clinical trials have demonstrated a beneficial effect from immunosuppressive therapy, despite inflammation being a consequence of an inappropriately activated immune system. Glucocorticoids and cyclosporine have independently been shown to worsen proteinuria and prognosis in some patients.

- Aspirin decreases pro-inflammatory thromboxane production. Low-dose aspirin (0.5 mg/kg PO q12–24h) may decrease platelet aggregation and prevent reductions in beneficial prostaglandins. Aspirin therapy should be initiated once serum albumin is < 2.2–2.5 g/dL, or when serum antithrombin is known to be decreased (regardless of albumin concentration).

CONTRAINdicATIONS

Some glomerular disease subtypes, particularly membranous glomerulopathy prior to onset of azotemia, may favorably respond to immunosuppressive drugs. Biopsy is recommended prior to attempting immunosuppressive therapy. If a biopsy cannot be obtained, then immunosuppression can be considered in dogs with serum creatinine > 3.0 mg/dL, progressive azotemia, or severe (< 2.0 g/dL) hypoalbuminemia and inadequate responses to standard therapy alone.

PRECAUTIONS

- Dosages of highly protein-bound drugs and/or drugs eliminated by the kidneys (e.g., aspirin) may require adjustment.
- ACE inhibitors should be used cautiously in azotemic patients. Once serum creatinine is approx. > 3.5 g/dL, reduced ACE inhibitor doses should be considered. Serum creatinine should be monitored 4–7 days after dosage increase to evaluate the status of azotemia.



FOLLOW-UP

PATIENT MONITORING

- UPC—is the least invasive method to assess progression or remission of GN.
- Magnitude of proteinuria will also decrease as nephrons are lost to progressive disease, interpret changes in the UPC ratio in light of serum creatinine changes.
- Monitor serum urea nitrogen, creatinine, albumin, and electrolyte concentrations, blood pressure, and body weight at each evaluation.
- Ideal reexamination schedule in stable patients is 1, 3, 6, 9, and 12 months after initiation of treatment.

PREVENTION/AVOIDANCE

Do not breed animals with suspected familial disease.

POSSIBLE COMPLICATIONS

- Nephrotic syndrome
- Hypertension
- Chronic renal insufficiency or failure
- Thromboembolic disorders

EXPECTED COURSE AND PROGNOSIS

- Guarded to poor
- Often progress despite treatment



MISCELLANEOUS

SYNOMYMS

- Glomerulonephropathy
- Protein-losing nephropathy

SEE ALSO

- Amyloidosis
- Lyme Borreliosis
- Nephrotic Syndrome
- Proteinuria

ABBREVIATIONS

- ACE = angiotensin-converting enzyme
- CKD = chronic kidney disease
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- GBM = glomerular basement membrane
- RBC = red blood cell
- WBC = white blood cell

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Client Education Handout
available online

GLUCAGONOMA



BASICS

OVERVIEW

- Glucagonoma is an uncommon pancreatic islet cell tumor originating from the alpha cells, which secrete glucagon. Glucagonomas may secrete other hormones as well, such as gastrin, pancreatic polypeptide and in rare cases insulin.
- Excess circulating glucagon results in increased protein catabolism, lipolysis, gluconeogenesis, and glycogenolysis. The culmination of these biochemical changes results in hyperglycemia, hypoaminoacidemia, anemia, and weight loss. Glucagon can also exert a secretory effect on the small intestine, leading to diarrhea.
- Glucagonomas can affect numerous organ systems, including musculoskeletal, integumentary, endocrine, gastrointestinal, nervous/behavioral, and hepatobiliary.

SIGNALMENT

- Dog—rare; older animals
- Cat—no reports to date

SIGNS

- The hallmark sign is a characteristic dermatopathy most commonly called NME or necrolytic migratory erythema. This has also been reported in the veterinary literature as metabolic epidermal necrosis, superficial necrolytic dermatitis, hepatocutaneous syndrome, and diabetic dermatopathy.
- Skin lesions include erythema, erosions, and crusting generally located around mucocutaneous junctions (perineum, face, and genitalia), distal extremities, and footpads. Lesions are often pruritic with hyperkeratotic and painful footpads. In many cases, footpads are the only affected area.
- Other systemic signs may include lethargy, polyuria/polydipsia, diarrhea, secondary pyoderma and/or yeast infections, and weight loss.

CAUSES & RISK FACTORS

The etiology of glucagonoma is unknown; however, glucagonomas are commonly represented in multiple endocrine neoplasia syndrome.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Glucagonoma should always be added to the differential list when the presence of skin lesions consistent with NME is found; however, additional and more common differentials should include nonspecific liver disease and hypoaminoacidemia.
- Metabolic epidermal necrosis has been associated with diabetes, pancreatic tumors, and hepatic disease. Other dermatopathy

differentials include pemphigus foliaceus, systemic lupus erythematosus, vasculitis, food dermatoses, vitamin A responsive dermatosis, and zinc deficiency dermatopathy.

- It is important to note that mild-moderate hyperglucagonemia can be seen secondary to non-glucagonoma diseases such as liver disease, pancreatic disease, chronic renal failure, starvation, bacteremia, diabetic ketoacidosis, and hyperadrenocorticism.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—may be normal; however, normocytic, normochromic anemia and/or mature neutrophilia is common.
- Biochemistry—may be normal; however, mild liver enzyme and/or total bilirubin elevations with mild hyperglycemia and/or hypoalbuminemia may be noted.
- Bile acid and liver function tests are generally within normal limits.
- Urinalysis—decreased urine specific gravity is common. If secondary diabetes mellitus is present, glucosuria may be present.

OTHER LABORATORY TESTS

- Plasma glucagon levels are generally extremely elevated (i.e., > 1,000 pg/mL); however, normal to mildly elevated glucagon levels do not rule out glucagonoma.
- Plasma amino acid levels are generally severely reduced and are thought to be pathophysiologically associated with the development of NME.
- Zinc levels are generally reduced and are also thought to be pathophysiologically associated with the development of NME.
- Fructosamine may be elevated in patients with secondary diabetes mellitus.

IMAGING

- Ultrasonography—useful to detect pancreatic glucagonomas, peripancreatic metastases, and hepatic metastases.
- CT, MRI, PET scans, selective visceral angiography, and somatostatin receptor scintigraphy (octreoscan and radioiodinated MIBG) are used to increase glucagonoma detection sensitivity in humans

DIAGNOSTIC PROCEDURES

Increased blood serum glucagon and clinical signs consistent with NME are indicative of glucagonoma, but the definitive diagnosis can only be made by biopsy, histopathological examination, and documentation of immunohistochemical glucagon expression. Immunohistochemical assays for other pancreatic and gastrointestinal hormones are commonly performed.

DIAGNOSTIC PROCEDURES

- Skin biopsies taken from affected glucagon-associated NME lesions typically histopathologically exhibit severe superficial to mid-epidermal edema, diffuse parakeratotic hyperkeratosis, and irregular epidermal hyperplasia. This triad of histopathologic

findings is commonly referred to as a “red, white, and blue” pattern.

- Biopsies taken from the primary glucagonoma (and/or metastases) typically histopathologically exhibit pleomorphic islet cells with fine cytoplasmic granules and occasional mitoses with immunohistochemical glucagon expression (and often other secretory hormones).



TREATMENT

- Surgical excision of non-metastatic primary pancreatic glucagonoma represents the best chance for cure. Unfortunately, there is a high rate of post-operative morbidity and mortality reported in dogs. Furthermore, glucagonoma syndrome reported in people is associated with thromboembolic disease, which can further exacerbate morbidity and mortality.
- Combined debulking (primary tumor and/or metastases) and octreotide medical therapy can temporarily resolve skin lesions and provide relief.
- If surgery and/or octreotide therapy are not possible, symptomatic palliative therapies may be beneficial and include high-protein diet with egg whites (approximately two to four egg whites/day for a 25-kg dog), zinc supplementation (may be beneficial in the face of normal serum zinc levels) as outlined below, and fatty acid supplementation.
- Secondary bacterial and/or yeast skin infections are common and should be appropriately treated.



MEDICATIONS

DRUG(S)

- Octreotide, a somatostatin analog that inhibits the conversion of preproglucagon to glucagon, may be beneficial in patients with unresectable and/or metastatic glucagonoma. Side effects reported in human use include injection site pain, vomiting, diarrhea, and cholestasis. The safe and effective dosage of octreotide (or long-acting lanreotide) has not been reported in dogs; however, 10–20 µg/dog SC q8–12h has been reported, whereas a one-time safe dose of 50 µg/dog SC has been reported in healthy dogs.

- Chemotherapeutics have been utilized in human glucagonoma syndrome. Doxorubicin and streptozotocin appear to have the best, albeit, limited activity. The use of streptozotocin as an islet-cell lytic agent has been reported previously in a small number of dogs with insulinoma, but has not been reported in dogs with glucagonoma.

- Glucocorticoids may improve the secondary pruritis of the skin lesions in NME but are not recommended for use in glucagonomas as they are likely to exacerbate hyperglycemia,

GLUCAGONOMA

since many glucagonoma patients have secondary diabetes mellitus.

- Intravenous amino acids (500 mL of essential amino acids added to saline or lactated Ringer's solution given over 12 hours or 10% amino acid solution at 24 mL/kg given over 8–12 hours in a large central vein) have shown variable improvement in skin lesions in dogs. Treatments may be repeated every 1–2 weeks if effective until clinical signs abate or resolve.
- Sulfur/salicylic acid-based shampoos or very mild shampoos may help remove crusts, soften skin, and improve the pain and/or pruritus associated with footpad and/or skin lesions.
- Oral zinc sulfate 10 mg/kg/day or zinc methionine 2 mg/kg/day or zinc gluconate 3 mg/kg/day may be considered.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Glucocorticoids may exacerbate hyperglycemia if secondary diabetes mellitus is present.



FOLLOW-UP

- Serial blood work should be performed post-operatively to ensure the prior hyperglucagonemia (and any other abnormalities) is resolving and continues to be within normal limits.
- Strong considerations should be made for serial follow-up ultrasounds and three-view chest radiographs to monitor for metastasis.



MISCELLANEOUS

SEE ALSO

- Diabetic Hepatopathy
- Superficial Necrolytic Dermatitis

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging
- NME = necrolytic migratory erythema

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(CONTINUED)

GLUCOSURIA



BASICS

DEFINITION

Positive, semiquantitative urine glucose concentration detected via routine laboratory tests (e.g., reagent test strips). Low concentrations normally present (2–10 mg/dL in humans) are undetectable using routine screening tests. Persistent glucosuria (via screening tests) is abnormal (pathologic).

PATHOPHYSIOLOGY

- Glucose is freely filtered through the glomerular capillaries; therefore, blood and glomerular filtrate have equivalent glucose concentrations.
- Glucose is actively reabsorbed from the proximal renal tubular lumen by sodium-glucose linked transporters in the epithelial cell brush border. Physiologic levels of filtered glucose are mostly removed during health with excreted levels too low to detect using screening tests).

Hyperglycemic Glucosuria

- Glucosuria will be present when plasma glucose concentration exceeds the renal tubular epithelial transport maximum (T_m) (approximately 170–180 mg/dL for dogs, 260–310 mg/dL for cats). If hyperglycemia is present, determine whether glucosuria is transient or persistent.

Transient

- Physiologic—usually transient and associated with release of endogenous “stress” hormones (catecholamines, glucagon, glucocorticoids); especially common in cats. Serum may be normoglycemic or hyperglycemic at urine collection because different concentrations of glucose excreted in urine over time equilibrate in the bladder.
- Pharmacologic—may occur following administration of glucose-containing solutions (e.g., dextrose, total parenteral nutrition). Some hormones (adrenocorticotrophic hormone, glucocorticoids, glucagon, adrenaline, progesterone) and drugs (epinephrine, morphine, phenothiazine, xylazine in cats, diazoxide, l-asparaginase) may cause glucosuria.
- Toxic—ethylene glycol.
- Pathologic—possible with acute pancreatitis.

Persistent

Pathologic—diabetes mellitus, hyperadrenocorticism (\pm), pheochromocytoma, glucagonoma, acromegaly, progesterone (endogenous or exogenous), extreme stress, chronic liver disease, \pm CNS lesions.

Normoglycemic Glucosuria

- Impaired renal proximal tubular epithelial cell reabsorptive capacity.

Congenital

Primary glucosuria, following an overnight fast (Scottish terriers).

Fanconi syndrome (basenji dogs; also sporadic in Norwegian elkhounds, Shetland sheepdogs, miniature schnauzers, Labrador retrievers, border terriers, whippets, Yorkshire terriers, and mixed-breed dogs); decreased reabsorption of glucose, amino acids, and phosphorus plus decreased secretion of hydrogen ions.

Acquired

- Fanconi syndrome due to toxicity such as heavy metal poisoning (lead, mercury, cadmium, uranium or copper associated hepatitis) or dried chicken treats made in China, drugs (gentamicin, cephalosporins, outdated tetracycline, cisplatin, streptozotocin, amoxicillin), chemicals (Lysol, maleic acid).
- Acute renal failure with significant tubular lesions (\pm).

SYSTEMS AFFECTED

- Renal/Urologic—normoglycemic patients have abnormal renal tubular epithelial cell function. Dogs with Fanconi syndrome may develop metabolic acidosis and CKD with secondary multisystem involvement. Glucosuria predisposes to bacterial urinary tract infection.
- Endocrine—hyperglycemic patients may have diabetes mellitus and/or hyperadrenocorticism.
- Liver—copper associated hepatitis; centrilobular hepatitis with copper accumulation, increased serum ALT and ALP; \pm total bilirubin; decreased albumin, urea nitrogen, fasting ammonia concentrations, prolonged hemostasis testing.

SIGNALMENT

- Frequently adult dogs and cats develop persistent hyperglycemic glucosuria due to adult onset diabetes mellitus.
- Dogs with congenital Fanconi syndrome typically develop clinical disease due to defective reabsorption of glucose and amino acids at 4–5 years of age; males and females are equally affected.
- Familial renal tubular disorders have been reported (see “Pathophysiology”).
- Primary renal glucosuria (Scottish terriers) may be recognized at an early age as an incidental finding.
- Copper associated hepatitis with acquired Fanconi syndrome (Labrador retrievers).
- Dogs (any breed or age) fed dried chicken treats made in China.

SIGNS

Clinical signs are variable depending upon the primary cause.

Historical Findings

- Persistent glucosuria results in polyuria (osmotic diuresis), leading to compensatory polydipsia.
- Glucosuria predisposes to urinary tract infections; resultant signs are associated with upper and/or lower urinary tract infection.
- Breed (see “Pathophysiology”) and therapeutic history (see “Pathophysiology”) are important.

Physical Examination Findings

- Patients with hyperglycemic glucosuria may exhibit systemic signs; see Diabetes Mellitus chapters.
- Patients with normoglycemic glucosuria may have normal body functions.

- Dogs with Fanconi syndrome may develop signs of metabolic acidosis, electrolyte abnormalities, and CKD.

CAUSES

Hyperglycemic Glucosuria

Transient

- Physiologic—stress; common in cats
- Pharmacologic—see “Pathophysiology”

Persistent

- Diabetes mellitus (100% of patients); insulin deficiency or resistance.
- Hyperadrenocorticism (5–10% of patients); insulin resistance.
- Acute pancreatitis (\pm); insulin deficiency.
- Other less common causes—CNS lesions, pheochromocytoma, increased growth hormone concentration due to increased progesterone (endogenous or exogenous) or acromegaly, glucagonoma, chronic liver failure (due to failure to metabolize glucagon).

Normoglycemic Glucosuria

Congenital

- Primary renal glucosuria (Scottish terrier).
- Fanconi syndrome (see “Pathophysiology”).
- Congenital diseases may be associated with renal dysfunction (Norwegian elkhound).

Acquired

- Acute renal failure associated with significant proximal tubular lesions
- Fanconi syndrome (see “Pathophysiology”)
- CKD (rare)

RISK FACTORS

Vary with underlying causes



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Persistent hyperglycemic glucosuria in fasted patients is frequently associated with endocrinopathies (diabetes mellitus, hyperadrenocorticism).
- Acute pancreatitis.
- Renal tubular reabsorptive dysfunctions cause normoglycemic glucosuria.
- Stressed patients frequently exhibit mild transient hyperglycemia and glucosuria.

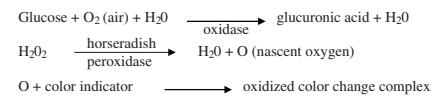
LABORATORY FINDINGS

Screening Tests

Normally negative (urine glucose concentration below detection).

Glucose Oxidase Tests

- Specific for glucose; more sensitive (~40–100 mg/dL) than copper reduction methods.



- Glucose oxidase, peroxidase, and a color indicator are impregnated into reagent test strips; react specifically with glucose at room

GLUTEN ENTEROPATHY IN IRISH SETTERS



BASICS

OVERVIEW

A rare inherited disease in which there is a predisposition to develop a sensitivity to dietary gluten present in wheat and other grains. In affected dogs, there is villous atrophy, reduced brush border enzyme expression, lymphocytic infiltration of the intestinal mucosa, and goblet cell hyperplasia.

SIGNALMENT

- Irish setter breed.
- Signs develop in young to middle-aged dogs.
- Genetic transmission of gluten sensitive enteropathy is likely under the control of a single major autosomal recessive locus.
- Gluten enteropathy has not been reported in other dog breeds or in cats.

SIGNS

- Poor weight gain (or weight loss)
- Poor body condition
- Mild small intestinal diarrhea that can be intermittent
- Variable vomiting

CAUSES & RISK FACTORS

The enteropathy and clinical signs are exacerbated by gluten-containing diet.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Inflammatory bowel disease
- Infectious diseases such as *Giardia*, hookworms, and roundworms
- Metabolic abnormalities
- Exocrine pancreatic insufficiency

CBC/BIOCHEMISTRY/URINALYSIS

- Biochemistry can be unremarkable or may show panhypoproteinemia
- CBC may show eosinophilia

OTHER LABORATORY TESTS

- Serum folate concentrations are subnormal in some patients, reflecting chronic malabsorption in the jejunum.
- Other tests are recommended to rule out other differentials, such as fecal flotation to rule out enteric parasites and serum trypsin-like immunoreactivity to rule out exocrine pancreatic insufficiency.
- Serum TLI and cobalamin concentrations are usually unremarkable.

IMAGING

Not useful

DIAGNOSTIC PROCEDURES

Intestinal biopsy specimens (jejunal) obtained via endoscopy or laparotomy.

PATHOLOGIC FINDINGS

- Histologic examination of jejunal biopsy specimens from affected dogs reared on a wheat-containing diet reveals partial villus atrophy and accumulation of intraepithelial lymphocytes.
- Jejunal abnormalities improve following gluten withdrawal but recur with gluten challenge.



TREATMENT

Treatment is on an outpatient basis. Avoid diets containing gluten (wheat, rye, barley, triticale, brewers yeast, and wheat starch for the life of the animal).



MEDICATIONS

DRUG(S)

Folate (0.5–2 mg PO q24h for 2–4 weeks) if serum folate concentration is markedly subnormal (< 4 µg/L).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A

G



FOLLOW-UP

Consider periodic assay of serum folate (q6–12 months)



MISCELLANEOUS

ABBREVIATION

- TLI = trypsin-like immunoreactivity

Suggested Reading

Cave N. Adverse food reactions. In: Washabau RJ, Day MJ, eds., Canine and Feline Gastroenterology. St. Louis: Elsevier, 2013, p. 403.

Hall EJ, German AJ. Diseases of the small intestine. In: Ettinger SJ, Feldman EC, eds., Textbook of Veterinary Internal Medicine, 7th ed. St. Louis: Elsevier, 2010, p. 1557.

Author Krysta Deitz

Consulting Editor Stanley L. Marks

GLYCOGEN STORAGE DISEASE



BASICS

OVERVIEW

- Also known as glycogenoses: rare inherited disorders of defective or deficient enzyme activity governing glycogen metabolism.
- Tissue glycogen accumulation—leads to organ enlargement and dysfunction; may affect liver, heart, skeletal muscle, kidney, and CNS.
- Impaired hepatic glycogenolysis—leads to symptomatic hypoglycemia (neuroglycopenia).
- Classification—based on enzymatic defect and primary organ(s) involvement: more than 12 types in humans, four types in dogs (Ia, II, III, and VII), 1 type in cats (IV).

SIGNALMENT

- Clinical signs manifest in juveniles—may be days to months after birth.
- Type Ia (von Gierke's disease)—Maltese puppies. Autosomal recessive mutation of glucose-6-phosphatase gene (gene symbol: *G6PC*).
- Type II (Pompe's disease)—Swedish Lapland, Finnish and Swedish Lapphund dogs; onset by 6 months of age. Autosomal recessive, single mutation in acid α -glucosidase (gene symbol: *GAA*).
- Type III (Cori's disease)—young female German shepherds, curly-coated retrievers. Autosomal recessive mutation in glycogen debranching enzyme (gene symbol: *AGL*).
- Type IV (Andersen disease)—Norwegian forest cats; may be stillborn or fade shortly after birth; may manifest signs at 5–7 months with progressive neurologic decline. Autosomal recessive mutation in glycogen branching enzyme (complex rearrangement mutation (gene symbol *GBE1*)).
- Type VII (Tarui disease)—English Springer, American Cocker, whippets, mixed breeds; PFK (M-PFK) muscle isoform single missense mutation; different missense mutation in Wachtelhunds. Adult dogs, no sex predilection.
- Autosomal recessive inheritance—Maltese, Lapland, Lapphund, English Springer spaniels, Norwegian forest cats, other M-PFK affected breeds; also suspected in German shepherds.

SIGNS

- Depend on enzymatic defect.
- Type Ia (Maltese puppies)—failure to thrive; mental depression; hypoglycemia; abdominal distention; hepatomegaly; death or euthanasia by 60 days of age.
- Type II (Lapland dogs)—vomiting and regurgitation related to megaesophagus; progressive muscle weakness; cardiac changes; death before 2 years of age.
- Type III (German shepherds, curly-coated retrievers)—depression; weakness; stunted; abdominal distention from hepatomegaly; mild hypoglycemia, high liver enzymes and CK.
- Type IV (Norwegian forest cats)—perinatal death common; intermittent fever; generalized muscle tremors; muscle atrophy;

weakness progressing to tetraparesis; sudden death from myocardial degeneration and terminal dysrhythmia. Glucose administration can enable cats to survive to adulthood.

- Type VII (English Springer spaniels)—compensated hemolytic anemia; episodic weakness, exercise-induced with intravascular hemolysis; hemoglobinuria; one patient with a progressive myopathy at 11 years of age—no liver effect.

CAUSES & RISK FACTORS

Deficiencies

- Type Ia—glucose-6-phosphatase
- Type II—acid- α -glucosidase
- Type III—amylo-1,6-glucosidase
- Type IV—glycogen branching enzyme (α -1,4-d-glucan)
- Type VII—phosphofructokinase



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- High index of suspicion for diagnosis.
- Breed affiliation—familial history.
- Differentiate other causes of juvenile hypoglycemia—malnutrition; endoparasitism; transient fasting hypoglycemia; portosystemic vascular anomaly.
- Other causes of muscular weakness—infectious diseases; endocrinopathy; immune-mediated causes; hypokalemia; other neuromyopathies.

CBC/BIOCHEMISTRY/URINALYSIS

- Types I and III—hypoglycemia
- Type I: lactic acidemia, increased cholesterol, triglycerides, uric acid
- Type VII—anemia; reticulocytosis; pigmenturia, no hepatic effects

OTHER LABORATORY TESTS

Genetic testing: type I—in Maltese dogs, type II: in Lapland and Lapphund dogs, type III in curly-coated retrievers, type IV in Norwegian forest cats, type VII in breeds listed previously and *in vitro* erythrocyte testing.

IMAGING

- Type II—thoracic radiography; cardiomegaly and megaesophagus.
- Types Ia and III—abdominal radiography; hepatomegaly.
- Abdominal ultrasonography—hepatomegaly, hyperechoic parenchyma consistent with hepatic glycogen accumulation.
- Types II and IV—echocardiography may reveal cardiac changes.

DIAGNOSTIC PROCEDURES

- Tissue enzyme analysis and glycogen determination
- Electromyography—depends on disorder
- Electrocardiography—depends on disorder
- Genetic testing

PATHOLOGIC FINDINGS

- Type Ia—emaciation; massive hepatomegaly due to hepatocyte glycogen and lipid vacuolation and similar change in renal tubular epithelium.
- Type II—glycogen

accumulation in skeletal, smooth, and cardiac muscle.

- Type III—hepatomegaly due to hepatic glycogen accumulation; also in skeletal muscle.
- Type IV—generalized muscle atrophy; glycogen accumulation: skeletal muscle, CNS, and peripheral nervous system.
- Type VII—polysaccharide deposits in skeletal muscle.



TREATMENT

NURSING CARE

- Supportive care.
- Types I and III—may require intravenous or SC dextrose for management of hypoglycemic crisis; long-term management usually futile.
- Gene therapy with adeno-associated virus vector experimentally survived type 1a dogs.

DIET

Control hypoglycemia (types I and III) with frequent feedings of a high-carbohydrate diet until diagnosis is confirmed; glucose solutions usually used.

CLIENT EDUCATION

- Advise that specimens be submitted for genetic/enzyme characterizations.
- Discuss known mechanisms of inheritance to modify breeding programs.



MEDICATIONS

DRUG(S)

N/A



FOLLOW-UP

- Monitor for hypoglycemia.
- Cull parents from breeding programs.
- Prognosis—poor; most patients with glycogen storage disorders causing hypoglycemia and hepatomegaly and stunted growth die or are euthanized owing to progressive deterioration.



MISCELLANEOUS

SEE ALSO

- Lysosomal Storage Disease
- Mucopolysaccharidoses
- Portosystemic Vascular Anomaly, Congenital

ABBREVIATIONS

- CK = creatine kinase
- CNS = central nervous system

Suggested Reading

Walvoort HC. Glycogen storage disease type II in the Lapland dog. Vet Q 1985; 7:187–190.

Author Sharon A. Center

Consulting Editor Sharon A. Center

GLYCOGEN-TYPE VACUOLAR HEPATOPATHY



BASICS

DEFINITION

- Glycogen-type vacuolar hepatopathy (VH)—reversible hepatocellular cytosolic vacuolation.
- Reflects many primary disorders including: glucocorticoid treatment, hyperadrenocorticism, atypical adrenal hyperplasia (sex hormone hyperplasia), chronic systemic illnesses (inflammatory, neoplastic), and rarely, congenital glycogen storage disorders.
- Typified by high ALP activity—usually without hyperbilirubinemia or hepatic insufficiency.
- Similar but remarkably severe VH in hepato-cutaneous disease (See Diabetic Hepatopathy); may reflect chronic phenobarbital administration.
- Glycogen VH may coexist with cytosolic lipid vacuolation—comparatively rare in dogs but may associate with: idiopathic hyperlipidemia, diabetes mellitus, hypothyroidism, and rare inborn errors of glycogen/lipid metabolism.

PATOPHYSIOLOGY

- Glucocorticoids—induce reversible increase in hepatocyte glycogen within 2–3 days; injectable or topical drug induces most severe VH compared to PO or topical (ocular, cutaneous, aural) routes.
- Cell expansion—causes hepatomegaly; ballooning degeneration leads to parenchymal collapse; when severe, nodularity grossly mistaken for cirrhosis.
- Variable response to glucocorticoids among dogs relates to: (1) drug type, (2) route, (3) dose, (4) treatment duration, (5) individual sensitivity; VH may follow low-dose, short-term oral treatment.
- VH may reflect: stress response, cytokines, or acute-phase response initiated by non-hepatic systemic disorders or neoplasia (especially lymphoma), without exogenous glucocorticoid exposure or adrenal disease.
- VH common in dogs with gallbladder mucocele.

SYSTEMS AFFECTED

- Hepatobiliary—normal hepatic function usually; severe degenerative VH can lead to hepatic dysfunction, jaundice, ascites, and liver failure.
- All systems affected by steroid hormones or a primary systemic disease.

INCIDENCE/PREVALENCE

- Dogs—common, often accompanies primary necroinflammatory liver disorders.
- Cats—rare; liver vacuolation with triglyceride accumulation more common (see Hepatic Lipidosis).

SIGNALMENT

Species

Dog; rarely cat

Breed Predilections

Breeds predisposed to hyperadrenocorticism develop glycogen VH (e.g., miniature poodles, Dachshunds, Boxers, Boston terriers), Scottish terriers (sex hormone adrenal hyperplasia, hyperlipidemia), and others with hyperlipidemia (miniature Schnauzers, Shetland sheepdogs) may develop mixed glycogen/lipid VH.

Mean Age and Range

- Middle-aged to old dogs—spontaneous hyperadrenocorticism ($> 75\%$ older than 9 years); chronic systemic inflammation or neoplasia.
- Dogs of any age—iatrogenic VH subsequent to glucocorticoid administration.
- Young dogs or cats—genetic glycogen storage disease.

SIGNS

General Comments

- Reflect glucocorticoids or underlying systemic illness.
- Rarely, signs of hepatic disease or failure; hepatic failure can develop with severe chronic VH.
- HE observed in some dogs with hepato-cutaneous syndrome (see Diabetic Hepatopathy).

Historical Findings

- Glucocorticoid excess—polyuria and polydipsia; polyphagia; endocrine alopecia; abdominal distention: weak muscles, loss of elasticity; skeletal muscle weakness; excessive panting; lethargy; friable skin; bruising tendencies; urinary tract infections, may be asymptomatic; corneal ulcer.
- Adrenal sex hormone hyperplasia—may display some signs of glucocorticoid excess but often fewer and less severe; endocrine alopecia may be the only sign; some dogs remain asymptomatic except for chronic progressive marked ALP activity and degenerative VH.
- Other causes—depend on system affected; chronic phenobarbital may cause severe VH.
- Sex hormone hyperplasia causing VH may increase risk for dysplastic hepatic foci and hepatocellular carcinoma (e.g., Scottish terriers).

Physical Examination Findings

- Hepatomegaly.
- Relate to steroid hormone excess or underlying disease; depends on severity and duration.

CAUSES

- Glucocorticoid administration.
- Typical hyperadrenocorticism (spontaneous).
- Atypical adrenal hyperplasia—overproduction of cortisol precursor sex hormones (spontaneous).

- Systemic disease provoking acute-phase response or stress—e.g., severe dental disease, inflammatory bowel disease, chronic pancreatitis, systemic neoplasia (especially lymphoma), chronic infections (urinary tract, skin), hypothyroidism, many others.

RISK FACTORS

- Pharmacologic doses of glucocorticoids.
- Breeds at risk for hyperadrenocorticism.
- Breeds at risk for hyperlipidemia—often also demonstrate combined glycogen VH: miniature Schnauzers, Shetland sheepdogs, Beagles.
- Dogs receiving chronic phenobarbital.

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DIAGNOSIS

DIFFERENTIAL DIAGNOSES

- Other diffuse hepatopathies (especially those causing hepatomegaly and increased ALP activity)—passive congestion; neoplasia (primary or metastatic to liver); necroinflammatory liver disease; anticonvulsant hepatopathy; hepatomegaly due to amyloid (rare).
- VH distinguishing features—most dogs have fold increase in ALP $>$ ALT or AST; increased cholesterol, normal serum bilirubin; normal/mild increase in TSBA; heterogeneous or homogeneous hyperechoic hepatic parenchyma on ultrasonography (nodules or “Swiss cheese” pattern); characteristic cytology: hepatocytes engorged due to expanded “rarefied” cytoplasm.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Depends on underlying disease
- Non-regenerative anemia—anemia of chronic disease or hypothyroidism
- Relative polycythemia—steroid excess
- Stress leukogram—hyperadrenocorticism; glucocorticoid exposure; stress of illness
- Thrombocytosis—neoplasia; hyperadrenocorticism; splenic disease

Biochemistry

- ALP markedly increased; ALP glucocorticoid isoenzyme cannot differentiate cause of VH as other liver disorders also induce this isoenzyme; variable GGT, ALT, AST activity.
- Serum albumin and total bilirubin—usually normal; high bilirubin usually implicates another hepatobiliary or hemolytic process.
- Hypercholesterolemia: hyperadrenocorticism, sex hormone adrenal hyperplasia; breed-related hyperlipidemias; hypothyroidism; pancreatitis; nephrotic syndrome.

OTHER LABORATORY TESTS

- ALP glucocorticoid isoenzyme—see above, lacks specificity and thus, clinical utility.
- TSBA—may be modestly increased; ammonia tolerance test—usually normal.

GLYCOGEN-TYPE VACUOLAR HEPATOPATHY

(CONTINUED)

- Pituitary adrenal axis—ACTH-response test or LDDST, \pm HDDST, and endogenous ACTH may help differentiate non-adrenal illness, adrenal or pituitary disorders.
- Urine cortisol:creatinine ratio—at-home urine collection helps rule out hyperadrenocorticism; high ratio may reflect stress or non-adrenal illness.
- Adrenal ultrasound imaging: nodules, adrenomegaly; consider dog size and age.
- If VH confirmed (liver biopsy) and underlying cause not evident, patient asymptomatic or symptomatic for adrenal disease: assess cortisol and sex hormone panel with ACTH response test.
- Thyroid testing—rules out hypothyroidism.
- Triglycerides (fasting)—hyperlipidemia.
- cPLI—may indicate “sub-clinical” pancreatic inflammation or inflammatory bowel disease.

IMAGING

- Abdominal radiography—reveals hepatomegaly or other underlying conditions.
- Thoracic radiography—may reveal lymphadenopathy, metastatic disease, cardiac or pulmonary disorders.
- Abdominal ultrasonography—discloses hepatomegaly, diffuse hyperechoic hepatic parenchyma or multifocal nodular “mottling”; multifocal lesions suggest nodules (“Swiss cheese pattern”) formed by progressive hepatocellular ballooning degeneration; may disclose underlying primary visceral abnormalities (e.g., mesenteric lymphadenopathy, neoplasia) or adrenal disorders (size/shape): adrenals may be large with hyperadrenocorticism, sex hormone adrenal hyperplasia, chronic stress or neoplasia.

DIAGNOSTIC PROCEDURES

- Hepatic fine-needle aspiration cytology—22 gauge, 2.5–3.75 cm (1–1.5 in.) US-guided needle aspiration; target nodules and normal parenchyma.
- Cytology—glycogen vacuolation is common in many primary liver disorders. Used to rule out vacuolar change; cannot definitively confirm illness caused only by VH.
- Hepatic biopsy—verifies VH; excludes other primary hepatic disease; pursue if a systemic disorder is not discovered explaining high ALP and VH; use US-guided Tru-Cut needle biopsy to confirm VH but may miss primary hepatic disease, laparoscopy (recommended), or laparotomy (if visceral inspections and biopsies indicated).
- Cytologic features—hepatocellular cytosolic distention: “rarefaction” or granular appearance with increased cell fragility; canalicular bile casts may be observed; primary VH is not associated with inflammatory infiltrates; common association with extramedullary hematopoiesis (EMH) may be misinterpreted as suppurative inflammation.

- Tissue culture and sensitivity—if suppurative inflammation suspected, submit aerobic and anaerobic bacterial cultures.
- Coagulation assessments—PT, aPTT, fibrinogen, and mucosal bleeding time: usually normal; bench assessments have low predictive value in predicting iatrogenic hemorrhage; buccal mucosal bleeding time may be more relevant.

PATHOLOGIC FINDINGS

- Gross—variable; normal to moderate hepatomegaly; inconsistent surface irregularity; tan or pale color; confusion with cirrhosis if nodular severe degenerative VH.
- Microscopic—marked vacuolization and ballooning of hepatocytes; no consistent zonal distribution, foci of hepatic degeneration; focal aggregates of neutrophils due to EMH; severe degenerative VH leads to parenchymal collapse forming nodules surrounded by a thin partition with minimal collagen deposition.



TREATMENT

DIET

- Hyperlipidemia or pancreatitis—restrict dietary fat and fatty supplements.
- Obesity—gradual energy restriction; treat predisposing disorders.

SURGICAL CONSIDERATIONS

- Depends on underlying conditions.
- Adrenal masses may be resected.
- Hypophyseal masses—resection only by experienced surgeons; pituitary mass lesions may respond to radiation therapy.



MEDICATIONS

DRUG(S) OF CHOICE

- Depends on underlying disease.
- Pituitary-dependent hyperadrenocorticism or adrenal hyperplasia syndrome (sex hormone)—usually treated medically: op'-DDD (mitotane or Lysodren), trilostane or ketoconazole; op'-DDD preferred for sex hormone adrenal hyperplasia as Trilostane augments sex hormone accumulation; l-deprenyl and melatonin ineffective.
- Manage primary inflammatory disorders necessitating immunosuppressive or anti-inflammatory medications—use polypharmacy to minimize glucocorticoid exposure (see “Alternative Drugs”) if symptomatic or progressive VH.
- Neoplasia—tumor resection, chemotherapy or radiation, as appropriate.
- Dental disease—antibiotics and dentistry.
- IBD—hypoallergenic/hydrolyzed protein diets and immunomodulation (avoid glucocorticoids).

- Pyelonephritis, chronic dermatitis, or other infectious disorders—long-term antimicrobial treatment based on microbial culture and sensitivity tests; other appropriate medications.
- Hypothyroidism—supplemental thyroxine.

CONTRAINdications

- Avoid hepatotoxic drugs if severe VH.
- Beware of drug interactions if using ketoconazole for adrenal disease.
- Avoid drugs with hepatic ALP induction effects.

PRECAUTIONS

Glucocorticoids—caution in VH patients; use lowest effective dose regimen (e.g. alternate-day protocol if prednisone or prednisolone); special caution in hyperlipidemia: may worsen clinical signs of abdominal pain, vomiting, pancreatitis; increases insulin requirements in diabetes mellitus; may augment gallbladder mucocele formation; may provoke hepatic lipidosis in cats.

ALTERNATIVE DRUG(S)

Polypharmacy protocol—may reduce glucocorticoid usage in management of immune-mediated or inflammatory disorders; e.g. metronidazole, azathioprine, chlorambucil, cyclophosphamide, mycophenolate, or cyclosporine.



FOLLOW-UP

PATIENT MONITORING

- Hepatomegaly—abdominal palpation; imaging
- Normalizing enzymes—biochemistry
- Adrenal function—ACTH stimulation tests
- Neoplasia—physical exams and imaging
- Control of infection—repeat cultures
- Hyperlipidemia—assess gross plasma lipemia; measure triglycerides and cholesterol

PREVENTION/AVOIDANCE

- Limit glucocorticoid exposure.
- Use alternate-day therapy with prednisone/prednisolone; titrate to lowest effective dose; use alternative medications to control primary illness.

POSSIBLE COMPLICATIONS

Numerous—related to multisystemic effects of glucocorticoids and associated conditions.

EXPECTED COURSE AND PROGNOSIS

- Most patients are asymptomatic for VH despite high ALP; however, progressive degenerative hepatopathy leading to diffuse nodule formation and hepatic insufficiency may develop in chronic VH in dogs with high ALP activity.
- Laboratory and pathologic features reversible before degenerative parenchymal collapse.

(CONTINUED)

GLYCOGEN-TYPE VACUOLAR HEPATOPATHY

- Dogs with sex hormone hyperplasia, VH, and dysplastic hepatocellular foci appear at risk for development of hepatocellular carcinoma.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Pulmonary thromboembolism and myopathy due to hyperadrenocorticism
- Pancreatitis associated with hyperlipidemia
- Gallbladder mucocele

PREGNANCY/FERTILITY/BREEDING

Reproductive failure with glucocorticoid excess—testicular atrophy; abnormal estrus

SYNOMYS

- Glucocorticoid hepatopathy
- Steroid hepatopathy
- Corticosteroid hepatopathy
- Vacuolar change

SEE ALSO

- Diabetic Hepatopathy
- Hyperadrenocorticism (Cushing's Disease)—Cats
- Hyperadrenocorticism (Cushing's Disease)—Dogs
- Hyperlipidemia
- Gallbladder Mucocele

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- aPTT = activated partial thromboplastin time
- AST = aspartate aminotransferase
- cPLI = canine pancreatic lipase immunoreactivity
- EMH = extramedullary hematopoiesis
- GGT = gamma glutamyltransferase
- HDDST = high-dose dexamethasone suppression test

- LDDST = low-dose dexamethasone suppression test
- PT = prothrombin time
- TSBA = total serum bile acids
- US = ultrasonography
- VH = vacuolar hepatopathy

Suggested Reading

Corthright CC, Center SA, Randolph JF, et al. Clinical features of progressive vacuolar hepatopathy in Scottish Terriers with and without hepatocellular carcinoma: 114 cases (1980–2013). *J Am Vet Med Assoc* 2014; 245:797–808.

Sepesy LM, Center SA, Randolph JF, et al. Vacuolar hepatopathy in dogs: 336 cases (1993–2005). *J Am Vet Med Assoc* 2006; 229:246–252.

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G



**Client Education Handout
available online**

GRAPE, RAISIN, AND Currant Toxicosis



BASICS

OVERVIEW

Syndrome resulting from ingestion of grapes, raisins, sultanas, or Zante currants (*Vitis vinifera*).

SIGNALMENT

- Dogs are the only species in which toxicosis has been well described.
- No breed, sex, or age predisposition noted.
- Anecdotal reports of toxicosis in cats and ferrets exist, but data are lacking to confirm.

SIGNS

- Vomiting within 24 hours of ingestion; vomitus frequently contains ingested fruit.
- Diarrhea, anorexia, lethargy, and abdominal pain may occur.
- Within 24 hours to several days, dehydration with oliguria or anuria occurs.
- Death due to anuric renal failure or euthanasia.

CAUSES & RISK FACTORS

- Although amounts of raisins and grapes reported to cause toxicosis lie in the range 2.8–9.6 g/kg and 11–31 g/kg, respectively, a minimum toxic dose has not been established. Additionally, not all exposures of dogs to *Vitis vinifera* have resulted in clinical evidence of renal injury.
- Ingestion of sultanas, Zante currants, and other varieties of *Vitis vinifera* has also been associated with renal injury in dogs, but amounts associated with toxicosis have not been reported.
- Mechanism of toxicity and toxic principle are unknown. Inconsistent development of clinical signs resulting from ingestion of *Vitis vinifera* may reflect idiosyncratic reactions of individual dogs or a toxic principle that is of variable presence in the fruit due to variances in growing conditions.
- Until further toxicity data are available, all exposures of dogs to *Vitis vinifera* should merit veterinary attention.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other causes of acute renal failure—ethylene glycol, heavy metal toxicosis, nephrotoxic antibiotics (e.g., aminoglycosides), nonsteroidal anti-inflammatory drug

toxicosis, hemoglobinuria, myoglobinuria, leptospirosis, borreliosis, and vitamin D toxicosis.

CBC/BIOCHEMISTRY/URINALYSIS

- Hypercalcemia, hyperphosphatemia, high creatinine and blood urea nitrogen may develop within 24–48 hours of ingestion. Elevated creatinine and hyperphosphatemia tend to develop first, followed by elevation of BUN with calcium elevation tending to increase 48–72 hours after exposure. Differentiate from vitamin D₃ toxicosis, where calcium and phosphorus elevate first followed by elevations in BUN and creatinine as kidney injury develops.
- Hyperkalemia, hyperamylasemia, hyperlipasemia, and elevated ALT have also been reported.
- Isothrenuria, hyposthenuria, proteinuria, hematuria, and glucosuria have been reported.
- Granular casts may occur in the urine.

OTHER LABORATORY TESTS

Histopathology of kidneys reveals acute diffuse renal tubular degeneration and necrosis.



TREATMENT

- Gastrointestinal decontamination (induction of emesis, administration of activated charcoal) should follow ingestion of grapes or raisins by dogs.
- Fluid diuresis (2–3 times maintenance) for minimum of 48 hours is recommended, longer if renal failure develops. Fluid choice may vary with circumstance, but 0.9% NaCl is most commonly recommended.
- Monitor serum chemistry values, particularly renal values, for minimum of 72 hours, longer if renal failure develops.
- Correct fluid imbalances (e.g., dehydration).
- Monitor fluid in/out.
- Diuretics (e.g., furosemide, mannitol, dopamine) if oliguria or anuria develop.
- Hemodialysis or peritoneal dialysis may be required in anuric patients.



MEDICATIONS

DRUG(S)

- Emetics—3% hydrogen peroxide 2.2 mL/kg up to a maximum of 45 mL/dog

PO; may repeat once if first dose unsuccessful; apomorphine crushed and diluted with sterile saline and instilled in conjunctival sac, rinse eye after emesis, or 0.03 mg/kg IV.

- Activated charcoal—1–3 g/kg PO.

Management of Oliguric or Anuric Renal Failure

- Mannitol 0.25–0.5 g/kg of 20–25% solution IV over 15–20 minutes, repeat q4–6h or administer as CRI of 8–10% solution for 12–24 hours.
- Furosemide 2 mg/kg IV, repeat at 4 mg/kg if no diuresis within 1 hour; use with dopamine for best results.
- Dopamine 0.5–3 µg/kg/minute.

CONTRAINdications/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- In dogs developing renal insufficiency, monitor renal values until they return to normal.
- Some dogs may develop irreversible renal injury requiring lifelong management.
- Evidence of pancreatitis developed in 3 of 43 dogs with acute renal injury following *Vitis vinifera* ingestion.



MISCELLANEOUS

ABBREVIATION

ALT = alanine aminotransferase

INTERNET RESOURCES

Client education article (The Wrath of Grapes) at
http://www.aspca.org/sites/pro/files/grapes_3.pdf

Suggested Reading

Eubig PA, Brady MS, Gwaltney-Brant S, et al. Acute renal failure in dogs after ingestion of grapes or raisins: A retrospective evaluation of 43 dogs (1992–2002). J Vet Intern Med 2005, 19:663–674.

Mostrom MS. Grapes and raisins. In: Peterson M, Talcott PA, eds., Small Animal Toxicology, 3rd ed. St. Louis, MO: Saunders, 2006, pp. 569–572.

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HAIR FOLLICLE TUMORS



BASICS

OVERVIEW

- Two main types—trichoepithelioma/trichoblastoma, which arise from keratinocytes in the outer root sheath of the hair follicle (\pm hair matrix); and pilomatrixoma, which arises from the hair matrix.
- Both types—generally benign; a few published reports of malignant pilomatrixomas.
- Approximately 5% of all skin tumors in dogs, uncommon in cats.

SIGNALMENT

- Dog and cat.
- Age—usually > 5 years.
- No sex predisposition.
- Trichoepithelioma—common in dogs; rare in cats; golden retrievers, basset hounds, German shepherds, cocker spaniels, Irish setters, English springer spaniels, miniature schnauzers, and standard poodles may be predisposed; Persian and Siamese cats.
- Pilomatrixoma—uncommon in dogs and cats; Kerry blue terriers and miniature poodles may be predisposed; no known breed predisposition in cats.

SIGNS

- Usually a solitary mass.
- Trichoepithelioma—common on the lateral thorax and dorsal lumbar area (dogs) and head (cats).
- Pilomatrixoma—common on the back, shoulders, flanks, tail, and limbs.
- Firm, round, elevated, well-circumscribed, often hairless, or ulcerated dermoepithelial masses; cut surface gray (trichoepithelioma) or lobulated with white chalky areas (pilomatrixoma).

CAUSES & RISK FACTORS

Unknown, some genetic predisposition



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Distinguish from other tumors including basal cell tumor, squamous cell carcinoma, and keratoacanthoma, and from epidermal inclusion cysts.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Fine-needle aspiration and cytopathology
- Tissue biopsy and histopathology

PATHOLOGIC FINDINGS

- Fine-needle aspiration cytology—basaloid and ghost cells suggestive of pilomatrixoma in dogs.
- Trichoepithelioma—varies in degree of differentiation and site of origin (root sheath or hair matrix); horn cysts, lack of desmosomes, and differentiation toward hair follicle-like structures and formation of hair common.
- Pilomatrixoma—characterized by a variable proliferation of basophilic cells resembling hair matrix cells and fully keratinized, faintly eosinophilic cells with a central unstained nucleus (shadow cells); calcification common. Features of malignancy are present with the occasional malignant pilomatrixoma.



TREATMENT

Complete excision—curative with most cases



MEDICATIONS

DRUG(S)

- Isotretinoin (1 mg/kg q24h PO) was used to successfully control multiple pilomatrixomas in one dog.
- Multimodal analgesia recommended for painful lesions.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- Monitor for local recurrence.
- Prognosis usually excellent; multiple reports of metastatic disease with the less common canine malignant pilomatrixomas.



MISCELLANEOUS

Suggested Reading

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Author Louis-Philippe de Lorimier
Consulting Editor Timothy M. Fan

H

HALITOSIS



BASICS

DEFINITION

An offensive odor emanating from the oral cavity.

PATHOPHYSIOLOGY

- The sour milk odor accompanying periodontal disease may result from bacterial populations associated with plaque, calculus, unhealthy oral cavity tissues, decomposing food particles retained within the oral cavity, and tissue necrosis.
- Contrary to common belief, neither normal lung air nor stomach aroma contributes.
- The most common cause is periodontal diseases caused by plaque bacteria.
- A bacterial biofilm forms over a freshly cleaned and polished tooth as soon as the patient starts to salivate; bacteria attach to the pellicle within 6–8 hours; within days, the plaque becomes mineralized, producing calculus; as plaque ages gingivitis may progress into periodontitis (tooth support loss), the bacterial flora changes from a predominantly non-motile gram-positive aerobic coccoid flora to a more motile, gram-negative anaerobic population including *Prophyromonas*, *Bacteroides*, *Fusobacterium*, and *Actinomyces* spp.

- The rough surface of calculus attracts more bacteria, irritating the free gingiva; as the inflammation continues, the gingival sulcus is transformed into a periodontal pocket, which accumulates food debris and bacterial breakdown products, creating halitosis.
- The primary cause of malodor is gram-negative anaerobic bacteria that generates volatile sulfur compounds, such as hydrogen sulfide, methyl mercaptan, dimethyl sulfide, and volatile fatty acids.
- Volatile sulfur compounds may also play a role in periodontal disease, affecting the integrity of the tissue barrier, allowing endotoxins to produce periodontal destruction, endotoxemia, and bacteremia.

SYSTEMS AFFECTED

Gastrointestinal—oral cavity

SIGNALMENT

Species

Dogs and cats

Breed Predilections

Small breeds and brachycephalic breeds are more prone to oral disease because the teeth

are closer together, smaller animals live longer, and their owners tend to feed softer food.

Mean Age and Range

Older animals are predisposed.

SIGNS

- If due to oral disease, ptyalism (with or without blood), pawing at mouth, anorexia may occur.
- In most cases, no clinical signs other than the odor.

CAUSES

- Eating malodorous food.
- Metabolic—diabetes, uremia.
- Respiratory—rhinitis, sinusitis, neoplasia.
- Gastrointestinal—megaeosophagus, neoplasia, foreign body.
- Dermatologic—lip-fold pyoderma.
- Dietary—fetid foodstuffs, coprophagy.
- Oral disease—periodontal disease and ulceration, orthodontic, pharyngitis, tonsillitis, neoplasia, foreign bodies.
- Trauma—electric cord injury, open fractures, caustic agents damaging oral cavity.
- Infectious—bacterial, fungal, viral infections of oral cavity.
- Autoimmune diseases of oral cavity.
- Eosinophilic granuloma complex.



DIAGNOSIS

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal. Might see changes consistent with diabetes mellitus or renal disease.

IMAGING

Intraoral radiographs are appropriate to help diagnose causes of halitosis.

DIAGNOSTIC PROCEDURES

- Hydrogen sulfide, mercaptans, and volatile fatty acids are the primary components of halitosis; an industrial sulfide monitor can be used to measure sulfide concentration in peak parts per billion.
- Use of OraStrip QuickCheck Canine provides a quick, point-of-care test that detects thiols produced by the anaerobic bacterial that cause periodontal disease and provides results in the exam room, within 10 seconds.
- Other diagnostic procedures to evaluate periodontal disease include intraoral radiography, probing pocket depths, attachment levels, and tooth mobility.



TREATMENT

APPROPRIATE HEALTH CARE

- Once the specific cause of halitosis is known, direct therapy at correcting existing pathology. Often multiple teeth are extracted when advanced periodontal disease is the cause of halitosis.

CLIENT EDUCATION

- Halitosis is generally a sign of unhealthy oral cavity and should prompt oral assessment under general anesthesia, treatment, and prevention. Initiate preventive measures to ensure good oral health (e.g., twice daily brushing and/or wiping teeth).

SURGICAL CONSIDERATIONS

Oral assessment performed under general anesthesia with intraoral radiographs, treatment including extraction of teeth with greater than 50% support loss.



MEDICATIONS

DRUG(S) OF CHOICE

- Antibiotics are not indicated to treat halitosis.
- Controlling periodontal pathogens helps control dental infections and accompanying malodor. When accompanied by follow-up homecare, has been shown to decrease pocket depth.
- Weekly application of a plaque-retardant gel, has been shown to decrease plaque.
- The use of oral care products that contain metal ions, especially zinc, inhibits odor due to the affinity of the metal ion to sulfur; zinc complexes with hydrogen sulfide to form insoluble zinc sulfide; zinc interferes with microbial proliferation and calcification of microbial deposits (by interfering with the crystal development of calculus). Topical treatment with zinc ascorbate cysteine gel usually reduces halitosis within 30 minutes.



FOLLOW-UP

PATIENT MONITORING

Evaluate for recurrence of signs.

(CONTINUED)

HALITOSIS**PREVENTION/AVOIDANCE**

Daily brushing or friction wipes to remove plaque and control dental disease and odor; periodic veterinary examinations to monitor care.

EXPECTED COURSE AND PROGNOSIS

Varies with underlying cause.

**MISCELLANEOUS****SYNONYMS**

- Bad breath
- Fetor ex ore
- Fetor oris
- Foul breath
- Malodor

SEE ALSO

Periodontal Diseases

Suggested Reading

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Author Jan Bellows

Consulting Editor Heidi B. Lobprise



Client Education Handout available online

H

HEAD PRESSING



BASICS

DEFINITION

Compulsive pressing of the head against a wall or other object for no apparent reason.

PATHOPHYSIOLOGY

- Alterations in behavior—caused by lesions in the prosencephalon (i.e., cerebrum, limbic system, thalamus, and hypothalamus), particularly those affecting the limbic system and frontal and temporal cortices.
- Lesions may result in compulsive pacing; when an obstacle (e.g., a wall) is reached, the animal may press its head against it for long periods of time, apparently unable to turn and move away.
- Apparent inability to voluntarily move away—may reflect impaired integration of sensory information, leading to inappropriate behavior.

SYSTEMS AFFECTED

Nervous

GENETICS

N/A

INCIDENCE/PREVALENCE

N/A

SIGNALMENT

Dogs and cats of any age, breed, and sex

SIGNS

- Head pressing—just one sign of prosencephalic disease.
- Compulsive pacing and circling toward the side of the lesion; circling can be toward either side if lesion is centrally located.
- Change in learned behavior.
- Seizures.
- Contralateral postural reaction deficits.
- Contralateral visual deficits with normal pupillary light reflexes.
- Contralateral facial hypalgesia.

CAUSES & RISK FACTORS

- Anatomic—hydrocephalus, most commonly in young toy-breed dogs; lissencephaly (Lhasa apso).
- Metabolic—hepatic encephalopathy as a result of a portosystemic shunt or severe hepatic disease; severe hyper- or hyponatremia.
- Nutritional—very unusual since most pets are fed compounded diets; thiamin deficiency can occur in cats fed a diet of raw fish, if thiamin supplementation in canned food is insufficient or in cats with severe malabsorptive syndromes; however, vestibular signs predominate.
- Neoplastic—primary (e.g., glioma, meningioma) or metastatic (e.g., hemangiosarcoma) tumors affecting the brain; more common in older animals (> 6 years).
- Immune-mediated/inflammatory—granulomatous meningoencephalitis;

necrotizing encephalitides (Maltese encephalitis, pug encephalitis); meningoencephalitis of unknown etiology.

- Infectious (dogs)—viral (rabies virus, canine distemper virus), rickettsial (*Ehrlichia canis*, Rocky mountain spotted fever), protozoal (*Toxoplasma gondii*, *Neospora caninum*), or fungal (*Blastomyces*, *Cryptococcus*); rabies is of particular importance because neurons in the limbic system are frequently infected in carnivores.
- Infectious (cats)—viral (rabies, feline infectious peritonitis, feline leukemia virus [associated immunosuppression predisposes to other encephalitides and neoplasia], feline immunodeficiency virus [can cause encephalopathy primarily and can predispose to other encephalitides and neoplasia due to immunosuppression]); *Bartonella henselae*; *Cuterebra* migration; toxoplasmosis; *Cryptococcus* and other fungal infections.
- Toxic—e.g., lead poisoning.
- Trauma.
- Vascular—intracranial hemorrhage as a result of hypertension (consider in older cats with hyperthyroidism, diabetes or chronic renal insufficiency); bleeding disorder (either primary or secondary to rodenticide toxicity); ischemia (feline ischemic encephalopathy or secondary to systemic metabolic, inflammatory, or neoplastic disease).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

A newly blind animal might bump into objects, but rapidly recognizes his environment and acts visual; an animal with prosencephalic lesion continues bumping into objects despite normal ocular exam.

CBC/BIOCHEMISTRY/URINALYSIS

- May reflect a metabolic or toxic cause.
- Hepatic encephalopathy—decreased serum albumin, blood urea nitrogen, cholesterol, and glucose concentrations, with or without elevated ALP, ALT, and bilirubin concentrations; microcytic anemia may be present; ammonium biurate crystals may be present in the urine.
- Lead toxicity—basophilic stippling of erythrocytes; presence of reticulocytes and nucleated RBCs in the absence of anemia.
- Encephalitis—findings often unremarkable, but may reflect an inflammatory process (e.g., with fungal infection).
- CNS lymphoma—may see evidence of bone marrow involvement.

OTHER LABORATORY TESTS

- Bile acid tolerance—to diagnose hepatic encephalopathy; blood ammonia concentrations may also be elevated.
- Acute and convalescent serologic titers—to diagnose rickettsial, protozoal, fungal, and viral diseases; for some infections (e.g., canine

distemper virus, *Toxoplasma*, *Cryptococcus*), also measure CSF antibody or antigen (*Cryptococcus*) titers.

- Polymerase chain reaction on CSF and serum—to diagnose rickettsial, bacterial, protozoal, fungal, and viral diseases; sensitive and specific if the infectious agent is present in CSF or serum.
- Blood lead concentration—to diagnose lead toxicity.

IMAGING

- Thoracic radiography—recommended for older patients to identify metastatic disease.
- Abdominal ultrasonography—recommended for older patients if intra-abdominal neoplasia is suspected; indicated if a portosystemic shunt or other hepatic disease is suspected.
- Rectal scintigraphy—may be used to definitively diagnose a portosystemic shunt.
- Brain CT or MRI—to identify intracranial masses, malformations, skull fractures, inflammation, and hemorrhage.
- Ultrasonography of the brain via persistent fontanels—may be used to diagnose hydrocephalus in young dogs.

DIAGNOSTIC PROCEDURES

- Fundic examination—to identify chorioretinitis (evidence of infectious/inflammatory disease) and vascular lesions.
- Blood pressure measurement to identify hypertension.
- CSF analysis—to diagnose encephalitis.

PATHOLOGIC FINDINGS

Findings at necropsy will reflect the etiology.



TREATMENT

APPROPRIATE HEALTH CARE

- Severe clinical signs—hospitalization for diagnostic workup and treatment.
- Suspected rabies—quarantine outdoor animal with no vaccination or unknown vaccination history when rapidly progressive neurologic signs are present and animal lives in a rabies-endemic area; minimize the number of people in contact with the animal, and maintain a contact log; if neurologic signs deteriorate rapidly, euthanize the animal and send it to a public health laboratory to be tested for rabies.

NURSING CARE

- When hospitalized, patients should be monitored closely for deterioration in mental status and for seizures.
- Maintenance intravenous fluids may be necessary for patients with severe prosencephalic syndrome.
- The cage may need to be padded to avoid self-trauma if constantly head pressing and pacing.

(CONTINUED)

HEAD PRESSING**H**

- Eyes should be monitored regularly for development of corneal ulcers due to self-induced trauma.
- Central intravenous catheters should be placed in the saphenous vein rather than the jugular vein if possible, to avoid increasing intracranial pressure by occlusion of the jugular veins.

ACTIVITY

N/A

DIET

- Suspected hepatic encephalopathy—appropriate low-protein diet.
- Hand-feeding may be necessary in severely encephalopathic patients; risk of aspiration if the patient fails to prehend and swallow correctly.

CLIENT EDUCATION

- Specific to the underlying condition.
- Clients should be warned about the possibility of seizures, be provided with a description of a seizure and instructions on what to do if a seizure occurs.
- Clients should be provided with a description of signs of acute decompensation due to brain herniation.

SURGICAL CONSIDERATIONS

- If signs are due to intracranial disease, elevated intracranial pressure is likely and therefore there is a risk of herniation during anesthesia, with induction and recovery from anesthesia posing the highest risk. Patients should be ventilated carefully to ensure that their partial pressure of carbon dioxide remains within normal limits (35–45 mmHg).
- Hydrocephalus can be treated by placement of a ventriculo-peritoneal shunt.
- Brain neoplasia, in particular extra-axial tumors such as meningiomas, can be treated surgically if tumor location accessible.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Different causes require different treatment; do not initiate therapy until a diagnosis has been established.
- If patient's mental status deteriorates suggesting impending brain herniation, mannitol (0.25–1 g/kg IV over 10–30 minutes) or hypertonic saline (4 mL/kg of 7.5% or 5.3 mL/kg of 3%) can be used to transiently reduce intracranial pressure; treatment can be repeated but recurrent use will simply result in dehydration.
- Furosemide (0.7 mg/kg IV) given prior to administration of mannitol can complement the use of mannitol and prolong its effect.

CONTRAINdications

N/A

PRECAUTIONS

Sedatives should be used with caution in patients exhibiting head pressing because they prevent assessment of mental status changes and might suppress respiratory drive, causing an increase in pCO_2 and thus causing an increase in intracranial pressure.

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

- Periodic repeat neurologic examinations to monitor progress
- See specific diseases

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

N/A

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

- Rabies should be considered in endemic areas.
- Fungal infections may be zoonotic if spores are released; most likely to occur if exudative skin lesions are present.

SEE ALSO

- Brain Injury
- Encephalitis
- Hepatic Encephalopathy
- Hydrocephalus

ABBREVIATIONS

- ALP = alanine phosphatase
- ALT = alanine aminotransferase
- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- MRI = magnetic resonance imaging
- RBC = red blood cell

INTERNET RESOURCES

http://www.ivis.org/advances/Vite/braund1/chapter_frm.asp?LA=1#Cerebral_Syndrome.

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Author Natasha J. Olby

Consulting Editors Joane M. Parent

HEAD TILT



BASICS

DEFINITION

Tilting of the head away from its normal orientation with the trunk and limbs; usually associated with disorders of the vestibular system.

PATHOPHYSIOLOGY

- Vestibular system—coordinates position and movement of the head with that of the eyes, trunk, and limbs by detecting linear acceleration and rotational movements of the head; includes vestibular nuclei in the rostral medulla of the brainstem, vestibular portion of the vestibulocochlear nerve (CN VIII), and receptors in the semicircular canals of the inner ear.
- Head tilt—most consistent sign of diseases affecting the vestibular system and its projections to the cerebellum, spinal cord, cerebral cortex, reticular formation, and extraocular muscles (via medial longitudinal fasciculus); usually ipsilateral to the lesion.

SYSTEMS AFFECTED

Nervous—peripheral or CNS

SIGNS

- Ensure that abnormal head posture is true head tilt and not a head turn; i.e., turning of the head and neck to the side as if to turn in a circle.
- Head tilt may not be present if disease is bilateral.

CAUSES

Peripheral Disease

- Anatomic—congenital head tilt.
- Metabolic—hypothyroidism; pituitary chromophobe adenoma; paraneoplastic disease.
- Neoplastic—nerve sheath tumor of CN VIII; neoplasia of the bone and surrounding tissue (e.g., osteosarcoma, fibrosarcoma, chondrosarcoma, and squamous cell carcinoma).
- Inflammatory—otitis media and interna; primarily bacterial but also parasitic (e.g., *Otodectes*), and fungal; foreign body; nasopharyngeal polyp(s).
- Idiopathic—canine geriatric vestibular disease; feline idiopathic vestibular disease.
- Immune-mediated—cranial nerve neuropathy.
- Toxic—aminoglycosides, lead, hexachlorophene.
- Traumatic—fracture of tympanic bulla or petrosal bone; ear flush.

Central Disease

- Degenerative—storage disease; demyelinating disease; vascular event.
- Anatomic—hydrocephalus.
- Neoplastic—glioma, choroid plexus papilloma, meningioma, lymphoma, nerve sheath tumor, medulloblastoma, skull tumor (e.g., osteosarcoma); metastasis (e.g., hemangiosarcoma, melanoma).
- Nutritional—thiamin deficiency.
- Inflammatory, infectious—viral (e.g., FIP, canine distemper); protozoal (e.g., toxoplasmosis, neosporosis); fungal (e.g., cryptococcosis, blastomycosis, histoplasmosis, coccidioidomycosis, nocardiosis); bacterial (e.g., extension from otitis media and interna); parasitic (e.g., *Cuterebra* larvae); rickettsial (e.g., ehrlichiosis); algae (protothecosis).
- Inflammatory, non-infectious—granulomatous meningoencephalomyelitis, breed-specific meningoencephalitis (e.g., necrotizing encephalitis).
- Trauma—fracture petrosal bone with brainstem injury.
- Toxic—metronidazole.

• Inflammatory, non-infectious—granulomatous meningoencephalomyelitis, breed-specific meningoencephalitis (e.g., necrotizing encephalitis).

• Trauma—fracture petrosal bone with brainstem injury.

• Toxic—metronidazole.

RISK FACTORS

- Hypothyroidism
- Administration of ototoxic drugs
- Metronidazole treatment
- Thiamin-deficient diet
- Otitis externa, media, and interna



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Vestibular Disease

- Unilateral disease—head tilt usually toward side of the lesion; usually accompanied by other vestibular signs, e.g., abnormal nystagmus (resting, positional) with fast phase usually in the direction opposite the tilt, ventral deviation of the eye (vestibular strabismus) ipsilateral to the tilt observed with elevation of the head; ataxia and disequilibrium with tendency to fall, lean, and/or circle toward the side of the tilt.
- Bilateral disease—head tilt may be absent or mild on the more severely affected side; abnormal nystagmus may be present; physiologic nystagmus (e.g., normal vestibular nystagmus) may be depressed or absent; may have wide side-to-side swaying movements of the head (especially evident in cats); may have wide-based stance or a crouched posture with reluctance to move.
- Head tilt—localizes to peripheral (e.g., vestibular portion of cranial nerve VIII or receptors in the inner ear) or central (e.g., vestibular nuclei and their neuronal pathways) nervous system.
- Peripheral deficits—horizontal or rotatory nystagmus with fast phase opposite the head tilt; possible concomitant ipsilateral facial nerve paresis or paralysis and/or Horner's syndrome, and/or decreased tear production because of the close association of CN VIII with CN VII and the sympathetic nervous system in the petrosal bone and tympanic bulla.
- Central deficits—vertical, horizontal, or rotatory nystagmus that can change direction with position of the head; altered mentation; ipsilateral paresis and/or proprioceptive deficits; central signs related to cerebellum, rostral medulla, and pons; in some patients, multiple CN involvement.
- Paradoxical vestibular syndrome—with lesions in the caudal cerebellar peduncles, or flocculonodular lobes of cerebellum; vestibular signs (e.g., head tilt, nystagmus)

contralateral to the lesion whereas the cerebellar signs and proprioceptive deficits are ipsilateral to the lesion.

Non-vestibular Head Tilt and Head Posture

- Uncommon.
- Must differentiate from true vestibular head tilt.
- Unilateral midbrain lesions can cause severe rotation of the head (> 90°) toward the side opposite the lesion; no other vestibular signs; tilt corrects when patient is blindfolded.
- Adversive syndrome—observed with rostral thalamic or frontoparietal lobe lesions; head turn, neck curvature, and/or compulsive circling can be misinterpreted as vestibular deficits; may have postural reaction, menace, and/or sensory deficits that are contralateral to the lesion; compulsive turning is usually in large circles and without the disequilibrium and true head tilt of vestibular disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal
- Mild anemia—hypothyroidism
- Leukocytosis with neutrophilia—otitis media and interna
- Thrombocytopenia—ehrlichiosis
- Hypercholesterolemia—hypothyroidism
- High serum globulin concentration—FIP

OTHER LABORATORY TESTS

- T_4 , free T_4 , FT_4 , E_QD, and endogenous TSH levels—if hypothyroidism is suspected based on physical examination and associated unilateral or bilateral involvement of CN VIII and possibly VII.
- Bacterial culture and sensitivity—sample from myringotomy or surgical drainage of tympanic bulla if otitis media/interna is suspected.
- Microscopic examination of ear swab—parasites (e.g., *Otodectes*).
- Serologic testing—*infectious causes* (e.g., canine distemper; FIP; protozoal, fungal, rickettsial diseases).

IMAGING

- Radiographs of tympanic bullae and skull—normal radiographs do not rule out bulla disease.
- CT and MRI—valuable to confirm bulla lesions, CNS extension from peripheral disease, localize tumor, granuloma, and document extent of inflammation.

DIAGNOSTIC PROCEDURES

- CSF—from cerebello-medullary cistern; for evaluating central vestibular disease; detects inflammatory process; protein electrophoresis and titers to match with serologic testing if indicated; collection may put the patient at risk for herniation if elevated intracranial pressure.
- BAER—assess cochlear portion of CN VIII and brainstem auditory pathways; particularly valuable for evaluating peripheral vestibular disease, because some diseases may cause ipsilateral deafness (e.g., otitis media/interna), whereas other diseases (e.g., canine geriatric and feline idiopathic vestibular diseases) affect only the vestibular portion of CN VIII.
- Biopsy—bone, tissue in tympanic bulla when a tumor, polyp, or osteomyelitis is suspected; brainstem mass

(CONTINUED)

HEAD TILT

(e.g., cerebello-medullary angle) difficult to approach and remove surgically.

**TREATMENT**

- Inpatient versus outpatient—depends on severity of signs (especially vestibular ataxia), size and age of patient, and need for supportive care.
- Supportive fluids—replacement or maintenance intravenous fluids may be required in acute phase when disorientation, nausea, and vomiting preclude oral intake; especially important in geriatric patients.
- Activity—restricted according to degree of disequilibrium.
- Diet—as usual unless there is thiamin deficiency (e.g., exclusively fish diet without vitamin supplementation); restrict oral intake if nausea and vomiting; caution: aspiration secondary to abnormal body posture in patients with severe head tilt and disequilibrium or brainstem dysfunction.
- Discontinue drug if toxicity suspected.
- Surgical treatment—to drain bulla with otitis media, remove nasopharyngeal polyp in cats, and resect tumor, if accessible.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Otitis media and interna—broad-spectrum antibiotic (parenteral or oral) that penetrates bone while awaiting culture results; trimethoprim-sulfa (15 mg/kg PO q12h or 30 mg/kg PO q12–24h); first-generation cephalosporins, such as cephalexin (10–30 mg/kg PO q6–8h) or amoxicillin/clavulanic acid (Clavamox dogs, 12.5 mg/kg PO q12h, or cats, 62.5 mg/cat PO q12h; Clavaseptin 12.5 mg/kg PO q12h); treatment for 4–6 weeks.
- Hypothyroidism— T_4 replacement (dogs, levothyroxine 22 μ g/kg PO q12h) should be introduced gradually in geriatric patients, especially with cardiac disease; response varies, partly depending on the duration of signs (i.e., in some patients, neuropathy is not reversible).
- Infectious CNS—specific treatment, if indicated; for bacterial diseases, antibiotic that penetrates the blood-brain barrier (e.g., trimethoprim-sulfa, 15 mg/kg PO q12h; metronidazole 15 mg/kg q12h or 10 mg/kg q8h PO or slowly IV; third-generation cephalosporin, e.g., cefotaxime 25–50 mg/kg

IV q8h); for protozoal diseases, clindamycin (12.5–25 mg/kg PO q12h); for fungal diseases, itraconazole (dogs, 2.5 mg/kg PO q12h or 5 mg/kg PO q24h; cats, 5 mg/kg PO q12h), fluconazole (dogs, 5–8 mg/kg PO q12h, 10–12 mg/kg PO q24h; cats, 50 mg/cat PO q12–24h); prognosis usually poor for protozoal, fungal, and viral diseases (e.g., FIP).

- GME—usually initially treated with steroids: dexamethasone (0.25 mg/kg PO, IM q12h for 3 days; followed by prednisone (2 mg/kg PO q24h for 1–2 weeks; then decrease slowly); depending on progress, may need stronger immunosuppression—e.g., cytosine arabinoside 50 mg/m² q12h for four treatments repeated every 3 weeks (need to monitor CBC); radiation therapy.
- Trauma—supportive care (e.g., anti-inflammatory drugs, antibiotics, intravenous fluid administration); specific fracture repair or hematoma removal is potentially difficult considering the location.
- Canine geriatric and feline idiopathic vestibular disease—supportive care only.
- Cranial nerve polyneuropathy—response to prednisone good if the patient has a primary immune disorder.
- Thiamin deficiency—diet modification and thiamin replacement.

CONTRAINdications

Drugs potentially toxic to the vestibular system—aminoglycoside antibiotics; prolonged high-dose metronidazole.

PRECAUTIONS

- Trimethoprim-sulfa administration—keratoconjunctivitis sicca (dry eye).
- Avoid administering drugs into external ear canal (especially oil-based) if tympanic membrane is ruptured.

**FOLLOW-UP****PATIENT MONITORING**

- Repeat the neurologic examination as dictated by underlying cause.
- Head tilt may persist.
- Hypothyroidism—measure T_4 concentration 4–6 hours after treatment 3–4 weeks after initiation of thyroid therapy or dosing change.
- Repeat CSF and brain imaging—with some central vestibular disorders.
- Monitor tear production (Schirmer test) with trimethoprim-sulfa administration.

POSSIBLE COMPLICATIONS

- Progression of disease
- Brain herniation

EXPECTED COURSE AND PROGNOSIS

- Prognosis for central vestibular disorders usually poorer than peripheral vestibular disorders.
- Prognosis for canine geriatric and feline idiopathic vestibular syndromes is excellent.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Facial nerve paresis or paralysis
- Horner's syndrome

AGE-RELATED FACTORS

Canine geriatric vestibular syndrome affects older dogs.

H**SEE ALSO**

- Encephalitis
- Meningoencephalomyelitis, Granulomatous
- Nasal and Nasopharyngeal Polyps
- Otitis Media and Interna
- Vestibular Disease, Geriatric—Dogs
- Vestibular Disease, Idiopathic—Cats

ABBREVIATIONS

- BAER = brainstem auditory-evoked response
- CN = cranial nerve
- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- FIP = feline infectious peritonitis
- FT_4 E_QD = free T_4 by equilibrium dialysis
- GME = granulomatous meningoencephalomyelitis
- MRI = magnetic resonance imaging
- TSH = thyroid-stimulating hormone

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Consulting Editor Joane M. Parent



Client Education Handout available online

HEAD TREMORS (BOBBING), IDIOPATHIC—DOGS



BASICS

OVERVIEW

- Common, very specific, benign, often self-limiting, head and neck tremors in dogs.
- Commonly called head bobbing but idiopathic head tremors is more appropriate.
- Synonyms: episodic head tremor syndrome, bobble head doll syndrome, head shaking, head tremors, head wobbling, head nodding.
- A movement disorder is suspected, but the pathophysiology remains unknown.

SIGNALMENT

- All dog breeds can be affected. • Not reported in cats. • English bulldog (EB), French bulldog, Boxer, Doberman Pinscher (DP) and Labrador retrievers are predisposed.
- Reported prevalence of 19–38% in EB.
- Reports that males are over-represented in DP and EB. • Generally starts early in life (< 3 years old), but can start at any age.

SIGNS

Historical Findings

- Acute onset of head tremor episodes.
- Possible recent stressful event (heat, gestation, whelping with lactation, vaccination, illness, etc.). • Littermates may be affected (familial form identified in DP ≤ 1 year old).

Physical Examination Findings

- None if not currently experiencing an episode. • Typical vertical or horizontal rapid (4–8 Hertz or movements per second) head tremors—episodes last from a few seconds to a few hours. • Variable tremor episode frequency, duration, and inter-episode interval. • Occasional reports of abnormal dystonic posture (subtle head tilt, stiffness, floppiness) during episodes, but not between episodes. • Occasional reports of abnormal behavior (disorientation, sleepiness, agitation) immediately prior to an episode. • All dogs are reported to be responsive to their surroundings during the episode. • Rare reports of associated generalized seizure.
- Episodes can often be interrupted by distraction or treats. • Other neurologic abnormalities (ataxia, proprioceptive deficits, paresis, etc.) consistent with concurrent, unrelated neurologic disease (cervical spondylomyopathy in DP, hemivertebrae in bulldogs) are often noted.

CAUSES & RISK FACTORS

- Unknown pathophysiology. • Anatomic, neoplastic, and traumatic causes have been ruled out by different studies. • Genetic basis suspected but unproven. • May be triggered by a recent stressful event.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Tremogenic toxin (mycotoxin, permethrins, etc.). • Corticosteroid-responsive shaker/tremor syndrome.
- Hypomyelinating/dysmyelinating congenital or degenerative disease.
- Cerebellar disease (intention tremor).
- Hypocalcemia. • Hypoglycemia.
- Hypoadrenocorticism (electrolyte imbalance). • Epilepsy (focal or generalized seizures) or reactive seizures. • Stress.
- Muscle fatigue following exercise or associated with generalized weakness from myopathy, neuropathy or neuromuscular disease. • Viewing of a video provided by the client helps greatly in identifying this typical head movement and differentiating it from other types of tremor. • History and signalment differentiate head bobbing from many of these conditions.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

N/A

IMAGING

Magnetic resonance imaging might be considered if abnormalities other than typical head bobbing episodes noted.

DIAGNOSTIC PROCEDURES

Cerebrospinal fluid analysis and electrodiagnostic testing might be considered if abnormalities other than typical head bobbing episodes noted.

PATHOLOGIC FINDINGS

Have not been studied



TREATMENT

- No known effective treatment. • Attempts to interrupt the episodes by distracting the dog should be tried by the client. • If head bobbing episodes significantly impair crucial life functions such as eating or sleeping, or the quality of life of the dog, consult a veterinary neurologist for further recommendations.



MEDICATIONS

DRUGS

No known effective medication.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Commonly used antiepileptic drugs (phenobarbital, potassium bromide) have

multiple significant side effects and have not been proven unsuccessful at treating head bobbing. Their use is not warranted with this condition.



FOLLOW-UP

PREVENTION/AVOIDANCE

N/A

EXPECTED COURSE AND PROGNOSIS

- Self-limiting in 49% of EB in one study.
- Benign head tremor episodes may continue life-long at a variable frequency, usually decreasing over time. • Prognosis is excellent as head bobbing is not associated with a life-threatening condition.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Concurrent epilepsy may be present and may need to be addressed. • A thorough description of the idiopathic head tremor episodes needs to be obtained and variation from the typical pattern should be video-filmed and reviewed.

PREGNANCY/FERTILITY/BREEDING

Studies regarding the potential genetic transmission of this condition are under way.

ABBREVIATIONS

- EB = English bulldog • DP = Doberman pinschers

INTERNET RESOURCES

<https://www.youtube.com/watch?v=cVkrIAHIKVM>

Suggested Reading

Guevar J, De Decker S, Van Ham LML, Fisher A, Volk HA. Idiopathic head tremor in English Bulldogs. Mov Disord 2014, 29(2):191–194.

Wolf M, Bruehschwein A, Sauter-Louis C, Sewell AC, Fisher A. An inherited Episodic Head tremor Syndrome in Doberman Pinscher Dogs. Mov Disord 2011, 26(13):2381–2386.

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Client Education Handout
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HEARTWORM DISEASE-CATS



BASICS

OVERVIEW

- Disease caused by infection with *Dirofilaria immitis*. • Microfilaremia uncommon (<20%) and if present usually transient.
- Prevalence one-tenth that of unprotected dogs. • Low average worm burden. • Worms are physically smaller but recent evidence suggests lifespan is similar to that in the dog.

SIGNALMENT

- No age or breed predisposition. • Males more commonly infected naturally and easier to infect experimentally.

SIGNS

Historical Findings

- Coughing (this is relatively uncommon with heart failure). • Cough will commonly occur early in the disease prior to an established adult infection. • Heartworm-associated respiratory disease (HARD). • Clinical signs and pulmonary pathology that occurs 2–4 months post-infection even when an adult infection is never established. • Dyspnea.
- Vomiting (undetermined cause). • PTE frequently results in acute respiratory failure and death. • Vomiting and respiratory signs predominate in chronic disease.

Physical Examination Findings

- Usually normal. • Increased bronchovesicular sounds. • An arrhythmia, murmur, or gallop rhythm should increase the suspicion of primary cardiac disease.

CAUSES & RISK FACTORS

- Outdoor cats at increased risk (2:1). • FeLV infection is not a predisposing factor.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Asthma • Cardiomyopathy • Chylothorax
- *Aelurostrongylus abstrusus* infection
- *Paragonimus kellicotti* infection

CBC/BIOCHEMISTRY/URINALYSIS

- Varies with stage of disease • Mild nonregenerative anemia • Eosinophilia inconsistent • Concurrent basophilia should increase suspicion • Hyperglobulinemia

OTHER LABORATORY TESTS

Microfilaria Concentration Tests

Very low sensitivity, high specificity

Heartworm Antigen Tests

- ELISA or immunochromatographic tests.
- Tests that detect circulating HWAg are more specific than antibody tests. • A positive antigen test result is strong evidence of adult heartworm infection. • Low worm burdens (fewer than five worms) and single-sex infections commonly result in false-negative Ag tests. • Recent data suggests that heat

treatment of samples prior to testing may significantly increase the test sensitivity. Negative result does not rule-out heartworm disease; more than 40% of cats with adult infection are antigen-negative. Many cats are symptomatic (HARD) well before an antigen test would become positive.

Heartworm Antibody Tests

- ELISA or immunochromatographic tests.
- Tests that detect circulating antibodies to immature and adult heartworm antigen are the most sensitive tests for feline heartworm disease. • A positive result does not confirm an adult infection. Usually becomes positive within 4 months of infection. • The more intense the antibody response the more likely there is an adult infection. • May become negative in adult infections perhaps associated with Ag;Ab complexing.

IMAGING

Radiography

- Enlarged (pulmonary artery, > 1.6 times the width of the ninth rib). • Blunted, tortuous pulmonary arteries. • Patchy perivascular pulmonary infiltrates. • Pleural effusion may be present. • Chylothorax has been documented with spontaneously occurring and experimentally induced heartworm infections in cats.

Echocardiography

- Dilated main pulmonary artery.
- Identification of worms in heart or main pulmonary artery; most commonly seen in the right pulmonary artery but also in right ventricle and atrium (hyperechoic “=” sign).
- Sensitive test in the hands of an experienced echocardiographer. • Excludes or confirms other primary cardiac diseases (cardiomyopathy).



TREATMENT

- There is currently no approved or recommended medical adulticide therapy.
- Surgical or catheter-based extraction may be the most reasonable option. • Symptomatic cats should be stabilized (see below) prior to consideration of worm extraction.
- Spontaneous “cure” is probably more common in cats than dogs.



MEDICATIONS

DRUG(S)

Initial Stabilization

- Supplemental oxygen. • Theophylline (sustained release formulation) 15–25 mg/kg PO q24h in the evening. • Prednisolone 1–2 mg/kg PO q12–24h for 10–14 days; then gradually reduce. • Doxycycline therapy 10 mg/kg PO q24h for 30 days (to eliminate the endosymbiont *Wolbachia*) may hasten worm death and reduce the severity of

pulmonary inflammation secondary to worm embolization. • Cautiously balanced fluid therapy if indicated. • Medical adulticide therapy is not currently recommended.

- Supportive care for PTE the same as initial stabilization (see above).

CONTRAINdications/POSSIBLE INTERACTIONS

- Aspirin therapy—no documented benefit.
- Current information does not support the use of melarsomine (Immiticide) in cats.



FOLLOW-UP

PATIENT MONITORING

Serial evaluation of clinical response, thoracic radiographs, and heartworm antigen and antibody tests is most informative.

PREVENTION/AVOIDANCE

- Ivermectin 24 µg/kg PO every 30 days.
- Milbemycin oxime 0.5 mg/kg PO every 30 days. • Selamectin 6.6–12 mg/kg cutaneously every 30 days. • Moxidectin 1–2 mg/kg cutaneously every 30 days.
- Administration of these drugs in cats is not precluded by antibody or antigen seropositivity.



MISCELLANEOUS

ABBREVIATIONS

- ELISA = enzyme-linked immunosorbent assay • FeLV = feline leukemia virus
- HARD = heartworm-associated respiratory disease • HWAg = adult heartworm antigen
- PTE = pulmonary thromboembolism

INTERNET RESOURCES

2010 Guidelines for the Diagnosis, Treatment and Prevention of Heartworm (*Dirofilaria immitis*) Infection in Cats. The American Heartworm Society:
<https://heartwormsociety.org/images/pdf/2014-AHS-Feline-Guidelines.pdf>

Suggested Reading

- Little SE, Raymond MR, Thomas JE, Gruntmeir J, et al. Heat treatment prior to testing allows detection of antigen of *Dirofilaria immitis* in feline serum. *Parasites & Vectors* 2014; 7:1. doi:10.1186/1756-3305-7-1

Thomason JD, Calvert CA. Heartworm disease. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., *Manual of Canine and Feline Cardiology*, 5th ed. St. Louis, MO: Saunders Elsevier, 2015 (in press).

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Client Education Handout available online

HEARTWORM DISEASE—DOGS



BASICS

DEFINITION

Disease caused by infestation with *Dirofilaria immitis*

PATOPHYSIOLOGY

- Disease severity is directly related to the number of worms, duration of infestation, host response, and host activity level.
- Endothelial damage leads to myointimal proliferation and inflammation predisposing to periarterial edema.
- Lobar arterial enlargement, tortuosity, and obstruction cause impaired compliance, loss of collateral recruitment, pulmonary hypertension, and thrombosis.
- Pulmonary damage is exacerbated after the death of adult worms and with exercise.

SYSTEMS AFFECTED

- Respiratory—pulmonary hypertension (when severe), thromboembolism, allergic pneumonitis (some occult infections), eosinophilic granulomatosis (uncommon).
- Cardiovascular—severe pulmonary hypertension causes right ventricular hypertrophy and, in some dogs, right-sided congestive heart failure (R-CHF=ascites).
- Hemic/Lymphatic/Immune—venous inflow to the heart can become obstructed by worms causing traumatic hemolytic anemia and cardiogenic shock (caval syndrome).
- Renal/Urologic—immune-complex glomerulonephritis.

INCIDENCE/PREVALENCE

Virtually 100% in unprotected dogs living in highly endemic regions.

GEOGRAPHIC DISTRIBUTION

- Most common in tropical and subtropical zones
- Common along the Atlantic/Gulf coasts and Ohio/Mississippi river basins
- Diagnosed in all 50 states
- Ubiquitous—mosquito vector

SIGNALMENT

Breed Predilections

- Medium- to large-breed dogs > small dogs
- Outdoor dogs > indoor dogs

Mean Age and Range

Infestation can occur at any age; most affected dogs are 3–8 years old

Predominant Sex

Males affected more often than females

SIGNS

Historical Findings

- Dogs often asymptomatic or exhibit minimal signs such as occasional coughing (Class I).
- Coughing and exercise intolerance associated with moderate pulmonary damage (Class II).
- Cachexia, anemia, exercise intolerance, syncope, and/or ascites (R-CHF) in severely affected dogs (Class III).

Physical Examination Findings

- No abnormalities—dogs with mild (Class I) and some with moderate infestation (Class II).
- Labored breathing and/or crackles—dogs with severe pulmonary hypertension (Class III) or pulmonary thromboembolism.
- Tachycardia, weight loss, exercise intolerance, syncope, coughing, anemia, and dyspnea (Class III).
- Ascites, jugular vein distention/pulsation, and hepatomegaly indicate R-CHF (Class III).
- Hemoptysis—occasionally.
- Pale mucous membranes, dyspnea, weak pulses, hemoglobinemia, and hemoglobinuria (caval syndrome).

RISK FACTORS

- Residence in endemic regions
- Outside habitat
- Lack of prophylaxis
- Greater than 64°F all day, every day for at least 1 month
- Greater than 80°F every day for 10–14 days.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of pulmonary hypertension and thrombosis (e.g., hyperadrenocorticism, protein-losing nephropathy or enteropathy)
- Chronic obstructive lung disease
- Pneumonia
- Allergic lung disease
- Other causes of ascites (e.g., dilated cardiomyopathy)
- Other causes of hemolytic anemia (e.g., immune-mediated).

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia—absent, mild, or moderate depending on chronicity, severity of disease, and thromboembolic complications. Anemia associated with Class III.
- Eosinophilia and basophilia—vary.
- Inflammatory leukogram and thrombocytopenia associated with thromboembolism.
- Hyperglobulinemia—inconsistent finding.
- Hemoglobinemia—evident with caval syndrome and less often with thromboembolism.
- Proteinuria—common in dogs with severe and chronic infestation; caused by immune-complex glomerulonephritis or amyloidosis.
- Hemoglobinuria—caval syndrome or severe lysis with thromboembolism (Class III).

OTHER LABORATORY TESTS

- Highly specific, sensitive serologic tests that identify adult female *D. immitis* antigen; test 7 months after the end of the previous transmission season.
- Antigenemia absent in absence of adult female worms.
- Weak positive test verified by repeat testing using different test.
- Strong reaction indicates relative high worm burden or recent death of worms and is highly predictive of thromboembolic complications following adulticide therapy.
- Microfilaria identification tests are not recommended for routine heartworm screening; mainly used to

confirm weak positive antigen tests, determine microfilarial status prior to patients receiving milbemycin as heartworm preventative, and to identify microfilaria which may contribute to the development of resistance when treated chronically with macrolide preventative.

IMAGING

Radiographic Findings

- Use DV projection.
- Main pulmonary artery segment enlargement, lobar arterial enlargement, and tortuosity/pruning vary from absent (Class I) to severe (Class III).
- Right caudal artery > left caudal artery > cranial arteries.
- Parenchymal lung infiltrates of variable severity—surround lobar arteries; may extend into most or all of one or multiple lung lobes when thromboembolism occurs.
- Diffuse, symmetrical, alveolar, and interstitial infiltrates occasionally occur secondary to allergic reaction to microfilaria (allergic pneumonitis) in about 10% of occult infestations.

Echocardiographic Findings

- Often unremarkable; may reflect right ventricular dilation and wall hypertrophy, tricuspid regurgitation, pulmonary hypertension, small left heart due to under-loading (pulmonary obstruction/hypertension).
- Parallel, linear echodensities produced by heartworms may be detected in the right ventricle, right atrium, and pulmonary arteries.

DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

- Usually normal.
- May reflect right ventricular hypertrophy in dogs with severe infestation.
- Heart rhythm disturbances—occasionally seen (atrial premature contractions and atrial fibrillation most common) in severe infestation.

PATHOLOGIC FINDINGS

- Large right heart
- Pulmonary arterial myointimal proliferation
- Pulmonary thromboembolism
- Pulmonary hemorrhage
- Hepatomegaly and congestion in dogs with R-CHF



TREATMENT

APPROPRIATE HEALTH CARE

- Most dogs hospitalized during adulticide administration.
- Eliminate microfilaria with monthly prophylaxis and doxycycline/minocycline; milbemycin may cause rapid decrease in microfilaria numbers and should be used with caution in that scenario; dogs should be rendered microfilaria free 3 months post diagnosis.
- Hospitalization recommended for dogs experiencing thromboembolic complications.

(CONTINUED)

HEARTWORM DISEASE—DOGS**ACTIVITY**

Severely restrict activity for 4–6 weeks after adulticide administration.

CLIENT EDUCATION

- Good prognosis for animals with mild-to-moderate disease. • Post-adulticide pulmonary complications likely in patients with moderate-to-severe pulmonary artery pathology and those with high worm burden.
- Reinfestation can occur unless appropriate prophylaxis administered.

SURGICAL CONSIDERATIONS

- Treatment of choice for caval syndrome.
- Worm removal from right heart and pulmonary artery via jugular vein, by use of fluoroscopy and a long, flexible, alligator forceps or horsehair brush, is highly effective for treating high worm burden when employed by an experienced operator.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Stabilize animals with R-CHF with diuretics, ACE inhibitor, pimobendan, sildenafil, cage rest, and moderate sodium restriction before adulticide treatment.
- Stabilize pulmonary failure with oxygen supplementation, antithrombotic agents (e.g., aspirin or heparin), or anti-inflammatory dosages of corticosteroid depending on the clinical and radiographic findings.
- Adulticide drug: melarsomine dihydrochloride (Immiticide, 2.5 mg/kg IM/dose)—injections are given into the epaxial muscles using 22-gauge needles; apply pressure over the injection site during and after needle withdrawal. • Graded-kill protocol recommended in most cases; administer one injection followed in 1 month by two injections (first injection on left or right epaxial muscles, followed by injection on the opposite side 24h later). • For Class III in small dogs or severe Class III with high worm burden administer one injection every 4–6 weeks for a total of three injections. Maintain the strictest patient confinement practical for 4–6 weeks. Perform antigen test 6 months after third injection. • Allergic pneumonitis: administer prednisone or prednisolone (2 mg/kg PO q12–24h for several days) and then immediately administer Immiticide. • Rapid microfilaricidal therapy (e.g., milbemycin or high-dose ivermectin) not recommended by authors; eliminate the microfilaria with monthly prophylaxis and doxycycline/minocycline; confirm elimination of microfilaria by testing 3 months after initiating therapy.

PRECAUTIONS

- Adulticide treatment—not indicated in patients with renal failure, hepatic failure (icterus), or nephrotic syndrome. • Caval

syndrome—remove worms surgically and stabilize patient with conservative management for at least 1 month prior to adulticide therapy.

ALTERNATIVE DRUG(S)

- Sodium heparin (75–100 units/kg SC q8h), aspirin (5–7 mg/kg PO q24h), or low molecular weight heparin (dalteparin: 100 units/kg SC q12–24h) for 1–3 weeks before, during, and for 3 weeks after adulticide administration are controversial recommendations for the most severe cases of Class III disease; therapy is combined with strict, extended cage confinement. • Sodium heparin (200–500 units/kg SC q8h) is recommended for dogs with pulmonary thromboembolism or hemoglobinuria with goal of prolonging APTT 1.5–2 times baseline. • Soft or slow kill: ivermectin (6 µg/kg weekly) and doxycycline (10 mg/kg/day) combination may result in worm eradication with 9 months of therapy (generally not recommended due to possible promotion of resistance to the macrolides).
- Doxycycline/minocycline (5–10 mg/kg PO q12h) is used prior to adulticide therapy to kill *Wolbachia*, a gram-negative, intrafilarial bacterium that is associated with post-adulticide inflammation of the lungs and kidneys.

**FOLLOW-UP****PATIENT MONITORING**

Perform an antigen test 6 months after adulticide treatment. Some dogs with persistent, low-grade antigenemia may not require retreatment. Weak antigenemia indicates most worms killed, pulmonary pathology will improve, and ivermectin prophylaxis will eventually kill remaining worms.

PREVENTION/AVOIDANCE

- Heartworm prophylaxis should be provided for all dogs at risk. Authors recommend year-round prophylaxis. Otherwise begin with mosquito season and continue for 1 month following first frost. • Antigen test prior to starting preventive treatment. • Antigen test 7 months after end of previous season.
- Ivermectin (Heartgard, Iverhart, Triheart)—a highly effective, monthly preventive that can be given safely to microfilaremic dogs.
- Milbemycin oxime (Interceptor, Sentinel, Trifexis)—highly effective, monthly prophylaxis in which acute reactions may occur when given to microfilaremic dogs.
- Moxidectin (Advantage Multi)—a topical solution administered monthly. • Selamectin (Revolution)—a highly effective monthly topical preparation. • Administer to puppies soon after 8 weeks of age as dictated by seasonal risk. • All of the prophylactic drugs can be administered safely to collies at the

appropriate dosages. • For dogs infected with adult worms and not already taking prophylactic drug, any of the above drugs can be started immediately and should be started within one month of diagnosis. The authors recommend against using milbemycin in microfilaremic dogs. • The authors do not practice initiating prophylaxis and then delaying adulticide treatment for 1 or more months. • All macrocyclic lactones with combination doxycycline/minocycline should eliminate microfilaria in 1–3 months. • Due to the recent increase in the number of lack of efficacy (LOE) reports and the concern of possible heartworm resistance to the current heartworm preventives, dogs should be rendered microfilaria free 3 months post diagnosis.

POSSIBLE COMPLICATIONS

- Post-adulticide pulmonary thromboembolic complications—may occur up to 4–6 weeks after treatment; usually more severe in dogs with Class III disease and those not properly confined. • Thrombocytopenia and intravascular coagulation. • Melarsomine adverse effects—pulmonary thromboembolism (usually 7–30 days after therapy); anorexia; injection site reaction-myositis; lethargy or depression; elevation of hepatic enzymes; paresis/paralysis/altered mentation; lack of efficacy.

EXPECTED COURSE AND PROGNOSIS

- Class I—usually uneventful with excellent prognosis
- Class III—guarded prognosis with higher risk of complications

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Wolbachia

ANESTHESIA

When anesthesia/surgery required, delay heartworm treatment until after procedure.

PREGNANCY/FERTILITY/BREEDING

- Delay adulticide treatment. • Transplacental infestation by microfilaria can occur.

SEE ALSO

- Congestive Heart Failure, Right-Sided
- Disseminated Intravascular Coagulation
- Hypertension, Pulmonary
- Nephrotic Syndrome
- Pulmonary Thromboembolism

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HEAT STROKE AND HYPERTHERMIA



BASICS

DEFINITION

- Hyperthermia is defined as an elevation in body temperature above the normal range. Although published normal values for dogs and cats vary slightly, it is generally accepted that body temperatures $> 103^{\circ}\text{F}$ (39°C) are abnormal.
- Hyperthermia can be categorized into pyrogenic hyperthermia (pyrexia or fever) and non-pyrogenic hyperthermia.
- Heat stroke is a form of non-pyrogenic hyperthermia that occurs when heat-dissipating mechanisms of the body cannot accommodate excessive heat. This can lead to multisystem organ dysfunction. Temperatures of $106^{\circ}\text{F}+$ (41°C) without signs of inflammation are suggestive of non-pyrogenic hyperthermia.
- Malignant hyperthermia is an uncommon familial form of non-pyrogenic hyperthermia that can occur secondary to some anesthetic agents.
- Other causes of non-pyrogenic hyperthermia include excessive exercise, thyrotoxicosis, and hypothalamic lesions.

PATHOPHYSIOLOGY

- The hypothalamic set point is changed with true fever. This is most likely mediated via the endogenous pyrogen interleukin I.
- Non-pyrogenic hyperthermia does not change the hypothalamic set point.
- The critical temperature leading to multiple organ dysfunction is 109°F (42.7°C).
- The primary pathophysiologic processes of heat stroke are related to thermal damage, which can lead to cellular necrosis, hypoxemia, and protein denaturalization.
- Heat stroke and its sequelae can lead to SIRS.

SYSTEMS AFFECTED

- Cardiovascular—hypovolemia, cardiac arrhythmias, myocardial ischemia, and necrosis.
- Gastrointestinal—mucosal ischemia and ulceration, bacterial translocation and endotoxemia.
- Hemic/Lymphatic/Immune—hemoconcentration, thrombocytopenia, DIC.
- Hepatobiliary—hepatocellular necrosis.
- Musculoskeletal—rhabdomyolysis.
- Nervous—neuronal damage, parenchymal hemorrhage, and cerebral edema.
- Renal/Urologic—acute renal failure.

GEOGRAPHIC DISTRIBUTION

May be seen in any climate but more common in warm and/or humid environments.

SIGNALMENT

Species

- Dog and cat
- Cats uncommon

Breed Predilections

- May occur in any breed
- Longhaired animals
- Brachycephalic breeds

Mean Age and Range

- All ages but often age extremes
- Young dogs may tend to overexert
- Old dogs with preexisting disease

SIGNS

Historical Findings

- Identifiable underlying cause (warm environmental conditions, locked in car or other confined area without adequate ventilation, grooming accident associated with drying cages, excessive exercise, restricted access to water).
- Predisposing underlying disease: laryngeal paralysis, brachycephalic obstructive disease, cardiovascular disease, neuromuscular disease, previous history of heat-related disease.

Physical Examination Findings

- Panting
- Hypersalivation
- Hyperemic mucous membranes
- Pale mucous membranes
- Cyanosis
- Tachycardia
- Cardiac dysrhythmias
- Shock
- Respiratory distress
- Hematemesis
- Hematochezia
- Melena
- Petechiation
- Changes in mentation
- Seizures
- Muscle tremors
- Ataxia
- Coma
- Oliguria/anuria
- Respiratory arrest
- Cardiopulmonary arrest

CAUSES

- Excessive environmental heat and humidity (may be due to weather conditions or accidents such as enclosed in unventilated room, car, or grooming dryer cage).
- Upper airway disease.
- Exercise.
- Toxicosis (some compounds that lead to seizures, i.e., strychnine and metaldehyde).
- Anesthesia (malignant hyperthermia).

RISK FACTORS

- Previous history of heat-related disease
- Age extremes
- Heat intolerance due to poor acclimatization
- Obesity
- Poor cardiopulmonary conditioning
- Hyperthyroidism
- Underlying cardiopulmonary disease
- Brachycephalic breeds
- Thick hair coat
- Dehydration



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- If temperatures exceed 106°F (41°C) without evidence of inflammation should consider heat stroke.
- Panting and hypersalivation may not be seen with true fever as hypothalamic set point has been raised.

CBC/BIOCHEMISTRY/URINALYSIS

- May help to identify underlying disease process.
- May be beneficial in identifying sequelae to hyperthermia.
- CBC abnormalities may include stress leukogram, leukopenia, anemia, nucleated RBCs, thrombocytopenia, or hemoconcentration.
- Biochemistry profile may show azotemia, hyperalbuminemia, elevations in serum

enzymes; ALT, AST, CK, hypernatremia, hyperchloraemia, hyperglycemia, hypoglycemia, hyperphosphatemia, hyperkalemia, hypokalemia, hyperbilirubinemia.

Urinalysis may show hypersthenuria, proteinuria, cylindruria, hemoglobinuria, myoglobinuria.

OTHER LABORATORY TESTS

- Blood gas analysis may show mixed acid-base disorder, respiratory alkalosis, or metabolic acidosis.
- Lactate concentrations may be elevated due to impaired perfusion.
- Coagulation profile may indicate prolonged ACT, PT, or PTT. FDP or d-dimers may be positive. DIC may be present if PT and PTT are prolonged along with positive FDPs or d-dimers and thrombocytopenia. If available the measurement of antithrombin may be valuable.
- Thromboelastography may document hyper- or hypocoagulability.

IMAGING

- Thoracic radiographs may help identify underlying cardiopulmonary disease or predisposing factors.
- Abdominal radiographs and/or ultrasound may help identify underlying disease process.
- Computed tomography or magnetic resonance imaging may help identify hypothalamic lesion.

DIAGNOSTIC PROCEDURES

Continuous temperature monitoring



TREATMENT

- Early recognition is key.
- Immediate correction of hyperthermia; spray with water or immerse in water prior to transport to veterinary facility. Convection cooling with fans.
- Evaporative cooling such as alcohol on foot pads, axilla, and groin.
- Stop cooling procedures when temperature reaches 103°F to avoid hypothermia.
- Oxygen supplementation via oxygen cage, mask, or nasal catheter.
- Airway management in cases of laryngeal paralysis or edema.
- Ventilatory support if required.
- Fluid support with shock doses of crystalloids or colloids.
- Treat complications, seizures, DIC, renal injury, cerebral edema.
- Treat underlying disease or correct predisposing factors.

APPROPRIATE HEALTH CARE

- Patients should be hospitalized until temperature is stabilized.
- Most patients need intensive care for several days.

NURSING CARE

- External cooling; try to avoid ice as this may cause peripheral vasoconstriction and impede heat elimination. Shivering response is also undesirable as this creates heat.
- Fluid therapy; isotonic crystalloids can be administered at shock rates (90 ml/kg/hr for dogs, 45–60 mL/kg/hr for cats) based on clinical assessment. Synthetic colloids may

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HEAT STROKE AND HYPERTHERMIA

also be used to treat shock (20 mL/kg in dogs (5 mL/kg IV boluses), 5–10 mL/kg in cats (1–2 mL/kg boluses)). • Oxygen supplementation can be administered via mask, cage, or nasal cannula.

ACTIVITY

Restricted

DIET

Nothing per os until animal is stable

CLIENT EDUCATION

- Be aware of clinical signs.
- Know how to cool off animals.
- Seek veterinary care immediately.
- An episode of heat stroke may predispose pets to additional episodes.

SURGICAL CONSIDERATIONS

Tracheostomy may be required if upper airway obstruction is underlying cause or contributing factor.

**MEDICATIONS****DRUG(S) OF CHOICE**

- There are no specific drugs that are required for hyperthermia or heat stroke, therapy is dependent on clinical presentation.
- Prophylactic broad-spectrum antimicrobials may decrease the incidence of bacterial translocation. First-generation cephalosporins or potentiated penicillins (clavulanate/amoxicillin, sulbactam/ampicillin) in combination with fluoroquinolones provide excellent four quadrant coverage.
- Acute renal failure—dopamine continuous rate intravenous infusion (2–5 µg/kg/min), furosemide intravenously (2–4 mg/kg PRN) mannitol 0.5–1 g/kg as CRI.
- Cerebral edema—mannitol (1 g/kg IV over 15–30 minutes), furosemide (1 mg/kg IV) 30 minutes following mannitol infusion, corticosteroids (dexamethasone sodium phosphate (1–2 mg/kg IV), prednisone sodium succinate (10–20 mg/kg IV), methyl prednisolone (15 mg/kg IV). The use of corticosteroids is considered controversial due to adverse side effects in these patients.
- Ventricular arrhythmia—lidocaine bolus (2 mg/kg IV) followed by continuous rate intravenous infusion (25–75 µg/kg/min), procainamide (6–8 mg/kg IV).
- Metabolic acidosis—sodium bicarbonate (0.3 × BW (kg) × BE) give 1/3 to $\frac{1}{2}$ as bolus IV.
- DIC—fresh frozen plasma (20 mL/kg),

heparin doses vary widely (300–500 U/kg SC q 6–8h).

- Thrombocytopenia—severe thrombocytopenia with active bleeding can be treated with fresh whole blood, platelet-rich plasma, lyophilized platelets, or frozen platelet concentrate.
- Hemorrhagic vomiting diarrhea—broad-spectrum antibiotics, H₂-antagonists, or proton pump inhibitors in combination with sucralfate.
- Seizures—diazepam (0.5–1 mg/kg IV) or midazolam; phenobarbital (6 mg/kg IV as needed).

CONTRAINdications

- Nonsteroidal anti-inflammatory agents are not indicated in non-pyrogenic hyperthermia because the hypothalamic set point is not altered.
- The use of corticosteroids is considered controversial in heat stroke due to possible adverse effects.
- Cooling with ice, which may lead to peripheral vasoconstriction and poor heat dissipation.

PRECAUTIONS

Refer to manufacturer's recommendations.

POSSIBLE INTERACTIONS

Refer to manufacturer's recommendations.

**FOLLOW-UP****PATIENT MONITORING**

- Patients should be closely monitored during cooling-down period and for a minimum of 24 hours post-episode. Most animals must be monitored for several days depending on clinical presentation and clinical complications. Thorough physical examination should be performed daily. In addition the following parameters should be given consideration:
 - Body temperature
 - Body weight
 - Blood pressure
 - Central venous pressure
 - ACT
 - PT/PTT
 - D-dimers
 - ECG
 - Thoracic auscultation
 - Urinalysis and urine output
 - PCV, TP
 - CBC, biochemical profile
 - Venous blood gas analysis (electrolytes, lactate).

POSSIBLE COMPLICATIONS

- Cardiac dysrhythmias
- Organ failure
- Coma
- Seizures
- Acute renal failure
- DIC
- SIRS
- Sepsis/septic shock
- Pulmonary edema—acute respiratory distress (ARDS)
- Rhabdomyolysis
- Hepatocellular necrosis
- Respiratory arrest
- Cardiopulmonary arrest

EXPECTED COURSE AND PROGNOSIS

- Prognosis is dependent on underlying cause or disease process.
- Prognosis may be dependent on time lag between event and hospital admission.
- Prognosis is guarded dependent on complications that occur (renal failure and DIC) and duration of episode.
- May predispose animal to further episodes due to damage of thermoregulatory center.

**MISCELLANEOUS****SYNOMYMS**

- Heat exhaustion
- Heat prostration
- Heat-related disease
- Heat stroke

SEE ALSO

Fever

H

ABBREVIATIONS

- ACT = activated clotting time
- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- DIC = disseminated intravascular coagulopathy
- ECG = electrocardiogram
- FDP = fibrin degradation products
- PCV = packed cell volume
- PT = prothrombin time
- PTT = partial thromboplastin time
- RBC = red blood cell
- SIRS = systemic inflammatory response syndrome

Suggested Reading

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Client Education Handout available online

HELICOBACTER spp.



BASICS

DEFINITION

Helicobacter spp. are microaerophilic, Gram-negative, urease-positive bacteria that range from coccoid to curved to spiral.

PATHOPHYSIOLOGY

Helicobacter spp. in the Stomach

The discovery of an association of *Helicobacter pylori* with gastritis, peptic ulceration, and gastric neoplasia has fundamentally changed the understanding of gastric disease in humans. Putative mechanisms by which *H. pylori* alters gastric physiology in humans include disruption of the gastric mucosal barrier (due to secretion of phospholipases and vacuolating cytotoxins) and alteration of the gastric secretory activity (e.g., decreased somatostatin secretion leading to hypergastrinemia and hyperchlorhydria). *H. pylori* infection in humans has also been associated with increased secretion of proinflammatory cytokines, tumor necrosis factor- α , and nitric oxide. Several *Helicobacter* spp other than *H. pylori* have been isolated from the stomach of dogs and cats. Typically, multiple species of *Helicobacter* are present. To date *H. pylori*, the most important species affecting humans, has only been identified in a single colony of laboratory cats. A possible cause-effect relationship of *Helicobacter* spp. and gastric inflammation in cats and dogs remains unresolved; inflammation or glandular degeneration accompanies *Helicobacter* spp. in some but not all dogs and cats. Experiments to determine the pathogenicity of *H. pylori* in SPF cats and *H. pylori* and *H. felis* in gnotobiotic dogs demonstrated gastritis, lymphoid follicle proliferation, and humoral immune responses after infection.

HELICOBACTER spp. IN THE LIVER AND INTESTINES

The role of *Helicobacter* spp. in intestinal and hepatic disease in dogs and cats is unclear. Several *Helicobacter*-like organisms (HLOs) have been identified in the large intestine and feces from normal and diarrheic dogs and cats. *H. canis* has also been isolated from the liver of a dog with active, multifocal hepatitis.

SYSTEMS AFFECTED

Gastrointestinal—stomach: *Helicobacter* spp. may lead to gastritis in some dogs and cats; intestines: diarrhea can be observed in some dogs with *H. canis*.

Hepatobiliary—acute hepatitis has been associated with *H. canis*.

GENETICS

No genetic basis for susceptibility to *Helicobacter* spp. infection has been established.

INCIDENCE/PREVALENCE

Gastric Helicobacter spp.

- Gastric HLOs are highly prevalent in dogs and cats—evidence for HLOs has been shown in 86% of random-source cats, 90% of clinically healthy pet cats, 67–86% of clinically healthy pet dogs. • HLOs have been demonstrated in gastric biopsy specimens in 57–76% of cats and 61–82% of dogs presented for investigation of recurrent vomiting. • To date *H. pylori* has been identified only in a single colony of laboratory cats.

Enterohepatic Helicobacter spp.

- H. canis* has been isolated in 4% of 1,000 dogs evaluated. • However, only a single case of *H. canis*-associated hepatitis has been reported. • The prevalence of *H. fennelliae* and *H. cinaedi* remains undetermined.

GEOGRAPHIC DISTRIBUTION

- H. pylori* infection in human beings has a higher prevalence in less-developed countries.
- No information available for dogs and cats.

SIGNALMENT

Species

Dog and cat

Mean Age and Range

- Gastric infection with *Helicobacter* spp. appears to be acquired at a young age. • The dog with *H. canis*-associated hepatitis was 2 months old.

SIGNS

Historical Findings

- Asymptomatic presence of *Helicobacter* spp. is common. • Vomiting, anorexia, abdominal pain, weight loss, and/or borborygmus have all been reported in dogs and cats with gastric *Helicobacter* spp. • *H. canis* in dogs may be associated with diarrhea. • Vomiting, weakness, and sudden death was reported in a dog with hepatic *H. canis*.

Physical Examination Findings

- Usually unremarkable. • May have signs of dehydration from fluid and electrolyte loss due to vomiting and/or diarrhea.

CAUSES

Gastric Helicobacter spp.

- H. felis*, *H. heilmannii*, and *H. baculiformis* have been identified in cats. • *Helicobacter felis*, *H. bizzozeronii*, *H. salomonis*, *H. heilmannii*, *H. bilis*, *Flexispira rappini*, and *H. cynogastericus* have been identified in dogs.

Enterohepatic Helicobacter spp.

- H. bilis*, *H. canis*, *H. cinaedi*, and *Flexispira rappini* have been identified in feces from normal and diarrheic dogs. • *H. cinaedi* has been identified in one cat, but its significance is unknown. • *H. canis* has been reported in one dog with acute hepatitis.

RISK FACTORS

Poor sanitary conditions and overcrowding may facilitate the spread of infection.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

General Comments

There is a high prevalence of *Helicobacter* spp. in both dogs and cats. Therefore, exclusion of other causes of gastric disease and a positive identification of *Helicobacter* spp. are crucial before a diagnosis of gastrointestinal disease due to *Helicobacter* spp. can be suspected.

Gastric Helicobacteriosis

Must be distinguished from other causes of vomiting (both primary and secondary gastrointestinal diseases that can cause vomiting).

Intestinal Helicobacteriosis

Must be distinguished from other causes of diarrhea (both primary and secondary gastrointestinal diseases).

Hepatic Helicobacteriosis

Must be distinguished from other causes of hepatobiliary disease.

CBC/BIOCHEMISTRY/URINALYSIS

- May reflect fluid and electrolyte abnormalities secondary to vomiting and/or diarrhea. • May reflect changes consistent with hepatic disease in patients with *H. canis*-associated hepatitis.

OTHER LABORATORY TESTS

- Examination of impression smears of gastric mucosa or gastric washings using May-Grünwald-Giemsa, gram, or Diff-Quik stain is sensitive for *Helicobacter* spp. and can easily be performed, but this test cannot distinguish between different HLOs.

- Rapid-urease test—requires gastric biopsy specimen, but is easy to perform in patients that undergo gastroduodenoscopy. • ^{13}C -urea breath or blood test has been shown to be reliable in identifying infected dogs, but is currently not commercially available.

- Bacterial culture requires special techniques and media and is impractical. • PCR of DNA extracted from biopsy specimens or from gastric juice. • Serologic tests (ELISA) measure circulating IgG in serum, but this test cannot distinguish between different HLOs. • Histopathology enables the definitive diagnosis of gastric *Helicobacter* spp. infection, but cannot distinguish between different HLOs.

IMAGING

Abdominal radiography and ultrasonography are usually normal in patients with *Helicobacter* spp. infection alone.

DIAGNOSTIC PROCEDURES

Gastric Helicobacteriosis

In cases of *Helicobacter* spp.-associated gastritis, endoscopy may reveal superficial nodules that suggest hyperplasia of lymphoid

(CONTINUED)

follicles, diffuse gastric rugal thickening, punctate hemorrhages, and erosions.

Hepatic Helicobacteriosis

Hepatic biopsy/histopathology (Warthin-Starry staining) and culture.

PATHOLOGIC FINDINGS

- Identification of HLOs requires special staining of tissue samples with Warthin-Starry or modified-Steiner stain. Routine H&E staining may reveal larger HLOs, but smaller organisms are often missed.
- In cases of *Helicobacter* spp.–associated gastric disease: lymphocytic-plasmacytic gastritis and lymphoid follicle hyperplasia; rarely neutrophilic infiltrations. Gastric ulcers have not been reported in dogs and cats.
- In cases of *H. canis*–associated hepatitis: hepatocellular necrosis; infiltration of the hepatic parenchyma with mononuclear cells, and spiral-shaped to curved bacteria predominantly in biliary canaliculi.



TREATMENT

APPROPRIATE HEALTH CARE

- The pathogenicity of *Helicobacter* spp. in dogs and cats is still unclear. Therefore, there are no generally accepted guidelines for the treatment of *Helicobacter* spp. infections in dogs and cats.
- Currently there is no indication for treating asymptomatic animals with a *Helicobacter* spp. infection.
- Eradication of gastric *Helicobacter* spp. should only be considered in infected dogs and cats that have compatible clinical signs that cannot be attributed to another disease process.

NURSING CARE

Fluid therapy in dehydrated patients.

DIET

Easily digestible diets in patients with gastrointestinal signs.

CLIENT EDUCATION

Explain the difficulty of establishing a definitive diagnosis, the high prevalence of infections with HLOs in normal dogs and cats, the potential for recurrence, and the zoonotic potential, though minimal, of these infections.



MEDICATIONS

GENERAL COMMENTS

- A triple therapy (combination of two antibiotics and one antisecretory drug) is effective in humans with *H. pylori* infection, with cure rates of approximately 90%.
- Combination therapy may eliminate *Helicobacter* spp. infections in dogs and cats less effectively than in humans.
- Treat for 2–3 weeks.

DRUG(S) OF CHOICE

Antibiotics (Two Antibiotics with One Antisecretory Agent)

- Clarithromycin (dogs, 5 mg/kg PO q12h; cats, 62.5 mg/cat PO q12h).
- Metronidazole (dogs, 11–15 mg/kg PO q12h; cats, 12.5 mg/kg PO q12h).
- Amoxicillin (22 mg/kg PO q12h).
- Azithromycin (5 mg/kg PO q24h).
- Tetracycline (20 mg/kg PO q8h).
- Bismuth subsalicylate has mucosal protectant, anti-endotoxemic, and weak antibacterial properties; it remains unclear which property is responsible for its beneficial effects in HLO infections (0.22 mL/kg of 130 mg/15 mL solution of Pepto-Bismol PO q4–6h).

Antisecretory Agents (One with Two Antibiotics)

- Omeprazole (0.7–1 mg/kg PO q12h)
- Famotidine (0.5 mg/kg PO q12–24h)
- Ranitidine (1–2 mg/kg PO q12h)

Intestinal and Hepatic Helicobacter spp. in Dogs

A combination of amoxicillin and metronidazole at above dosages may be effective.

CONTRAINdicATIONS

Hypersensitivity to one of the antibiotics.

ALTERNATIVE DRUG(S)

Patients with HLO infections and gastritis that do not respond to antibiotic therapy usually are given immunosuppressive therapy (prednisolone, or others) for inflammatory bowel disease with gastric involvement.



FOLLOW-UP

PATIENT MONITORING

• Serologic tests are not useful to confirm eradication of gastric HLOs—serum IgG titers may not decrease for up to 6 months after a cleared infection.

• ^{13}C -urea breath and blood tests have been evaluated to monitor the eradication of HLOs in dogs and cats, but these tests are currently not commercially available.

• If vomiting persists or recurs after cessation of combination therapy, a repeat endoscopic biopsy to determine whether the infection has been successfully eradicated may be necessary.

PREVENTION/AVOIDANCE

Avoid overcrowding and poor sanitation.

EXPECTED COURSE AND PROGNOSIS

- The efficacy of therapeutic regimens currently employed in dogs and cats for eradicating *Helicobacter* spp. infections is questionable.
 - Metronidazole (20 mg/kg PO q12h), amoxicillin (20 mg/kg PO q12h), and famotidine (0.5 mg/kg PO q12h) for 14 days effectively eradicated *Helicobacter* spp. in 6 of 8 dogs when evaluated 3 days post-treatment, but all dogs were recolonized by day 28 after completion of treatment.
 - Clarithromycin (30 mg/cat PO q12h), metronidazole (30 mg/cat PO q12h), ranitidine (20 mg/cat PO q12h), and bismuth subsalicylate (40 mg PO q12h) for 4 days was effective in eradicating *H. heilmannii* in 11 of 11 cats by 10 days, but two cats were reinfected 42 days post-treatment.
 - Amoxicillin (20 mg/kg PO q8h), metronidazole (20 mg/kg PO q8h), and omeprazole (0.7 mg/kg PO q24h) for 21 days transiently eradicated *H. pylori* in 6 cats, but all were reinfected 6 weeks post-treatment.
- (Note: this dose of metronidazole has the potential for toxicity.)

HELICOBACTER spp.

H

MISCELLANEOUS

ASSOCIATED CONDITIONS

Other gastric diseases

AGE-RELATED FACTORS

Gastric HLOs appear to be acquired at a young age.

ZOONOTIC POTENTIAL

- The high prevalence of *Helicobacter* spp. in dogs and cats raises the possibility that household pets may serve as a reservoir for the transmission of *Helicobacter* spp. to human beings.
- *H. pylori*, *H. heilmannii*, and *H. felis* have been isolated from humans with gastritis.
- *H. fennelliae* and *H. cinaedi* have been isolated from immunocompromised humans with proctitis and colitis.
- *H. cinaedi* and *H. canis* have been associated with septicemia in humans.
- *H. pylori* has not been identified in pet dogs or pet cats.

PREGNANCY/FERTILITY/BREEDING

Avoid metronidazole and tetracycline in pregnant animals.

SYNONYMS

- Gastric spiral bacterial • *Gastrospirillum*

SEE ALSO

- Gastritis, Chronic • Vomiting, Chronic

ABBREVIATIONS

- ELISA = enzyme-linked immunosorbent assay
- HLO = *Helicobacter*-like organism
- PCR = polymerase chain reaction

Suggested Reading

Leib MS, Duncan RB, Ward DL. Triple antimicrobial therapy and acid suppression in dogs with chronic vomiting and gastric *Helicobacter* spp. J Vet Intern Med 2007, 21:1185–1192.

Simpson KW, Neiger R, DeNovo R, Shering R. The relationship of *Helicobacter* spp. infection to gastric disease in dogs and cats. J Vet Intern Med 2000, 14:223–227.

Authors Jan S. Suchodolski and Jörg M. Steiner

Consulting Editor Stanley L. Marks



**Client Education Handout
available online**

HEMANGIOSARCOMA, BONE



BASICS

OVERVIEW

- A highly metastatic malignant tumor of the vascular endothelium.
- Primary bone HSA is rare and accounts for < 5% of all canine bone tumors.
- Difficult to differentiate metastatic from primary bone lesions based upon radiographs.
- Can arise from various appendicular sites; while the rib is most common axial location.
- Extremely rare in cats.

SIGNALMENT

- Dog and rarely cat.
- Golden retrievers, Labrador retrievers, and German shepherds predisposed.
- Typically middle-aged to older dogs; older cats.
- Possible slight predisposition for male dogs.

SIGNS

- Appendicular—pain/lameness, soft tissue swelling/mass, pathologic fracture.
- Axial—myelopathy consequent to vertebral body collapse and spinal cord compression; thoracic wall swelling with rib involvement, signs related to hemorrhagic pleural effusion if involving ribcage.

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Radiography—other primary or metastatic bone tumors (i.e., osteosarcoma, fibrosarcoma, chondrosarcoma).
- Osteomyelitis (bacterial or fungal).
- Histopathology—can be difficult to differentiate from the vascular telangiectatic subtype of OSA without immunohistochemistry.

CBC/BIOCHEMISTRY/URINALYSIS

Abnormalities less common than with splenic hemangiosarcoma but may include:

- Regenerative anemia
- Thrombocytopenia
- Leukocytosis.

OTHER LABORATORY TESTS

N/A

IMAGING

- *Radiography*—may reveal poorly marginated osteolytic lesion with minimal periosteal reaction; pathologic fractures possible.
- *Thoracic radiography*—should be used to screen for pulmonary metastasis.
- *Abdominal and cardiac ultrasonography*—should be used to screen for primary visceral tumors (spleen, liver, heart) and metastatic lesions.
- *CT scan*—can better define the extent of bone tumor for surgical excision (especially axial lesions) and provides a more sensitive assessment for pulmonary metastasis.

DIAGNOSTIC PROCEDURES

- Excisional biopsy is the preferred method for diagnosis.
- An incisional biopsy may yield a diagnosis but due to the vascular nature of the tumor, blood contamination within the specimen may preclude a diagnosis or prevent differentiation between HSA and telangiectatic OSA.

PATHOLOGIC FINDINGS

- *Gross findings*—a dark, friable mass often within the medullary cavity of the bone.
- *Histopathology*—anaplastic mesenchymal cells arranged in chords separated by a collagenous background for vascular channels and spaces filled with red blood cells, thrombi, and necrotic debris.
- Can use immunohistochemistry for von Willebrand factor (factor VIII-related antigen) or CD31/platelet endothelial cell adhesion molecule (PECAM) to confirm endothelial cell origin.



TREATMENT

- Aggressive surgical excision of primary tumor.
- Amputation is required if appendicular.
- Axial tumors may be more difficult to resect.
- Radiation therapy may be used for palliation of bone-related pain or as an adjuvant to marginal resection of axial lesions.
- Adjuvant chemotherapy is indicated due to high metastatic potential.



MEDICATIONS

DRUG(S)

- Doxorubicin: 30 mg/m² IV dogs > 15 kg; 1 mg/kg IV dogs < 15 kg q2–3 weeks for 5 cycles; cats 1 mg/kg IV q3 weeks for 5 cycles.
- Metronomic cyclophosphamide (12.5–15 mg/m² PO q24h) in combination with an NSAID (e.g., piroxicam 0.3 mg/kg PO q24h) may be used concurrent with doxorubicin and as a long-term maintenance therapy.
- Vincristine (0.5–0.7 mg/m²) and cyclophosphamide (200–250 mg/m²) q21 days can be used in rescue setting.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Doxorubicin administration can lead to gastrointestinal, bone marrow, cardiac, renal, hypersensitivity, and extravasation toxicities.
- Doxorubicin can lead to cumulative cardiotoxicity in dogs.
- Cyclophosphamide can lead to sterile hemorrhagic cystitis in dogs.
- NSAIDs can lead to gastrointestinal toxicity and liver/kidney damage.



FOLLOW-UP

PATIENT MONITORING

- Physical examination, laboratory work, thoracic radiography, and abdominal ultrasonography every 3 months after the completion of therapy.
- If treated with metronomic chemotherapy, routine monthly urinalysis recommended to screen for sterile hemorrhagic cystitis.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Pathologic fracture.
- Bone lesions, especially within the rib, and visceral metastatic lesions may rupture, resulting in clinical signs related to effusion or anemia.

EXPECTED COURSE AND PROGNOSIS

- Aggressive course of disease with high risk for metastasis.
- Median survival time for bone presentation not well-defined due to rarity of cases.
- Less than 10% of patients survive 1 year following surgery alone; prognosis with addition of chemotherapy not defined but may be similar to that associated with the splenic presentation.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Chemotherapy drugs may be carcinogenic and mutagenic.

ABBREVIATIONS

- CT = computed tomography
- HSA = hemangiosarcoma
- NSAIDs = nonsteroidal anti-inflammatory drugs
- OSA = osteosarcoma

Suggested Reading

Thamm DH. Hemangiosarcoma. In:

Withrow SJ, Vail DM, eds. Small Animal Clinical Oncology, 5th ed. St. Louis, MO: Saunders/Elsevier, 2013, pp. 679–699.

Authors Craig A. Clifford and Christine Mullin

Consulting Editor Timothy M. Fan

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HEMANGIOSARCOMA, HEART



BASICS

OVERVIEW

- A highly metastatic malignant tumor of the vascular endothelium.
- The most common cardiac tumor in dogs.
- Can be a primary or metastatic site.
- Most tumors involve the right atrium or right auricular appendage.
- Metastasis can be multi-organ including lungs, kidneys, muscle, peritoneum, etc.

SIGNALMENT

- Dog and rarely cat.
- German shepherds, Labrador retrievers, golden retrievers predisposed.
- Typically middle-aged to older animals.
- Possible slight predisposition for male dogs.

SIGNS

- Signs most commonly related to pericardial effusion, cardiac tamponade, and right-sided congestive heart failure.
- *Historical findings*—include collapse, lethargy, weakness, anorexia, cough, dyspnea, vomiting, and exercise intolerance.
- *Physical examination findings*—include muffled heart and lung sounds, arrhythmias, pulse deficits, pulsus paradoxus, jugular vein distention, and hepatomegaly.

CAUSES & RISK FACTORS

- Dogs—genetic abnormalities including overexpression of the oncogene STAT3, mutations within tumor suppressor genes *p53* and *PTEN*, and overexpression of angiogenic factors such as vascular endothelial growth factor and angiopoietins.
- Cats—none identified.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other cardiac neoplasia
- Idiopathic hemorrhagic pericardial effusion
- Other causes of right heart failure or arrhythmias

CBC/BIOCHEMISTRY/URINALYSIS

- Regenerative anemia
- Thrombocytopenia
- Poikilocytosis—acanthocytes, schistocytes, spherocytes
- Leukocytosis characterized by mature neutrophilia

OTHER LABORATORY TESTS

Coagulation panel (PT, PTT, D-dimers, fibrinogen)—criteria for DIC present in up to 50% of patients.

IMAGING

- *Radiography*—thoracic radiographs may reveal the presence of a globoid cardiac silhouette, pleural effusion, and pulmonary metastasis.
- *Ultrasonography*—abdominal ultrasonography can be used to screen for visceral metastatic disease or primary splenic or hepatic lesions, omental nodules, and free abdominal fluid (hemoabdomen).

- *Echocardiography*—useful for identifying and removing pericardial effusion and determining the location and extent of tumor involvement.
- *Advanced imaging*—cardiac-gated MRI or CT scan can be used to help determine surgical resectability.

DIAGNOSTIC PROCEDURES

- Definitive diagnosis requires a tissue biopsy.
- Thoracoscopy can be used to visualize the tumor and obtain pericardial biopsies.
- Cytologic evaluation of pericardial fluid rarely provides a definitive diagnosis.
- Electrocardiography may reveal arrhythmias.

PATHOLOGIC FINDINGS

- *Gross findings*—solitary hemorrhagic, friable masses within the right side of the heart.
- *Histopathology findings*—atypical mesenchymal cells forming irregular blood-filled vascular spaces within a tumor mass. Often abundant necrosis and hemorrhage.



TREATMENT

- Periodic pericardiocentesis can provide temporary symptomatic relief from cardiac tamponade.
- Thoracoscopic pericardectomy (pericardial window) can be performed as a palliative procedure to lower the risk of life-threatening cardiac tamponade.
- Surgical tumor excision provides the best chance of long-term tumor control but is restricted to the atrial appendage and/or small areas of the right atrial wall.
- The use of doxorubicin chemotherapy in the measurable disease setting can provide clinical benefit for a median of ~4 months.



MEDICATIONS

DRUG(S)

- Doxorubicin (30 mg/m^2 IV dogs $> 15 \text{ kg}$; 1 mg/kg IV dogs $< 15 \text{ kg}$ q2–3 weeks for 5 cycles).
- Metronomic cyclophosphamide ($12.5\text{--}15 \text{ mg/m}^2$ PO q24h) in combination with an NSAID (e.g., piroxicam 0.3 mg/kg PO q24h) may be used concurrent or as an alternative to doxorubicin.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Doxorubicin administration can lead to gastrointestinal, bone marrow, cardiac, renal, hypersensitivity, and extravasation toxicities.
- Doxorubicin can lead to cumulative cardiotoxicity in dogs.
- Cyclophosphamide can lead to sterile hemorrhagic cystitis in dogs.
- NSAIDs can lead to gastrointestinal toxicity and liver/kidney damage.



FOLLOW-UP

PATIENT MONITORING

- Physical examinations, blood work, thoracic radiographs, and cardiac ultrasounds every 2–3 months after the completion of therapy.
- If treated with metronomic chemotherapy, monthly urinalysis recommended to screen for sterile hemorrhagic cystitis.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Congestive heart failure secondary to pericardial effusion and cardiac tamponade.

EXPECTED COURSE AND PROGNOSIS

- Prognosis guarded to poor, increased risk for acute death due to cardiac tamponade or fatal arrhythmias.
- Median survival < 1 month without treatment, ~ 4 months with doxorubicin, possibly longer if tumor resection performed.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Chemotherapy drugs may be carcinogenic and mutagenic.

ABBREVIATIONS

- DIC = disseminated intravascular coagulation
- HSA = hemangiosarcoma
- PT = prothrombin time
- PTT = partial thromboplastin time

Suggested Reading

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HEMANGIOSARCOMA, SKIN



BASICS

OVERVIEW

- A highly metastatic malignant tumor of the vascular endothelium.
- Primary tumor develops within dermal or subcutaneous tissues.
- Accounts for ~14% of all HSA in dogs.
- Metastatic risk dependent upon grade and location within the tissues (stage).
- Subcutaneous/intramuscular lesions may represent metastasis from a primary visceral tumor.

SIGNALMENT

- Dog and cat.
- Pit bull, boxer, and German shepherd affected more commonly than other breeds.
- Dermal hemangiosarcoma—whippet, greyhound, and related breeds.
- Median age, 9 years; range, 4.5–15.6 years.

SIGNS

Dermal

- Firm, raised, dark nodules/masses on the limbs, head, face, ears, prepuce, nasal planum, and ventral abdomen.
- When caused by ultraviolet radiation on the ventral abdomen/inguinal region, often appear as several small blood blister-like nodules.

Subcutaneous/Intramuscular

- Usually solitary mass but multiple masses may occur.
- Masses are typically larger than dermal tumors.
- Firm or soft, fluctuant masses with or without associated bruising.
- Intratumoral bleeding is common.
- Pelvic limbs are commonly affected, but may arise in any location.
- In cats, the flank, ventral abdomen, inguinal region, and cervical region are most commonly affected sites.

CAUSES & RISK FACTORS

- Dermal HSA associated with ultraviolet radiation (actinic keratosis), especially in sparsely haired and lightly pigmented skin.
- Subcutaneous HSA may be secondary to prior ionizing radiation therapy.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Trauma-induced subcutaneous hematoma
- Other sarcomas
- Mast cell tumor

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal.
- Possible mild regenerative anemia and thrombocytopenia if tumor hemorrhage.

OTHER LABORATORY TESTS

Coagulation panel (PT, PTT, D-dimers, fibrinogen)—may see changes compatible

with DIC if large, bleeding subcutaneous or intramuscular tumor.

IMAGING

- *Radiography*—thoracic radiographs are used to screen for pulmonary metastatic disease characterized by coalescing miliary pattern, or nodular/generalized miliary interstitial pattern.
- *Ultrasonography*—abdominal ultrasonography should be performed to screen for metastatic (or primary) splenic or hepatic lesions, omental nodules, and free abdominal fluid (hemoabdomen).
- *Echocardiography*—can be used to identify right atrial masses (better identified when at least some degree of pericardial effusion is present).
- *Advanced imaging*—MRI/CT can be used for staging and surgical planning purposes.

Note: True dermal HSA are generally benign and may not require an extensive staging process.

DIAGNOSTIC PROCEDURES

Cytology

- Often unrewarding due to insufficient cell numbers and blood contamination.
- Neoplastic cells are spindle, oval, flamed, or stellate shape with anisocytosis and anisokaryosis, single round, oval, or pleomorphic nuclei with prominent nucleoli, low nuclear cytoplasmic ratio, and moderate-to-abundant basophilic and usually vacuolated cytoplasm.

PATHOLOGIC FINDINGS

- *Gross findings*—can include well circumscribed blood blister-like nodules confined to the dermis or more invasive and often poorly circumscribed hemorrhagic tumors within the subcutaneous and intramuscular space.
- *Histopathologic findings*—characterized by neoplastic mesenchymal cells forming irregular vascular channels with solid areas composed of severely anaplastic stromal cells.
- Allows differentiation between hemangioma and HSA and dermal versus subcutaneous/intramuscular origin.
- Some areas may not resemble vascular structures, so immunohistochemistry for von Willebrand factor (factor VIII-related antigen) or CD31/platelet endothelial cell adhesion molecule (PECAM) can be used to confirm endothelial cell origin.

Histologic Staging System

- Stage I—confined to dermis
- Stage II—subcutaneous involvement
- Stage III—intramuscular involvement



TREATMENT

Aggressive surgical excision is the first-line treatment of choice.

- Definitive radiation therapy may be used postoperatively for the control of microscopic residual tumor burden.

- Palliative (hypofractionated) radiation may be used for treatment of non-resectable macroscopic tumor burden, providing response rates of up to 60% and survival times of < 100 days.

- Doxorubicin chemotherapy has been associated with moderate response rates (up to 46%) and MST ~130 days for non-resectable tumors (subcutaneous/intramuscular).
- Metronomic chemotherapy can be used to delay time to locoregional recurrence after surgery given its anti-angiogenic effect.



MEDICATIONS

DRUG(S)

- Doxorubicin (30 mg/m^2 IV dogs $> 15 \text{ kg}$; 1 mg/kg IV dogs $< 15 \text{ kg}$ q2–3 weeks for 5 cycles).
- Metronomic cyclophosphamide ($12.5\text{--}15 \text{ mg/m}^2$ PO q24h) in combination with an NSAID (e.g., piroxicam 0.3 mg/kg PO q24h) may be used concurrent or as an alternative to doxorubicin.

CONTRAINdications/POSSIBLE INTERACTIONS

- Doxorubicin administration can lead to gastrointestinal, bone marrow, cardiac, renal, hypersensitivity, and extravasation toxicities.
- Doxorubicin can lead to cumulative cardiotoxicity in dogs.
- Evaluate cardiac function with echocardiography prior to, during, and after therapy in breeds predisposed to dilated cardiomyopathy (i.e., Great Dane, St. Bernard, Irish wolfhound) and those patients with clinical evidence of heart disease.
- Cyclophosphamide can lead to sterile hemorrhagic cystitis in dogs. Incidence with metronomic dosing not yet defined; is typically < 10% with conventional dosing.
- NSAIDs can lead to gastrointestinal toxicity and liver/kidney damage.

ALTERNATIVE DRUG(S)

Immunotherapy: A medicinal mushroom extract made from the *Coriolus versicolor* mushroom containing polysaccharide peptide may have efficacy in dogs with HSA.



FOLLOW-UP

PATIENT MONITORING

- Physical examinations, bloodwork, thoracic radiographs, and abdominal ultrasounds every 2–3 months after the completion of therapy.
- If treated with metronomic chemotherapy, routine monthly urinalysis recommended to screen for sterile hemorrhagic cystitis.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Tumor hemorrhage

(CONTINUED)

EXPECTED COURSE AND PROGNOSIS

- Dermal HSA—prognosis very good with treatment. MST in dogs of 987 days with surgery alone; disease-free interval in cats > 450 days with surgery alone.
- Subcutaneous HSA—higher metastatic risk but prognosis can be good with aggressive treatment. MST of 172 days for dogs undergoing surgery alone versus > 1,100 days if surgery and adjuvant doxorubicin chemotherapy.
- Intramuscular HSA—MST of 272 days with surgery and doxorubicin chemotherapy.
- High risk of locoregional recurrence and distant metastasis with stage II (SQ) and III (IM) HSA.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Other ultraviolet-induced skin tumors such as squamous cell carcinoma.

PREGNANCY/FERTILITY/BREEDING

Chemotherapy drugs may be carcinogenic and mutagenic.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Chemotherapy drugs may be carcinogenic and mutagenic.

ABBREVIATIONS

- CT = computed tomography
- DIC = disseminated intravascular coagulation
- HSA = hemangiosarcoma
- MRI = magnetic resonance imaging
- MST = median survival time
- IM = intramuscular
- NSAIDs = nonsteroidal anti-inflammatory drugs
- PT = prothrombin time
- PTT = partial thromboplastin time
- SQ = subcutaneous

Suggested Reading

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HEMANGIOSARCOMA, SKIN

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H

HEMANGIOSARCOMA, SPLEEN AND LIVER



BASICS

OVERVIEW

- A highly metastatic malignant tumor of the vascular endothelium.
- Accounts for up to 70% of all canine splenic tumors.
- Primary tumor rupture leads to acute hemorrhage, collapse, and often sudden death.
- Highly metastatic tumor that spreads early in the course of disease via hematogenous and intra-abdominal implantation routes.
- Metastasis can be to any organ including lungs, kidneys, muscle, peritoneum, omentum, lymph nodes, mesentery, adrenal glands, spinal cord, brain, subcutaneous tissue, and diaphragm.

SIGNALMENT

- Dog and rarely cat.
- German shepherd, Labrador retriever, golden retriever predisposed.
- Typically middle-aged to older animals.
- Possible slight predisposition for male dogs.

SIGNS

- *Historical findings*—can be variable and include weakness, lethargy, dyspnea, cough, inappetance, and weight loss.
- *Physical examination findings*—pale mucous membranes, arrhythmias, tachypnea, abdominal distension, and palpable cranial abdominal mass.

CAUSES & RISK FACTORS

- Dogs—genetic abnormalities including overexpression of the oncogene STAT3, mutations within tumor suppressor genes *p53* and *PTEN*, and overexpression of angiogenic factors such as vascular endothelial growth factor and angiopoietins.
- Cats—none identified.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Anticoagulant rodenticide ingestion.
- Other splenic and hepatic masses: hematoma, hemangioma, hepatoma, lymphoma, leiomyosarcoma, liposarcoma, splenic cyst, hepatocellular carcinoma, hepatic cyst.

CBC/BIOCHEMISTRY/URINALYSIS

- Regenerative anemia with nucleated red blood cells
- Thrombocytopenia
- Poikilocytosis—acanthocytes, schistocytes, spherocytes
- Leukocytosis characterized by mature neutrophilia
- Elevated liver enzymes

OTHER LABORATORY TESTS

Coagulation panel (PT, PTT, D-dimers, fibrinogen)—criteria for DIC present in up to 50% of patients.

IMAGING

Radiography

- Abdominal radiographs may identify a cranial abdominal mass and evidence for abdominal fluid (loss of serosal detail).
- Thoracic radiographs are used to screen for pulmonary metastatic disease characterized by coalescing miliary pattern, or nodular/generalized miliary interstitial pattern.

Ultrasonography

- Abdominal ultrasonography is used for the detection of splenic or hepatic lesions, omental nodules, and free abdominal fluid (hemoabdomen).
- Echocardiography is used to identify right atrial masses (better identified when at least some degree of pericardial effusion is present).

Advanced Imaging

MRI/CT provides high sensitivity and specificity in determining benign from malignant processes of the liver and spleen.

STAGE OF DISEASE

- Stage I—tumor confined to one organ, no rupture
- Stage II—ruptured tumor
- Stage III—measureable metastatic disease

DIAGNOSTIC PROCEDURES

- Abdominocentesis to characterize fluid accumulation—usually a serosanguineous fluid or hemorrhagic non-clotting effusion. Can compare PCV of effusion to peripheral blood PCV to confirm blood loss.
- Cytology—diagnostic yield for HSA is reported to be low (< 25%).

PATHOLOGIC FINDINGS

- *Gross findings*—solitary or multiple hemorrhagic, friable masses or nodules within the spleen and/or liver.
- *Histopathology findings*—atypical mesenchymal cells forming irregular blood-filled vascular spaces within a tumor mass. Often abundant necrosis and hemorrhage. Some areas may not resemble vascular structures, so immunohistochemistry for von Willebrand factor (factor VIII-related antigen) or CD31/platelet endothelial cell adhesion molecule (PECAM) can be used to confirm endothelial cell origin.



TREATMENT

- Balanced isotonic electrolyte solutions ± colloids to correct hypovolemic shock and reduced cardiac output.
- Fresh whole blood or packed red blood cell transfusion to replace reduced oxygen-carrying capacity from acute bleeding.

- Fresh frozen plasma if coagulopathy or signs of DIC present.

- Splenectomy or liver lobectomy are the standard of care surgical procedures and initial treatment of choice. Removes macroscopic tumor burden and lessens the ongoing risk of acute death from hemorrhage. Surgery alone is palliative, with median survival times of 1–3 months without adjuvant chemotherapy.
- The use of doxorubicin-based chemotherapy has been consistently shown to improve remission duration and survival times.
- Metronomic chemotherapy may offer benefit vs. surgery alone as a sole therapy or when used concurrent to or following doxorubicin chemotherapy.



MEDICATIONS

DRUG(S)

- Doxorubicin (30 mg/m^2 IV dogs $> 15 \text{ kg}$; 1 mg/kg IV dogs $< 15 \text{ kg}$ q2–3 weeks for 5 cycles).
- Metronomic cyclophosphamide ($12.5\text{--}15 \text{ mg/m}^2$ PO q24h) in combination with an NSAID (e.g., piroxicam 0.3 mg/kg PO q24h) may be used concurrent or as an alternative to doxorubicin.

CONTRAINdications/POSSIBLE INTERACTIONS

- Doxorubicin administration can lead to gastrointestinal, bone marrow, cardiac, renal, hypersensitivity, and extravasation toxicities.
- Doxorubicin can lead to cumulative cardiotoxicity in dogs.
- Cyclophosphamide can lead to sterile hemorrhagic cystitis in dogs.
- NSAIDs can lead to gastrointestinal toxicity and liver/kidney damage.

ALTERNATIVE DRUG(S)

- Immunotherapy:
 - Liposomal muramyl tripeptide phosphatidylethanolamine (L-MTP-PE), a synthetic macrophage activator derived from mycobacterial cell wall, when given concurrent to a doxorubicin/cyclophosphamide protocol, was associated with the longest reported survival times (MST 273 days) for this disease. This agent is not currently commercially available in the US.
 - An allogeneic HSA vaccine, when given concurrent to doxorubicin, was associated with a MST of 182 days but is not currently commercially available.



FOLLOW-UP

PATIENT MONITORING

- Physical examinations, blood work, thoracic radiographs, and cardiac ultrasounds

(CONTINUED)

HEMANGIOSARCOMA, SPLEEN AND LIVER

every 2–3 months after the completion of therapy.

- If treated with metronomic chemotherapy, routine monthly urinalysis recommended to screen for sterile hemorrhagic cystitis.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Death due to acute hemorrhage or fatal tachyarrhythmias.

EXPECTED COURSE AND PROGNOSIS

- Prognosis guarded to poor.
- Median survival time with surgery alone (dogs): 19–65 days.
- Median survival time with surgery plus chemotherapy (dogs): 145–179 days.
- Mean time to progression in cats: 4–5 months.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Chemotherapy drugs may be carcinogenic and mutagenic.

SEE ALSO

N/A

ABBREVIATIONS

- CT = computed tomography
- DIC = disseminated intravascular coagulation
- HSA = hemangiosarcoma
- MRI = magnetic resonance imaging
- MST = median survival time
- NSAIDs = nonsteroidal anti-inflammatory drugs
- PT = prothrombin time
- PTT = partial thromboplastin time

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H

HEMATEMESIS



BASICS

DEFINITION

The vomiting of blood

PATHOPHYSIOLOGY

A disruption in the gastric or upper small intestinal mucosal barrier leading to inflammation and bleeding. Coagulopathies can also present with hematemesis. An animal may also vomit blood that originated in the oral cavity or respiratory system and was swallowed.

SYSTEMS AFFECTED

- Gastrointestinal—*inflammation, trauma, ulceration, neoplasia, and/or foreign body in the oral cavity, pharyngeal area, esophagus, stomach, and/or duodenum.*
- Cardiovascular—acute, severe hemorrhage may result in tachycardia, systolic heart murmur, and/or hypotension.
- Hematologic—coagulopathy with gastrointestinal hemorrhage can lead to hematemesis.
- Respiratory—respiratory hemorrhage with ingestion can lead to hematemesis.

GENETICS

N/A

INCIDENCE/PREVALENCE

True incidence unknown

SIGNALMENT

Species

Dog and, less commonly, cat

Breed Predilections

There appears to be an overrepresentation of chow chows and Siamese cats with gastric adenocarcinoma.

Mean Age and Range

All ages

Predominant Sex

Male dogs have increased incidence of gastric carcinoma

SIGNS

Historical Findings

• Vomiting with blood—blood in the vomitus may appear as fresh flecks of blood, blood clots, or digested blood, which looks like coffee grounds. • Melena can be observed. • Anorexia. • Abdominal pain (may assume the praying position).

Physical Examination Findings

- Abdominal pain
- Melena
- If patient is anemic—tachycardia, heart murmur, pallor, weakness, and/or collapse.

CAUSES

Coagulopathies

- Thrombocytopenia
- Thrombocytopathia—von Willebrand's disease, NSAIDs, drugs, uremia
- Hyperviscosity syndrome
- Disseminated intravascular coagulopathy
- Anticoagulant rodenticide toxicity
- Coagulation factor deficiency
- Liver failure
- Polycythemia

Drugs

NSAIDs, glucocorticoids

Gastrointestinal Diseases

- Inflammatory bowel disease
- Gastric, or duodenal neoplasia
- Gastric, or duodenal foreign body
- Gastric or intestinal volvulus or torsion
- Hemorrhagic gastroenteritis
- Gastroduodenal ulcers
- Gastroesophageal intussusception

Toxicity

- Heavy metal poisoning (arsenic, zinc, thallium, iron, or lead)
- Plant intoxication (dieffenbachia, sago palm, mushroom, castor bean)
- Chemical intoxication (phenol, ethylene glycol, corrosive agents, psoriasis creams—vitamin D analogues)
- Pesticide/rodenticide toxicity (cholecalciferol)
- Snake bite
- Aflatoxins
- Bee sting

Infectious Diseases

- Gastrointestinal parasitism
- Pythiosis (fungal oomycete)
- Viral, fungal, or bacterial gastroenteritis
- Virulent systemic feline calicivirus
- Rickettsial infections

Metabolic Diseases

- Renal failure
- Liver disease
- Hypoadrenocorticism
- Pancreatitis

Neoplasia

- Mastocytosis
- Gastrinoma
- Oral, nasal, respiratory (blood is swallowed and subsequently vomited), or gastrointestinal tumors
- APUDomas

Neurologic Diseases

- Head trauma
- Spinal cord disease

Respiratory Diseases

- Nasal disease—neoplasia, fungal infection
- Pulmonary and airway disease—neoplasia, severe pneumonia, fungal infection, foreign body, heartworm disease
- Mediastinal neoplasia

Stress/Major Medical Illness

- Septic or hypovolemic shock
- Severe illness
- Burns
- Heat stroke
- Major surgery
- Sustained strenuous exercise
- Trauma
- Systemic hypertension
- Thromboembolic disease
- Hypotension

RISK FACTORS

- Administration of ulcerogenic drugs—NSAIDs or glucocorticoids
- Critically ill patients
- Hypovolemic or septic shock
- Thrombocytopenia
- Concurrent administration of NSAIDs and glucocorticoids



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hemoptysis—thoracic radiographs may reveal presence of airway or pulmonary disease.
- Regurgitation or vomiting of swallowed blood from extragastrointestinal diseases (e.g., oropharyngeal, nasopharyngeal, and cutaneous diseases).
- Ingestion and vomiting of foreign materials or foods that

look like fresh or digested blood (e.g., oral iron).

CBC/BIOCHEMISTRY/URINALYSIS

- If acute (3–5 days) blood loss—nonregenerative anemia (normocytic, normochromic, minimal reticulocytosis).
- If blood loss > 5–7 days in duration—regenerative anemia (macrocytic, reticulocytosis).
- If chronic blood loss—iron-deficiency anemia (microcytic, hypochromic, variable reticulocytosis, with or without thrombocytosis).
- ± thrombocytopenia.
- ± panhypoproteinemia with alimentary hemorrhage.
- May have mature neutrophilia or left shift neutrophilia with sepsis and/or gastroduodenal ulcer perforation.
- BUN: creatinine ratio may be elevated with gastrointestinal hemorrhage, but will also be increased with dehydration.

OTHER LABORATORY TESTS

- Fecal occult blood test may be false positive if dog is not on a non-meat diet for 3 days prior to test.
- Fecal flotation—to screen for gastrointestinal parasitism.
- Coagulation profile—if a coagulopathy is suspected.
- Bile acids—if liver disease is suspected.
- ACTH stimulation—if hypoadrenocorticism is suspected.

IMAGING

- Abdominal radiography may identify a gastric or duodenal foreign body or mass, pancreatitis, pneumoperitoneum, effusion or changes consistent with kidney, pancreas, or liver disease.
- Thoracic radiographs may reveal esophageal foreign body or mass, gastroesophageal intussusception, mediastinal mass, pulmonary or airway disease, and/or pulmonary metastasis.
- Abdominal ultrasound may identify a gastric or duodenal mass, gastric or duodenal wall thickening or altered layering, gastric ulcer, and/or abdominal lymphadenopathy.
- Abdominal ultrasound can also screen for abnormalities in the pancreas, liver, kidneys, and other abdominal organs as source of hematemesis.
- Gastrointestinal scintigraphy may be used to localize gastrointestinal blood loss.

DIAGNOSTIC PROCEDURES

- Endoscopy to evaluate the mucosal appearance of the esophagus, stomach, and upper small intestinal tract once extragastrointestinal causes are ruled out.
- Biopsy mucosal lesions and submit for histopathology to determine the nature of the underlying gastrointestinal disease.
- Abdominocentesis may identify septic peritonitis.
- Obtain fine needle aspirates or biopsy specimens of cutaneous or intra-abdominal masses to identify neoplasia/disease.

PATHOLOGIC FINDINGS

- Gastroduodenal inflammation and hemorrhage.
- Ulcers may have more necrosis, microthrombi, and hemorrhage, and deeper penetration than erosions.

(CONTINUED)

HEMATEMESIS**TREATMENT****APPROPRIATE HEALTH CARE**

- Treat any underlying causes.
- Treat on an outpatient basis if the cause is identified and removed, vomiting is not excessive, and gastroduodenal bleeding is minimal.
- Inpatients—those with severe gastroduodenal bleeding, ulcer perforation, excessive vomiting, and/or shock.

NURSING CARE

- Intravenous fluids to maintain hydration.
- May need aggressive intravenous fluid treatment for shock—crystalloids and/or colloids.
- Severe hypoproteinemic patients may require colloids and/or plasma to increase vascular oncotic pressure.
- May need transfusions (whole blood or packed red blood cells) in patients with severe gastroduodenal hemorrhage.
- Patients with underlying coagulopathies may need whole blood or fresh frozen plasma to replace clotting factors.
- In severe cases of hematemesis—to stop the gastrointestinal bleeding, ice water lavage (10–20 mL/kg remaining in stomach for 15–30 minutes) or lavage with norepinephrine (8 mg/500 mL) diluted in ice water can be attempted.

DIET

- Discontinue oral intake if vomiting.
- When feeding is resumed, feed small amounts in multiple feedings.

CLIENT EDUCATION

- NSAIDs should be administered to pets only under the guidance of a veterinarian.
- Administration of NSAIDs (including COX-2 inhibitors) can result in gastroduodenal ulcerations and perforations.
- Adverse effects of NSAIDs can be reduced by giving drug with food and concurrent administration of a synthetic prostaglandin E₁ analogue (e.g., misoprostol).

SURGICAL CONSIDERATIONS

Surgical treatment is indicated if medical treatment fails after 5–7 days, hemorrhage is uncontrolled, gastroduodenal ulcer perforates, and/or potentially resectable tumor is identified.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Histamine (H₂) receptor antagonists competitively inhibit gastric acid secretion and are the initial drug of choice (ranitidine 1–2 mg/kg SC, PO, IV q8–12h, dog and cat; famotidine 0.5–1 mg/kg PO, IV q12–24h, dog and cat; nizatidine 5 mg/kg PO q24h, dog). H₂ receptor antagonists differ in potency and duration of action. Famotidine is most potent followed by ranitidine. Treat for

at least 6–8 weeks. Rebound gastric acid hypersecretion may occur when H₂ blockers are discontinued but can be minimized by tapering the dose as it is discontinued.

- H₂-receptor antagonists are less potent than proton pump inhibitors.
- Antacids neutralize gastric acid and some induce local synthesis of mucosal protectants but must be given at least four to six times/day to be effective. Owner compliance with this regimen is often poor.
- Sucralfate suspension (0.5–1 g PO q6–8h) protects ulcerated tissue (cytoprotection) by binding to ulcer sites, adsorbing pepsin and bile salts, and stimulating prostaglandin synthesis. Binding is greater in duodenal than gastric ulcers.
- Antibiotic(s) with activity against enteric gram negative bacteria and anaerobes should be given parenterally if a break in gastrointestinal mucosal barrier is suspected or aspiration pneumonia is present.
- Antiemetics (chlorpromazine 0.5 mg/kg q6–8h SC, IM, IV, dog and cat; prochlorperazine 0.1–0.5 mg/kg q6–8h SC, IM, dog and cat; ondansetron 0.5 mg/kg IV q12h, dog; 0.2 mg/kg IV q12h, cat; metoclopramide 1–2 mg/kg/24h CRI, dog and cat; maropitant 1 mg/kg SC q24h for 5 days, dog; 2 mg/kg PO q24h for 5 days, dog) are administered if vomiting occurs frequently or results in significant fluid losses.
- Proton pump inhibitors (omeprazole 1 mg/kg PO q12–24h, dog; pantoprazole 1 mg/kg IV dogs)—omeprazole is the most potent inhibitor of gastric acid secretion; treatment of choice for gastrinomas with evidence of metastasis or non-resectable disease and gastroduodenal disease that has not responded to H₂ blocker therapy.

CONTRAINdications

Avoid drugs that might damage the gastroduodenal mucosal barrier (e.g., NSAIDs and corticosteroids).

POSSIBLE INTERACTIONS

- H₂ blockers prevent uptake of omeprazole by oxyntic cells.
- Sucralfate may alter absorption of other drugs. Thus, it should be given on an empty stomach 2 hours before or after other oral drugs.
- Antacids may alter oral absorption and renal elimination of other drugs.

ALTERNATIVE DRUG(S)

Misoprostol, synthetic prostaglandin analogue, (3 µg/kg PO q8–12h) with antisecretory and cytoprotective actions helps prevent NSAID-induced ulcers. There may be some efficacy in treating gastroduodenal ulcerations from other causes.

**FOLLOW-UP****PATIENT MONITORING**

- Improvement in some cases may be assessed on resolution of clinical signs; packed cell

volume, total protein, fecal occult blood, and BUN may help to detect continued blood loss.

- Depending on the underlying cause of the hematemesis, specific laboratory or imaging tests may be necessary to monitor response to therapy.

PREVENTION/AVOIDANCE

- Avoid gastric irritants (e.g., NSAIDs, corticosteroids).
- Concurrent use of misoprostol or PPI with NSAIDs; PPI may be preferable because they are therapeutic as well.
- Administer NSAIDs with food.
- COX-2 selective or dual LOX/COX inhibitors may have less adverse gastrointestinal effects than nonselective NSAIDs.

POSSIBLE COMPLICATIONS

- Severe blood loss
- Sepsis
- Ulcer perforation

H**EXPECTED COURSE AND PROGNOSIS**

- Varies with underlying causes.
- Patients with malignant gastric neoplasia, renal failure, liver failure, pythiosis, systemic mastocytosis, sepsis, and/or gastric perforation—guarded-to-poor prognosis.
- Hematemesis secondary to NSAID administration, coagulopathies, inflammatory bowel disease, or hypoadrenocorticism—prognosis may be good to excellent, depending on severity of disease.
- Hematemesis secondary to heat stroke, toxicities, and snake bites can have variable prognoses.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Anemia

PREGNANCY/FERTILITY/BREEDING

Synthetic prostaglandins (e.g., misoprostol) cause abortion.

SEE ALSO

- Gastroduodenal Ulcer Disease
- Melena

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone
- COX = cyclooxygenase
- LOX = lipoxygenase
- NSAID = nonsteroidal anti-inflammatory drug
- PPI = proton pump inhibitor

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HEMATURIA



BASICS

DEFINITION

Blood in urine

PATHOPHYSIOLOGY

Secondary to loss of endothelial integrity in urinary tract, clotting factor deficiency, or thrombocytopenia.

SYSTEMS AFFECTED

- Renal/Urologic • Reproductive
- Hemic/Lymphatic/Immune

SIGNALMENT

Dog and cat • Familial hematuria in young animals; neoplasia in older animals • Females at greater risk for UTI

SIGNS

Historical Findings

Red-tinged urine with or without pollakiuria

Physical Examination Findings

- Palpable mass in patients with neoplasia
- Abdominal pain in some patients
- Enlarged and/or painful prostate gland in males • Petechiae or ecchymoses in patients with coagulopathy

CAUSES

Systemic

- Coagulopathy • Thrombocytopenia
- Vasculitis

Upper Urinary Tract

- Anatomic—e.g., cystic kidney disease and familial malformations • Metabolic—e.g., nephrolithiasis • Neoplastic—e.g., renal lymphoma, adenocarcinoma, and hemangiosarcoma • Infectious—e.g., leptospirosis, FIP, and bacteria
- Inflammatory—e.g., glomerulonephritis
- Idiopathic • Trauma

Lower Urinary Tract

- Anatomic—e.g., bladder malformations
- Metabolic—e.g., uroliths • Neoplasia—e.g., transitional cell carcinoma and lymphosarcoma
- Infectious—e.g., bacterial, fungal, and viral disease • Idiopathic—cats (idiopathic cystitis)
- Traumatic • Cyclophosphamide-induced hemorrhagic cystitis

Genitalia

- Metabolic—e.g., estrus • Neoplastic—e.g., transmissible venereal tumor, leiomyoma, and prostatic adenocarcinoma • Infectious—e.g., bacterial and fungal disease • Inflammatory—e.g., benign prostatic hyperplasia • Trauma

RISK FACTORS

Breed predisposed to urolithiasis (e.g., Dalmatians and urate urolithiasis), coagulopathy (e.g., Dobermanns and von Willebrand disease), or neoplasia (e.g., Scottish terriers and transitional cell carcinoma).



DIAGNOSIS

See Figure 1.

DIFFERENTIAL DIAGNOSIS

Other causes of discolored urine (e.g., myoglobinuria, hemoglobinuria, and bilirubinuria)

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

Substantial doses of vitamin C (ascorbic acid) may cause false-negative reagent test strip results; newer generations of reagent strips are more resistant to interference by reducing substances such as ascorbic acid.

Disorders That May Alter Laboratory Results

- Common urine reagent strip tests for blood are designed to detect red blood cells, hemoglobin, or myoglobin. • Low urine specific gravity (polyuric syndromes) lyses RBCs. • Bacteriuria (bacterial peroxidase) causes false-positive reagent test strip results.
- Formalin preservative causes false-negative reagent test strip results.

Valid if Run in a Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Thrombocytopenia and severe anemia in some patients. • Azotemia in some patients with bilateral renal disease. • RBCs (> 5–10 RBC/hpf) and possibly infectious agents seen in urine sediment. • Crystalluria in some patients with urolithiasis.

OTHER LABORATORY TESTS

- ACT or clotting profile to rule out coagulopathy. • Bacterial culture of urine to identify urinary tract infection.
- Examination of an ejaculate to identify prostatic disease.

IMAGING

Ultrasonography, radiography, and possibly contrast radiography are often useful in localizing the underlying cause.

DIAGNOSTIC PROCEDURES

- Biopsy of mass lesion
- Vaginourethroscopy in females or urethrocystoscopy in males and females



TREATMENT

- Hematuria may indicate a serious disease process. • Urolithiasis and renal failure may require diet modification. • Urinary tract infection may be associated with another disease, local (e.g., neoplasia and urolithiasis) or systemic (e.g., hyperadrenocorticism and diabetes mellitus), that also requires treatment.



MEDICATIONS

DRUG(S) OF CHOICE

- Blood transfusion may be necessary if patient is severely anemic • Crystalloids to treat dehydration • Antibiotics to treat urinary tract infection and septicemia
- Heparin for DIC

CONTRAINDICATIONS

Immunosuppressive drugs, except to treat immune-mediated disease.

POSSIBLE INTERACTIONS

Intravenous contrast media can cause acute renal failure.



FOLLOW-UP

PATIENT MONITORING

Depends on primary or associated diseases

POSSIBLE COMPLICATIONS

- Anemia • Hypovolemia if severe hemorrhage • Ureteral or urethral obstruction due to blood clots



MISCELLANEOUS

AGE-RELATED FACTORS

- Neoplasia tends to occur in older animals
- Immune-mediated diseases tend to occur in young adult animals

ZOONOTIC POTENTIAL

Leptospirosis

SEE ALSO

- Coagulation Factor Deficiency
- Crystalluria • Cylindruria • Dysuria and Pollakiuria • Feline Idiopathic Lower Urinary Tract Disease • Glomerulonephritis
- Hemoglobinuria and Myoglobinuria
- Lower Urinary Tract Infection chapters
- Nephrolithiasis • Prostatitis and Prostatic Abscess • Prostomatomegaly • Proteinuria
- Pyelonephritis • Thrombocytopenia
- Urolithiasis chapters

ABBREVIATIONS

- ACT = activated clotting time • DIC = disseminated intravascular coagulation • FIP = feline infectious peritonitis • RBC = red blood cell • UTI = urinary tract infection

Suggested Reading

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Author Joseph W. Bartges

Consulting Editor Carl A. Osborne



Client Education Handout
available online

(CONTINUED)

HEMATURIA

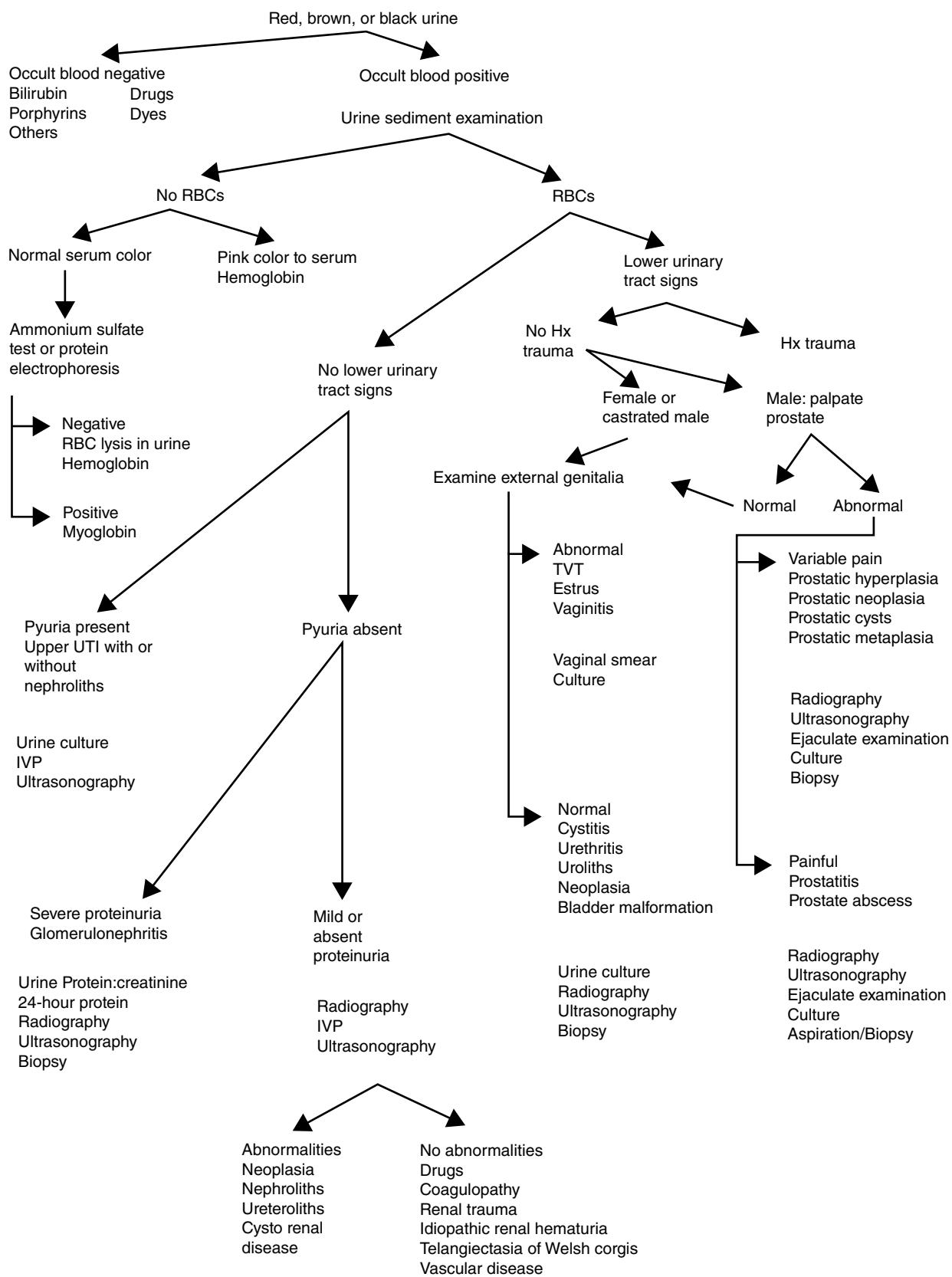


Figure 1.

Algorithm for the diagnosis of red, brown, or black urine.

HEMOGLOBINURIA AND MYOGLOBINURIA



BASICS

DEFINITION

Positive, semiquantitative urine heme (also reported as occult blood) concentration detected via routine laboratory tests (e.g., reagent test strip).

PATHOPHYSIOLOGY

- Hemoglobin released from RBC during intravascular hemolysis (hemoglobinemia) is bound (high-affinity) to haptoglobin, thereby inhibiting oxidative tissue destruction.
- Hemoglobin-haptoglobin complexes are too large to pass through normal glomerular capillaries and are removed by the reticuloendothelial system, mainly in the spleen. Haptoglobin becomes saturated when hemoglobin concentration is high; free hemoglobin (4 heme-containing chains, 64,000 daltons) rapidly dissociates into unstable dimers (32,000 daltons) small enough to pass through glomerular capillaries, resulting in hemoglobinuria (red discoloration). Free hemoglobin undergoes fluid-phase endocytosis (via megalin and tubulin receptors expressed at the apical membrane) in renal tubular epithelial cells. Globin is degraded while free heme is catabolized by heme oxygenase, resulting in lipid peroxidation and Fe deposition. In addition, an acidic intratubular environment favors hemoglobin precipitation, cast formation, and tubular obstruction.
- Methemoglobinemia causes an analogous disease process.
- In contrast, myoglobin, a single heme-containing chain (approximately 17,500 daltons), is released from muscle following decreased energy supply or injury. Interaction of heme with the protein portion (globin) allows myoglobin to carry oxygen without oxidation of ferrous (Fe^{2+}) to ferric (Fe^{3+}) iron. Myoglobin is freely and rapidly cleared by passing through the glomerular barrier (small size, no carrier protein) and plasma remains colorless. However, myoglobin accumulation in urine causes brown discoloration while an acidic environment favors precipitation, cast formation, and tubular obstruction. In addition, myoglobin enters proximal renal tubular epithelial cells via megalin and tubulin receptors, where it causes lipid peroxidation without release of free iron (via redox cycling of the heme center). Alkaline conditions prevent myoglobin-induced lipid peroxidation by (1) stabilizing the reactive ferryl myoglobin complex and (2) decreasing myoglobin precipitation in renal tubules.

SYSTEMS AFFECTED

Renal/Urologic—hemoglobin, methemoglobin, and myoglobin are

nephrotoxic, especially when decreased renal perfusion and acidic conditions are present.

SIGNALMENT

- Bedlington terrier—inherited copper toxicosis can cause hemolysis due to copper release from the liver into the blood. Although copper-associated liver disease has been reported in other breeds of dogs, only Bedlington terriers have been reported to have a hemolytic outcome.
- English springer spaniel, American cocker spaniel, English cocker spaniel, cocker spaniel—inherited phosphofructokinase deficiency may cause intravascular hemolysis with hemoglobinuria and myopathy.
- Racing sled dogs and greyhounds—exertional myopathy can result in myoglobinuria.
- Old English sheepdog—exertional lactic acidosis with hemoglobinuria.
- Neonatal isoerythrolysis in cats—(blood type B queen with type A or AB kittens) British shorthair, Cornish Rex, Devon Rex, Abyssinian, Birman, Himalayan, Persian, Scottish fold, and Somalia breeds; neonates die within 2 days.

SIGNS

General Comments

A diversity of clinical signs may be associated with specific causes; see “Causes.”

Historical Findings

Breed and drug treatment history are particularly important; see “Causes.”

Physical Examination Findings

- Signs associated with anemia (pale mucous membranes, tachycardia, lethargy, icterus).
- Signs associated with muscle damage (tenderness, bruising).

CAUSES

Hemoglobinuria

- Oxidative damage—drugs (acetaminophen, benzocaine, vitamin K₃, new methylene blue, phenacetin, phenazopyridine, monensin sodium); food (onions, garlic); heavy metals (copper, zinc).
- Physical agents—burns, heat stroke, crush injury, electric shock, IV hypotonic fluid administration, microangiopathy (e.g., disseminated intravascular coagulopathy, *D. immitis* caval syndrome).
- Toxins (loss of membrane integrity)—snake (e.g., Eastern diamondback, Eastern coral) or spider (e.g., brown recluse) venom.
- Infectious agents—babesiosis (e.g., *B. canis*), leptospirosis (e.g., *L. icteroheemorrhagica*), cytauxzoonosis (e.g., *C. felis*), mycoplasmosis (e.g., *M. hemofelis*).
- Immune-mediated—idiopathic immune-mediated hemolytic anemia, incompatible blood transfusion, isoerythrolysis (e.g., type B queen with type A or AB kittens).

- Deficiencies—hypophosphatemia (e.g., following insulin treatment in diabetes mellitus patients).

- Genetic associated—PK deficiency, copper toxicity.

- Other—retroperitoneal hemorrhage.

Myoglobinuria

- Myositis—*infectious* (e.g., toxoplasmosis, neosporosis), eosinophilic (German shepherd dog, other breeds), *immune-mediated*.
- Genetic-associated—X-linked muscular dystrophy (e.g., golden retriever, Weimaraner, rottweiler, Samoyed, Groenendael shepherd, miniature schnauzer); glycogenoses (storage diseases)—Type II (spitz), Type III (German shepherd dog), Type VII (springer spaniel colony, one American cocker spaniel); mitochondrial abnormalities (Clumber spaniel, Sussex spaniel, possibly Old English sheepdog).
- Toxins (loss of membrane integrity)—snake (e.g., coral) or spider (e.g., brown) venom.
- Physical—ischemia, crush injury, compartment syndrome.
- Excessive body temperature (e.g., heat stroke, prolonged seizures).
- Extreme exercise.

RISK FACTORS

- Genetic predisposition (see “Signalment”)
- Exposure to specific drugs or toxins
- Certain infectious agents
- Extreme physical exertion
- Heat stroke
- Snake or spider venom



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Urine reagent test strip heme (occult blood) pads detect RBC, hemoglobin (or methemoglobin), and myoglobin; the following assist with differentiation:
 - Clear plasma/serum with RBC or RBC ghost cells in urine sediment suggests hematuria.
 - Hemolyzed plasma/serum (not related to collection) suggests hemoglobinuria.
 - Chocolate-colored whole blood suggests methemoglobinuria.
 - Clear plasma/serum with an increased CK concentration and clinical evidence of muscle damage suggests myoglobinuria.
 - False-positive results (see “Laboratory Findings”).

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

- Vitamin C (ascorbic acid) administration may cause false-negative reagent test strip results.
- Hemoglobin-based oxygen carriers (Oxyglobin) administration causes positive reagent test strip results.

(CONTINUED)

HEMOGLOBINURIA AND MYOGLOBINURIA

H

Disorders That May Alter Laboratory Results

- Hyposthenuria (low urine specific gravity) may cause *in vitro* RBC lysis (no intact RBC in sediment) with a positive reaction.
- Bacteriuria may cause a false-positive result (bacterial peroxidase).
- Oxidizing reagents (e.g., from disinfectants) may cause a false-positive result.
- Free hemoglobin from transfused blood or blood products may cause a positive reaction.
- Formalin causes false-negative results.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Proteinuria.
- Intravascular hemolysis—decreasing PCV (may be accompanied by leukocytosis), blood smear abnormalities (RBC parasites, Heinz bodies, RBC ghost cells [complement mediated]), bilirubinemia, increased ALT activity, bilirubinuria.
- Rhabdomyolysis—increased CK and AST activities.

OTHER LABORATORY TESTS

- Ammonium sulfate precipitation test—mix 5 mL urine with 2.8 g ammonium sulfate and centrifuge; hemoglobin precipitates, myoglobin remains in solution. Dark precipitate is suggestive for hemoglobinuria, dark supernatant is suggestive of myoglobinuria, and if both are dark, hemoglobin and myoglobin are present.
- New methylene blue stained blood smear to detect Heinz bodies.
- Methemoglobin detection confirms toxin as oxidant.
- Haptoglobin concentration is decreased with intravascular hemolysis.
- Increased serum copper or zinc concentration.
- DNA test for PFK deficiency.

IMAGING

Abdominal radiography or ultrasonography—coins, hardware or other metal objects in the gastrointestinal tract; abnormal liver size in patients with copper-associated hepatopathy.

DIAGNOSTIC PROCEDURES

- Liver biopsy to measure copper concentration
- Forced exercise (e.g., Old English sheepdog)



TREATMENT

- Copious fluids to maintain renal function (50% of sodium as sodium bicarbonate if acidosis is present to avert precipitation and peroxidation).
- Avoid stress in anemic patients.
- Avoid hyperventilation in PFK-deficient patients.
- Exercise-induced hematuria has a benign, self-limiting course.
- See suspected causes for specific treatment.



MEDICATIONS

DRUG(S) OF CHOICE

Vary with underlying cause.

CONTRAINDICATIONS

See list of causes for contraindicated drugs.

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

PCV, pO₂, urinalysis, serum creatinine, ALT (copper-associated), CK (myopathy-associated).

POSSIBLE COMPLICATIONS

Renal damage (failure) may develop.



MISCELLANEOUS

AGE-RELATED FACTORS

Neonatal isoerythrolysis

ZOONOTIC POTENTIAL

- Leptospirosis
- Toxoplasmosis

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYNS

Pigmenturia

SEE ALSO

See "Causes"

ABBREVIATIONS

- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- CK = creatine kinase
- PCV = packed cell volume
- PFK = phosphofructokinase
- RBC = red blood cell

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Consulting Editor Carl A. Osborne

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HEMOTHORAX



BASICS

OVERVIEW

- Accumulation of blood in pleural space.
- Can develop acutely due to trauma or a coagulopathy, or chronically over time.
- Cardiovascular and respiratory systems commonly affected.

SIGNALMENT

Any age, breed, or sex of dogs and cats

SIGNS

- Peracute to acute onset—hypovolemic signs can occur before sufficient blood volume accumulates in the pleural space to impair respiration. • Respiratory distress, tachypnea. Honking cough in dogs with rodenticide poisoning. Ecchymoses along ventral cervical and thoracic inlet areas. • Pale mucous membranes. • Weakness and collapse.
- Weak, rapid pulse. • Ventral thoracic dullness; dorsal hyperresonance if concurrent pneumothorax.

CAUSES & RISK FACTORS

- Trauma—bleeding artery or vein of the thoracic wall, mediastinum, or thoracic spine; damaged heart, lungs, thymus, or diaphragm; herniated abdominal viscera (liver or spleen).
- Neoplasia—involving any structure adjacent to the pleural cavity. • Coagulopathies—can be congenital or acquired; rodenticide ingestion common; liver failure; cholangiohepatitis with concurrent small bowel disease. • Lung lobe torsion. • Acute thymic hemorrhage in young animals.
- *Dirofilaria immitis*, *Spirocerca lupi*, *Angiostrongylus vasorum*.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pulmonary contusion. • Pneumothorax.
- Diaphragmatic hernia. • Flail chest.
- Non-hemorrhagic pleural effusions—chyothonax; pyothorax; modified transudates; transudates. • Congestive heart failure.

CBC/BIOCHEMISTRY/URINALYSIS

- PCV and hemoglobin—reflect blood loss after initial fluid compartment shifts have occurred. • Platelet count may be low (~100,000) with acute blood loss. • Very low platelet count (<20,000) consistent with spontaneous bleeding. • Peripheral smear evaluation—less than 3–5 platelets/hpf indicates thrombocytopenia. • Chemistry panel may reveal low glucose, BUN, albumin, and cholesterol with liver failure.

OTHER LABORATORY TESTS

Fluid Analysis

- Hemorrhage-produced effusion—PCV and protein content similar to that of the peripheral

blood; platelets commonly seen on cytology. • Inflammation- or vascular-congestion related effusion—PCV < 8%. • Neoplasia or lung lobe torsion—PCV can be low or mid-range. • Cytologic examination—often fails to identify malignant causes.

Coagulation Tests

- Prolonged ACT or PT/PTT suggestive of coagulopathy. • Prolonged PT, APTT, and low platelet count—suggestive of DIC.
- Positive D-dimer aids in detecting DIC.
- Specific factor analysis—needed to diagnose congenital defect or acquired coagulopathy.
- Buccal mucosal bleeding time—identifies platelet function defect or vasculitis.

IMAGING

• Radiology—reveals pleural effusion varying from a diffuse increase in radiopacity to ventral leafing, interlobar fissures, and localized pleural densities. • Can see associated lesions (e.g., rib fractures, pneumothorax or pneumomediastinum, mediastinal hemorrhage, pulmonary contusions, diaphragmatic lesions, and masses). • Lobar consolidation with vesicular gas pattern suggestive of lung lobe torsion.

• Ultrasound—confirm pleural effusion; look for masses, lung lobe torsion, and herniation of liver, gallbladder, spleen, or bowel. • In stable patients without a coagulopathy—evacuation of pleural space may allow better radiographic visualization of masses or other pathology.

DIAGNOSTIC PROCEDURES

- Thoracentesis (contraindicated if clotting abnormality). • Surgical exploration—may be necessary to establish a diagnosis; if imaging does not suggest the appropriate side to enter, the left side is recommended or use median sternotomy. Preoperative computed tomography can be helpful.



TREATMENT

- Acute—judicious use of IV fluids. Try to get systolic blood pressure above 90 mm Hg using synthetic colloids, crystalloids and/or hypertonic saline to correct hypovolemia.
- Coexisting pneumothorax—generally requires needle thoracentesis or tube thoracostomy. • Plasma, specific clotting factors, and/or blood transfusion can be needed to restore clotting factors or provide RBCs for oxygen transport. • Pulmonary contusion—may require ventilator support.
- Severe or recurrent thoracic hemorrhage—may require surgical exploration. • Oxygen therapy. • Maintenance of body heat. • Most coagulopathic cases have respiratory difficulty associated with soft tissue bleeding rather than pleural hemorrhage and therefore rarely require evacuation of pleural fluid to resolve tachypnea. • Autotransfusion.



MEDICATIONS

DRUG(S)

- Hypovolemia—see Shock, Hypovolemic.
- Vitamin K₁—5 mg/kg SC loading dose (using a small gauge needle) followed by 1.5–2.5 mg/kg PO q12h for 21–30 days. Takes 12 hours or more to carboxylate clotting factors and restore activity.
- Analgesics—systemically or as nerve blocks for trauma. • Broad-spectrum antibiotics—when indicated.

CONTRAINdications/POSSIBLE INTERACTIONS

Avoid aspirin and other NSAIDs.



FOLLOW-UP

PATIENT MONITORING

- Clinical signs, respiratory rate and effort, heart rate. • Temperature. • Urine production. • Relief from pain. • Follow-up radiographs at 48-hour intervals until stable.
- Coagulation panel in 48 hours if coagulopathy diagnosed, and 48 hours after discontinuing vitamin K supplementation.

POSSIBLE COMPLICATIONS

- Pyothorax. • Sepsis. • Entrapment and constriction of lungs by scar tissue and fibrosis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Peritonitis—with penetrating wounds (e.g., gunshot) into the abdomen. • Esophageal perforation.

SEE ALSO

- Rodenticide Toxicosis—Anticoagulants
- Disseminated Intravascular Coagulation
- Lung Lobe Torsion • Pleural Effusion
- Pulmonary Contusions

ABBREVIATIONS

- ACT = activated clotting time • APTT = activated partial thromboplastin time
- DIC = disseminated intravascular coagulation • NSAID = nonsteroidal anti-inflammatory drug • PCV = packed cell volume • PT = prothrombin time • PTT = partial thromboplastin time • RBC = red blood cell

Suggested Reading

Berry CR, Gallaway A, Thrall DE, Carlisle C. Thoracic radiographic features of anticoagulant rodenticide toxicity in fourteen dogs. Vet Radiol Ultrasound 1993, 34:391–396.

Author Bradley L. Moses

Consulting Editor Lynelle R. Johnson

HEMOTROPHIC MYCOPLASMOSIS (ALSO HEMOPLASMOSIS)



BASICS

OVERVIEW

Red blood cell destruction and anemia caused by parasite attachment to the external surface of RBCs, nutrient scavenging by parasite from RBC, and immune response by the host.

SIGNALMENT

- Dog and cat.
- Acute disease most common in young cats, chronic form most common in adults.
- In cats, more common in males.
- Acute disease in splenectomized dogs, chronic disease in non-splenectomized dogs.
- Kennel-raised beagles are at increased risk for infection.
- No sex prevalence in dogs.

SIGNS

Cats

- For *M. haemofelis* infection:
 - Variable disease severity ranging from inapparent infection (chronic disease) to marked anemia and death (acute disease).
 - Intermittent fever (only 50% of the time) during the acute phase, depression, weakness, anorexia, anemia, pale mucous membranes, splenomegaly, and (occasionally) icterus.
- For *Candidatus M. haemominutum* infection:
 - Usually results in inapparent infection.
 - Minimal or no decrease in hematocrit.
- For *Candidatus M. turicensis*:
 - Limited information regarding natural infection.
 - Moderate anemia following experimental infection.

Dogs

- Mild or inapparent signs (e.g., pale mucous membranes and listlessness)—except when dogs have been splenectomized or splenic function is altered.
- High prevalence of chronic, inapparent infection in kennel-raised Beagles, which may be a threat to the validity of research results.

CAUSES & RISK FACTORS

- Caused by bacteria previously classified in the genus *Haemobartonella*, but these organisms are now recognized to be mycoplasmas (hemotropic mycoplasmas or hemoplasmas) based on genetic determinations.
- *Mycoplasma haemofelis* (previously classified as the large form of *Haemobartonella felis*), *M. haemominutum* (previously classified as the small form of *H. felis*), and *M. haemocanis* (previously classified as *H. canis*).
- *M. haemofelis* infection in cats generally causes more severe disease than does *M. haemominutum* infection.
- Cats—anemia more severe if FeLV-infected.

- Dogs—likelihood of severe anemia greatly increased if splenectomized or with pathologic changes in the spleen.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of hemolytic anemia, including AIHA, babesiosis (not in cats in the United States), cytauxzoonosis (cats only), Heinz body hemolytic anemia, microangiopathic hemolytic anemia, pyruvate kinase deficiency, and phosphofructokinase deficiency (dogs only).
- Differentiated from AIHA only by recognition of parasites in blood (stained blood film or species-specific PCR-based assays)—both disorders (IMHA and/or *M. haemofelis* infection) may be Coombs' test positive.
- *Babesia* and *Cytauxzoon* species are protozoal organisms that differ in morphology from these mycoplasmal organisms.
- New methylene blue stains used to identify Heinz bodies.
- Enzyme assays or specialized DNA tests used to diagnose pyruvate kinase and phosphofructokinase deficiencies.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia, most often present with reticulocytosis in animals with clinically important infections—may appear poorly regenerative if a precipitous decrease in PCV has occurred early in the disease or if there are other concurrent disorders (e.g., FeLV or FIV infections in cats).
- Autoagglutination may be seen in feline blood samples after they cool to below body temperature.
- Variable total and differential leukocyte counts of little diagnostic assistance.
- Slight hemoglobinuria rarely observed; no hemoglobinuria reported.
- Hyperbilirubinemia may be measured and/or seen clinically at times but is seldom severe.
- Substantial bilirubinuria seen in some dogs.
- Abnormalities related to anemic hypoxia may be shown by clinical chemistry profiles, but profile can be normal.
- Hypoglycemia possible in moribund cats or if slow to separate blood cells from plasma or serum.

OTHER LABORATORY TESTS

- Routine blood stains (e.g., Wright-Giemsa) to identify organisms in blood films, which must be examined for organisms before treatment is begun.
- Organism may detach from RBCs in stored blood collected with EDTA.

- Reticulocyte stains cannot be used because punctate reticulocytes in cats appear similar to the parasites.

- Organisms must be differentiated from precipitated stain, refractile drying or fixation artifacts, poorly staining Howell-Jolly bodies, and basophilic stippling.

- Feline organisms—small blue-staining cocci, rings, or rods on RBCs, often many parasites for *M. haemofelis*; small rods or coccoid organisms in low numbers for *Candidatus M. haemominutum*; parasites not conclusively seen in blood for *Candidatus M. turicensis*.

- Canine organisms—commonly form chains of organisms that appear as filamentous structures on the surface of RBCs.
- Parasitemia is cyclic and thus organisms not always identifiable in blood (especially in cats).
- PCR-based assays can detect parasites in blood below the number required to make a diagnosis by a stained blood film.

DIAGNOSTIC PROCEDURES

- In patients with nonregenerative anemia, bone marrow biopsy should be performed to detect other disorders (e.g., myeloproliferative disorders).
- PCR testing of blood donor cats and dogs is strongly recommended.



TREATMENT

- Without therapy, mortality with *M. haemofelis* infection may reach 30% in cats.
- Outpatient treatment unless severely anemic or moribund.
- Blood transfusions required when the anemia is considered life-threatening.
- IV administration of glucose-containing fluid recommended in moribund animals.



MEDICATIONS

DRUG(S)

- Doxycycline (5 mg/kg PO q12h), tetracycline (20 mg/kg PO q8h), or oxytetracycline (20 mg/kg PO q8h) should be given for a minimum of 3 weeks and up to 6 weeks for elimination.
- Preliminary findings indicate that enrofloxacin (5 mg/kg PO q24h) for 2 weeks may be efficacious in cats.
- Glucocorticoids, such as prednisolone (1–2 mg/kg PO q12h), may be given to severely anemic animals; gradually decrease dosage as the PCV increases.

HEMOTROPHIC MYCOPLASMOSES (ALSO HEMOPLASMOSES) (CONTINUED)

CONTRAINdications/POSSIBLE

INTERACTIONS

- Esophageal strictures have been reported in cats following doxycycline administration.
- Tetracycline antibiotics may produce fever or evidence of gastrointestinal disease in cats.
- Enrofloxacin at dosages above 5/mg/kg/day may cause retinotoxicity.
- Chloramphenicol should not be used to treat cats because it causes dose-dependent erythroid hypoplasia.



FOLLOW-UP

- Examine animal after 1 week of treatment to confirm that PCV has risen.
- Alert owners that cats may remain carriers even after completion of treatment but seldom relapse with disease once PCV returns to normal.
- Cats have protective immunity against *Mycoplasma haemofelis* reinfection for some period of time.



MISCELLANEOUS

ABBREVIATIONS

- AIHA = autoimmune hemolytic anemia
- HIV = human immunodeficiency virus
- PCR = polymerase chain reaction

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BASICS

OVERVIEW

- Amyloidosis—disorders of diverse etiology sharing common feature of deposition of extracellular insoluble fibrillar β -pleated proteinaceous matrix with distinctive staining properties and fibrillar ultrastructure.
- Amyloid—derived from diverse primary proteins, sometimes an acute phase reactant.
- Amyloid may accumulates as a focal or systemic process secondary to inflammatory or lymphoproliferative disorders or as a familial genetic disorder.
- Familial amyloidosis—certain kindreds of purebred cats; certain breeds and kindreds of dogs; syndromic inflammatory disorders.
- Multiple organs commonly involved; clinical signs often reflect renal involvement.
- Liver amyloid accumulation—insidious; associates with variable liver enzymes, severe hepatomegaly, coagulopathies, liver rupture leading to hemoabdomen (cats), or liver failure.

SIGNALMENT

- Dogs—Chinese Shar-Pei with cyclic “Shar-Pei fever syndrome”; Akita with cyclic fever and polyarthropathy; Collie with “Gray Collie syndrome”; usually develop renal signs first although some develop hepatic insufficiency.
- Cats—Oriental shorthair, Siamese, Devon rex, domestic shorthair cats; usually < 5 years of age when first symptomatic (hepatic signs and coagulopathies predominate); familial in Abyssinians (renal signs predominate). Upper respiratory viral infection proposed to trigger amyloidosis in Siamese.

SIGNS

Historical Findings

- Episodic fever and swollen hocks—Shar-Pei
- Episodic polyarthropathy, pain, and signs of meningitis—Akita
- Acute lethargy, cyclic
- Anorexia and vomiting, episodic
- Polyuria and polydipsia

Physical Examination Findings

- Pallor
- Abdominal effusion—hemorrhage or ascites
- Jaundice: unusual
- Hepatomegaly with amyloid deposition
- Edema: due to hypoalbuminemia secondary to pathologic proteinuria
- Joint pain: Akita, Shar-Pei syndromes
- Non-localized pain, meningeal pain, and abdominal discomfort: with different inflammatory disorders promoting amyloid

CAUSES & RISK FACTORS

- Familial immunoregulatory disorders
- Chronic infections—coccidioidomycosis; blastomycosis; tick-borne diseases
- Cyclic neutropenia—Gray Collie syndrome

- Bacterial endocarditis
- Chronic inflammation (e.g., SLE).
- Neoplasia



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Chronic hepatic inflammation
- Infiltrative hepatic neoplasia
- Primary or rodenticide induced coagulopathy
- Glomerulonephritis
- Pyelonephritis
- SLE
- Abdominal trauma
- Peritonitis
- Meningitis
- Immune-mediated or infectious polyarthropathy

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia secondary to hepatic hemorrhage or liver lobe rupture or chronic inflammation.
- Leukocytosis with a left shift during febrile episodes in Shar-Pei and Akita.
- Normal or high: liver enzymes, total bilirubin, and serum bile acids; may be normal with severe hepatic amyloid deposition.
- Azotemia with severe renal infiltration: glomeruli targeted in dogs (proteinuria), renal interstitium targeted in cats (azotemia).
- Proteinuria: dogs—glomerular amyloid.
- Dilute urine—renal involvement or failure.
- Feline systemic amyloidosis—involves multiple organ systems: thyroid, cardiac, renal, intestine, pancreatic, bone marrow, lymph nodes, adrenals.

OTHER LABORATORY TESTS

- Coagulation tests—normal to prolonged clotting times, hyperfibrinogenemia.
- Synovial fluid—dogs with joint swelling or pain: suppurative nonseptic inflammation.
- CSF—if meningeal pain, increased protein and suppurative inflammation.

IMAGING

- Abdominal radiography—hepatomegaly; variable renal size; abdominal effusion.
- Abdominal ultrasonography—hepatomegaly: hypoechoic parenchyma (diffuse amyloid); variable renal size with normal or equivocally hypoechoic parenchyma (renal amyloid); inconsistent mesenteric lymphadenopathy; thickened gut wall (amyloid deposition); abdominal effusion.

DIAGNOSTIC PROCEDURES

- Fine-needle aspiration cytology—may disclose amorphous fibrillar material.
- Liver or other tissue biopsy.
- Abdominocentesis—hemorrhagic (esp. cats) or transudative effusion (diffuse hepatopathy).

PATHOLOGIC FINDINGS

Gross

Liver—normal to pale color; large, firm to friable; hemorrhages (subcapsular hematomas, capsular tears) to overt rupture.

Microscopic

- Liver—diffuse acellular amorphous material in the space of Disse, associated with hepatic cord atrophy; may primarily involve blood vessels in portal triads (Abyssinian cats).
- Cats with systemic amyloidosis may have amyloid deposited in many organs and endocrine tissue.
- Amyloid stains amorphous pink with routine hematoxylin and eosin; may stain turquoise blue with Masson's trichrome; Congo red staining with bright field: amyloid is salmon pink but with polarized light is birefringent (β -pleated sheet structure refracts polarized light) and apple green.



TREATMENT

- Warn client that hepatic amyloidosis is difficult to treat; guarded to poor prognosis.
- Dictated by severity of clinical signs.
- No curative treatment; manage underlying disease; colchicine as described below may reduce organ amyloid deposition.
- Fluids—for dehydration.
- Blood transfusion—for acute blood loss; essential in cats with hepatic amyloid induced liver lobe rupture.
- Diet—individually tailored to organ function.
- Liver failure—consider measures appropriate for hepatic encephalopathy as appropriate.
- Pathologic proteinuria—see Nephrotic Syndrome.
- Surgical intervention—hepatic lobe resection as emergency measure for catastrophic bleeding from fractured liver lobe in cats; histologic features may describe centrilobular necrosis due to anemia-induced hypoxia; amyloid may be overlooked without special stains.



MEDICATIONS

DRUG(S)

- Colchicine—dogs: 0.03 mg/kg PO q24h; may block amyloid deposition in early disease or control deposition in chronic disorders in dogs; modulates expression of adhesion molecules and chemotactic factors; causes microtubule polymerization by binding to tubulin blocking cell mitosis in cells such as neutrophils. Effects attenuate inflammatory response triggering acute phase protein (amyloid precursor) production. Monitor

HEPATIC AMYLOID

(CONTINUED)

CBC for bone marrow toxicity; observe patient for enteric side effects (vomiting, diarrhea [bloody]), beware of toxicity if co-administered with p450 blocking drugs (e.g., ketoconazole, omeprazole, cimetidine). Use colchicine without added probenecid. Limited experience in cats.

- DMSO—Controversial treatment; use medical grade only; dogs: 80 mg/kg given as no more than a 33% solution in sterile water, PO, three times a week; may promote dissolution of amyloid fibrils or provide anti-inflammatory or anti-amyloid effect. Side effects: garlic odor and objectionable taste. Sterile solutions have also been prepared and administered SQ. In humans this treatment given PO daily (3–20 g/patient) has benefit in polysystemic amyloidosis but not renal amyloidosis associated with renal failure.

POSSIBLE INTERACTIONS

- Colchicine combined with probenecid may cause vomiting as probenecid prolongs residence time of colchicine.
- Colchicine toxicity if co-administered with p450 cytochrome inhibitor drugs.

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FOLLOW-UP

- Shar-Pei—with hepatic amyloid may survive > 2 years; most have episodes of fever and cholestasis; some resolve clinical signs and diminish hepatic amyloid with colchicine.
- Akitas with cyclic clinical signs—grave prognosis.
- Cats surviving liver hemorrhage eventually succumb to renal failure and other polysystemic effects of deposited amyloid.



MISCELLANEOUS

SEE ALSO

Amyloidosis

ABBREVIATIONS

- CSF = cerebrospinal fluid
- DMSO = dimethyl sulfoxide
- SLE = systemic lupus erythematosus

Suggested Reading

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HEPATIC ENCEPHALOPATHY



BASICS

DEFINITION

- Hepatic encephalopathy (HE) defines a broad spectrum of neurobehavioral signs.
- Associated with: (1) acute liver failure, (2) portosystemic bypass without intrinsic liver disease (portosystemic vascular anomaly [PSVA] shunt), (3) hepatic fibrosis/cirrhosis associated with portal hypertension and acquired portosystemic shunts (APSS).
- Direct metabolic/physiologic dysregulations responsible for HE are potentially reversible.

PATHOPHYSIOLOGY

- Multifactorial origin.
- Ammonia best studied toxin; ammonia and glutamate function as neurotoxins adversely affecting astrocytes (site of ammonia detoxification to glutamine). Hyperammonemia causes astrocyte swelling and oxidative stress.
- Complex pathophysiology—energy failure (neuroglycopenia), altered cerebral pH, calcium ion flux, abnormalities of glutamatergic, GABAergic and catecholaminergic neurotransmission; perturbed aromatic amino acid metabolism (preferential systemic utilization of branched chain gluconeogenic amino acids), increased cerebral levels of endogenous benzodiazepine-like substances; inflammatory cytokines, oxidative injury; each factor contributes to electrophysiologic derangements. An altered blood-brain barrier likely contributes to pathophysiologic changes.
- Neurobehavioral abnormalities predominate with most signs attributed to gut-derived substances (bacterial and protein metabolism), particularly ammonia.

SYSTEMS AFFECTED

- Nervous—abnormal cerebral function predominates; decreased awareness and function progresses to somnolence, coma, or agitation progressing to seizures; aggression and seizures more likely in cats with PSVA.
- GI—vomiting, diarrhea, and anorexia.
- Renal/urologic—ammonium biurate urolithiasis; renal pelvic and cystic calculi.

GENETICS

- PSVA—polygenic inheritance of extrahepatic PSVA in small breed dogs (see Portosystemic Vascular Anomaly, Congenital).
- Certain chronic hepatopathies have increased prevalence in some breeds (see Chronic Hepatitis; Copper Associated Hepatopathy).

INCIDENCE/PREVALENCE

Uncommon disorder

SIGNALMENT

Species

Dog and cat

Breed Predilections

- PSVA—usually purebred dogs; increased occurrence in certain breeds (see Portosystemic Vascular Anomaly, Congenital) and mixes of these.
- Chronic hepatitis and copper associated hepatopathy more common in certain breeds (see topics).

Mean Age and Range

- PSVA—usually young animals
- Acquired liver disease with APSS—any age

Predominant Sex

None

SIGNS

General Comments

- Neurologic—usually coordinates with meal ingestion (particularly high protein, e.g., red meat); systemic infection; GI hemorrhage; dehydration; azotemia; constipation; catabolism; hemolysis; blood transfusion; certain drugs.
- Temporary resolution of signs with: dietary protein restriction, ± antibiotic or lactulose treatment, ± resolution of associated conditions.
- Prolonged recovery from sedation or anesthesia—reduced elimination of drugs removed by first pass extraction.
- Ammonium biurate obstructive uropathy.

Historical Findings

- Episodic abnormalities.
- Learning disabilities (difficult to train).
- Lethargy/Somnolence → coma.
- Anorexia/Vomiting; ptalism especially cats.
- Polyuria and polydipsia.
- Disorientation—aimless wandering; compulsive pacing; head pressing.
- Amaurotic blindness.
- Seizures—neurologic prodrome.
- Signs more frequent in cats than in dogs—ptalism; seizures; aggression; disorientation; ataxic stupor.
- More frequent in dogs than cats—compulsive behavior, e.g., head pressing, circling, aimless wandering, vocalizing; vomiting; diarrhea; PU/PD; hematuria, pollakiuria, and dysuria-ammonium biurate urolithiasis.

Physical Examination Findings

- PSVA—cats may have normal size, but most have stunted stature; microhepatia; and golden-copper colored iris (non-blue-eyed and non-Persian cats; no green iris color).
- PSVA dogs may have normal size, but are usually stunted; microhepatia, increased incidence of cryptorchidism (one study).
- Acquired liver disease—depends on chronicity and formation of APSS; ascites common in dogs with HE due to acquired liver disease and vacillates in severity; variable coagulopathies (uncommon).
- Lower urinary tract signs—obstructive uropathy due to ammonium biurate urolithiasis; imparts orange/brown color to urine.

CAUSES

- PSVA—congenital malformations.
- APSS—secondary to splanchnic portal hypertension (cirrhosis, sinusoidal fibrosis; intrahepatic AV malformation, intolerant to PSVA shunt attenuation); see Hypertension, Portal; Portosystemic Shunting, Acquired.
- Acute hepatic failure—induced by drugs, toxins, or infection (see Hepatic Failure, Acute; Hepatotoxins).

RISK FACTORS

- Alkalosis, hypokalemia, hypoglycemia.
- Certain anesthetics and sedatives.
- Certain drugs: e.g., methionine, tetracycline, antihistamines.
- Enteric bleeding—most common acute precipitating cause of HE.
- Transfusion—stored blood products may contain high concentrations of ammonia; incompatible blood transfusions; heme potently provokes HE.
- Infections.
- Constipation.
- Catabolism—disorders causing muscle wasting; large amounts of ammonia are transiently detoxified by storage in muscle.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Lead toxicosis
- Urinary tract infection—other urolithiasis
- Intestinal parasitism
- Primary gastrointestinal disease
- Hypoglycemia: many causes
- Toxoplasmosis
- Congenital CNS disease or malformation—hydrocephalus; storage diseases
- CNS neoplasia
- Acute ethylene glycol or xylitol toxicosis
- Infectious diseases—rabies; canine distemper
- Thiamin deficiency—Wernicke's encephalopathy (especially cats)
- Drug intoxications; recreational human drugs

CBC/BIOCHEMISTRY/URINALYSIS

CBC

PSVA and APSS—RBC microcytosis; mild non-regenerative anemia; poikilocytosis (cats); target cells (dogs); APSS—± jaundice.

Biochemistry

- Low BUN and creatinine—reflect PU/PD, high GFR, and reduced hepatic synthesis.
- Hypoglycemia—young toy breed dogs with PSVA; fulminant hepatic failure; cirrhosis.
- Low cholesterol—common; PSVA and APSS; fulminant hepatic failure.
- Liver enzymes—variable with APSS depending on cause; ALP usually high in young patients with PSVA owing to bone isoenzyme.

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HEPATIC ENCEPHALOPATHY

(CONTINUED)

- Bilirubin—normal with PSVA but may be high with APSS depending on cause.
- Hypoalbuminemia—common with APSS but inconsistent and mild with PSVA.

Urinalysis

- Low concentration—common with PSVA.
- Ammonium urate crystalluria—causing hematuria, pyuria, and proteinuria due to mechanical inflammation and infection secondary to metabolic calculi.

OTHER LABORATORY TESTS

- Blood ammonia—sensitive but inconsistent indicator of HE; fasting hyperammonemia unreliable; blood ammonia values less reliable than TSBA owing to analytic/methodologic issues and because samples cannot be mailed for analysis; ammonia tolerance testing—most reliable method for detecting ammonia intolerance (administer NH₄Cl; **caution:** may induce HE).
- TSBA—confirms hepatic insufficiency or shunting associated with HE.
- Coagulation tests—PSVA: abnormalities usually not associated with bleeding; APSS: increased PT, APTT, PIVKA, and low fibrinogen reflect severity of liver dysfunction, synthetic failure, DIC, and vitamin K adequacy.
- Protein C: low activity in dogs with substantial shunting, liver failure, PLE, DIC.
- Abdominal effusion—acquired liver disease; hepatic AV malformation; pure or modified transudate.
- Liver zinc values—often low (< 120 µg/g dry weight liver tissue).

IMAGING

See Portosystemic Vascular Anomaly, Congenital; Portosystemic Shunting, Acquired

DIAGNOSTIC PROCEDURES

- Hepatic aspiration—cannot differentiate disorders causing portosystemic shunting.
- Liver biopsy—open surgical wedge biopsy or laparoscopic sampling (cup biopsy forceps) to collect tissue from several liver lobes.
- Tru-Cut needle biopsy: may inadequately sample tissue.

PATHOLOGIC FINDINGS

- Gross—liver changes reflect underlying disorder; rare brain herniation in acute HE.
- Microscopic—liver lesions: define causal hepatic disorders and identify portal hypoperfusion associated with portosystemic shunting; CNS lesions: polymicrocavitation and Alzheimer type II astrocyte changes—**inconsistent** in dog.



TREATMENT

APPROPRIATE HEALTH CARE

- Depends on underlying condition.
- PSVA—surgical correction preferred; chronic medical treatment possible for some.

NURSING CARE

- Depends on underlying condition; eliminate factors promoting HE.
- Improve dietary protein tolerance by concurrent oral or rectal (enema) treatments (see "Medications") and altered protein intake (type, quantity).
 - If hepatic coma—discontinue oral medications.
 - Avoid risk factors.
 - Fluids—balanced crystalloids but avoid lactate if fulminant hepatic failure, if hypoglycemic supplement fluids with 2.5–5.0% dextrose; provide 20–30 mEq/L potassium chloride (not to exceed 0.5 mEq/kg/h) titrated according to needs; sodium-restricted fluids with acquired liver disease associated with ascites, and/or marked hypoalbuminemia.
 - B-soluble vitamins (2 mL/L fluids).

ACTIVITY

Keep patient warm, inactive, and hydrated.

DIET

- Adequate calories—avoid catabolism and maintain muscle mass (site for temporary ammonia detoxification/storage).
- Dietary protein restriction—cornerstone of medical management; use commercially formulated diets for liver disease or moderate renal insufficiency; dogs: dairy and soy protein best sources; 2.5 g protein /kg bodyweight; cats: pure carnivores must have meat-derived protein; 3.5 g protein/kg bodyweight.
- Good-quality vitamin supplements—vitamin metabolism perturbed with liver disease and losses in urine. S-adenosylmethionine preferred to methionine supplementation: 20 mg/kg PO/d.
- Ensure thiamin repletion—avoids Wernicke's encephalopathy; 50–100 mg daily for 3 days in cats, then in water-soluble vitamins in fluids; **caution:** anaphylactoid reactions may occur with injectable thiamin.
- Partial parenteral nutrition—if short-term inappetence; may reduce muscle catabolism.
- Total parenteral nutrition if > 5 days inappetence and enteral route unavailable; use of branched-chain amino acid solutions remains controversial.

CLIENT EDUCATION

- HE—often episodic; relapse if underlying disorder cannot be eliminated.
- Train owner to administer enemas and to judiciously adjust medications PRN.
- PSVA—surgical ligation may be curative but also may cause adverse complications (see Portosystemic Vascular Anomaly, Congenital); postoperative clinical signs may persist requiring chronic nutritional and medical management.
- APSS—depends on underlying cause.

SURGICAL CONSIDERATIONS

- See Portosystemic Vascular Anomaly, Congenital
- APSS—do not ligate



MEDICATIONS

DRUG(S)

- Medications increasing dietary protein tolerance alter enteric flora or condition, reduce production/availability of substances provoking HE.
 - Antibiotics—spectrum altering intestinal flora (aerobic and anaerobic) or their products; first choice antimicrobial selections: systemic metronidazole (7.5 mg/kg q12h) or amoxicillin (esp. cats, 12.5–25 mg/kg PO q8–12h); combined with lactulose; **caution** if using neomycin (10–22 mg/kg PO q12h) as chronic administration may result in renal and otic toxicity (approximately 3% absorbed systemically).
 - Local antimicrobials used in enemas: same dosages as oral but do not administer by both oral and rectal routes.
 - In humans, rifaximin (semisynthetic rifamycin derivative) is as effective as lactulose and neomycin in treatment of HE and has a favorable safety and tolerability profile, but is expensive. There is no data accumulated for its utility for HE in animals. Suggested dose in dogs 5 mg/kg PO q24h or q12h.
 - Nonabsorbable-fermented carbohydrates—lactulose, lactitol, or lactose (milk products, if lactase deficient); decrease production/absorption of ammonia; promote a cathartic effect; trap nitrogen in bacteria; lactulose most commonly used (start at 0.5–1.0 mL/kg q8–12h and titrate up to therapeutic goal of passage of 2 or 3 soft stools/day); may also administer as enema for acute hepatic encephalopathy and coma *after* cleansing enemas remove debris.
 - Probiotics with nonabsorbable-fermented carbohydrates may be advantageous for altering gut flora to diminish HE toxin production (remains controversial).
 - Enemas—*cleansing enemas* (warmed polyionic fluids) mechanically clean colon (10–15 mL/kg, until clear return); *retention enemas* deliver fermentable substrates or directly alter colonic pH and organisms: diluted lactulose, lactitol, or lactose (1:2 in water); neomycin in water (do not exceed PO dose, do not dose PO and rectally); diluted Betadine (1:10 in water, *rinse well in 15 min*); diluted vinegar (1:10 in water).
 - Zinc supplementation—two urea cycle enzymes require zinc; measure baseline plasma zinc, (dose 1–3 mg/kg elemental zinc PO using zinc acetate); titrate dose using sequential plasma zinc measurements: avoid > 800 µg/dL.
 - Cerebral edema—complicates acute HE; head-up posture (15–20° incline); mannitol (1 g/kg diluted in saline, over 30 min); nasal oxygen; N-acetylcysteine (140 mg/kg IV diluted 1:2 in saline given through non-pyrogenic filter; then 70 mg/kg q8h);

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HEPATIC ENCEPHALOPATHY

glucocorticoids controversial, may promote enteric bleeding.

- Salvage therapy for intractable HE (experimental)—L-ornithine—L-aspartate (humans, rats: 180–300 mg/kg/day divided into three doses); L-carnitine (100 mg/kg PO or IV), may attenuate hepatic encephalopathy-associated hyperammonemia.
- If epileptic seizure activity—Keppra (levetiracetam) is the preferred anticonvulsant as it is minimally metabolized in liver and largely excreted in urine; secondary anticonvulsants include: zonisamide (caution: sulfa drug, rare idiopathic hepatotoxicity) and lastly, KBr (complicated by fluid therapy) as preferred anticonvulsants to phenobarbital.

CONTRAINDICATIONS

Avoid drugs metabolized by the liver.

PRECAUTIONS

- Use anesthetics, sedatives, tranquilizers, potassium-wasting diuretics, analgesics, and highly protein-bound drugs cautiously.
- If possible, avoid drugs reliant on hepatic metabolism, biotransformation, or excretion.
- Consider altered pharmacokinetics; reduced first-pass extraction due to portosystemic shunting; low albumin reduces protein binding increasing free drug-receptor interaction.

POSSIBLE INTERACTIONS

Drugs that affect or depend on hepatic metabolism—e.g., cimetidine, chloramphenicol, barbiturates, ketoconazole.

**FOLLOW-UP****PATIENT MONITORING**

- Re-evaluate patient's at-home behavior, demeanor, body condition and weight.

- Monitor albumin and glucose—in patients with non-correctable disorders; adjust nutrition.

- Monitor electrolytes—especially potassium; avoid hypokalemia as it aggravates hyperammonemia.

PREVENTION/AVOIDANCE

Avoid dehydration, azotemia, hemolysis, constipation, enteric bleeding, endoparasitism, infusion of stored blood, ammonium challenge, urinary tract infections (especially with urease-producing organisms, e.g., *Staphylococcus*), hypokalemia, hypomagnesemia, and alkalemia.

POSSIBLE COMPLICATIONS

Permanent neurologic damage (rare)

EXPECTED COURSE AND PROGNOSIS

- Depends on underlying disorder.
- Acute or chronic hepatic failure—may be fully or partially reversible, or patient may die.

**MISCELLANEOUS****AGE-RELATED FACTORS**

PSVA—surgical outcome may be good in young and old patients; medically treat HE before anesthesia/surgery.

SYNOMYS

- Hepatic coma
- Portosystemic encephalopathy

SEE ALSO

- Arteriovenous Malformations of the Liver
- Hepatic Failure, Acute
- Portosystemic Shunting, Acquired
- Portosystemic Vascular Anomaly, Congenital

ABBREVIATIONS

- APSS = acquired portosystemic shunt
- APTT = activated partial thromboplastin time
- AV = arteriovenous
- CNS = central nervous system
- DIC = disseminated intravascular coagulation
- GABA = γ -aminobutyric acid
- GFR = glomerular filtration rate
- HE = hepatic encephalopathy
- PIVKA = proteins invoked by vitamin K absence or antagonism
- PLE = protein-losing enteropathy
- PT = prothrombin time
- PSVA = portosystemic vascular anomaly
- TSBA = total serum bile acids

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**Client Education Handout
available online**

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HEPATIC FAILURE, ACUTE



BASICS

DEFINITION

- Severe acute hepatic injury incapacitating the ability to meet synthetic, metabolic, and detoxification needs.
- Sudden loss of > 75% of functional hepatic mass due to acute, massive hepatic necrosis.
- May lead to catastrophic multi-organ dysfunction/failure in a previously healthy individual; may rapidly progress to death.

PATOPHYSIOLOGY

- Necrosis—secondary to insufficient perfusion, hypoxia, hepatotoxins or their adducts (drugs, other xenobiotics, toxins), heat excess, or infectious agents.
- Severity of hepatic dysfunction depends on insult type and lobular (zonal) distribution.
- Reduced perfusion or hypoxia usually affect zone 3 (pericentral or centrilobular region).
- Ingested toxins—affect zone where toxin is metabolized or adducts formed, or where there is specific organelle tropism or propensity for oxidative injury (copper accumulation increases zone 3 vulnerability).
- Accompanied by enzyme leakage and markers of impaired liver function, hyperbilirubinemia and acute onset splanchnic hypertension due to sinusoidal or centrilobular collapse.
- Lethal organ failure associated with coagulopathy, enteric hemorrhage, acute onset hepatic encephalopathy (HE).
- Hepatic failure—associates with a myriad of metabolic derangements: i.e., altered glucose homeostasis, protein synthesis (albumin, transport proteins, procoagulants, and anticoagulants), and detoxification capabilities.

SYSTEMS AFFECTED

- Hepatobiliary—hepatocellular necrosis; hepatic failure, and jaundice.
- Nervous—HE; cerebral edema.
- Gastrointestinal—vomiting; diarrhea; melena; hematochezia due to acute splanchnic hypertension ± coagulopathy.
- Hemic/Lymphatic/Immune—pro- and anticoagulant factor imbalances; DIC.
- Renal/Urologic—renal tubule damage from certain toxins or physiologic vasoconstriction; tubular injury: i.e., copper associated hepatopathy, leptospirosis, xylitol toxicity, NSAID toxicity.
- Hyperdynamic circulatory status: low systemic and pulmonary vascular resistance, increased cardiac output and metabolic rate, systemic hypotension; this associates with endotoxemia, TNF- α , dehydration, and splanchnic hypertension.

INCIDENCE/PREVALENCE

- Variable depending on pre-existent liver disease: i.e. hepatocellular copper accumulation, chronic immune-mediated

hepatitis or cholangitis.

- Panlobular hepatic necrosis leading to acute liver failure is uncommon; examples: idiosyncratic drug toxicity: dogs—zonisamide, phenobarbital, primidone, diphenhydantoin, NSAIDs (e.g., carprofen), xylitol; cats—diazepam; dogs or cats—sulfa-antibiotics; primary toxins: dogs and cats—primary copper accumulation, acetaminophen; dogs—zonisamide, xylitol, cycad (sago palm), blue-green algae, *Amanita* mushrooms, aflatoxin; infectious disease: dogs—leptospirosis, infectious canine hepatitis.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

More common in dog than in cat

Breed Predilections

Breeds with apparent predisposition to chronic hepatitis and copper associated hepatopathy (e.g., Labrador retriever, Doberman pinscher) may have higher risk. e.g., Labrador retrievers and NSAID toxicity enhanced by copper associated hepatopathy.

Mean Age and Range

N/A

Predominant Sex

N/A

SIGNS

- Acute-onset nonspecific clinical signs; lethargy, inappetence, GI disturbances (vomiting, small intestinal diarrhea may be bloody), PU/PD.
- Tender hepatomegaly.
- Bleeding tendencies.
- Jaundice.
- Hepatic encephalopathy.
- Seizures.

CAUSES

Drugs

- See Hepatotoxins.
- Drug related toxicities may be *intrinsic* (direct) or *idiosyncratic* (unpredictable, unrelated to dose) presenting consequent to immune-mediated hypersensitivity or metabolic injury.

Biologic Toxins

See Hepatotoxins

Infectious Agents

See Hepatotoxins

Thermal Injury

- Heat stroke
- Whole-body hyperthermia
- Cancer treatment

Hepatic Hypoxia

- Thromboembolic disease, shock, DIC.
- Acute circulatory failure from any cause.
- Acute centrilobular necrosis (zone 3).

RISK FACTORS

- Administration of any potentially hepatotoxic substance or drug.
- Exposure to environmental toxins (e.g., *Amanita* mushroom, foodborne aflatoxin, cycad [sago palm] ingestion, blue-green algae, artificial sweetener xylitol (gum, candy)—dogs.

- Enzyme inducers (e.g., phenobarbital)—may increase risk for certain toxicities by enhancing xenobiotic toxin formation: e.g., acetaminophen toxicity is greatly enhanced by phenobarbital.
- Indiscriminate substance ingestion—puppies; polyphagic animals.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Severe acute pancreatitis or gastroenteritis—differentiated via laboratory tests and imaging.
- Acutely decompensated chronic liver disease—distinguished by review of medical records, blood tests, abdominal ultrasonography, and liver biopsy.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia and panhypoproteinemia—bleeding, marrow toxicity, direct enteric toxicity.
- Thrombocytopenia—bleeding, DIC, or portal hypertension.
- Liver enzyme activity—high acute ALT and AST; smaller increases ALP and GGT.
- Hypoglycemia—grave prognosis (cats esp.).
- Hypocholesterolemia—impaired synthesis or enteric loss with hemorrhage.
- Normal to low BUN concentration: reduced urea cycle function, PU/PD.
- Hyperbilirubinemia: initially absent.
- Bilirubinuria may precede hyperbilirubinemia—always abnormal in cats.
- Ammonium urate crystalluria signifies hyperammonemia, hepatic insufficiency or portosystemic shunting.
- Acquired Fanconi's syndrome—granular casts and renal glucosuria indicate proximal tubule injury (e.g., carprofen, copper, leptospirosis, other toxicities especially in dogs).

OTHER LABORATORY TESTS

- TSBA—high values indicate hepatic dysfunction, cholestasis, or portosystemic shunting.
- Plasma ammonia concentration—high values coincide with high TSBA, confirm hepatic insufficiency; hyperammonemia inconsistent but reflected by ammonium biurate crystalluria; hyperammonemia may reflect concurrent myonecrosis.
- Coagulation tests—coagulation factor deficiencies, platelet dysfunction, low fibrinogen, low antithrombin or protein C activity, and DIC suggest severe liver failure, decompensated DIC, or enteric losses with hemorrhage.

IMAGING

- Abdominal radiography—may identify a normal to slightly large liver ± effusion.
- Abdominal ultrasonography—may disclose non-hepatic disorders (e.g., pancreatitis), altered circulation (ratio hepatic vein:portal vein), altered liver echogenicity or surface contour reflecting chronic injury (e.g., remodeling implicated by heterogeneous liver texture, nodularity, or hepatofugal portal

(CONTINUED)

blood flow); rule out biliary obstruction as source of hyperbilirubinemia. • Brain MRI—may disclose early cerebral edema.

OTHER DIAGNOSTIC PROCEDURES

- Liver biopsy—confirms necrosis and characterize lesion zonal distribution.
- Fine-needle liver aspirate may identify hepatocellular degeneration, copper accumulation, dysplastic hepatocytes observed with cycad (sago palm) or aflatoxin ingestion; canalicular cholestasis. Many toxins lead to microvesicular hepatocellular lipid vacuolation.

PATHOLOGIC FINDINGS

- Gross—slightly large, mottled liver.
- Microscopic—confirms necrosis; zonal involvement; may assist in determining underlying cause: hypoxia leading to zone 3; certain toxins cause zone 1 or 3 necrosis; reticulin staining confirms zonal involvement, confirms retention or loss of reticulin substructure that orchestrate organized regeneration.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient—intensive care required.

NURSING CARE

- **Caution:** Delay inserting central catheters until bleeding diatheses controlled with vitamin K₁, fresh frozen plasma, or fresh whole blood. No advantage to prophylactic FFP administration as this may contribute to onset of HE and cerebral edema. • Fluids—non-lactate-containing; initially at a resuscitation rate; monitor peripheral blood pressure and pulse oximetry. Mixed acid-base disturbances common. • Colloid replacement—with low oncotic pressure from bleeding and protein loss; plasma always preferred; synthetic colloids are second line. Avoid dextran 70 and Hetastarch (as these may promote bleeding) and human albumin (may induce fatal acute allergic reaction).
- Potassium, phosphate, glucose—supplement as appropriate; low phosphate, potassium and glucose aggravate HE and other clinical signs, complicating critical supportive care. • Fluid regimen—adjust for maintenance needs after achieving normovolemia; typically provide one-third of normal maintenance rate with polyionic crystalloids if concurrently giving slow CRI of synthetic colloid. Avoid colloids if possible as these leak from the microvasculature (exacerbated with some toxicities that affect endothelium) and disturb signaling that triggers albumin and transporter protein synthesis. • Supplemental oxygen—if pulse oximetry $\leq 90\%$ saturation. • If suspect cerebral edema: use 30° head up elevation, consider mannitol, other interventions.

- Predisposition to infection from enteric bacterial translocation—cover with broad-spectrum antimicrobials; patient may not manifest fever or leukocytosis with infection. Sepsis/SIRS—major risks for cerebral edema. • Early administration of N-acetylcysteine may improve microvascular perfusion, tissue oxygenation, and mitigate oxidative damage; dosing: see below.

ACTIVITY

Restricted activity—conserves energy and metabolites for healing and regeneration.

DIET

- Intractable vomiting— withhold PO food until controlled; use antiemetics (see below).
- When enteric nutrition contraindicated (somnolent patient) use total or partial parenteral nutrition until enteral feeding route established; < 5 days advised. • If enteric nutrition chronically compromised, establish total parenteral nutrition (TPN) feeding catheter; use TPN formula with normal nitrogen content unless HE; branched-chain amino acids remain controversial. • Enteral feeding—small volume, frequent meals; optimize digestion and assimilation, minimize enteric toxin formation contributing to HE.
- Diet composition—use normal protein (nitrogen) content in tolerant patients; moderate protein restriction if HE (2.5 g protein/kg bodyweight) but strive to maintain a positive nitrogen balance for hepatic regeneration. • Supplemental vitamins are essential—water-soluble (2-fold normal); vitamin K₁ (0.5–1.5 mg/kg SC or IM, three doses at 12-h intervals, then once-to-twice weekly); vitamin E (10 IU/kg PO or by injection q24h). • Probiotic/Prebiotic yogurt: may protect against enteric bacterial translocation; tolerated dairy protein source if HE; controversial.

CLIENT EDUCATION

- Acute hepatic failure is a serious condition.
- Some patients succumb despite optimal treatment. • Cause of panlobular injury (e.g., exposure to a drug or toxin) should be investigated but may remain unconfirmed.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

Drugs for Vomiting

- Metoclopramide—1–2 mg/kg/day CRI for intermittent mild vomiting; contraindicated if spironolactone used for ascites mobilization.
- Ondansetron—0.5–1.0 mg/kg IV q24h.
- Chlorpromazine—0.5 mg/kg SC, IM, or rectally, q8–24h) for severe vomiting; ensure volume expansion first as causes alpha blockade vasodilation.

HEPATIC FAILURE, ACUTE

- Maropitant—1.0 mg/kg SC q24h.
- Histamine H₂-blocker—famotidine (0.5–1.0 mg/kg IM or SC q12–24h) if enteric bleeding; reserve cimetidine (0.5 mg/kg q8–12h) for purposeful P450 cytochrome inhibition.
- Omeprazole (0.5–1.0 mg/kg PO q12–24h) or pantoprazole may induce P450 cytochrome-associated drug interactions; 24–48 h delay in onset of action.

Drugs for Hepatic Encephalopathy

- Lactulose—0.5–2.0 mL/kg PO q8h; or rectally if PO hazardous; goal is soft feces.
- Probiotic yogurt (see above).
- Metronidazole—7.5 mg/kg PO q12h or rectally if PO hazardous.
- Rifaximin—5–10 mg/kg PO or rectally q12h (non-absorbed antibiotic alters enteric flora).
- Neomycin—22 mg/kg PO or rectally q12h; **caution:** may be ototoxic and renal toxic if increased absorption with reduced gut integrity.

H

Treatment of Cerebral Edema Associated with Hepatic Encephalopathy

- Mannitol—1 g/kg over 10–20 min, filtered; if brisk diuresis does not occur (~1 h), check for excessive volume expansion (plasma osmolality, blood pressure) and renal function.
- Furosemide—0.5–1.0 mg/kg IV q8–24h increases free water excretion and reduces CSF production; monitor hydration and serum potassium; avoid dehydration and hypokalemia that provoke or worsen HE.
- *Vasopressin V₂ antagonists* (aquaretics) may assist with management of diuretic resistant ascites. Tolvaptan successful in dogs with experimentally induced (rapid pacing) congestive heart failure. Human dose in cirrhosis is 7.5 mg/day; tolvaptan is metabolized exclusively in the liver primarily by cytochrome P450; dose undetermined in dogs with liver disease.

Drugs for Coagulopathy

Fresh whole blood or fresh frozen plasma—if clinically significant bleeding.

Free Radical Scavengers and Antioxidants

- For ongoing damage (membrane injury), reperfusion injury, and hypoxia.
- Vitamin E—10 IU/kg PO q24h.
- N-acetylcysteine—140 mg/kg IV or PO; IV use 10% solution diluted 1:2 in saline, administer via 0.25 μm non-pyrogenic filter; follow with 70 mg/kg q6–12h.
- S-adenosylmethionine (SAMe) as a GSH donor, use proven bioavailable product)—20 mg/kg PO q24h on empty stomach; multiple benefits: essential intermediary metabolites, GSH synthesis, promotes liver regeneration, antifibrotic, anti-inflammatory.

HEPATIC FAILURE, ACUTE

(CONTINUED)

Hepatoprotectants

- Silibinin (milk thistle), efficacy reported for *Amanita* toxicity and certain other toxins; use product complexed with polyunsaturated phosphatidylcholine (PPC), 2–5 mg/kg PO q24h.
- Ursodeoxycholic acid—if chronic liver injury or high bile acids persist, 10–15 mg/kg divided q12h PO, best absorbed if given with food.

Blocking Enterohepatic Circulation

Cholestyramine: 30–40 mg/kg mixed with water PO q24h; bile acid binding resin that can absorb certain toxins in the alimentary canal that undergo enterohepatic circulation diminishing their systemic availability, e.g., anecdotal, sago palm (cycad toxin).

CONTRAINDICATIONS

- Ideally, drugs biotransformed primarily in the liver, altering liver perfusion, or metabolizing enzyme activity should be avoided; may be difficult as many drugs are metabolized in hepatic pathways or eliminated in bile.
- Vitamin C—100–500 mg q24h, *avoid* if high liver iron or copper concentrations; ascorbate may augment transition metal-associated oxidative injury; no substantiation for vitamin C administration in liver failure.

PRECAUTIONS

Administration of stored whole blood or packed RBCs may precipitate or exacerbate HE in dogs with hepatic failure because of spontaneously generated ammonia during storage.

POSSIBLE INTERACTIONS

Compromised hepatic metabolism

ALTERNATIVE DRUG(S)

Case-based considerations



FOLLOW-UP

PATIENT MONITORING

- Temperature, pulse, respiration, and mental status—q1–2h until stable.
- Maintain

vigilance for infection, especially catheter-induced.

- Bodyweight—twice daily guides fluid therapy; bodyweight and condition used to assess nitrogen and energy allowances.
- Acid-base, electrolyte balances (especially potassium and phosphate), and glucose—q12–24h for the first 72 h.
- Sequential measurements of: liver enzymes, bilirubin, cholesterol, and fibrinogen q2–3 days provide evidence of recovery.

PREVENTION/AVOIDANCE

- Vaccinate dogs against infectious canine hepatitis virus.
- Avoid indiscriminate ingestion of hepatotoxins and environmental exposure.
- Consider drugs as potential toxins.

POSSIBLE COMPLICATIONS

- Hypoglycemia
- Uncontrolled GI bleeding and DIC
- HE, cerebral edema, brain herniation
- Chronic hepatic insufficiency, cirrhosis, fibrosis from postnecrotic scarring
- Acute renal failure
- Death

EXPECTED COURSE AND PROGNOSIS

Prognosis—depends on extent of liver injury, etiopathogenesis, supportive nursing care.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Pancreatitis
- Sepsis/Endotoxemia/Shock
- Bleeding diathesis; severe enteric hemorrhage; DIC
- Renal failure
- Hepatic encephalopathy

ZOONOTIC POTENTIAL

- Toxins (?)
- Leptospirosis

SYNOMYMS

- Acute hepatic necrosis
- Fulminant hepatic failure

SEE ALSO

- Ascites
- Coagulopathy of Liver Disease
- Hepatic Encephalopathy
- Hepatitis, Infectious (Viral) Canine
- Hepatotoxins
- Hyperbilirubinemia
- Icterus
- Renal Failure, Acute

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- BUN = blood urea nitrogen
- CRI = constant rate infusion
- CSF = cerebrospinal fluid
- DIC = disseminated intravascular coagulation
- GGT = γ -glutamyltransferase
- GSH = glutathione
- HE = hepatic encephalopathy
- PU/PD = polyuria, polydipsia
- TSBA = total serum bile acids

Suggested Reading

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Client Education Handout
available online

HEPATIC LIPIDOSIS



BASICS

DEFINITION

- Feline hepatic lipidosis—> 80% of hepatocytes accumulate substantial triglyceride vacuoles that distend the cytosolic compartment, causing canalicular compression, severe cholestasis, and liver dysfunction.
- Untreated—leads to progressive metabolic dysregulation and death.
- Develops secondary to a primary disease or condition causing anorexia or catabolism.

PATHOPHYSIOLOGY

- Cats have a unique propensity to accumulate triglyceride filled hepatocellular vacuoles.
- Causal factors—energy and protein deficits; increased peripheral fat mobilization; increased hepatic triglyceride synthesis; impaired hepatic β -oxidation of fatty acids; reduced hepatocellular triglyceride exportation.
- Cytosolic triglyceride vacuoles displace organelles to cell periphery, associate with organelle dysfunction, and canalicular compression.
- Hepatic failure—with rare overt HE.

SYSTEMS AFFECTED

- Hepatobiliary—severe intrahepatic cholestasis, hepatic dysfunction or failure
- Gastrointestinal—anorexia; vomiting
- Musculoskeletal—peripheral tissue wasting
- Nervous—HE, ptalism, moribund condition
- Hemic/Lymphatic/Immune—abnormal RBC shapes (poikilocytes), Heinz body hemolysis
- Renal/Urologic—potassium wasting; renal tubule triglyceride accumulation

INCIDENCE/PREVALENCE

Most common severe feline hepatopathy in North America causing jaundice.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Cat, rarely dog (toy breed puppies; also see Glycogen Storage Disease).

Breed Predilection

N/A

Mean Age and Range

Middle-aged adult cats: 8 (1–16 years)

Predominant Sex

N/A

SIGNS

Historical Findings

- Anorexia, hyporexia, weight loss, sarcopenia
- Jaundice
- Lethargy, weakness progressing to collapse
- Vomiting, diarrhea, or constipation

- Ptyalism: may reflect food aversion or HE
- Neck ventriflexion: weakness, electrolyte depletion: potassium, phosphate; thiamin deficiency
- Abnormalities due to underlying disease

Physical Examination Findings

- Jaundice
- Hepatomegaly
- Dehydration
- Weakness—neck ventriflexion, recumbency
- Ptyalism
- Collapse/Obtunded
- Others, depending on underlying or primary disease; HE (rarely overt)

CAUSES

"Idiopathic" Hepatic Lipidosis

“Idiopathic” = inappropriate terminology; antecedent health problems are discoverable in > 85% of cases causing anorexia or malassimilation; remainder have food deprivation.

Secondary Hepatic Lipidosis

- Primary liver disease—PSVA; CCHS; EHBDO; cholelithiasis; neoplasia
- Gastrointestinal—obstruction; neoplasia (lymphosarcoma); IBD; pancreatitis
- Urogenital disease—renal failure, CIN, lower urinary tract syndrome
- Neurologic conditions: cannot eat
- Infectious diseases—toxoplasmosis; FIP; FIV- or FeLV-related disorders
- Hyperthyroidism
- Vitamin B₁₂ deficiency (may predispose cats to HL)
- Many other systemic conditions or toxins
- Rapid weight loss protocol

RISK FACTORS

- Obesity
- Anorexia, negative nitrogen balance
- Catabolism or rapid weight loss
- Vitamin B₁₂ deficiency



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Primary liver disease—CCHS, cholelithiasis, EHBDO, or neoplasia (esp. lymphosarcoma) important considerations differentiated by abdominal ultrasonography, liver aspiration, and liver biopsy.
- PSVA—rarely confused; diagnosis by ultrasound or colorectal scintigraphy, and lab testing.
- Hepatic toxoplasmosis or FIP—liver biopsy, serology, immunohistochemistry.
- Pancreatitis—differentiated by ultrasonography, serum tests (low fPLI rules down likelihood of pancreatic inflammation, high values with local inflammation or pancreatitis; inconsistent amylase, lipase), pancreatic aspiration cytology, gross inspection, biopsy.

- Gastrointestinal disease—IBD differentiated by endoscopic or full-thickness bowel biopsies; obstruction differentiated by abdominal survey or contrast radiography and ultrasonography.

- Toxicities—suspected based on history (e.g., oral diazepam, acetaminophen, methimazole).
- Hyperthyroidism—serum thyroid panel.

CBC/BIOCHEMISTRY/URINALYSIS

- Hematology—poikilocytes common; non-regenerative anemia; hemolytic anemia: severe hypophosphatemia or Heinz bodies (low GSH); leukogram reflects underlying disorder.
- Biochemistry—hyperbilirubinemia; high ALP, ALT activity; normal or mild increase in GGT if no primary necro-inflammatory disorder of biliary or pancreatic tissue; low BUN; normal creatinine; variable glucose (hypoglycemia rare); variable cholesterol, albumin, globulins (high globulins with inflammatory disease); hypokalemia (associated with failure to survive, refeeding phenomenon); severe hypophosphatemia (< 2 mg/dL) complicates initial 72 h of feeding (refeeding syndrome).
- Urinalysis—lipiduria and unconcentrated urine common; ammonium biurate crystalluria not seen; renal potassium wasting (some cats).

OTHER LABORATORY TESTS

- Prolonged coagulation times—PT, APTT, ACT, esp. PIVKA in > 50% tested cats; fibrinogen usually normal; abnormalities correct with parenteral vitamin K₁ therapy.
- Hyperammonemia—uncommon.
- Serum bile acids—high before hyperbilirubinemic; redundant test if hepatobiliary jaundice.
- B₁₂ deficiency—may increase susceptibility to HL and appears to compromise recovery.

IMAGING

Survey Abdominal Radiography

- Hepatomegaly
- May note features of underlying disorder

Abdominal Ultrasonography

- Diffuse hyperechoic hepatic parenchyma reflects hepatic lipid vacuolation.
- Look for primary disease causing HL.

DIAGNOSTIC PROCEDURES

- Fine-needle liver aspiration cytology: > 80% hepatocytes with severe cytosolic vacuolation; biopsy rarely needed to confirm HL
- Definitive diagnosis HL—based on history, clinical features, high ALP, diffuse hyperechoic hepatic parenchyma, severe hepatocyte lipid vacuolation on aspiration cytology; cannot rule out underlying primary hepatic disorders (e.g., CCHS, EHBDO, PSVA) with these tests.
- Liver biopsy—definitive diagnosis of underlying “primary” liver disorders; *done only if poor response to therapy or high GGT*.

H

HEPATIC LIPIDOSIS

(CONTINUED)

Caution: stabilize cat before anesthesia and biopsy to reduce risk of death.

- Vitamin K₁ (0.5–1.5 mg/kg SC or IM) three doses at 12-h intervals, at least 12 h *before*: aspiration sampling, liver biopsy, jugular vein catheterization, or feeding appliance insertion to reduce risk of severe iatrogenic bleeding.

PATHOLOGIC FINDINGS

- Gross—diffuse hepatomegaly, smooth surface; friable greasy consistency, yellow/pale color with reticulated appearance; sample floats in formalin.
- Microscopic—diffuse, severe hepatocellular vacuolation; large (macrovesicular) or small (microvesicular) vacuolation.
- Oil Red O—on frozen tissue confirms lipid; but not typically necessary.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—necessary for recumbent cats or those with neck ventriflexion (indicates severe electrolyte disturbance: potassium or phosphate, or thiamin deficiency).
- Discharge for home care after stabilization and enteral feeding route established, and demonstrated to be problem free.
- Frequent reevaluations—imperative.
- Outpatient—reduces stress and thereby facilitates recovery in some cats.

NURSING CARE

- Balanced polyionic fluids—*avoid* lactate and dextrose supplementation. Acetate may not be metabolized quickly; 0.9% NaCl preferred.
- Potassium chloride supplementation is important, use sliding scale (see Hypokalemia).
- Phosphate supplements usually needed (see Hypophosphatemia) at initial feeding (refeeding syndrome).
- Magnesium supplements rarely needed; low Mg may rarely complicate potassium repletion.

Correct Hypophosphatemia

- Serum phosphate < 2.0 mg/dL reflects refeeding syndrome; may provoke: anorexia, vomiting, weakness, myonecrosis, ileus, hemo-lysis, and neurologic signs confused with HE.
- Treatment—potassium phosphate initial dose 0.01–0.03 mmol/kg/h IV (commercial parenteral phosphate = 3 mmol/mL phosphate = 93 mg/mL elemental phosphorus); monitor serum phosphate q6h; discontinue when stable phosphate > 2 mg/dL. **Caution:** reduce IV potassium chloride supplement to avoid iatrogenic hyperkalemia.

Correct Hepatic GSH Depletion

- Low liver GSH is confirmed in HL; routine GSH measurements are not available;

increased risk for oxidant injury from primary diseases, lipid accumulation; or hypophosphatemia-induced energy deficit (low ATP).

- Crisis intervention for low hepatic GSH or Heinz body anemia—NAC (140 mg/kg IV, then 70 mg/kg IV, 10% solution diluted 1:2 in saline; administer through 0.22–0.25 micron non-pyrogenic filter; administer over 20 minutes).
- When enteral feeding established, change to SAMe: 200 mg/cat PO q24h, use form with confirmed bioavailability/efficacy; need for dosing on empty stomach complicates use.

ACTIVITY

Activity may augment gastric motility when gastroparesis complicates feeding (chronic vomiting); early recovery phase cats too weak.

DIET

- Nutritional support—cornerstone of recovery.
- High-protein, high-calorie feline diet essential.
- Energy—50–60 kcal/kg ideal weight/day; gradual transition to full energy requirement over 3–5 days; feed multiple small meals/day.
- Forced alimentation usually required.
- Forced oral feeding may cause food aversion.
- Tube feeding—initially by nasogastric tube transitioned to esophageal tube after hydration and electrolyte status improves, and vitamin K₁.
- Avoid laparotomy for gastric feeding tube insertion; cats with HL have high mortality.
- Cautiously offer PO food daily to assess interest in food.
- Human stress formula enteral diets (not recommended)—require supplemental arginine (or citrulline), and taurine.

SUPPLEMENTS

- Supplements improve survival in severely affected cats.
- Medical grade L-carnitine (250–500 mg/day). Carnitine supplements have wide variability in bioavailability; Carnitor (liquid medical grade carnitine) recommended. Carnitine has been confirmed to increase and sustain fatty acid oxidation in overweight cats undergoing weight loss, as in HL (see Suggested Readings).
- Taurine (250–500 mg/day).
- Thiamin (50–100 mg/day).
- Vitamin B₁₂ (initially, 1 mg IM or SC once); determine chronic vitamin B₁₂ needs by sequential B₁₂ values (weekly intervals).
- Water-soluble vitamins in fluids (2 mL/L).
- Vitamin E (10 IU/kg/day) in food.
- Thiol donors (NAC, SAMe): as above.
- Potassium gluconate (for hypokalemia), reduces fluid potassium supplements.
- Marine oil in food (2000 mg q24h).

CLIENT EDUCATION

- Warn client—sequential biochemical assays needed to assess recovery.

- Educate client about feeding tube use/care and may be retained for 4–6 months.
- Advise client—recurrence unlikely; liver function will not be chronically compromised.

SURGICAL CONSIDERATIONS

- Avoid surgical interventions until hydration, electrolyte depletions, Vit. K₁ deficiency, Heinz body anemia alleviated.
- Exploratory laparotomy and liver biopsy (if indicated)—inspect for underlying disorders; biopsy pancreas, stomach, and small bowel.



MEDICATIONS

DRUG(S)

- Vitamin K₁—recommended for all cats with suspected HL; see dose above, avoid overdosage: oxidant hemolysis and liver injury.
- Drugs to ameliorate HE (see Hepatic Encephalopathy) usually not needed.
- Emesis control—metoclopramide: for vomiting, nausea, and gastroparesis (0.2–0.5 mg/kg SC q8h, 30 min before feeding, or as a CRI IV drip at 0.01–0.02 mg/kg/h or 1–2 mg/kg/day); dolasetron (0.5–0.6 mg/kg q24h IV, SC, PO); or maropitant (1 mg/kg IV, SC, PO q24h, 5 days max); famotidine: to avert damage to lower esophagus if vomiting (0.5–1.0 mg/kg q12–24h).
- Systemic antibiotics—as appropriate for concurrent infections.

CONTRAINdications/ PRECAUTIONS

- Adjust dosages of medications relying on hepatic metabolism or excretion.
- Avoid benzodiazepines and barbiturates—interact with neuroreceptors provoking HE.
- Appetite stimulants (e.g., diazepam, oxazepam, cyproheptadine, mirtazapine)—do not provide dependable energy intake; some produce sedation; diazepam rare fulminant hepatic failure.
- Avoid injectable medications with a propylene glycol carrier; may lead to hemolysis in cats with low GSH.
- Ursodeoxycholic acid—likely not beneficial; may be injurious in HL; may promote taurine deficiency due to conjugation.
- Dextrose supplements—may provoke hepatic triglyceride accumulation.
- Avoid tetracyclines or stanazolol—these promote triglyceride deposition leading to HL.
- Avoid propofol—(phenol derivative) may provoke hemolysis 12 h after infusion in cats with Heinz body anemia; some HL cats recover slowly; alternatively use gas anesthesia.

(CONTINUED)

HEPATIC LIPIDOSIS**FOLLOW-UP****PATIENT MONITORING**

- Body weight, condition, hydration, electrolytes; judicious adjustment of energy, fluid, and electrolyte provisions important.
- Serum bilirubin—declines within 2 weeks of adequate management; predicts recovery.
- Liver enzyme activity—slow to normalize; do not predict recovery.
- Discharge for home care—when vomiting is controlled, gastroparesis resolved, bilirubin declining, patient ambulatory, and tube-feeding apparatus is problem-free.
- Tube feeding—discontinued only after confirmed voluntary food consumption.

PREVENTION/AVOIDANCE

- Obesity—prevent; weight reduction must not exceed 2.0% bodyweight per week.
- Caution owner to verify food intake during weight loss regimens and during at-home stress.

POSSIBLE COMPLICATIONS

- Feeding tube malfunction or obstruction—tube obstructions relieved with: papaya juice, carbonated soft drink, or pancreatic enzyme slurry; 15-min dwell time, warm water flush.
- Rare HE after dietary support introduced.
- Hepatic failure can lead to death.
- Untreatable underlying causal disorder.

EXPECTED COURSE AND PROGNOSIS

- Optimal response to tube feeding and nutritional supplements—recovery in 3–6 weeks.

- Therapy as described—85% recovery of severely affected animals.
- Underlying disease influences outcome.
- HL rarely recurs.
- HL does not cause chronic liver dysfunction.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Primary liver disorders
- Pancreatitis
- Malassimilation: various causes
- Diabetes mellitus
- Neoplasia—hepatic and systemic
- Hepatic encephalopathy (rare)
- Systemic illness limiting nutrition intake

SYNOMYMS

- Fatty liver syndrome
- Hepatosteatosis
- Feline hepatic vacuolation
- Vacuolar hepatopathy
- Vacuolar degeneration

SEE ALSO

- Cholangitis/Cholangiohepatitis Syndrome
- Hepatic Encephalopathy

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- CCHS = cholangitis/cholangiohepatitis syndrome
- CIN = chronic interstitial nephritis
- EHBD = extrahepatic bile duct obstruction
- fPLI = feline pancreatic lipase

- GGT = gamma glutamyltransferase
- GSH = glutathione
- HE = hepatic encephalopathy
- HL = hepatic lipidosis
- IBD = inflammatory bowel disease
- NAC = *N*-acetylcysteine
- PIVKA = proteins invoked by vitamin K absence or antagonism
- PSVA = portosystemic vascular anomaly
- SAMe = *S*-adenosylmethionine

Suggested Reading

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**Client Education Handout
available online**

H

HEPATIC NODULAR HYPERPLASIA AND DYSPLASTIC HYPERPLASIA



BASICS

OVERVIEW

Hepatic Nodular Hyperplasia (HNH)

- Benign parenchymal feature in middle-aged to older dogs; non-encapsulated, ≤ 2 cm (rarely up to 5 cm), expansile nodule of hepatocellular hyperplasia, maintaining a modified lobular architecture with recognizable central and portal elements that are irregularly spaced, organized hepatic cord structure 1 cell wide, without marginal parenchymal collapse or fibrosis (is not a regenerative nodule), smooth margins; hepatocyte phenotype may be similar to surrounding parenchyma but may contain glycogen or lipid vacuoles.
- May associate with increased liver enzymes in elderly dogs, especially ALP.
- Clinical concern derives from association with increased liver enzyme activity and US detection of hepatic nodules or hepatic nodularity during exploratory surgery.
- Variable US appearance.
- Biopsy specimens must include affected and unaffected liver for appropriate interpretation.
- Nodular hyperplasia may be mistaken for regeneration secondary to chronic hepatitis or hepatocellular neoplasia (adenoma) with needle core biopsies or when only nodular tissue without normal hepatic tissue is sampled.

Hepatocellular Dysplastic Hyperplasia (HDH)

- Potentially pre-neoplastic proliferative hepatocellular foci in dogs with glycogen-type VH; non-encapsulated, variably sized, reduced reticulin substructure, expansile nodules of non-vacuolated hepatocytes forming wide (2 cells wide, normal = 1 cell width) disorganized hepatic cords, an irregular (serrated) margin interfacing with adjacent "normal VH" affected hepatocytes, and lacking remodeled marginal lesions (fibrosis, parenchymal collapse).
- Associates with VH-related increased liver enzymes, dominated by increased ALP activity.
- Recognized as an antecedent hepatic lesion in dogs developing hepatocellular carcinoma (e.g., Scottish terriers, also other breeds) and is seemingly associated with increased sex hormone concentrations (androgens, progestins).
- Variable US appearance depending on size, number, distribution.
- May be mistaken for nodular regeneration without special stains to detail reticulin substructure and collagen fibril deposition.

SIGNALMENT

HNH

- Age-related lesion.

• Nodules develop by 6–8 years of age; one study documented lesions in all geriatric dogs > 14 years of age.

HDH

- Associated with glycogen-type VH
- Reflect adrenal hyperplasia syndromes

SIGNS

Physical Examination Findings

- HNH does not cause clinical illness.
- Large nodules that rupture and bleed or nodules impairing hepatic sinusoidal perfusion likely represent misdiagnosed hepatic adenomas or well-differentiated hepatocellular carcinoma.
- HDH is associated with glycogen-type VH syndromes (see Glycogen-Type Vacuolar Hepatopathy).

CAUSES & RISK FACTORS

- HNH etiology—unknown; metabolic factors, prior injurious events. In humans associated with infarcts but no evidence of this in dogs.
- HDH etiology—may represent hormonal influence promoting neoplastic transformation (sex hormone-related adrenal hyperplasia).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Necroinflammatory liver disease—regenerative nodular hyperplasia involves the entire liver; formation of irregular nodules of variable size that are segregated by parenchymal collapse, often marginated by fibrous connective tissue; demonstrate loss of lobular architecture, sinusoidal fibrosis, reduced reticulin substructure, and wide disorganized hepatic cords.
- Neoplasia. Hepatic adenoma—mass lesions with margins reflecting expansile compression on normal adjacent liver, encapsulated, hepatic cords double wide, disorganized, reduced reticulin substructure, and minimal atypia. Hepatocellular carcinoma—single or multiple confluent or separate mass lesions, margins reflecting irregular expansile compression on normal adjacent liver, partially encapsulated, variable width of disorganized hepatic cords > 2 cells, multiple phenotypes differing from adjacent normal tissue, variable atypia (may be well differentiated), may display pseudoglandular pattern associated with giant canaliculi, well-vascularized with arterial twigs; retention of some normal lobular elements possible (primarily at the periphery).

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—no association with HNH; for HDH see Glycogen-Type Vacuolar Hepatopathy.
- Biochemistry profile—increased serum ALP activity may be encountered with HNH and

HDH; may range 2.5 to 16-fold normal; higher with HDH and VH syndrome, see Glycogen-Type Vacuolar Hepatopathy); usually normal total protein, albumin, bilirubin, and cholesterol.

- Urinalysis—no consistent findings.

OTHER LABORATORY TESTS

TSBA—usually normal, unless lesions are diffuse and severe.

IMAGING

- Abdominal radiography—no abnormalities except hepatomegaly with HDH due to VH.
- Abdominal US—variable echogenicity relating to histologic features, nodule number and size, and associated VH. HNH often not noted until liver grossly inspected at surgery or laparoscopy.

DIAGNOSTIC PROCEDURES

- Aspiration cytology—may yield normal hepatocytes, hepatocytes with cytosolic rarefaction and fragility consistent with VH (glycogen retention), or cells with discrete lipid (triglyceride) vacuoles (HNH); occasional binucleate hepatocytes may reflect cell proliferation or other concurrent disease (common in PSVA/MVD); hepatocytes may be small with size variation in HDH. Liver biopsy—collection of a needle biopsy specimen may not clearly differentiate HNH lesion because of small specimen size; definitive diagnosis requires targeted sampling of a large-enough tissue specimen to include lesion and adjacent normal hepatic tissue. HDH may be recognized on needle samples.
- Recommended biopsy methods—laparoscopy, open wedge biopsy during laparotomy, or multiple 14-g needle samples.
- Special stains—reticulin staining illustrates hepatocyte reticulin substructure, lobular collapse/remodeling, and changes associated with nodule margins. Masson's trichrome staining illustrates collagen deposition and remodeling typical of regenerative nodules secondary to chronic liver injury; PAS staining with and without amylase pre-digestion confirms excess glycogen in vacuolated hepatocytes (See Glycogen-Type Vacuolar Hepatopathy).

PATHOLOGIC FINDINGS

- HNH gross—single or multiple mass lesions, rarely > 2 cm in diameter; color similar to adjacent normal hepatic tissue or paler if vacuolated with glycogen or lipid.
 - HDH gross—single or multiple lesions, usually small, may appear darker colored compared to adjacent tissue.
- Microscopic—see previously.



TREATMENT

- Usually none required; rupture of large nodules indicates hepatocellular carcinoma misdiagnosis; may necessitate blood

HEPATIC NODULAR HYPERPLASIA AND DYSPLASTIC HYPERPLASIA

transfusion and emergency mass excision. Palliate or alleviate underlying cause of VH. • HDH: recommend biochemical assessments for rising ALP or ALT that may indicate transformation of mass lesion to a neoplastic phenotype; US inspection of adrenal glands for adrenomegaly or nodules, US surveillance for expanding mass lesions that should be surgically removed; assess pituitary adrenal axis for typical or atypical hyperadrenocorticism; if increased sex hormones $> 2.5 \times$ upper reference interval consider adrenal modulation with agent that does not increase sex hormones.



MEDICATIONS

DRUG(S)

- HDH: if increased sex hormones, progressive VH, nodule formation, increasing ALP, or confirmed hepatocellular carcinoma (after mass resection) consider adrenal modulation with a drug that does not increase sex hormone concentrations (Lysodren or Mitotane); Trilostane increases sex hormone concentrations and would be inappropriate.
- Scottish terrier syndrome does not respond to adrenal modulation; instead use surveillance to detect emerging hepatocellular carcinoma.



FOLLOW-UP

PATIENT MONITORING

- Quarterly biochemical profiles
- Sequential abdominal US to evaluate progression of hepatic nodules
- See Glycogen-Type Vacuolar Hepatopathy for related disorders

POSSIBLE COMPLICATIONS

Distinction of HNH from neoplastic foci is not possible based only on clinical, laboratory, or imaging data although lesions > 2 cm are unlikely to be this diagnosis.

EXPECTED COURSE AND PROGNOSIS

More extensive numbers of nodules may develop in some dogs with HNH and HDH; HDH predicts risk for primary hepatocellular neoplasia which requires surveillance and surgical treatment.



MISCELLANEOUS

SEE ALSO

- Cirrhosis and Fibrosis of the Liver
- Chronic Hepatitis

- Glycogen-Type Vacuolar Hepatopathy
- Hepatocellular Adenoma
- Hepatocellular Carcinoma

ABBREVIATIONS

- HDH = hepatic dysplastic hyperplasia
- HNH = hepatic nodular hyperplasia
- PAS = periodic acid-Schiff
- TSBA = total serum bile acids
- US = ultrasound
- VH = vacuolar hepatopathy

Suggested Reading

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HEPATITIS, CHRONIC



BASICS

DEFINITION

- Hepatic injury associated with active necroinflammatory liver injury.
- Nonsuppurative inflammation—most common; lymphocytes, plasma cells, macrophages, occasional neutrophils.
- Chronicity—progressive remodeling, regenerative nodule formation, fibrosis, eventuating in cirrhosis (see Fibrosis and Cirrhosis of the Liver).

PATHOPHYSIOLOGY

- Multitude of initiating events cause hepatic injury that alter hepatic architecture, damage membranes and/or organelles, and activate cytokine and cell-mediated immune responses; hepatic components become targeted foci. • Initial injury may include infectious agents, toxins, or therapeutic agents but cause often remains undetermined.
- Inflammatory cells, including predominantly lymphocytes (T-cells, NK T-cells), Kupffer cells (hepatic macrophages resident in the lumen of sinusoids), and neutrophils are initial effector cells; INF-g, TNF-a, FasL, IL-4, and numerous chemokines and oxidative free radicals are commonly involved.
 - Oxidant injury an important pathomechanism of membrane and organelle injury.
 - Initial zone of injury demarcates area of necroinflammatory response—zone 1 (periportal) common in many forms of idiopathic hepatitis whereas zone 3 incriminates Cu associated injury, NSAID and other toxins, or repeated ischemic/hypoxic insult.
 - Lesions progression is variable and may include portal and periportal lymphoplasmacytic infiltrates, interface hepatitis with piecemeal necrosis of the limiting plate and variable lobular necroinflammatory activity. Chronic inflammation—progressive fibrosis with bridging between involved zones.
 - Bridging fibrosis and regenerative nodules distort lobular architecture leading to cirrhosis.
 - Progressive development of cholestasis.
 - Cirrhosis and hepatic failure—late stage.
 - Cirrhosis—consequence of chronic fibrogenesis and hepatic regenerative response; typified by: regenerative nodules; reduced functional hepatic mass; collagen deposition along sinusoids and/or around portal triads that compromises sinusoidal perfusion.
 - Fibrosis—usually reflects chronic injury; associated with release of cytokines/mediators that stimulate ECM production or accumulation.
 - Cirrhosis/fibrosis—leads to hepatic dysfunction, sinusoidal hypertension; intrahepatic shunting in collagenized sinusoids or through recanalized vascular pathways within fibrotic partitions between regenerative nodules.
 - Sinusoidal hypertension—leads to (1) hepatofugal portal

venous flow (away from the liver), (2) mesenteric splanchnic hypertension, (3) formation of APSS, (4), episodic HE, (5) splanchnic pooling of blood, decreased effective blood volume, renal sodium and water retention that culminate in ascites formation, (6) portal hypertensive enteric vasculopathy predisposing to enteric bleeding.

SYSTEMS AFFECTED

- Hepatobiliary—inflammation; necrosis; cholestasis; fibrosis.
- GI—emesis; diarrhea; anorexia, portal hypertension leads to ascites formation and propensity for enteric bleeding (portal hypertensive gastroenteric vasculopathy).
- Neurologic—HE.
- Hemic—RBC microcytosis reflecting APSS; bleeding tendencies: failed factor synthesis or activation or thrombocytopenia; coagulopathy (advanced stage).
- Renal/Urologic—PU/PD; isosthenuria; ammonium biurate crystalluria (advanced stage).
- Endocrine/Metabolic—hypoglycemia if end-stage liver failure (provoked by prolonged inappetence).
- Respiratory—tachypnea if tense ascites; bicavity effusion (leakage across diaphragm (rare), pulmonary edema (rare)).
- Nervous—HE (advanced stage).

GENETICS

- Breed or familial predisposition for chronic hepatitis—Doberman pinscher, Labrador retriever, West Highland white terrier, and Dalmatians may develop chronic hepatitis related to low tolerance to Cu levels in commercial diets; Cocker spaniel, standard poodle, Maltese, Skye terrier, others.
- Inherited copper associated hepatopathy only proven in the Bedlington terrier—autosomal recessive, genetic test available.

INCIDENCE/PREVALENCE

N/A

SIGNALMENT

Species

Dog

Breed Predilection

See under genetics

Mean Age and Range

Average age 6–8 years (range 2–14 years)

Predominant Gender

Inconsistent among reports for any breed

SIGNS

General Comments

- Initially—vague and nonspecific.
- Later—relate to complications of portal hypertension (e.g., HE, ascites, gastroduodenal bleeding), and impaired hepatic function.

Historical Findings

- May be no signs in early disease.
- Lethargy.
- Anorexia, weight loss, vomiting, reduced body condition.
- Polyuria and polydipsia.
- Jaundice (late stage).
- Ascites (late stage, signifies onset of portal hypertension and development of APSS, fibrosis, cirrhosis)

- Hepatic encephalopathy (late stage, cirrhosis)

Physical Examination Findings

- May be no signs in early disease.
- Lethargy, poor coat, declining body condition.
- Variable jaundice.
- Liver size—normal to small, depends on chronicity.

Late Stage Physical Findings

- Ascites.
- Hepatic encephalopathy.
- Obstructive uropathy: ammonium biurates.
- Bleeding tendencies—variable, uncommon.

CAUSES

- Chronic necroinflammatory, oxidant, or immune-mediated liver injury has many causes.
- Infectious—canine hepatitis virus; leptospirosis, enteric portal bacteremia or endotoxemia affiliated with IBD; accidental parenteral administration of intranasal *Bordetella* vaccine.
- Immune-mediated—autoimmune with positive ANA; acquired immune sensitization, nonsuppurative inflammation.
- Toxic—copper associated hepatopathy; acute or chronic exposure to drugs—predictable or idiosyncratic toxicity: e.g., azole antifungals, trimethoprim-sulfa, zonisamide, phenobarbital, primidone, phenytoin, CCNU, NSAIDs (esp. carprofen); repeat exposure to environmental or food-borne toxins, e.g., dimethylnitrosamine, aflatoxin, cycad, cyanobacteria.

RISK FACTORS

- Immunostimulants (vaccinations?) and molecular mimicry of cell epitopes by infectious agents or infection of sinusoidal endothelium may promote inflammatory reactions associated with chronic hepatitis.
- Cu associated hepatopathy—neopeptope formation from oxidant injury.
- Hepatic iron accumulation: supplementation.
- Drugs—inducers or inhibitors of microsomal enzymes or conditions diminishing hepatic antioxidant status may augment liver damage from certain toxins.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute hepatitis—history; liver biopsy.
- Congenital portosystemic shunt (PSVA)—abdominal ultrasonography; radiographic or multisector CT contrast venography (latter preferred); colorectal scintigraphy; liver biopsy.
- Primary hepatic neoplasia—radiography or ultrasonography; cytology; biopsy.
- Metastatic neoplasia or carcinomatosis.
- Chronic pancreatitis.
- Causes of abdominal effusion—hypoalbuminemia; right heart failure; carcinomatosis (see Hypertension, Portal); bile peritonitis.
- Other causes of portal hypertension—see Hypertension, Portal.
- Jaundice—EHBO; bile peritonitis, hemolysis.

(CONTINUED)

CBC/BIOCHEMISTRY/URINALYSIS**Hemogram**

CBC—nonregenerative anemia; RBC microcytosis if APSS; variable leukogram, thrombocytopenia; low total protein if chronic disease

Biochemistry

High liver enzymes; variable total bilirubin, albumin, BUN, glucose, and cholesterol; hepatic failure suggested by low albumin, BUN, glucose, and cholesterol, in the absence of other explanations

Urinalysis

Variable urine concentration; bilirubinuria; ammonium biurate crystalluria if APSS

OTHER LABORATORY TESTS

- TSBA—variable depending on extent of hepatic remodeling, sinusoidal hypertension, and cholestasis.
- Ammonia intolerance—reflects APSS; insensitive to cholestatic changes.
- Coagulation tests—reflect panlobular injury and/or chronicity; early disease has no abnormalities but perhaps high fibrinogen; advanced stage or severe panlobular injury may note prolonged PT, APTT, and PIVKA, low fibrinogen, increased FDP or D-dimers (**note:** some D-dimer tests are too sensitive for differential diagnostic utility); coagulation tests reflect severity of liver dysfunction, synthetic failure, DIC, and vitamin K adequacy (see Coagulopathy of Liver Disease); low protein C activity suggests APSS or hepatic failure.
- Abdominal effusion—chronic liver disease or portal hypertension: pure or modified transudate.
- Liver zinc values—low with chronic disease and especially if APSS.
- Serologic tests—for possible infectious agents, e.g., leptospirosis, rickettsial diseases, *Borrelia*, *Bartonella*, endemic fungal agents.
- ANA titer—for potential autoimmune-mediated disease; **note:** low level positive titers are nonspecific.
- Immunohistochemical staining of liver sample—confirm infectious agent or origin of infiltrative cells.

IMAGING**Abdominal Radiography**

- Microhepatia—suggests late-stage disease
- Abdominal effusion—obscures image
- Ammonium biurate calculi—radiolucent unless combined with radiodense minerals

Ultrasonography

- Liver size depends on disease stage; microhepatia in late stage.
- Normal to variable parenchymal and biliary tract echogenicity; may note nodularity and irregular liver margins.
- APSS—tortuous vessels caudal to left kidney or near splenic vein with Doppler color flow interrogation.
- Abdominal effusion—visualize small pockets; US facilitates sampling.
- Uroliths (tiny to large)—renal pelvis or urinary bladder; may signify ammonium biurate urolithiasis.
- Rule out—EHBD (jaundice,

high enzymes); identify mass lesions, cholelithiasis; GB mucocele; cholecystitis, choledochitis; cystic lesions (abscess). Enables fine needle aspiration—cytology and cholecystocentesis for bile collection.

Colorectal/Splenoportal Scintigraphy

- 99M-Technetium pertechnetate isotope time activity curve displays first isotope distribution: delivery to liver = no shunting, delivery to heart = shunting.
- CRS—sensitive and noninvasive, detects portosystemic shunting but cannot differentiate PSVA from APSS.
- SPS—offers no diagnostic advantage, is invasive and requires US-guided splenic injection.

DIAGNOSTIC PROCEDURES**Aspiration Cytology**

Fine-needle aspiration cytology—*cannot define* fibrosis or nonsuppurative inflammation; *cannot* recommend therapy. May identify hepatic vacuolation and canalicular cholestasis: common changes observed in canine liver disorders; neoplasia; infectious agents. Cannot definitively diagnose chronic hepatitis, hepatic fibrosis, or copper associated hepatopathy with cytology.

Liver Biopsy

- Liver biopsy—needed for definitive diagnosis; acquire biopsies from multiple lobes.
- Tru-Cut needle biopsy—18G needle core too small for accuracy; use 14–16 G.
- Laparoscopy—best biopsy method; permits gross visualization, documents APSS, biopsy access to multiple liver lobes and focal lesions.

Bacterial culture

Aerobic and anaerobic and sensitivity of liver and bile; use bile containing particulate debris for best sample—bacteria are found tangled with biliary precipitates.

Metal analyses

Determine copper, iron, and zinc concentrations (dry matter basis). Low zinc commonly associated with portosystemic shunting; high iron common in necroinflammatory disorders, contributes to oxidative injury; copper analysis results may reflect sampling of regenerative nodules or fibrotic regions or regions of parenchymal extinction, leading to low measurements compared to intact parenchyma. Digital scanning of biopsy slide stained with rhodanine can accurately quantify liver copper concentration.

PATHOLOGIC FINDINGS

- Gross—early: no gross change; late stage: microhepatia with irregular surface or margins (fine or coarse nodules), tortuous APSS.
- Microscopic—nonsuppurative inflammation involving zone of necroinflammatory injury; variable cholestasis and biliary hyperplasia; piecemeal and/or bridging necrosis; interface hepatitis; disruption of limiting plate in zone 1 lesions; in late-stage disease: bridging between or

HEPATITIS, CHRONIC

within zones; regenerative nodules, and transition to cirrhosis.

Histopathology

- Immune-mediated hepatitis—periportal, lobular, or centrilobular lymphoplasmacytic infiltrates, hepatic cord disorganization, sinusoidal fibrosis (space of Disse), biliary hyperplasia (ductular reaction).
- Cu hepatopathy: initially centrilobular, may evolve to immune-mediated hepatitis.
- Cirrhosis—diffuse lesion; fibrosis associated with nodular regeneration and hepatic lobule distortion; periportal/sinusoidal fibrosis.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Inpatient—for diagnostic testing and therapy in overtly ill dogs.
- Outpatient—if condition is stable at diagnosis; slowly titrated onto medical therapy.

NURSING CARE

- Depends on underlying condition.
- Fluid therapy—balanced polyionic fluids supplemented to correct electrolyte aberrations or hypoglycemia; restrict sodium if ascites.
- Water-soluble vitamins (2 mL/L fluids).
- Ascites: managed with sodium-restricted diet, enforced rest, diuretics (furosemide combined with spironolactone); see Cirrhosis and Fibrosis of the Liver.
- Therapeutic abdominocentesis—aseptic procedure for removing large-volume symptomatic ascites compromising food intake, ventilation, or sleep; if diuretics and sodium restriction ineffectual.
- For diuretic-resistant ascites: calculate sodium intake against measured renal sodium excretion (collect urine over 12 hours, measure sodium and creatinine in well-mixed sample, and in sera); guides adjustments in management (i.e., increase sodium restriction vs. increase diuretic).

ACTIVITY

Keep patient warm, inactive, and hydrated; inactivity may promote hepatic regeneration, euglycemia, and ascites mobilization.

DIET

- Adequate calories and protein—avoid catabolism to maintain muscle mass (attenuates hyperammonemia); monitor body condition.
- Dietary protein—restrict quantity ONLY if signs of HE (see Hepatic Encephalopathy) or observed ammonium biurate crystalluria; feed balanced diet; if HE, avoid fish and red meat source protein (dogs).
- Meal frequency—feed several small meals per day to optimize nutrient assimilation.
- Sodium restriction—with ascites or severe hypoalbuminemia: < 100 mg/100 kcal or < 0.2% dry matter basis formula.
- Good-quality vitamin supplement—vitamin metabolism perturbed with liver

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HEPATITIS, CHRONIC

(CONTINUED)

disease and losses in urine; avoid copper supplements if copper associated hepatopathy.

- Thiamin—ensure repletion to avoid Wernicke's encephalopathy; 50–100 mg PO q24h; caution: anaphylactoid reactions may occur with injectable thiamin.
- Partial parenteral nutrition—may consider, if short-term inappetence to minimize catabolism.
- Total parenteral nutrition—if inappetence lasts > 7 days; branched-chain amino acids remain controversial in dogs with liver dysfunction.
- Fat restriction rarely needed.

CLIENT EDUCATION

- Control rather than cure is the expected goal; medications usually will be required for life; disease is cyclic; quarterly evaluations important.
- Inform client of the lack of long-term veterinary studies proving efficacy of single or polypharmacy approaches; recommendations derived from clinical experience, studies in humans, and animal disease models.
- Antifibrotics may reduce fibrosis but limited evidence; fibrosis diminished by control of inflammation and underlying primary process.
- Attenuate factors provoking HE—dehydration; azotemia, infection; catabolism; hypokalemia; alkalemia; high protein meals; endoparasitism; enteric bleeding; certain drugs.

SURGICAL CONSIDERATIONS

- APSS—do not ligate nor band the vena cava.
- Cirrhosis—high anesthetic risk; gas anesthesia preferred—isoflurane or sevoflurane.



MEDICATIONS

DRUG(S) OF CHOICE

- Treatments for specific etiologies: chelate Cu if copper associated hepatopathy); withdraw potentially hepatotoxic drugs.
- No clinical trials prove efficacy of specific regimens to date.

Copper Chelation

See Copper Associated Hepatopathy

Immunomodulation

- *Prednisolone/prednisone*—2–4 mg/kg daily PO; taper to lowest effective dose (e.g., 0.25–0.5 mg/kg PO q48h); for data on survival effect see reference. If ascites: use dexamethasone to avoid mineralocorticoid effect (to account for increased potency, divide prednisone dose by 8–10 for dexamethasone dose), SID q2–4 days; for data on canine survival influence see reference.
- *Azathioprine*—in dogs: 1–2 mg/kg PO q24h; use loading SID dose for 3–5 days then titrate to q48h; contraindicated in cats (toxic); in dogs: combined with prednisone, antioxidants, antifibrotics (PPC), and possibly cyclosporine. During chronic therapy, titrate dose by 25–50% reduction after 2–6 months

based on sequential biochemistries showing improvements (e.g., declining total bilirubin and liver enzyme activity); monitor CBC and biochemistry profile q7–10 days for first month to ensure absence of hematopoietic, hepatic, and pancreatic toxicity; if acute hematopoietic toxicity, stop therapy, allow recovery, then reintroduce at 25% dose reduction; if insidious chronic hematopoietic toxicity (after months) or acute cholestatic liver or pancreatic injury, discontinue therapy.

- *Mycophenolate mofetil*—similar mechanism of effect as azathioprine; dose: 10–15 mg/kg PO q12h; eliminated by hepatic glucuronidation and renal excretion; monitor as for azathioprine and titrate dose similarly. May have fewer side effects than azathioprine.
- *Microemulsified cyclosporine*—5 mg/kg PO q24h; limited long-term experience; variable response.

Ursodeoxycholic Acid

Immunomodulatory, hepatoprotectant, antifibrotic, choleretic, anti-endotoxic, antioxidant; dose 7.5 mg/kg PO q12h; administered with food for best assimilation; tablets have best bioavailability; may prepare aqueous solution; safe; maintain indefinitely.

Antifibrotics

- Immunomodulators, SAMe, silibinin, vitamin E: also are considered antifibrotics as these interrupt signaling processes promoting activation of sinusoidal myofibrocytes and collagen production.
- *Polyunsaturated phosphatidylcholine* (PPC)—antifibrotic, immunomodulatory, antioxidant, hepatoprotectant effects; dose: 25 mg/kg/day PO with food. Use PhosChol® form (preformed active ingredient: dilinolylphosphatidylcholine); beneficial in some forms of liver disease (humans, animal models); may provide a corticosteroid-sparing effect allowing reduced glucocorticoid dosing; safely prescribed without liver biopsy.
- *Colchicine*—imparts anti-inflammatory, antifibrotic, and immunomodulatory effects; 0.25–0.03 mg/kg PO q24–48h; controversial evidence for benefit reducing fibrosis in human liver disorders; mechanism of action is via polymerization of microtubules curtailing collagen formation; metaphase arrest may provoke GI and bone marrow toxicity; neurologic adverse effects described in humans; avoid form complexed with probenecid (prolongs drug retention time); used when fibroplasia is the overriding histologic feature but not in ductal plate malformations.
- *Silibinin with PPC*—hepatoprotectant (studied against numerous toxins), antifibrotic, and antioxidant effects, may also promote hepatocellular regeneration; no meta-analysis in humans confirms beneficial influence in chronic hepatitis that does not have a viral cause. Even that category remains controversial. 2–5 mg/kg/day PO (PPC complexed form only). May alter

glucuronidation of some drugs, unclear if causes drug interactions.

Antioxidants

- *Vitamin E*— α -tocopherol, 10 IU/kg PO q24h.
- *S-Adenosylmethionine (SAMe)*—use bioavailable proven GSH donor) 20 mg/kg/day enteric-coated tablet PO given on empty stomach for best absorption.
- *Avoid vitamin C (ascorbate)*—if high tissue copper or iron concentration, augments oxidant injury associated with transition metals.
- *Zinc (zinc acetate)*—antioxidant; antifibrotic, blocks enteric copper uptake, required for urea cycle enzymes. Elemental zinc 1.5–3 mg/kg PO daily supplement if low liver zinc concentration (< 120 μ g/g dry weight liver; adjust dose using sequential plasma zinc concentrations (avoid plasma \geq 800 μ g/dL).

Hepatoprotectants

- Ursodeoxycholate, vitamin E, SAMe provide hepatoprotectant effects in addition to other benefits.
- *Silibinin*—efficacy unclear, use PPC complexed form (bioavailable), 2–5 mg/kg PO q24h.

Bleeding Tendencies

See Coagulopathy of Liver Disease

Gastrointestinal Signs/Hemorrhage

- *Histamine type-2 receptor antagonists*—famotidine 0.5–2 mg/kg PO, IV, SC q12–24h.
- *HCl pump inhibitors*—omeprazole 1.0 mg/kg q24h PO or pantoprazole 1 mg/kg q24h IV. Omeprazole may induce P450 cytochrome-associated drug interactions and may have a 24–48 h delayed onset of action.
- Some clinicians recommend chronic treatment with HCl pump inhibitors to minimize gastrointestinal bleeding and ulceration that may become a chronic problem.
- *Sucralfate*—gastroprotectants 0.25–1.0 g/10 kg PO q8–12h; titrate to effect, beware of drug interactions as sucralfate may bind other medications, reducing bioavailability.
- Eliminate endoparasitism.

Specific Conditions

Ascites

- Restrict activity and sodium intake; combine with diuretic therapy.
- *Dietary sodium restriction*—(0.2% dry matter basis or < 100 mg/100 kcal).
- *Diuretics*—slowly mobilize effusion with combination of: furosemide (0.5–2 mg/kg IV, SC, PO q12h) and spironolactone (0.5–2 mg/kg PO q12h; loading spironolactone is important, use doubled dose once); recheck and adjust dose at 4- to 7-day intervals by 25–50%. Titrate dose to response, may use q48h or intermittently to mobilize recurrent ascites.

(CONTINUED)

- *Therapeutic large volume abdominocentesis*—if ascites is nonresponsive to mobilization in 7–14 days with concurrent diuretics and sodium restriction; may require fluid support as a result of intravascular to abdominal fluid shift causing postcentesis hypotension syndrome and acute renal failure.
- *Consider vasopressin V₂ antagonists* (aquaretics) with low-dose diuretics for treatment of resistant ascites; tolvaptan has been used experimentally in dogs at 10 mg/kg without adverse effects to mobilize water.

HE

See Hepatic Encephalopathy

CONTRAINDICATIONS

- NSAIDs—avoid; potentiate enteric bleeding; may worsen ascites; potentially centrilobular hepatic necrosis-hepatotoxic metabolites.
- Avoid drugs requiring hepatic metabolism whenever possible.

PRECAUTIONS

- Diuretics—dehydration, hypokalemia, alklosis worsen HE.
- Glucocorticoids—increased susceptibility to infection, enteric bleeding, sodium and water retention, protein catabolism and HE.
- Avoid drugs or reduce dose if first-pass hepatic extraction, if require hepatic conjugation or biotransformation e.g. metronidazole—reduce conventional dose to 7.5 mg/kg PO q12h (often used for HE).
- Zinc overdose may cause hemolysis.

ALTERNATIVE DRUG(S)

- Dexamethasone—if ascites, replace prednisone or prednisolone with this drug to remove mineralocorticoid effect); divide pred. dose by 7–10, administer q3–4 days; taper dose to observed efficacy.
- Mycophenolate: alternative for azathioprine.

**FOLLOW-UP****PATIENT MONITORING**

- At-home behavior, body condition, muscle mass, weight—adjust protein and energy intake to nitrogen tolerance and apparent energy needs.
- CBC, biochemistry, and

urinalysis—monthly or quarterly, depends on patient status; look for signs of drug toxicity, disease remission, synthetic function, ammonium biurate urolithiasis, and urinary tract infections.

- Serial monitoring of TSBA—usually does not add prognostic or diagnostic information.
- Abdominal girth: reflects ascites volume.
- Azathioprine, mycophenolate, colchicine—monitor for possible bone marrow toxicity (serial CBCs), GI toxicity, and other effects.

POSSIBLE INTERACTIONS

- Avoid medications that alter hepatic biotransformation or excretion pathways (e.g., cimetidine, quinidine, ketoconazole).
- Avoid concurrent treatment with metoclopramide if spironolactone used for diuresis (causes aldosterone release).

POSSIBLE COMPLICATIONS

HE, septicemia, bleeding—may be life-threatening; DIC—may be a terminal event.

EXPECTED COURSE AND PROGNOSIS

- Chronic hepatitis can be a cyclic disease with occasional flare-ups indicated by sequential assessment of liver enzymes.
- Some dogs achieve solid long-term remission.
- Some dogs with Cu associated hepatopathy can achieve permanent remission of apparent “immune-mediated” inflammation upon effective Cu chelation and appropriate nutritional management.
- Presence of ascites indicates severe disease with shorter survival.
- Severe disease complicated by development of APSS have HE and ascites may require occasional hospitalizations for adjustment of nutritional and medical interventions.
- Sodium restriction and diuretics may require titration to achieve optimal control of ascites.

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

- Dogs with leptospirosis-associated chronic liver disease (rare) may shed organisms.

HEPATITIS, CHRONIC

- *Bartonella*; rickettsial agents (endemic vectors).

SEE ALSO

- Ascites
- Copper Associated Hepatopathy
- Diabetic Hepatopathy
- Hepatic Encephalopathy
- Hepatic Failure, Acute
- Hepatic Fibrosis and Cirrhosis
- Hepatitis, Chronic
- Hypertension, Portal
- Portosystemic Shunting, Acquired

ABBREVIATIONS

- ACT = activated clotting time
- APSS = acquired portosystemic shunt(s)
- APTT = activated partial thromboplastin time
- ARF = acute renal failure
- Cu = copper
- EHBDO = extrahepatic bile duct occlusion
- FasL = fas-ligand
- FDP = fibrin degradation products
- HE = hepatic encephalopathy
- IL-4 = interleukin 4
- INF-g = interferon gamma
- NSAID = nonsteroidal anti-inflammatory drugs
- PPC = polyunsaturated phosphatidylcholine
- PIVKA = proteins invoked by vitamin K absence or antagonism
- PSVA = portosystemic vascular anomaly
- PT = prothrombin time
- TNF-a = tumor necrosis factor alpha
- TSBA = total serum bile acids

Suggested Reading

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Consulting Editor Sharon A. Center



**Client Education Handout
available online**

H

HEPATITIS, GRANULOMATOUS



BASICS

DEFINITION

- Uncommon necroinflammatory hepatitis.
- Characterized by histiocytes/macrophages, lymphocytes, plasma cells, and variable neutrophilic infiltrates forming granulomas that efface normal hepatic structure.
- May reflect infectious agents, immune-mediated or immunoregulatory disorder, or a proliferative/neoplastic histiocytic syndrome.
- May localize to the liver or involve multisystemic disease (spleen, lymph nodes, bone marrow).
- Copper associated hepatopathy— involves unique “copper granulomas” distinct from this syndrome; having histologically stainable copper-protein aggregates.

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PATHOPHYSIOLOGY

- May initiate by infection with: bacteria (eubacterial, mycobacterial, chlamydial), viral, parasitic, protozoal, or fungal agents.
- May reflect immune-mediated or immunoregulatory disorders, or an adverse drug or xenobiotic interaction (herbal, holistic supplements).
- May reflect proliferative histiocytic syndromes or histiocytic neoplasia.
- Hepatocyte necrosis—reflects insufficient perfusion and hypoxia (sinusoidal invasion or collapse), cytokines or cytotoxic cell injury (histiocytes, lymphocytes), hepatotoxins including: xenobiotics (drugs, toxins, bacterial products, herbal or holistic remedies).
- Severity of hepatic dysfunction—reflects lobular distribution and density of infiltrates.
- Toxins—affect zone where they are metabolized (adducts formed), where there is specific organelle tropism or oxidative injury.
- Zone 3 copper accumulation—can augment zone 3 (centrilobular region) injury.
- Liver injury is accompanied by enzyme leakage reflecting regional involvement; hyperbilirubinemia occurs with diffuse injury, canalicular damage, or biliary tree involvement; sinusoidal injury can cause sinusoidal hypertension leading to splanchnic hypertension, ascites, and development of acquired portosystemic shunts (APSS).
- Severe diffuse lobular involvement can lead to liver failure, coagulopathy, enteric hemorrhage from acute portal hypertension, and acute-onset hepatic encephalopathy (HE).
- Hepatic failure—associated with a myriad of metabolic derangements, i.e., altered glucose homeostasis, protein synthesis (albumin, transport proteins, procoagulants, and anticoagulants), and detoxification capabilities; often lethal.

SIGNALMENT

- No breed, sex, or age predilection

- More common in dog than in cat

SIGNS

Historical Findings

- Nonspecific clinical signs, lethargy
- Anorexia, vomiting, diarrhea, weight loss
- Polyuria or polydipsia

Physical Examination Findings

- Normal liver size to severe hepatomegaly
- Abdominal pain: vague, due to hepatic capsule distention
- Distended abdomen—ascites; hepatomegaly
- ± Splenomegaly—granulomatous process
- ± Lymphadenopathy
- ± Jaundice
- ± Fever
- ± Tachypnea: abdominal distention, pulmonary disease involvement
- Late stage: bleeding tendencies, ascites, HE

CAUSES & RISK FACTORS

- Systemic fungal infection—histoplasmosis; blastomycosis; coccidioidomycosis; pythiosis
- Bacterial infection—Brucella; Nocardia, Borrelia, *Propionibacterium acnes*, mycobacteria; Bartonella
- Rickettsial infections
- Parasitism—visceral larval migrans; liver flukes, schistosomiasis; dirofilariasis
- Virus—FIP
- Protozoal—Toxoplasma; visceral Leishmania
- Neoplasia—histiocytic neoplasia, lymphoma
- Hemophagocytic histiocytic sarcoma
- Reactive or proliferative histiocytosis
- Immune-mediated disease
- Drug reactions
- Xenobiotics: holistic or herbal remedies
- Treats or food products from countries with unregulated manufacturing processes
- Idiopathic



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Widely disparate features initiate pursuit of diagnostic considerations; drug history must be carefully reviewed; consideration of splenic and/or bone marrow involvement necessary to rule out histiocytic neoplasia.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—inflammatory or stress leukogram; nonregenerative anemia (chronic inflammation); spherocytes: microangiopathic, immune-mediated anemia, or histiocytic hemophagocytic syndrome; moncytosis with chronic inflammation/infection.
- Biochemistry—high liver enzymes; variable: bilirubin, hypoglycemia; hypoalbuminemia, low BUN; high or low total proteins; high globulins; may note electrolyte abnormalities with fluid and acid-base disturbances,

hypcholesterolemia with hemophagocytic histiocytic sarcoma.

- Urinalysis—may be normal or demonstrate: bilirubinuria, proteinuria, RBCs, WBCs, cellular and other casts.

OTHER LABORATORY TESTS

- Serum bile acid concentrations—often high with massive hepatic involvement or APSS.
- Coagulation assays—normal, except with end-stage liver failure.
- Acute phase proteins may be increased: certain globulins, fibrinogen, C-reactive protein, protein C, antithrombin.
- Serologic tests—titers must be evaluated with caution in regard to infectious agents; consider convalescent titers; increased IgM titers to toxoplasmosis support active infection, serology for *Bartonella* should be considered.
- Molecular diagnostic tests: PCR or fluorescent *in situ* hybridization (FISH: for eubacterial organisms, other) on liver tissue can confirm certain infectious agents not visualized on histopathology; mycobacterial PCR and Bartonella PCR are necessary.
- Antinuclear antibody titer—positive with SLE but low positive titers are nonspecific.
- Bacterial cultures—liver tissue, bile, or blood; mycobacterial cultures grow slowly (months); mycobacteria may be better detected using PCR; tissue staining (Ziehl-Neelsen, Fite Faraco for mycobacteria) should be done; however, staining in humans with granulomatous mycobacteria is often negative.

IMAGING

- Abdominal radiography—may identify a normal to large liver, abdominal mass; ascites may obscure details.
- Abdominal ultrasonography—liver size and parenchymal pattern (diffuse vs. focal); defines mass lesions; other visceral lesions may include splenomegaly and lymphadenopathy; confirms abdominal effusion; US imaging enables diagnostic sample collection.

OTHER DIAGNOSTIC PROCEDURES

- Aspiration sampling—hepatic parenchyma; other visceral lesions (esp. spleen, bone marrow) and abdominal effusion.
- Liver biopsy—definitive diagnosis of granulomatous reaction but usually does not define cause. Copper-specific stain and copper quantification in liver (dry weight basis) should be completed; copper concentration may be calculated from digitally scanned biopsy stained with rhodanine (Cornell University).
- *Special Tissue Stains for Infectious Agents:* Gram stain, Modified Steiner's, Ziehl Neelsen and Fite Faraco (mycobacteria), periodic acid-Schiff, Grocott's methenamine silver (GMS).
- Consider bone marrow aspirate/core: histiocytic neoplasm, lymphoma, infectious disease.

(CONTINUED)

HEPATITIS, GRANULOMATOUS**PATHOLOGIC FINDINGS**

- Gross—hepatomegaly; normal or finely irregular surface; firm texture; blunted margins; may have abdominal effusion.
- Microscopic—pyogranulomatous reaction, variable zonal orientation and infiltration.

**TREATMENT**

- Inpatient vs. outpatient—dictated by severity of clinical signs.
- Fluid therapy—balanced polyionic solution for dehydration; may require dextrose (2.5–5%); judicious potassium supplements.
- Nutritional support essential; provide positive nitrogen balance; do not restrict protein if lacking signs of hepatic encephalopathy.
- Inform client that the causes of this syndrome (e.g., FIP, neoplasia) are often difficult to confirm and treat.
- If granulomatous response associates with copper, see Copper Associated Hepatopathy.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Remove drug, herbal, or holistic therapies considered possible causes of granulomatous hepatic reaction.
- Depends on cause; see specific chapters for infectious disorders.
- Immunomodulation—if immune-mediated mechanisms suspected and survey for infectious etiology negative.
- Idiopathic disease (no underlying cause or possible markers of immune-mediated process)—glucocorticoids combined with azathioprine or mycophenolate has been proven successful. **Caution:** may exacerbate undetected infectious conditions.

- Vomiting—antiemetics (e.g., metoclopramide 0.2–0.5 mg/kg PO or SC q6–8h; ondansetron 0.5–1.0 mg/kg 30 minutes before feeding, q12–24h); maropitant (1.0 mg/kg SC, PO, maximum 5 days).
- Gastrointestinal bleeding—H₂-receptor antagonist: famotidine 0.5–2 mg/kg PO, IM, SC q12–24h or omeprazole 1.0 mg/kg PO q24h; sucralfate gastroprotection.

POSSIBLE INTERACTIONS

- Consider potential drug-associated pathologies because of the broad spectrum of possible causes.
- Consider adjusting drugs requiring hepatic activation, biotransformation, or elimination.
- Immunosuppression—may worsen clinical signs in primary infectious disorders.

**FOLLOW-UP****PATIENT MONITORING**

- Routine monitoring: fluids, acid-base and electrolyte balance, and general response.
- Sequential hematologic, biochemical, imaging, and serologic evaluations.

POSSIBLE COMPLICATIONS

- Chronic hepatitis, fibrosis or cirrhosis
- Hepatic failure
- Coagulopathy

EXPECTED COURSE AND PROGNOSIS

- Depends on primary cause.
- Prognosis usually guarded at best, owing to multisystemic nature of this syndrome.

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

- Brucellosis—main causal agent of concern.
- Blastomycosis, coccidioidomycosis, Bartonellosis, Leishmania—not directly

contagious; pet may serve as environmental exposure sentinel.

SEE ALSO

- Bartonellosis
- Leishmaniasis
- Blastomycosis
- Coccidioidomycosis
- Histoplasmosis
- Pythiosis
- Feline Infectious Peritonitis (FIP)
- Leptospirosis
- Lupus Erythematosus, Systemic (SLE)
- Mycobacteria

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HEPATITIS, INFECTIOUS (VIRAL) CANINE



BASICS

OVERVIEW

- Viral disease of dogs (Canidae) caused by CAV-1 serologically homogeneous and antigenically distinct from respiratory CAV-2.
- Infection—targets parenchymal organs (especially liver), eyes, and endothelium.
- Oronasal exposure—viremia (4–8 days); virus shed in saliva and feces; initial dispersal to hepatic macrophages (hepatocellular Kupffer cells) and endothelium; replicates in Kupffer cells; damages adjacent hepatocytes producing massive viremia when released.
- Adequate antibody response clears organs in 10–14 days; virus persists in renal tubules and may be shed in urine for 6–9 months.
- Chronic hepatitis—after infection in dogs with only partial neutralizing antibody response.
- Cytotoxic ocular injury—anterior uveitis; leads to classic “hepatitis blue eye”. Develops in ~1% of dogs after MLV vaccine.
- Virus can be shed for 6–9 mths in urine.

H

SIGNALMENT

- Dogs and other Canidae
- No breed or sex predilections
- Most common in dogs < 1 year of age

SIGNS

- Depend on immunologic status of host and degree of initial cytotoxic injury.
- Peracute—fever; CNS signs; vascular collapse; DIC; death within hours.
- Acute—fever; anorexia; lethargy; vomiting; diarrhea; hepatomegaly; abdominal pain; abdominal effusion; vasculitis (petechia, bruising); DIC; lymphadenopathy; rarely, nonsuppurative encephalitis.
- Uncomplicated—lethargy; anorexia; transient fever; tonsillitis; vomiting; diarrhea; lymphadenopathy; hepatomegaly; abdominal pain.
- Late—20% of cases develop anterior uveitis and corneal edema 4–6 days post-infection; recover within 21 days; may progress to glaucoma and corneal ulceration. May be the only clinical feature of inapparent infection.

CAUSES & RISK FACTORS

- CAV-1
- Unvaccinated dogs susceptible



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Canine herpesvirus (neonatal)
- Other infectious hepatopathies
- Leptospirosis
- Granulomatous hepatitis
- Toxic hepatitis

- Fulminant infectious disease—e.g., parvovirus, canine distemper

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—schistocytes; leukopenia during acute viremia, followed by leukocytosis with reactive lymphocytosis and nucleated RBCs.
- Biochemistry—liver enzyme activity high initially, begin to decline within 14 days; low glucose and albumin reflect fulminant hepatic failure, vasculitis, and endotoxemia; low sodium and potassium levels reflect GI losses; hyperbilirubinemia if survive several days.
- Urinalysis—proteinuria (glomerular injury); granular casts (renal tubule damage); bilirubinuria consistent with jaundice.

OTHER LABORATORY TESTS

- Coagulation tests—reflect severity of liver injury and DIC.
- Serology for antibodies to CAV-1—fourfold rise in IgM and IgG; recent vaccine-induced antibodies confuse interpretation.
- Viral isolation—anterior segment of eye, kidney, tonsil, and urine; difficult in parenchymal organs (especially liver) unless first week of infection.

IMAGING

- Abdominal radiography—normal or large liver; poor detail due to effusion.
- Abdominal ultrasonography—may observe hepatomegaly, hypoechoic parenchyma (multifocal or diffuse pattern), and effusion.

DIAGNOSTIC PROCEDURES

- Liver biopsy, cytologically evident intranuclear hepatocyte inclusions—aspirates
- Viral culture
- Acute and convalescent serology

PATHOLOGIC FINDINGS

- Acute—edema and hemorrhage of lymph nodes; serosal visceral hemorrhages; liver large, dark-mottled; edematous gallbladder; fibrinous exudate on liver, gallbladder, and other viscera; splenomegaly; renal infarcts; abdominal effusion. Perivasculär necrosis in liver and other organs; widespread centrilobular to panlobular necrosis. Liver is discolored; abdominal effusion also observed in canine herpesvirus in neonates.
- Chronic—small, fibrotic or cirrhotic liver.



TREATMENT

- Usually inpatient.
- Fluid therapy—balanced polyionic fluids; avoid lactate if fulminant hepatic failure; carefully monitor fluids to avoid overhydration in context of increased vascular permeability.
- Judicious potassium (and other electrolyte) supplementation since electrolyte depletion may augment HE.

- Avoid neuroglycopenia—supplement fluids with dextrose (2.5–5.0%) as necessary.
- Blood component therapy for coagulopathy; blood component preferred to synthetic colloids for support of colloidal osmotic pressure; widespread vasculitis and DIC allow rapid systemic third space colloid dispersal.
- Overt DIC—fresh blood products and low molecular weight heparin (e.g., enoxaparin 100 U/kg [1 mg/kg] q24h). See Coagulopathy of Liver Disease.
- Nutritional support—frequent small meals as tolerated; optimize nitrogen intake; inappropriate protein restriction may impair tissue repair and regeneration; nitrogen restriction advised only if overt signs of HE.
- If oral feeding not tolerated, provide partial parenteral nutrition (maximum of 5 days) or, preferably, total parenteral nutrition.



MEDICATIONS

DRUG(S)

- Prophylactic antimicrobials—transmural passage of enteric bacteria/and endotoxemia with hepatic failure; e.g., ticarcillin (33–50 mg/kg q6–8h) combined with metronidazole (reduce conventional dose to 7.5 mg/kg IV q8–12h) and fluoroquinolone.
- Antiemetics—metoclopramide (0.2–0.5 mg/kg PO or SC q6–8h or CRI); ondansetron (0.5–1.0 mg/kg PO q12h); maropitant (1 mg/kg/day SC).
- Gastroprotection—H₂-receptor antagonists (e.g., famotidine 0.5 mg/kg PO, IV, SC q12–24h) and sucralfate (0.25–1.0 g PO q8–12h).
- Manage HE (see Hepatic Encephalopathy).
- Ursodeoxycholic acid—choleretic and hepatoprotectant (10–15 mg/kg daily in two divided doses, with food); give indefinitely if chronic hepatitis.
- Antioxidants—vitamin E (10 IU/kg/day PO), N-acetylcysteine IV (140 mg/kg load, then 70 mg/kg q8h) until PO route possible; transition to S-adenosylmethionine (SAMe, 20 mg/kg/day PO, dose on empty stomach) when patient can tolerate oral medications until liver enzymes normalize or indefinitely if chronic hepatitis.

CONTRAINDICATIONS

Consider severity of liver injury, protein depletion, and age in calculating drug dosages.



FOLLOW-UP

PATIENT MONITORING

- Monitor fluid, electrolyte, acid-base, and coagulation status to adjust supportive measures.
- Monitor for acute renal failure.

(CONTINUED)

HEPATITIS, INFECTIOUS (VIRAL) CANINE**PREVENTION/AVOIDANCE**

MLV vaccination—at 6–8 weeks of age; two boosters 3–4 weeks apart until 16 weeks of age; booster at 1 year; highly effective vaccine; boosters may not be needed.

POSSIBLE COMPLICATIONS

- Fulminant hepatic failure
- Hepatic encephalopathy
- Septicemia
- Acute renal failure
- DIC
- Glaucoma
- Chronic hepatitis

EXPECTED COURSE AND PROGNOSIS

- Peracute—poor prognosis; death within hours.
- Acute—variable: guarded to good prognosis.
- Poor antibody response (titer 1:16–1:50)—chronic hepatitis may develop.

- Good antibody response (titer > 1:500 IgG)—complete recovery in 5–7 days possible.
- Recovered patients—may develop chronic liver or renal disease.

**MISCELLANEOUS****AGE-RELATED FACTORS**

- Maternal antibody—may protect some pups for first 8 weeks; depends on maternal antibody concentration and efficacy of passive transfer.
- Vaccination of pups with high levels of passively acquired antibodies—successful at 14–16 weeks of age.

SEE ALSO

- Herpesvirus Infection—Dogs
- Disseminated Intravascular Coagulation

- Hepatic Encephalopathy
- Hepatic Failure, Acute
- Renal Failure, Acute
- Chronic Hepatitis
- Uveitis

ABBREVIATIONS

- CAV-1 = canine adenovirus-1
- CRI = constant rate infusion
- GSH = glutathione
- HE = hepatic encephalopathy
- MLV = modified live virus

Suggested Reading

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HEPATITIS, SUPPURATIVE AND HEPATIC ABSCESS



BASICS

OVERVIEW

- Bacterial infection involving the hepatobiliary system; variable in size and distribution.
- Distribution and lobular involvement—variable; multifocal microabcessation; diffuse suppurative cholangitis/cholangiohepatitis; cholecystitis; choledochitis, or discrete focal necrosuppurative lesions; lesions associate with pyogenic bacteria.
- Large abscesses commonly associate with hepatocellular carcinoma (HCA) in dogs where opportunistic organisms populate necrotic regions.

H

SIGNALMENT

- Dog and cat.
- No breed predilection.
- Hepatic abscesses—most common in old dogs with HCA in necrotic foci, or secondary to immunosuppression or diabetes mellitus; in neonates may develop subsequent to omphalitis.
- Suppurative septic cholangitis/cholangiohepatitis—most common in young-middle-aged male cats secondary to retrograde bile duct infection or hematogenous distribution of translocated enteric bacteria via the portal vein.
- Cholestatic disorders (e.g., EHBO, GB mucocele) predispose to enteric bacterial translocation due to reduced delivery of bile acids and secretory IgA (normally regulate the enteric bacterial population and reduce enteric bacterial translocation); cholestasis also impairs canalicular bacterial egress from the liver.

SIGNS

Historical Findings

- Lethargy
- Gastrointestinal signs: vomiting, diarrhea
- Weight loss
- Polyuria and polydipsia
- Trembling
- Fever
- May become jaundiced

Physical Examination Findings

- Fever
- Abdominal pain: cranial abdomen
- Dehydration
- Hepatomegaly: focal, with large abscess
- Coagulopathy
- Effusion: abdominal distention or fluid wave
- May develop jaundice
- Endotoxemia: tachycardia, tachypnea, hypotension, hypoglycemic collapse

CAUSES & RISK FACTORS

- Hematogenous infection via the portal vein, hepatic artery, or umbilical vein.

- Biliary tree obstruction, preexisting hepatobiliary or pancreatic disease, and inflammatory bowel disease: predispose to enteric bacterial translocation.
- Ascending biliary tract infection.
- Cholecystoenterostomy.
- HCA with necrotic foci.
- Compromised immune responses: diabetes mellitus, glucocorticoid administration, hyperadrenocorticism, hypothyroidism, chemotherapy, immune-mediated disorders managed with immunosuppressives.
- Penetrating wounds.
- Complication of hepatic biopsy or other surgery.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infectious or necroinflammatory disease—most patients are febrile.
- Hepatic abscess—fever, abdominal pain, and/or hepatomegaly (especially if risk factors).
- Pancreatitis or pancreatic abscess.
- Hepatobiliary neoplasia.
- Gastrointestinal obstruction or perforation.
- Peritonitis or other intra-abdominal abscess.
- Cholecystitis, choledochitis, cholelithiasis.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—neutrophilic leukocytosis with a left shift and toxic WBC changes; monocytosis; thrombocytopenia; nonregenerative anemia.
- Biochemistry—variably increased ALT > ALP activity; low albumin, hyperglobulinemia, inconsistent hyperbilirubinemia, and hypoglycemia; features reflecting endotoxemia (Gram-negative bacterial infection).
- Urinalysis—usually normal; bilirubinuria; proteinuria; culture may or may not disclose hematogenously dispersed organisms.

OTHER LABORATORY TESTS

- Serum bile acids—may be high; depends on the extent or zonal location of hepatic involvement, cholestasis, or may reflect sepsis-related cholestasis.
- Coagulation tests and RBC morphology (schistocytes)—consistent with DIC.

IMAGING

Abdominal Radiography

- Hepatomegaly; single lobe if isolated abscess, diffuse organomegaly with suppurative cholangiohepatitis or hepatitis.
- Hepatic mass effect if large abscess or abscessed primary hepatic neoplasia.
- Reduced abdominal detail (focal or diffuse) if effusion or peritonitis.
- Gas in hepatic parenchyma or biliary tree (gas-producing bacteria): emphysematous.

Ultrasonography

- Best noninvasive method of abscess detection (> 0.5 cm lesions); solitary, variably echogenic, cavitated lesions hyperechoic rim.
- Dystrophic tissue mineralization or entrapped gas—appear hyperechoic.
- Highly echogenic interface with cavitated mass—may be gas; combination with an abdominal effusion and hyperechoic perilesional effect supports an abscess.
- Multiple masses—some appear complex.
- Miliary abscesses—cannot discern from other parenchymal hepatic disorders.
- Suppurative septic CCHS—image not unique from nonsuppurative CCHS.

DIAGNOSTIC PROCEDURES

Cytology

- Cytologic evaluations are essential; histologic specimens may not reveal bacterial organisms.
- Samples—effusion; aspirate hepatic parenchyma and discrete lesions with ultrasound guidance; cholecystocentesis: transhepatic approach, collect liquid bile and biliary debris (particulates).
- Stains—Wright-Giemsa for cytologic bacterial detection; Gram stain for morphology.
- Look for bacteria within biliary debris, in WBCs, and for signs of a primary or predisposing disease (e.g., neoplasia, VH reflecting adrenal disease or diabetes mellitus).

Culture and Sensitivity Testing

- If suppurative or pyogranulomatous reaction (cytology)—culture for aerobic and anaerobic bacteria and fungal organisms.
- Blood (aerobic and anaerobic cultures)—more likely to be positive if multiple abscesses.
- Polymicrobial infections: ~30%.
- Gram-negative bacteria: common; *E. coli* (most common); *Klebsiella* spp.; *Pseudomonas* spp.; *Enterobacter* spp.; *Proteus* spp.; *Serratia marcescens*; *Citrobacter* spp.
- Gram-positive bacteria: *Enterococcus* spp. (most common); *Staphylococcus* spp.; *Streptococcus* spp.
- Anaerobic organisms: least common; *Clostridium* spp. (most common of these); *Propionibacterium acnes*; *Bacteroides* spp. suggests polymicrobial infection and facilitates growth of other bacteria.



TREATMENT

- Inpatient—if signs of sepsis.
- IV fluids and antibiotics—essential.
- Fluid support—correct dehydration; rectify acid-base and electrolyte disturbances.
- Abscess—drain via hepatic lobectomy during laparotomy or under ultrasound

(CONTINUED)

HEPATITIS, SUPPURATIVE AND HEPATIC ABSCESS

guidance before surgery; in some patients (e.g., endotoxic shock) ultrasound facilitated drainage is best; after drainage, monitor body temperature, liver enzymes, WBC count, and sequentially image with ultrasound (monitor abscess size, focal or diffuse peritonitis); judiciously repeat drainage (may require insertion of an indwelling catheter for short-term continuous drainage).

- In middle age/older dogs—be prepared to liver lobectomy for abscess removal and possible wide-margin resection of an HCA.
- If EHBDO—biliary decompression essential; antimicrobials must be administered IV before surgical manipulations (biliary decompression) to avoid septicemia (see Biliary Obstruction).



MEDICATIONS

DRUG(S)

- Antibiotics—initially based on cytology and Gram stain, then adjusted based on culture and sensitivity results; continue for 2–4 months, perhaps longer.
- Initial treatment—combine antimicrobials to cover possible polymicrobial infection (common aerobic and anaerobic pathogens); common effective empirical combination includes: ticarcillin (25–50 mg/kg over 15 min. CRI) or amoxicillin clavulanate (10–20 mg/kg PO q12h), enrofloxacin (2.5 mg/kg PO or SC q12h dogs or cats; may use 5 mg/kg PO or SC q12h in dogs), and metronidazole (15 mg/kg IV q12h; reduce dose by 50% if hepatic dysfunction or severe

cholestasis) or clindamycin (10–16 mg/kg SC per day; reduce dose if hepatic dysfunction or severe cholestasis to 5 mg/kg SC per day).

- Choleretics advised if biliary tree involved, but if EHBDO *NOT UNTIL* biliary decompression (see Bile Duct Obstruction (Extrahepatic); Cholangitis/Cholangiohepatitis Syndrome).
- Antioxidants advised (see Chronic Hepatitis).

CONTRAINdications

- Aminoglycosides—do not use until normal hydration because of potential for renal injury; also, may not penetrate abscess capsule.
- Avoid drugs metabolized or excreted by the liver or those known to be hepatotoxic if compromised liver function; adjust dosages or frequency of drugs if suspect reduced hepatic elimination, cholestasis, or hepatic dysfunction.



FOLLOW-UP

PATIENT MONITORING

- Assess vital signs and physical condition.
- Sequential ultrasound examinations—monitor for abscess recrudescence or suppurative peritonitis.

POSSIBLE COMPLICATIONS

- DIC
- Septicemia/Endotoxemia
- Fulminant hepatic failure
- Septic peritonitis
- Acute renal failure

EXPECTED COURSE AND PROGNOSIS

- Favorable prognosis—early detection and aggressive antimicrobial treatment, with judicious surgical intervention.
- Guarded prognosis—concurrent disorders, especially unresectable primary hepatic neoplasia.



MISCELLANEOUS

ABBREVIATIONS

- ALP =alkaline phosphatase
- ALT =alanine aminotransferase
- AST =aspartate aminotransferase
- CCHS =cholangitis/cholangiohepatitis syndrome
- CRI =constant rate infusion
- EHBDO =extrahepatic bile duct obstruction
- GB =gallbladder

Suggested Reading

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HEPATOCELLULAR ADENOMA



BASICS

OVERVIEW

- A benign liver tumor of epithelial origin.
- May be more common than primary malignant liver tumors.

SIGNALMENT

- Rare in dog and very rare in cat • Affected dogs commonly > 10 years of age • Breed predispositions unknown

SIGNS

- Usually asymptomatic; however, when clinically signs present, symptoms may be nonspecific. Typically incidental finding.
- Acute tumor rupture may cause hemoperitoneum with resultant weakness and hypovolemic shock-like symptoms.
- Occasionally, large tumors may cause cranial abdominal pain, vomiting, and inappetance.

CAUSES & RISK FACTORS

Definitive cause or risk factors for tumor development are unknown.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hepatocellular carcinoma • Hepatic nodular hyperplasia • Hepatic abscess
- Abdominal mass • Splenomegaly

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Usually unremarkable.
- Anemia—regenerative anemia if tumor is bleeding, or anemia of chronic disease.
- Leukocytosis with a left shift—large tumors with necrotic centers (rare).

Biochemistry

- Liver enzymes variable. • ALP, ALT, AST—normal or mild to markedly high.
- Serum total bilirubin values—usually normal.

Urinalysis

Unremarkable

OTHER LABORATORY TESTS

- Serum bile acids are usually normal unless tumor growth compromises hepatic perfusion and biliary flow. • Coagulation abnormalities consistent with DIC occur rarely with large necrotic or hemorrhagic tumors.

IMAGING

Radiography

- May demonstrate a single mass lesion or apparent asymmetry of hepatic silhouette.
- Rarely, gas in necrotic center of tumor.

Abdominal Ultrasonography

May identify discrete mass effect with variable echogenicity, ranging from normal liver echogenicity to mixed echogenicity, presence

of multiple nodules, or cystic mass appearance.

Abdominal Computed Tomography

- May allow for improved assessment regarding surgical feasibility, especially for large tumors, or tumors associated with critical structures, such as the gallbladder.
- May detect additional lesions, depending on the contrast enhancement protocol.

DIAGNOSTIC PROCEDURES

• Hepatic aspiration cytology with ultrasonographic guidance may allow the identification of normal hepatocytes or cells with mild atypia. This diagnostic will not be useful to differentiate between benign and low-grade malignant hepatic tumors, but will be useful to exclude other neoplastic diseases, such as lymphoma. • Hepatic biopsy with Trucut needle; several core biopsies are necessary to provide enough tissue for histopathologic characterization. Due to the overlap between the hepatocellular adenoma and the low-grade hepatocellular carcinoma, it may be difficult to obtain a definitive diagnosis. • Abdominal exploratory surgery followed by mass resection (liver lobectomy) and histopathology is the best way to obtain a definitive diagnosis and treat the disease.

PATHOLOGIC FINDINGS

Gross Pathology

- Usually well-circumscribed single nodules < 10 cm in diameter. • May be yellow-brown.
- Often soft, highly vascular, and friable.
- Occasionally multiple. • Occasionally very large (> 20 cm).

Microscopic Findings

- May be difficult to distinguish from nodular hyperplasia, normal liver tissue, or low-grade hepatocellular carcinoma. • Usually well-defined trabecular pattern; not necessarily encapsulated. • Compression of adjacent hepatic parenchyma common.
- Mitotic figures infrequent. • Affected liver cells resemble normal hepatocytes but often are larger and have a clear cytosol.



TREATMENT

• Surgical resection for large tumors, or tumors that cause clinical signs or organ dysfunction. • Bleeding tumor—requires immediate emergency care: hemodynamic stabilization, blood transfusion, and exploratory surgery. • Transarterial embolization or chemo-embolization is an experimental option for large, non-resectable tumors. In such cases, referral to an oncologic surgeon or experienced boarded surgeon is strongly advised, as many large tumors are actually resectable.

SURGICAL CONSIDERATIONS

- Excision recommended for large, single-mass lesions. • Between 60% and 70%

of the liver can be resected if the patient is healthy, and appropriate postoperative supportive care is available. • Biopsy local lymph nodes, normal appearing liver and any abnormal tissue identified during the exploratory surgery is of paramount importance.



MEDICATIONS

None



FOLLOW-UP

PATIENT MONITORING

- Liver enzymes—sequential evaluation, especially if they were elevated at the time of diagnosis. • Abdominal ultrasonography—every 3–4 months for the first year; preferred method of reevaluation.

POSSIBLE COMPLICATIONS

Risk of tumor necrosis and massive abdominal hemorrhage if not resected.

EXPECTED COURSE AND PROGNOSIS

Excellent



MISCELLANEOUS

SYNONYMS

Hepatoma—a confusing term that should be avoided; refers to hepatocellular carcinoma in human medicine and hepatocellular adenoma in veterinary medicine.

SEE ALSO

Hepatocellular Carcinoma

ABBREVIATIONS

- ALP = alkaline phosphatase • ALT = alanine aminotransferase • AST = aspartate aminotransferase • DIC = disseminated intravascular coagulation

Suggested Reading

Cave TA, Johnson V, Beths T, et al.

Treatment of unresectable hepatocellular adenoma in dogs with transarterial iodized oil and chemotherapy with and without an embolic agent: A report of two cases. J Vet Comp Oncol 2004, 1:191–199.

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HEPATOCELLULAR CARCINOMA



BASICS

OVERVIEW

- Malignant epithelial liver tumor.
- Accounts for about 50% of malignant hepatic tumors.
- Metastasis to regional lymph nodes, lungs, and peritoneal cavity in dogs is associated with the nodular and diffuse forms of hepatocellular carcinoma.

SIGNALMENT

- Uncommon in dogs and rare in cats.
- Affected dogs commonly > 10 years of age.
- No breed predispositions, although golden retrievers, miniature schnauzers, and male dogs are overrepresented in some studies.

SIGNS

- Typically absent until disease is advanced, unless it causes biliary obstruction
- Many times incidental finding
- Lethargy
- Weakness
- Anorexia
- Weight loss
- Polydipsia
- Diarrhea
- Vomiting
- Hepatomegaly (asymmetric)—consistent; precedes development of overt clinical signs
- Abdominal hemorrhage

CAUSES & RISK FACTORS

- Unknown
- May be associated with chronic inflammation or hepatotoxicity



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hepatic adenoma
- Nodular hyperplasia
- Biliary cystadenoma
- Bile duct adenoma/carcinoma
- Metastatic neoplasia
- Polycystic liver disease—less common form; fibrous stroma hyperplasia with anaplastic duct cells; few cysts
- Hepatic lymphoma
- Hepatic hemangiosarcoma
- Hepatic carcinoid

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Usually unremarkable.
- Anemia was detected in > 50% of cases with massive hepatocellular carcinoma in one study.
- Anemia may be regenerative if tumor is bleeding.
- Leukocytosis with a left shift—tumors with necrotic centers.

Biochemistry

- Liver enzymes variable.
- ALT, AST, ALP, and GGT—may be significantly elevated.
- Serum total bilirubin values—usually normal.
- May note hypoalbuminemia, hypoglycemia, and hypcholesterolemia.

OTHER LABORATORY TESTS

- Serum bile acids—normal unless tumor impairs hepatic perfusion and biliary flow.
- Coagulation parameters—may see abnormalities consistent with DIC in patients

with massive or necrotic tumors, or intra-abdominal bleeding.

IMAGING

Radiography

- May demonstrate a single-mass lesion, apparent asymmetry of hepatic silhouette, or hepatomegaly.
- Rarely, gas in necrotic center of tumor.
- Loss of serosal detail in case of hemoabdomen.

Abdominal Ultrasonography

- Discrete mass lesion with variable echogenicity, depending on the presence of intratumoral necrosis, hemorrhage, gas, or cystic cavities.
- Massive enlargement of a single liver lobe is occasionally observed.
- Mixed echogenic pattern—most common.
- Nodular pattern of lesions.

CT/MRI

May be indicated when tumor is suspected to involve critical anatomical structures, (major vessels, bile duct), and do help plan the surgical approach and inform owners on the risk associated with surgery.

DIAGNOSTIC PROCEDURES

- Aspiration cytology—to exclude other types of neoplasia (lymphoma, sarcoma, etc.).
- Aspirate cytology cannot reliably differentiate between hepatocellular carcinoma and benign hepatocellular proliferation (adenoma, hyperplasia).
- Surgical hepatic biopsy for confirmation.
- If tumor is not surgically resectable, ultrasound-guided needle biopsy may be useful in obtaining definitive diagnosis.

PATHOLOGIC FINDINGS

- Three clinical subtypes of this tumor are described—massive, nodular, and diffuse.
- Nodular forms account for 30% and diffuse types account for 10% of all reported hepatocellular carcinomas in dogs, and both types involve multiple liver lobes.
- Massive form that is confined to one lobe accounts for about 60% of canine hepatocellular carcinoma cases.
- Color varies from almost white to normal liver color.
- Presence of necrotic center.
- Diffusely infiltrated tumors may not be grossly apparent other than hepatomegaly.



TREATMENT

SURGICAL CONSIDERATIONS

- Complete excision (liver lobectomy) recommended when possible. Excision with microscopically dirty margins can still afford durable tumor control and long survival times.
- Massive form is often amenable to surgical resection.
- Nodular and diffuse forms are often not amenable to surgery.
- Between 60% and 70% of the liver lobes

can be resected if the patient is healthy and is given appropriate postoperative care.



MEDICATIONS

DRUG(S)

No medical treatment options have been successful in reducing tumor recurrence or risk for metastasis.



FOLLOW-UP

PATIENT MONITORING

- Abdominal ultrasonography: 2 weeks postoperative for baseline and every 3–4 months for the first year.
- Abdominal CT and/or MRI are more sensitive than ultrasonography for detection of small, recurrent lesions.
- Monitor liver enzymes serially.

POSSIBLE COMPLICATIONS

Risk of tumor necrosis and massive abdominal hemorrhage if unresected.

EXPECTED COURSE AND PROGNOSIS

- Prognosis is variable; histologic classification is not prognostic.
- Massive forms treated with surgery have a better prognosis than do the nodular or diffuse forms.
- Median survival of dogs with massive form treated with surgery may be > 1,460 days.
- Local tumor recurrence or de-novo tumor growth is not uncommon.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Polycystic liver disease in cats

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- AST = aspartate transaminase
- CT = computed tomography
- GGT = gamma-glutamyltransferase
- MRI = magnetic resonance imaging

Suggested Reading

Liptak JM, Dernell WS, Monnet E, et al. Massive hepatocellular carcinoma in dogs: 48 cases (1992–2002). J Am Vet Med Assoc 2004, 225(8):1225–1230.

Liptak JM, Dernell WS, Withrow SJ. Liver tumors in cats and dogs. Compend Contin Educ Pract Vet 2004, 26:50–56.

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HEPATOMEGLALY



BASICS

DEFINITION

Large liver detected on physical examination, abdominal radiography, ultrasonography, or direct visualization. Liver size—adult dog: ~3.5–5% body weight; neonatal liver: 4.5–5% body weight.

PATHOPHYSIOLOGY

- Liver size: influenced by factors (hepatotrophic) produced by splanchnic viscera (pancreas dominates) delivered in portal blood.
- Enlargement causes: (1) sinusoidal capacitance (blood pooling) or (2) parenchymal or sinusoidal accumulation of cells, substrates, or storage products.

Diffuse or Generalized

- Inflammatory—immune-mediated, infectious, pyogranulomatous hepatitis; classified by infiltrative cell type.
- Lymphoreticular hyperplasia—response to antigens or accelerated erythrocyte destruction.
- Congestion—impaired venous drainage.
- Infiltration—cellular (neoplastic, primary hepatocellular, metastatic) or excessive glycogen, lipid, or rarely, metabolic products (genetic diseases) in hepatocyte cytosol, amyloid in space of Disse.
- Cystic lesions.
- Cholestasis—extrahepatic bile duct obstruction (EHBDO); intrahepatic cholestasis causing bile duct distention.
- Extramedullary hematopoiesis (EMH).

Nodular, Focal, or Asymmetric

- Neoplasia
- Hemorrhage
- Infection or inflammation
- Hepatic nodular hyperplasia
- Nodular regeneration
- Arteriovenous malformation—involved lobe larger than other lobes; other lobes atrophied
- Asymmetric regeneration after large-volume resection or panlobular necrosis
- Cystic lesions
- Liver lobe torsion: acute venous congestion
- Malformations; atretic liver lobes

SYSTEMS AFFECTED

- Gastrointestinal—gastric compression or distension.
- Peritoneal effusion—sinusoidal hypertension.
- Pulmonary—reduced ventilatory space from diaphragmatic compression.
- General/vague pain—stretched liver capsule.

SIGNALMENT

- Dog and cat
- Old animals more commonly affected

SIGNS

Historical Findings

- Abdominal distention or palpable mass
- Abdominal discomfort—vague location
- Depends on underlying cause

Physical Examination Findings

- Dogs—liver palpable beyond costal margin (normal liver palpable in some breeds)
- Cats—liver palpable > 1.5 cm beyond costal margin (normal liver palpable in some cats)
- May remain undetected in obese animals

CAUSES

Inflammation

- Infectious or chronic (early) hepatitis
- Acute toxic hepatopathy—many causes
- Feline CCHS
- EHBDO
- Lymphoreticular/Pyogranulomatous—immune-mediated disease (hemolytic anemia, systemic lupus erythematosus, idiopathic), infectious disorders
- Venous outflow obstruction—sinusoidal occlusion syndrome

Congestive Hepatopathy

- Increased central venous pressure—right-sided congestive heart failure—tricuspid valve disease; cardiomyopathy; congenital anomaly (cor triatriatum dexter); neoplasia; pericardial disease; heartworm disease; pulmonary hypertension; severe arrhythmias.
- Vena caval or hepatic vein occlusion—thrombosis; tumor invasion or extramural caval occlusion; heartworm vena cava syndrome; vena caval stenosis or congenital kink; diaphragmatic hernia; intrahepatic hepatic vein occlusion (Budd-Chiari syndrome).
- Sinusoidal occlusion syndrome: xenobiotics or herbal toxicity (e.g., pyrrolizidine alkaloids).
- Liver lobe torsion (acute).

Infiltration

- Neoplasia
- Metabolic abnormalities—amyloid; lipid (see Hepatic Lipidosis [cats]), glycogen (see Glycogen-Type Vacuolar Hepatopathy [dogs]); cats and dogs: neonatal, diabetes mellitus, hyperlipidemic syndromes; metabolic storage disorders.
- Lymphohistiocytic/Pyogranulomatous—infECTious disease, immune response, antigen stimulation, neoplasia (histiocytic/dendritic).

Extramedullary Hematopoiesis

Regenerative anemias—hemolytic (immune-mediated, congenital, metabolic, infectious); oxidant injury; erythroparasitism; severe blood loss, bone marrow failure; idiopathic.

Neoplasia

- Infiltrative, diffuse, or large focal tumors.

- Primary hepatic—lymphoma; hepatocellular carcinoma; cholangiocarcinoma (bile duct carcinoma).
- Metastatic—lymphosarcoma, hemangiosarcoma, fibrosarcoma, leiomyoma/sarcoma, neuroendocrine, osteosarcoma, others.

Major Bile Duct Obstruction

- Pancreatitis; pancreatic neoplasia
- Neoplasms in porta hepatis: bile duct carcinoma, lymphoma
- Granuloma/Fibrosis of common bile duct
- Inspissated bile syndrome, choledochal cyst, or gallbladder mucocele
- Cholelithiasis
- Proximal duodenitis; duodenal foreign body
- Fluke migration (cats)

Cystic Lesions

- Primary single hepatic or biliary cysts
- Acquired cysts—tumors
- Ductal plate malformations and polycystic diseases—may be associated with renal cysts (common in Persian cats)
- Biliary cystadenoma (cats)
- Hepatic abscesses (cystic cavitation); hepatocellular carcinoma housing abscess

Other

- Drugs—corticosteroids (see Glycogen-Type Vacuolar Hepatopathy), phenobarbital (dogs)
- Hepatic nodular hyperplasia (rare cause)
- Acromegaly—cats

RISK FACTORS

- Cardiac disease
- Heartworm disease
- Neoplasia
- Primary hepatic disease—inflammatory, neoplastic, or cystic
- Corticosteroids—exogenous or endogenous
- Phenobarbital treatment
- Poorly controlled diabetes mellitus
- Anorexia in obese cats—hepatic lipidosis
- EHBDO
- Certain anemias—diffuse hepatic EMH



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Similar Signs

Distinguish from other disorders causing visceromegaly (gastric, splenic), cranial abdominal masses or effusions via radiography and ultrasonography.

Differential Causes

- Cardiac disorders (e.g., heart murmur, weak femoral pulses, hepatojugular reflex, jugular distention and pulses, muffled heart sounds).
- Symptomatic anemia (pallor with or without jaundice); tachycardia; tachypnea; exercise intolerance; bounding pulses.
- Parenchymal liver disease—lethargy,

(CONTINUED)

HEPATOMEGLALY**H**

- anorexia, vomiting, diarrhea, weight loss, variable liver enzymes, jaundice, coagulopathies, HE, PU/PD, ascites.
- VH (dog)—signs of hyperadrenocorticism or adrenal hyperplasia or other chronic disease imposing stress.
 - Hepatic lipidosis—jaundice in obese hyporexic cat, poorly controlled diabetes mellitus (dog or cat); puppies or kittens.

CBC/BIOCHEMISTRY/URINALYSIS**CBC**

- Identify anemia and cause; spherocytes (immune-mediated hemolytic anemia, microangiopathic anemia); schistocytes (vascular shearing-microangiopathic, vena cava syndrome, hemangiosarcoma, DIC), Heinz bodies (oxidant injury); erythroparasitism (*Mycoplasma haemofelis*, *Babesia*).
- Circulating blast cells—myeloproliferative or lymphoproliferative disease.
- Nucleated red cells—EMH, splenic disease.
- Macrocytosis and non-regenerative anemia—FIV, FeLV.
- Thrombocytopenia—increased consumption or destruction; reduced production.
- Thrombocytosis—neoplasia; inflammation; hyperadrenocorticism; splenic disease.

Biochemistry

- Inflammatory hepatic disorders—usually high liver enzyme activity; variable hyperglobulinemia, bilirubin and albumin values.
- Reticuloendothelial hyperplasia—variable liver enzyme activity.
- Primary hepatic neoplasia—moderate to markedly increased liver enzyme activity (ALP, GGT, ALT).
- Metastatic neoplasia—variable liver enzymes; occasionally high calcium or globulin.
- Infiltrative disorders—minor liver enzyme changes; variable hyperbilirubinemia.
- VH (dogs)—markedly high ALP; high cholesterol with increased glucocorticoids or sex steroids.
- Hepatic lipidosis (cats)—high ALP, AST, and ALT; minor increase in GGT unless concurrent pancreatitis, CCHS, or EHBDO.
- Storage diseases—few abnormalities.
- EHBDO—markedly high ALP, GGT, other enzymes; high bilirubin and cholesterol.
- Cystic lesions—normal, except with hepatic abscess (markedly high ALT and AST) or cholangitis/cholangiohepatitis (high ALP, ALT, GGT).
- Phenobarbital-associated—high liver enzymes (especially ALP in dog).
- Nodular hyperplasia—normal or moderately high ALP, elderly dogs.

OTHER LABORATORY TESTS

- FeLV and FIV testing—cats.
- Buffy coat—circulating blasts (neoplasia).

- Coagulation panel—DIC common with hemangiosarcoma or diffuse lymphoma; prolonged coagulation times common with EHBDO > 5 days; (especially PIVKA test).
- TSBA—high in diffuse disorders or EHBDO; *redundant test if nonhemolytic* jaundice.
- Pituitary-adrenal axis testing (dogs)—see Glycogen-Type Vacuolar Hepatopathy; Hyperadrenocorticism (Cushing's Syndrome)—Cats; Hyperadrenocorticism (Cushing's Syndrome)—Dogs.
- Heartworm testing—in endemic areas.
- Fungal serology—in endemic areas.
- Other serology—e.g., Rickettsial, *Bartonella*, *Leishmania*, *Toxoplasmosis*.

IMAGING**Abdominal Radiography**

- Hepatomegaly—rounded margins extend beyond costal arch; caudal-dorsal gastric displacement; caudal displacement: cranial duodenal flexure, right kidney, transverse colon.
- May suggest cause.

Thoracic Radiography

- Three views (lateral [right, left], dorsal-ventral)—metastasis, other disorders, cranial displacement of diaphragm.
- Cardiac, pulmonary, pericardial, and vena caval disorders usually need US imaging.
- Sternal lymphadenopathy—reflects abdominal inflammation or neoplasia.
- Puppies, kittens, and deep inspirations—spurious hepatomegaly.

Abdominal Ultrasonography

- Liver size and surface contour.
- Diffuse enlargement with normal echogenicity—congestion; cellular infiltration (lymphoma); inflammation; EMH; reticuloendothelial hyperplasia.
- Diffuse enlargement with hypoechoic parenchyma—normal variation; congestion, lymphoma, diffuse sarcoma; amyloidosis.
- Diffuse enlargement with hyperechoic parenchymal (minor nodularity)—lipid or glycogen; inflammation; fibrosis; lymphoma.
- Diffuse enlargement with hypoechoic nodules—neoplasia; abscesses; VH (dog); cystic lesions (ductal plate malformations, polycystic liver disease).
- Identify EHBDO.
- Identify concurrent abdominal diseases—kidneys; intestines; lymph nodes; effusion; interrogation of porta hepatis for obstructions and lymphadenopathy.
- Cannot distinguish benign from malignant disease.
- Identify abdominal effusion—distribution and echogenic patterns.

OTHER DIAGNOSTIC PROCEDURES

- Electrocardiography/Echocardiography**
Characterize cardiac conduction, structure, function, pulmonary pressure gradient.

Fine-Needle Aspiration

- Procedure—22-gauge, 2.5–3.75 cm (1–1.5 in) needle; diffusely large liver directly aspirated without US; focal lesions aspirated under US guidance.
- Cytology—may disclose infectious agents, vacuolar change, neoplasia, inflammation, or EMH; definitive diagnosis seldom confidently confirmed (false-positive and -negative results).
- Hepatic biopsy—if US rules out EHBDO, cytology does not indicate septic inflammation or neoplasia, and no obvious diagnoses; percutaneous ultrasound-guided Tru-Cut needle biopsy for suspected neoplasia or amyloid (avoid if abscess or EHBDO possible); otherwise, best sampling with laparoscopic or surgical exploratory approaches.
- Microbial culture—aerobic and anaerobic bacterial; fungal as appropriate.
- Staining—hematoxylin & eosin (routine); reticulin (architectural substructural remodeling, infiltration, compression), Masson's trichrome (collagen deposition); rhodanine (copper); PAS (glycogen, with and without amylase pre-digestion); acid-fast stain (mycobacteria if granulomatous inflammation); Congo red (amyloid); Oil Red O (lipid, requires frozen section); infectious disease stains (see Hepatitis, Granulomatous).
- Coagulation testing—before liver sampling, consider measurement of PT, aPTT, fibrinogen, and buccal mucosal bleeding time (BMBT); lack of dependable prediction of iatrogenic hemorrhage with bench tests is recognized; BMBT may be more relevant.
- Abdominal effusion—cytology; protein content; culture; evaluate before tissue sampling.
- Pericardiocentesis—if pericardial tamponade.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Outpatient—except cardiac or hepatic failure.
- General supportive goals—eliminate or manage inciting cause; prevent complications; palliate derangements due to hepatic failure.
- Important derangements—dehydration and hypovolemia; HE; hypoglycemia; acid-base and electrolyte abnormalities; coagulopathies; enteric hemorrhage; sepsis; endotoxemia.

NURSING CARE

- Heart failure or ascites—impose sodium restriction: fluids and food (< 100 mg/100 kcal, < 0.2% dry matter basis food).
- Supplement potassium chloride if IV fluids—sliding scale (maintenance = 20 mEq/L fluid).
- Supplement B-soluble vitamins.

HEPATOMEGLALY

(CONTINUED)

- If Jaundiced—parenteral vitamin K before invasive procedures.

ACTIVITY

Restricted; initial cage rest in some disorders.

DIET

- Dietary protein—restrict only if HE.
- Well-balanced, adequate energy, positive nitrogen balance is essential; adequate vitamins and micronutrients.
- Sodium—restrict if cardiac failure or ascites.

CLIENT EDUCATION

- Treatment depends on underlying cause.
- Many causes are life-threatening, some less serious and amenable to treatment.
- Thorough diagnostic evaluations are essential for determining definitive diagnosis.

SURGICAL CONSIDERATIONS

- Resection of primary or focal hepatic mass lesions (neoplasia, abscess, compromising cyst)—biliary decompression if EHBDO.
- Pericardiectomy (thoracoscopic procedure)—if effusion recurs after initial pericardiocentesis.



MEDICATIONS

DRUG(S)

Varies with underlying cause.

CONTRAINDICATIONS

- Avoid hepatotoxic drugs.

- Vacuolar hepatopathy (dogs)—avoid glucocorticoids.
- Hepatic lipidosis (cats)—avoid catabolism or drugs that promote catabolism; avoid fasting.



FOLLOW-UP

PATIENT MONITORING

- Physical assessment and hepatic imaging—reassess liver size.
- CBC, biochemistry, TSBA—serial assessment of abnormalities and liver function; reticulocyte count with anemia.
- Thoracic radiography, electrocardiography, and echocardiography—reassess status.
- Pituitary-adrenal axis—adrenal disorders.
- Adjust drug dosages according to status of liver function, body condition, and weight.

POSSIBLE COMPLICATIONS

Many causes are life-threatening.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Certain infectious agents of concern

SEE ALSO

- Amyloidosis
- Anemia, Immune-Mediated

- Bile Duct Obstruction (Extrahepatic)
- Cholangitis/Cholangiohepatitis Syndrome
- Congestive Heart Failure, Right-Sided
- Ductal Plate Malformation (Congenital Hepatic Fibrosis)
- Glycogen Storage Disease
- Glycogen-Type Vacuolar Hepatopathy
- Hepatic Lipidosis
- Hepatitis, Granulomatous
- Hepatitis, Suppurative and Hepatic Abscess
- Hepatocellular Carcinoma

ABBREVIATIONS

- ALT = alanine aminotransferase
- ALP = alkaline phosphatase
- AST = aspartate aminotransferase
- APTT = activated partial thromboplastin time
- BMBT = buccal mucosal bleeding time
- CCHS = cholangitis/cholangiohepatitis syndrome
- EHBDO = extrahepatic bile duct obstruction
- EMH = extramedullary hematopoiesis
- GGT = gamma glutamyltransferase
- HE = hepatic encephalopathy
- PAS = periodic acid-Schiff
- PIVKA = proteins invoked by vitamin K absence or antagonism
- PT = prothrombin time
- TSBA = total serum bile acids
- VH = vacuolar hepatopathy

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HEPATOPORTAL MICROVASCULAR DYSPLASIA



BASICS

DEFINITION

- MVD describes intrahepatic microscopic vascular malformations diminishing hepatic perfusion in tertiary branches of the portal vein; this is accommodated by the compensatory increase in hepatic arterial perfusion; MVD lacks macroscopic portosystemic shunting but genetically associates with congenital portosystemic vascular anomalies (PSVA, shunts) as a component of a complex polygenic autosomal syndrome.
- Occurs as an isolated malformation or in association with PSVA.
- Clinically distinct from intrahepatic portal vein atresia that associates with numerous acquired portosystemic shunts (APSS).
- Histologic features—overlap with any condition impairing hepatopetal portal circulation (forward flow of splanchnic blood toward the liver).
- Clinicopathologic hallmark—increased total serum bile acid (TSBA) concentrations.
- Coexistence of MVD with PSVA explains: (1) failure of TSBA to normalize after complete PSVA occlusion (some dogs); and (2) inability to fully attenuate PSVA (some dogs).
- MVD diagnosis is confused by inappropriate terminology where “portal hypoplasia” has been proposed to describe features of portal venous hypoperfusion. “Hypoplasia” defines lack of development—impossible to ascertain from liver biopsy without clinical features and vascular imaging details; MVD is one of many causes of portal venous hypoperfusion.

PATOPHYSIOLOGY

- Malformations impairing intrahepatic portal venous perfusion deprive hepatocytes of splanchnic hepatotrophic factors—causing lobular atrophy and impairing rapid extraction of bile acids from the enterohepatic circulation.
- Compensatory increase in hepatic arterial perfusion (hepatic arterial buffer response) maintains liver viability.
- Absence of macroscopic portosystemic shunting directly into the systemic circulation explains the lack of clinical signs and hepatic encephalopathy (HE) in dogs with MVD.
- Finding signs consistent with HE in a dog thought to have MVD strongly indicates PSVA or APSS; in a young dog APSS develop with portal venous atresia, ductal plate malformation (DPM, with congenital hepatic fibrosis [CHF] phenotype), NCPH, or splanchnic portal venous thromboembolism (TE).

SYSTEMS AFFECTED

- Usually asymptomatic.
- May observe slow recovery from injectable anesthetics and apparent adverse drug reactions with

medications undergoing first-pass hepatic extraction or hepatic metabolism.

- If concurrent IBD—vomiting, diarrhea, inappetence, increased liver enzymes; may lead to centrilobular and/or portal tract inflammation; most severe in eosinophilic IBD.
- No HE in MVD—if HE identified, suspect PSVA or disorders causing APSS.
- Renal/Urologic—MVD dogs *DO NOT* develop ammonium biurate crystalluria/urolithiasis; if such is discovered, consider mistaken MVD diagnosis in a dog with PSVA, APSS, rare inborn errors of ammonia detoxification, or uric acid membrane transporter mutations (bulldogs, Black Russian terriers, Dalmatians, some cats).

GENETICS

- Compelling evidence supports inheritance of PSVA/MVD as a complex polygenic autosomal trait in many small pure-breed dogs.
- TSBA > 25 $\mu\text{M/L}$ designates phenotype (affected/not affected) PSVA/MVD trait, Cornell University.
- Unaffected parents may produce affected progeny due to suspected polygenic inheritance.

INCIDENCE/PREVALENCE

- Prevalence PSVA/MVD trait in small pure-breed dogs: 30–80%, varies with breed.
- Genetic association of MVD and PSVA in kindreds of certain breeds confirms that MVD is most common: 10–30:1 MVD:PSVA.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog

Breed Predilections

- Small breeds.
- Commonly affected breeds: Yorkshire terriers, Maltese, Cairn terriers, Tibetan spaniels, Shih Tzu, Havanese, miniature schnauzers, pugs, Papillon, Norfolk terriers, Bichon Frise, West Highland white terriers.
- Not identified in large-breed dogs.
- Not identified in cats.

Age and Range

MVD usually tested at 4–6 months of age using paired TSBA tests (collected before and 2 h after a meal); neonatal testing not advised; more reliable results at 4 months age.

SIGNS

Historical Findings

- Asymptomatic—unremarkable history; occasionally delayed anesthetic recovery or drug intolerance reported.
- Symptomatic dogs represent misclassified diagnosis (see “Pathophysiology”); PSVA (see Portosystemic Vascular Anomaly, Congenital) or disorders causing APSS.
- MVD dogs are not hyperbilirubinemic.
- MVD dogs do not

develop ascites.

- MVD is often recognized serendipitously during routine screening tests or diagnostic evaluations for unrelated health problems, or during TSBA testing in breeds with high PSVA/MVD prevalence.

- Important to consider and rule out other causes of increased TSBA; concurrent illnesses may complicate TSBA interpretation (e.g., GI malabsorption causes low TSBA values).

Physical Examination Findings

- Unremarkable
- HE, jaundice, or ascites: do not occur

CAUSES

Congenital inherited disorder

RISK FACTORS

Pure-bred small dog breeds and mixes of these breeds.

H



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- PSVA—suspected in symptomatic young dog with increased TSBA or HE; however, 20% of PSVA dogs are asymptomatic.
- Symptomatic dogs > 2 years of age—may have APSS caused by inflammatory, infiltrative, neoplastic, or toxic hepatopathies; DPM with CHF phenotype; rare PSVA dogs show late-onset signs (e.g., miniature schnauzers; dogs with portoazygous shunts) reflecting small relative shunt fraction; portal vein atresia (true intrahepatic portal hypoplasia) and NCPH (acquired loss of tertiary branches of the intrahepatic portal vein) associate with portal hypertension, ascites, and APSS.
- Histopathologic features of all disorders causing portal hypoperfusion are similar.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—normal.
- Biochemistry—generally unremarkable; hepatic enzyme activities normal (expect high ALP in young patients due to bone growth) or cyclically increased (ALT) if coexistent IBD or degenerative/inflammatory centrilobular lesions; mild hypoglobulinemia or hypoalbuminemia noted in ~50% of young dogs.
- Urinalysis—specific gravity within normal range, no ammonium biurate crystalluria.
- Hyperammonemia is not documented dogs with MVD, without portal atresia or PSVA.

OTHER LABORATORY TESTS

TSBA

- Paired pre- and postprandial TSBA—recommended diagnostic test; values > 25 $\mu\text{mol/L}$ confirm abnormal liver function or perfusion; “shunting pattern” common.
- Shunting pattern—postprandial TSBA concentrations 0.5- to 3-fold > preprandial

HEPATOPORTAL MICROVASCULAR DYSPLASIA

(CONTINUED)

TSBA occurs with MVD, PSVA, APSS. ~15–20% of dogs and ~10% of cats have fasting > postprandial TSBA; thus, random single TSBA in the “normal range” must be followed up by paired TSBA testing.

- $> 25 \mu\text{M/L}$ —cutoff for TSBA in dogs.
- No need to fast patient before meal-provoked enterohepatic bile acid challenge because of physiologic variables influencing fasting values; do not use “fasting” value ranges.
- Important TSBA testing strategy: food-initiated enterohepatic bile acid challenge is essential; verify meal consumption; feed typical size and meal type for that patient.
- Magnitude of TSBA increase: typically lower for MVD vs. PSVA; but wide overlap in values impairs utility of TSBA as a stand-alone test to distinguish MVD.
- Quantitative abnormal TSBA values cannot discriminate “severity” of MVD between dogs; sequential testing show vacillating abnormal values (reflect physiologic variables).

Clearance Studies

Cairn terriers with MVD had reduced clearance of an organic anion indicator dye (ICG), confirming reduced liver perfusion; this test has low clinical utility.

Protein C

- Protein C reflects severity of portosystemic shunting in dogs; is not validated in cats.
- Generalities: ° MVD: protein C usually $\geq 70\%$. ° Symptomatic PSVA: protein C $< 70\%$. ° Asymptomatic PSVA protein C may be $\geq 70\%$ more common in portoazygous PSVA.

IMAGING

- *Abdominal Radiography*—lack microhepatia and renomegaly observed in PSVA.
- *Abdominal Ultrasonography*—no macroscopic shunting vessel; liver size subjectively normal or “slightly” small; experienced operator may suspect portal hypoperfusion that may vary among lobes.
- *Mesenteric Portovenography*—subtle abnormalities of blunted small portal vein branches, protracted contrast “blush” due to truncation of tertiary portal branches that trap contrast. **Caution:** PSVA may be overlooked if radiographic portography only completed in a single recumbent posture.
- *Colorectal or Splenoportal Scintigraphy*—normal or slightly increased shunt fraction in MVD; rules out macroscopic shunt (PSVA, APSS); CRS may demonstrate irregular liver lobe perfusion in MVD.

DIAGNOSTIC PROCEDURES

- Liver biopsy—sample several liver lobes as MVD does not uniformly affect all liver lobes; **AVOID SAMPLING** caudate lobe as this receives perfusion from the first portal vein branch; is often the best perfused liver lobe.
- *Histologic Evaluation*—required for

definitive diagnosis of portal hypoperfusion but must be considered in context of clinical, clinicopathologic, and imaging details; rules out most acquired hepatobiliary disorders causing increased TSBA except portal TE and NCPH. • *US-Guided Needle Biopsies*—may not sample enough tissue for definitive diagnosis; limits sampling to 1 or 2 left-sided liver lobes. • *Surgical Wedge or Laparoscopic Liver Biopsies*—reliably diagnostic if biopsies of several lobes obtained.

PATHOLOGIC FINDINGS

Gross

- Normal appearance and liver size.
- Some liver lobes may appear small.

Microscopic

- Cannot discriminate MVD, PSVA, NCPH or extrahepatic portal venous TE/occlusion: without history, clinical findings, and imaging details.
- *Hepatic Histopathology Reflects Portal Venous Hypoperfusion:* (1) lobular atrophy—small hepatocytes, closely approximated portal tracts and centrilobular regions, miniaturized portal tracts; (2) increased arteriolar profiles in portal tracts and orphaned arterioles without other portal tract elements in parenchyma—physiologic compensatory increase in arteriolar perfusion likely involves the biliary arterial plexus, arteries are coiled in response to increased pressure and flow with formation of new arterial twigs; (3) lymphatic distention—in portal tracts, adjacent to hepatic veins, and variably, beneath the liver capsule; reflects increased ultralymph formation from arterialized sinusoidal perfusion.
- *Unique MVD Features:* (1) maldevelopment of tertiary portal vein branches—inconsistent perfused portal veins in portal tracts, portal veins may demonstrate dilated, thin-walled unusual appearance; (2) malposition of hepatic venules adjacent to portal triads sharing borders = “fusion complexes”; (3) prominent smooth “throttling musculature” of hepatic venules (influence transhepatic perfusion) suggests physiologic hypertrophy or constriction, perhaps reflecting increased pressure; (4) increased numbers of binucleated hepatocytes (esp. near portal tracts); (5) randomly distributed but mildly disorganized hepatic cords with occasional widened sinusoids (random distribution); (6) inconsistent involvement of hepatic lobes: normal, mild to severe.
- **Note:** liver biopsy in any dog ≤ 4 months of age demonstrates juvenile portal triads (small).



TREATMENT

APPROPRIATE HEALTH CARE

- Asymptomatic—requires no medical interventions except avoidance of drugs

dependent on hepatic first-pass extraction, conjugation, metabolism. • **DO NOT**

- **NEED:** ursodeoxycholic acid, S-adenosylmethionine (SAMe, unless chronically increased liver enzymes), silybin (milk thistle) or dietary protein restriction.
- Suspected HE and/or protracted vomiting or diarrhea—hospitalize for supportive care and diagnostic evaluations; these dogs have other disorders that may complicate MVD (see Hepatic Encephalopathy, Portosystemic Vascular Anomaly, Congenital, Inflammatory Bowel Disease, “Pathophysiology”). • Rarely, dogs with zone 3 degenerative changes develop a chronic progressive hepatopathy: leads to hepatic dysfunction, portal hypertension, and ascites; diagnosis requires hepatic imaging and liver biopsy; may require management for hepatic insufficiency and ascites; more common in Maltese, Shih Tzu, Bichon Frise, Yorkshire terriers.
- Confirmed MVD associated with nonsuppurative zone 3 inflammation (especially involving eosinophils) and IBD: usually managed with low-dose dexamethasone (0.05 mg/kg PO q48–72h, rather than prednisone to avoid mineralocorticoid supplementation which may provoke ascites), hypoallergenic diet (protein restriction if HE) or a hydrolyzed protein diet, and low dose metronidazole: 7.5 mg/kg PO q12h; if low protein C: add mini-dose aspirin 0.5 mg/kg PO q12–24h or clopidogrel. **Must have liver biopsy** to confirm need for glucocorticoid and anticoagulants.

NURSING CARE

N/A

ACTIVITY

N/A

DIET

- Dogs with MVD do not require a protein-restricted diet.
- Dogs with HE do not have simple MVD; these have complicated illnesses or PSVA—see Hepatic Encephalopathy and Portosystemic Vascular Anomaly, Congenital, and “Pathophysiology”.

CLIENT EDUCATION

- MVD cannot be culled from a kindred based on TSBA testing; parents with normal TSBA may produce progeny with MVD or PSVA; examination of TSBA in F1 and F2 progeny is the only method of defining optimal breeding strategy, at present.
- Counsel clients that TSBA values cannot be used to grade severity of MVD.
- TSBA testing should be used to identify MVD in juvenile dogs to avoid future diagnostic confusion: e.g., adult with non-hepatic illnesses.
- Protein C—**should not be used** as a screening test without TSBA. Asymptomatic PSVA may have normal protein C. TSBA are **ALWAYS** abnormal in PSVA unless testing is

(CONTINUED)

HEPATOPORTAL MICROVASCULAR DYSPLASIA

inadequate (lack of provocative tolerance test, or compromised enteric fat absorption).

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

For HE—see Hepatic Encephalopathy

CONTRAINDICATIONS

N/A

PRECAUTIONS

Beware of rare adverse reactions to drugs reliant on hepatic first-pass extraction or metabolism.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Asymptomatic dogs—no specific treatment/long-term follow-up has confirmed normal lifespan, no chronic illness, no progressive hepatic degeneration.
- Repeated TSBA tests are not advised as values remain abnormal and fluctuate due to physiologic variables that clients find difficult to understand.

PREVENTION/AVOIDANCE

Specific recommendations to eliminate MVD from a particular genetic line or breed are not possible at present. Based on information derived from large pedigrees of multiple dog breeds, simply breeding unaffected parents does not eliminate MVD from a kindred. In high-incidence kindreds remain vigilant for vaguely ill dogs that may have PSVA; surgical

exploration can miss PSVA as can portovenography if only a single recumbency is evaluated); CRS can definitively detect hepatofugal blood flow (portosystemic shunting) providing a quick YES/NO test for portosystemic shunting; protein C activity assists in differentiating dogs with PSVA from MVD to advise further expensive imaging but is not definitive as a stand-alone test.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

- Most dogs with MVD remain asymptomatic and have a normal lifespan.
- Progressive increase in magnitude of TSBA values with age (juvenile to adult) has been documented in MVD.
- Generally, TSBA tests in MVD dogs are not quantitatively related to histologic severity.
- Dogs with zone 3 degenerative lesions (described above) may develop progressive hepatopathy leading to HE, portal hypertension, APSS, ascites, and rarely portal venous thromboembolism; this is a *rare* syndrome.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Small-breed dogs with high incidence of PSVA affected.

AGE-RELATED FACTORS

TSBA can be used to screen young dogs (16 weeks of age) in breeds known to have high prevalence of PSVA/MVD.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Bitches with MVD carry litters to term.

SYNONYMS

- Congenital portal hypoperfusion
- Hepatic microvascular dysplasia
- Microscopic portovascular dysplasia

CONFUSED TERMINOLOGY

- Intrahepatic portal venous atresia is not a synonym for MVD
- Portal venous hypoplasia is not a synonym for MVD

SEE ALSO

- Ductal Plate Malformation (Congenital Hepatic Fibrosis)
- Hepatic Encephalopathy
- Portosystemic Vascular Anomaly, Congenital
- Portosystemic Shunting, Acquired

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- APSS = acquired portosystemic shunt
- CRS = colorectal scintigraphy
- ICG = indocyanine green
- MVD = microvascular dysplasia
- NCPH = non-cirrhotic portal hypertension
- PSS = portosystemic shunting
- PSVA = portosystemic vascular anomaly
- SPS = splenoportal scintigraphy
- TE = thromboembolism
- TSBA = total serum bile acids

H

Suggested Reading

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HEPATOTOXINS



BASICS

DEFINITION

- Endogenous or exogenous substances (drugs, xenobiotics, toxins) that cause hepatic injury.
- Direct—("Dose dependent") causes predictable injury.
- Idiosyncratic—("Dose independent" or "Type II") unpredictable.

PATOPHYSIOLOGY

- Liver highly susceptible because of location and central role in metabolic and detoxification pathways. Liver is most commonly reported organ associated with true adverse drug reactions.
- Mechanisms of damage are direct (active metabolic byproducts) or indirect (oxidative processes from free radical metabolites).
- May cause hepatocellular or cytolytic injury (necrosis and apoptosis), cholestasis, immunologic (innocent bystander or hapten-mediated), or mixed histopathologic patterns of injury.
- Susceptibility and severity of injury—affected by age, species, nutritional status, concurrent drug administration, antecedent disease, antioxidant status; level of hepatic copper accumulation; hereditary factors, and current or prior exposure to the same or similar compounds.

SYSTEMS AFFECTED

- Hepatobiliary
- Nervous—hepatic encephalopathy
- Renal—proximal tubular necrosis or renal tubular acidosis/Fanconi syndrome; hepatorenal syndrome (rare)

GENETICS

Some dog breeds seem predisposed to certain drug-associated hepatotoxicities.

SIGNALMENT

Species

- Dog and cat.
- Cats have lower endogenous detoxification abilities; are susceptible to GSH depletion; dogs have higher risk for hepatotoxicity to some agents due to comparatively lower hepatic GSH (e.g., acetaminophen, aflatoxins).

Breed Predilections

- Siamese cats—some kindreds have high risk (reduced glucuronide formation).
- Some dog breeds have high risk for selected drug toxicity—Dobermanns, Dalmatians, Samoyeds: trimethoprim sulfamethoxazole; Dobermanns: oxibendazole; Labrador retrievers: NSAIDs, Cocker spaniels and German shepherd: phenobarbital; herding breeds: MDR1-polymorphisms (deranged P-glycoprotein production) affecting various drugs or other pharmacogenetic factors.

Mean Age and Range

- Any age.
- Young animals (<16 weeks of age)—immature hepatic metabolic and excretory pathways; less discriminating toxin ingestion.

SIGNS

General Comments

- Signs may reflect chronic long-term or single acute exposure.
- Detailed history essential—environmental, drug, and past medical history.

Historical Findings

- Malaise to moribund state
- Hyporexia, vomiting, diarrhea, jaundice

Physical Examination Findings

- Variable body temperature (hypothermic to febrile), vomiting, diarrhea, weakness
- Icterus—overt or progressive (48–96 hours post-exposure)
- Ascites—rare (grave sign)
- HE or coma
- DIC secondary to liver necrosis—hemorrhage; petechia; ecchymosis

CAUSES

Any drug, toxin, or xenobiotic may cause hepatotoxicity, variable severity, any individual.

Commonly Reported Drugs (dogs and cats unless otherwise noted)

- Acetaminophen
- Anabolic steroids
- Azole antifungals
- Amiodarone
- Amoxicillin
- Azathioprine
- NSAID (dogs)
- CCNU (dogs)
- Cyclosporine
- Diazepam (cats)
- Doxycycline
- Glucocorticoids (dogs)
- Glucosamine-based joint supplements (dogs)
- Griseofulvin (cats)
- Ketoconazole
- Mebendazole (dogs)
- Methimazole (cats)
- Mitotane (Lysodren, op/DDD) (dogs)
- Oxibendazole (dogs)
- Phenytoin (dogs)
- Primidone (dogs)
- Phenobarbital (dogs)
- Stanozolol (cats)
- Sulfa antibiotics (dogs)
- Tetracycline
- Thiacetarsamide (dogs, cats)
- Trimethoprim-sulfadiazine (dogs)

Common Environmental Toxins

- Amanita mushrooms (amanitin-containing mushrooms)
- Aflatoxins/mycotoxins
- Blue-green algae (Cyanobacteria)
- Chlorinated compounds
- Cycad (sago palm nuts)
- Heavy metals (Pb, Zn, Mn, Ar, Fe, Cu)
- Phenolic chemicals (especially cats)
- Gossypol from cottonseed

Endotoxins

- Enteric organisms—*Clostridium perfringens*; Gram-negative organisms
- Food poisoning—*Staphylococcus*; *E. coli*; *Salmonella*

Nutritional/Herbal

- Atractylis gummifera
- Black cohosh
- Callilepis laureola
- Chaparral
- Comfrey extracts (pyrrolizidine alkaloids)
- Chinese herbal medicines (certain constituents, contents difficult to characterize)
- Germander
- Greater celandine
- Green tea extract
- Lipoic acid (cats)
- Kava kava (dogs)
- Licorice
- Lipoic acid (cats)
- Mistletoe
- Pennyroyal
- Senna
- Usnic acid
- Valerian
- Xylitol (sugar substitute; dogs)

RISK FACTORS

- Medications influencing hepatic metabolism (enzyme inducers and P450 inhibitors).
- Antecedent hepatic disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infectious disorders affecting liver/biliary tract: leptospirosis, cholecystitis, FIP, toxoplasmosis, rickettsial diseases (RMSF, ehrlichiosis).
- Acute necrotizing pancreatitis.
- Traumatic or hypoxic liver injury.
- Hepatic neoplasia
- Diagnosis of hepatotoxicity requires integration of history, environment, food, medications, and temporal relationship(s).

CBC/BIOCHEMISTRY/URINALYSIS

- PCV and total solids—often normal or high in acute hepatotoxicosis (shock or dehydration).
- ALT reflects cellular membrane damage and leakage of this cytosolic enzyme; may be 10- to 100-fold normal; monitor for subsequent decline over 3–28 days; prognosis not correlated with magnitude of increase. Increased ALT may precede increases in bilirubin and ALP.
- AST—may reflect more severe injury (mitochondrial) than ALT; also increased in myonecrosis.
- ALP—usually continues to rise for days/weeks while ALT falls.
- CK—high activity associated with myonecrosis; some hepatotoxins also damage muscle (e.g., feline diazepam toxicity); high AST with normal CK confirms hepatic damage.
- Bilirubin, Albumin, BUN, and glucose—variable.
- Glucosuria and granular casts if proximal renal tubular injury (e.g., carprofen, copper). Some toxins suppress hepatic enzyme synthesis impairing clinical recognition of hepatic injury (e.g., blue-green algae, aflatoxin).

OTHER LABORATORY TESTS

- Coagulation profile—PT, APTT, FDP, platelets, and AT variable; monitor for DIC. Buccal mucosal bleeding time if others unavailable.
- Low protein C activity: biomarker for blocked protein transcription in aflatoxicosis.
- Non-icteric—paired TSBA (pre- and post-meal) assess hepatic function.

IMAGING

- Abdominal radiography—acute toxicity: normal to large liver; chronic injury: variable liver size.
- Abdominal ultrasonography—variable echogenicity, hepatic size, and margins.

DIAGNOSTIC PROCEDURES

- Hepatic biopsy—seldom indicated in acute toxicity (excessive risk/unnecessary for diagnosis/treatment); more helpful in confusing chronic hepatic injury; laparoscopic sampling more dependable; if desire core needle biopsies, need multiple samples using 14- to 16-gauge biopsy needle.
- Fine needle aspiration helpful if find neoplasia or etiologic agents; many toxins induce hepatocyte lipid vacuolation; variable dysplastic cell morphology in aflatoxin and cycad toxicity.

(CONTINUED)

HEPATOTOXINS**PATHOLOGIC FINDINGS**

Variable, depends on toxin, mechanism of cell injury, acinar zone of metabolism or product accumulation, or vascular injury and chronicity.

**TREATMENT****APPROPRIATE HEALTH CARE**

Inpatient—critical care setting

NURSING CARE

- Prevention/correction of shock imperative.
- Fluid therapy—maintain hepatic perfusion to improve oxygenation and toxin removal; administer maintenance requirements—monitor oncotic pressure and ongoing losses/hydration status; administer colloid or plasma if albumin < 2.0 g/dL; fluid therapy—avoid lactate-containing fluids in fulminant hepatic failure.
- Colloid administration—plasma initially preferred for delivery of clotting and anticoagulant precursor proteins followed by cautious use of synthetic colloid, if warranted.
- Bleeding tendencies—provide vitamin K₁ (0.5–1.5 mg/kg SC or IM q12–24h); administer fresh whole blood or fresh frozen plasma as needed. (**Caution:** stored blood products may have high ammonia concentration, causing HE.)
- Nasal oxygen—if compromised peripheral perfusion (hypotension) or pulmonary edema; may improve oxygen delivery to hepatic tissue.
- Oxidant damage likely involved in most hepatotoxic events—administer thiol or GSH donors (see below); GSH important for direct conjugation of certain toxins, may facilitate detoxification of some metabolites, enhances antioxidant protection, helps correct cell redox status conferring resistance to apoptosis, promoting cell membrane repair, and cell regeneration.
- Monitor urine output—diuretics as appropriate; see Renal Failure, Acute.
- Hypoglycemia—administer dextrose (2.5–5%) to maintain euglycemia as needed.

DIET

- Protein—normal, unless overt HE.
- Nutritional support—Antiemetics (maropitant or ondansetron) and antidyspepsics (pantoprazole) lessen nausea/promote appetite. If normal body condition score and acute disease, can wait up to 48 h for patient to voluntarily ingest food. If not eating within 48 h, first preference is NE tube enteral nutrition.
- Energy—strict calculation cumbersome. Initial starting points are: bodyweight kg × 50 (dogs) and bodyweight kg × 45 (cats); modified based upon size, body condition and monitoring—begin with 10–20% of calculated requirement; gradually increase to full requirement over 3–5 days. PPN only if unable to feed enterally. PPN/TPN can cause

severe complications—only use if familiar with techniques/complications.

CLIENT EDUCATION

- Potential for 3–10 days of ICU.
- Many recover, but post-necrotic cirrhosis, acquired shunting, and chronic hepatitis can develop later.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Electrolyte supplementation—KCl (must monitor serum potassium).
- Short-acting glucocorticoids—for endotoxic shock (prednisolone sodium succinate)—controversial.
- Ampicillin or metronidazole theoretically protect against transmural migration of enteric flora.
- Antioxidant therapy—crisis intervention: *N*-acetylcysteine for acute or fulminant hepatic necrosis (140 mg/kg IV load, followed by 70 mg/kg IV q6–8h; give over 20 minutes not by CRI, dilute in saline, administer with non-pyrogenic 0.25 µm filter); when patient can accept oral medications and condition stabilizes, change to oral S-adenosylmethionine (SAMe; 20 mg/kg enteric-coated tablet PO q24h, on an empty stomach); vitamin E as d-α-tocopherol acetate (10 IU/kg q24h PO, although currently no evidence of clinically important benefit from vitamin E).
- B-complex vitamins—parenteral; co-factors for hepatic metabolism.
- Silybin (active component of silymarin [milk thistle extract]); prefer form complexed with phosphatidylcholine (2–5 mg/kg q24h PO); may augment liver regeneration and provide antioxidant, hepatoprotective, and antifibrotic effects.
- Ursodeoxycholic acid—primarily for chronic hepatopathies (15 mg/kg/day PO), give with food. Provide taurine supplementation in anorectic cats (obligate taurine bile acid conjugation).

CONTRAINdicATIONS

Avoid known hepatotoxic drugs and those that require or inhibit hepatic metabolism.

PRECAUTIONS

- Use drugs listed as hepatotoxins with caution.
- Use caution when catheterizing large vessels or doing diagnostic needle aspirates/biopsies if coagulopathy.

**FOLLOW-UP****PATIENT MONITORING**

- Prevent hypothermia.
- Monitor blood glucose, electrolytes, PCV—frequently; fluctuations occur rapidly in critically ill patients.
- CBC/platelet, serum biochemical analyses, coagulation tests—typically monitor q48h or as warranted.
- Monitor urine output.

PREVENTION/AVOIDANCE

Close scrutiny of environment and future medications

POSSIBLE COMPLICATIONS

- DIC or hemorrhage
- Hepatic encephalopathy
- Progressive hepatic failure
- Post-necrotic cirrhosis with acquired shunting/ascites

EXPECTED COURSE AND PROGNOSIS

- Usually need 2–5 days to estimate prognosis.
- Negative indicators: intractable emesis, hematemesis, intolerance to supportive treatments, oliguria, DIC, HE; decline of ALT with increasing bilirubin and/or lowering of serum albumin; lowering cholesterol.
- Positive indicator: ALT declining by 20–30% or more every 48–72 hours, with other evidence of improvement, is positive indicator.
- Post-necrotic cirrhosis—possible in 2–6 months.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Hepatitis
- Fibrosis
- Hepatic encephalopathy
- Hepatic lipidosis (cats)
- Icterus
- Ascites
- Hypoglycemia
- Sepsis

AGE-RELATED FACTORS

- Young animals may have greater exposure and risk for toxin ingestion.
- Older animals—may have diseases requiring drug therapies increasing their risk (e.g., cimetidine, phenobarbital, NSAIDs).

SEE ALSO

- Acetaminophen (APAP) Toxicosis
- Cirrhosis and Fibrosis of the Liver
- Hepatic Encephalopathy • Hepatic Failure, Acute
- Poisoning (Intoxication) Therapy

ABBREVIATIONS

- AT = antithrombin
- CCNU = chloroethylcyclohexylnitrosourea
- FDP = fibrin degradation products
- FIP = feline infectious peritonitis
- GSH = glutathione
- HE = hepatic encephalopathy
- MDR1 = multidrug resistance gene 1
- NE = nasoesophageal
- NSAID = nonsteroidal anti-inflammatory drug
- PIVKA = proteins invoked by vitamin K absence or antagonism
- PPN = partial parenteral nutrition
- RMSF = Rocky Mountain spotted fever
- TPN = total parenteral nutrition
- TSBA = total serum bile acids

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Client Education Handout
available online

HEPATOZOOONOSIS



BASICS

OVERVIEW

- Disease caused by infection with the protozoan *Hepatozoon americanum* or *Hepatozoon canis*. This chapter focuses on systemic infection with *Hepatozoon americanum*—the primary cause of American canine hepatozoonosis.
- Hepatozoon canis* is less prevalent in the United States than *Hepatozoon americanum*. It is also less virulent and infections are typically subclinical.
- Infection typically involves muscle and bone.
- Dogs—more common in the southern and southeastern United States.
- Cats—uncommon in the United States; one reported case from Hawaii.

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SIGNALMENT

- Dogs and rarely cats
- No age, breed, or sex predilections

SIGNS

- Lameness and stiff gait
- Waxing and waning fever
- Mucopurulent ocular discharge
- Hyperesthesia
- Weight loss and cachexia
- Polyuria and polydipsia in some cases if glomerulonephritis is present

CAUSES & RISK FACTORS

- Amblyomma maculatum*—tick ingestion.
- Ingestion of infected paratenic hosts (predation or scavenging).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Neoplasia
- Endocarditis
- Immune-mediated polyarthritis or polymyositis
- Chagas disease
- Leishmaniasis
- Meningitis/meningoencephalitis
- Hypertrophic osteopathy
- Ehrlichiosis
- Discospondylitis
- Hepatic failure

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilic leukocytosis, usually profound (20,000–200,000 WBC/ μ L) sometimes with a left shift.
- Anemia—mild to moderate, usually non-regenerative.
- Usually have a normal platelet count unless there is a co-infection.

- High serum ALP activity.
- Decreased urea nitrogen.
- Despite severe myositis, creatinine kinase concentrations are often within reference range.
- Hyperglobulinemia.
- Hypoalbuminemia.

OTHER LABORATORY TESTS

Blood films—in rare cases identify organisms in circulating neutrophils and monocytes.

IMAGING

Radiographs—pelvis, lumbar vertebrae, and long bones; reveal periosteal proliferation.

DIAGNOSTIC PROCEDURES

- Muscle biopsy
- Polymerase chain reaction on blood or muscle

PATHOLOGIC FINDINGS

- Cachexia.
- Muscle atrophy: “onion-skin” meronts and pyogranulomatous myositis.
- Enlarged liver and spleen—may contain meront stages on histopathology.
- Periosteal proliferation of bone.



TREATMENT

- Inpatient—for severe pain; provide symptomatic relief.
- Pain management—as for any musculoskeletal disease.
- General activity level and appetite—on pain level.
- Most dogs will require life-long treatment to maintain clinical remission.



MEDICATIONS

DRUG(S)

- Mostly palliative as no treatments have been shown to clear infection.
- Combination therapy (TCP) initially:
 - Trimethoprim = sulfadiazine—15 mg/kg PO q12h for 14 days.
 - Clindamycin—10 mg/kg PO q8h for 14 days.
 - Pyrimethamine—0.25 mg/kg PO q24h for 14 days.
- Followed with long-term therapy:
 - Decoquinate 10–20 mg/kg PO q12h for up to 33 months (possibly indefinite).
 - Ponazuril 10 mg/kg PO q12h for 28 days has shown promise as an alternative initial treatment. Long-term therapy with decoquinate is still necessary.
 - Glucocorticoids—may give temporary relief but are not routinely recommended.
 - NSAIDs.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

None



FOLLOW-UP

PATIENT MONITORING

- Difficult to monitor organisms in chronically infected dogs.
- Best to monitor for clinical improvement.

PREVENTION/AVOIDANCE

- Control ticks within the household or kennel.
- Avoid predation and scavenging.

POSSIBLE COMPLICATIONS

- Glucocorticoids—may exacerbate clinical disease.
- Radiographic changes may never occur.

EXPECTED COURSE AND PROGNOSIS

- Treatment typically results in improvement of clinical signs and quality of life but does not cure the infection.
- Treatment is likely to be needed for the remainder of the patient's life.
- If clinical relapse occurs, repeat of both initial and long-term treatments are recommended.



MISCELLANEOUS

ZOONOTIC POTENTIAL

No reported risk to humans

ABBREVIATIONS

- ALP = alkaline phosphatase
- NSAIDS = nonsteroidal anti-inflammatory drug
- TCP (trimethoprim-sulfa, clindamycin, and pyrimethamine)

Suggested Reading

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HERPESVIRUS INFECTION—DOGS



BASICS

OVERVIEW

CHV causes a systemic infection in immunologically naïve animals; systemic disease in pups <2–3 weeks of age is usually fatal; systemic infection in naïve pregnant dams causes fetal death, mummification, and abortion. Pups born to immune dams develop life-long infection. After primary infection, CHV becomes latent in neurons of sensory ganglia, but can reactivate when animals are stressed or are receiving immunosuppressive treatments leading to excretion in nasal secretions; reactivation associated with mild respiratory illness or mild to severe ocular disease. Prevalence of latent infection is high; CHV ocular disease in adult animals is common, but underdiagnosed.

- Mature non-pregnant animals usually have inapparent, localized infections in the nasopharynx or external genitalia.
- Localized genital infections reported in both sexes.

SIGNALMENT

• All members of the canine family are susceptible.

- Death usually occurs between 9 and 14 days after birth; range is from 1 day (prenatal infection) to about 1 month (neonatal infection).
- Most commonly reported in purebred dogs, although there is no breed predilection. Ocular signs associated with CHV are common, but underdiagnosed.

SIGNS

- Dyspnea.
- Serous to mucopurulent nasal discharge.
- Anorexia.
- Grayish yellow or green, soft, odorless stool.
- Persistent, agonizing crying.
- Encephalitic signs.
- Severe gasping before death.
- Petechial hemorrhages on the mucous membranes occasionally seen.
- Incubation period in neonatal pups is 4–6 days.
- Onset sudden; death occurs 12–36 hours later.
- Some pups are found dead without premonitory signs.
- Occasionally, pups with mild signs survive but often later develop ataxia, persistent vestibular signs, or blindness.
- Mature females may have lymphofollicular or hemorrhagic lesions in the vagina.
- Infertility—evidence of increased seroprevalence in kennels with reproductive problems.
- Conjunctivitis—CHV is a common cause of acquired idiopathic conjunctivitis.
- CHV ulcerative keratitis—common sequelae of recrudescent infections.

CAUSES & RISK FACTORS

- CHV—typical herpesvirus; only one serotype described; latent infection is endemic in domestic dogs; young, naïve females and their newborn pups at greatest risk.
- Closed breeding kennels—CHV endemic; infection is less common and most adults are immune; newly introduced breeding bitches at high

risk.

- Abortion storms with massive pup losses can occur when pregnant bitches maintained in private homes are assembled for whelping.
- Immunosuppressive drugs may provoke reactivation of latent CHV with associated transient ocular disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Bacteria (brucellosis, coliform bacteria, or streptococci), toxoplasmosis, toxic substances—no typical gross lesions of CHV.
- MVC (canine parvovirus type 1)—causes enteric or respiratory disease; no characteristic CHV lesions.
- Distemper and canine adenovirus type 1 (canine hepatitis)—uncommon; no characteristic CHV renal lesions.

CBC/BIOCHEMISTRY/URINALYSIS

Thrombocytopenia may occur

DIAGNOSTIC PROCEDURES

- Immunofluorescence or immunoperoxidase staining; reveal viral antigen in most organs, especially in the lesion areas.
- Cell cultures—viral isolation accomplished from several tissues, especially lung and kidney; refrigerate (don't freeze) samples.
- PCR from samples of suspected tissues; e.g., conjunctival swabs; PCR can be used to screen for naïve animals prior to breeding.

PATHOLOGIC FINDINGS

Gross

- Characteristic lesions—disseminated focal necrosis; hemorrhage in several organs.
- Kidneys—diffuse hemorrhagic areas, necrotic foci, and hemorrhagic infarcts pathognomonic.
- Lungs, liver, adrenal glands—diffuse foci of hemorrhage and necrosis.
- Small intestine variably affected.
- Lymph nodes and spleen—generalized enlargement; consistent finding.
- Panuveitis.

Histopathologic

- Foci of perivasculär necrosis—with mild cellular infiltration; kidney, lung, liver, spleen, small intestine, and brain.
- Lesions in the CNS of recovered pups—non-suppurative ganglionitis; meningoencephalitis; necrosis in the cerebellum and retina; acidophilic intranuclear inclusions may be observed but are not abundant.
- Necrotizing lesions—may be seen in fetal placentas.



TREATMENT

- Not recommended.
- Antiviral drug therapy—unsuccessful for systemic infection.
- Immune sera from recovered bitches—beneficial in reducing pup deaths when antiserum is given before onset of illness.

Topical cidofovir ophthalmic solution may be effective for ocular disease in adult animals—no controlled clinical trials as yet.



MEDICATIONS

DRUG(S)

N/A

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Use of systemic immunosuppressive drugs in adult animals may induce reactivation of latent CHV possibly leading to ocular disease (conjunctivitis and/or keratitis).

H



FOLLOW-UP

- Normal litters can be expected from bitches that have suffered pup losses or abortions.
- An inactivated subunit vaccine for pregnant bitches is available in Europe but benefit unknown.
- Isolate pregnant dams, especially young bitches, when introduced into a kennel; adults commonly shed latent CHV in nasal secretions for 1–2 weeks after encountering newly introduced dogs.
- Surviving pups may suffer deafness, blindness, encephalopathy, or renal damage.



MISCELLANEOUS

AGE-RELATED FACTORS

- Dogs of all ages susceptible.
- Fatal illness occurs only in pups infected during the neonatal period (1–10 days after birth).

PREGNANCY/FERTILITY/BREEDING

Infection of dams during last 3 weeks of gestation—fetal infections with death and mummification, or ill pups that die shortly after birth.

ABBREVIATIONS

- CHV = canine herpesvirus
- CNS = central nervous system
- MVC = minute virus of canines
- PCR = polymerase chain reaction

Suggested Reading

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Author John S. Parker

Consulting Editor Stephen C. Barr

HIATAL HERNIA



BASICS

OVERVIEW

• Hiatal herniation – when abdominal contents (most commonly the stomach), herniate cranial to the diaphragm into the thorax through the esophageal hiatus. Four types of hernia have been described:
◦ Type I (sliding hiatal hernia; most common)
◦ Type II (paraesophageal hiatal hernia)
◦ Type III (includes elements of both type I and II)
◦ Type IV (herniation of organs other than the stomach)
• Congenital and acquired hiatal hernias have been reported. Acquired most commonly associated with severe upper respiratory disease (brachycephalic syndrome, laryngeal paralysis).

H

SIGNALMENT

- Dogs and less commonly cats
- Prevalence—higher in English bulldogs, Shar-Peis and other brachycephalic breeds. Type I more commonly congenital and therefore seen in younger animals.

SIGNS

Typically recognized in young animals 2–6 months of age. Signs can coincide with weaning. Most signs secondary to GER and esophagitis.
• Regurgitation
• Dysphagia
• Hypersalivation
• Lip smacking
• Inability to gain weight
• Vomiting
• Respiratory distress
• Anorexia
• Weight loss

CAUSES & RISK FACTORS

Congenital. Acquired—traumatic event ± severe upper respiratory disease; brachycephalic airway syndrome.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Physical examination findings are generally unremarkable unless aspiration pneumonia or chronic weight loss are present.
- Distinguish from other causes of weight loss or regurgitation.

CBC/BIOCHEMISTRY/URINALYSIS

No specific abnormalities. May find inflammatory leukogram secondary to associated pneumonia.

OTHER LABORATORY TESTS

N/A

IMAGING

Thoracic Radiographic Findings—Cranial displacement of stomach. Soft tissue mass in the caudal thorax adjacent to diaphragm. Gas-filled viscera in thorax. Hiatal hernia is infrequently diagnosed on survey thoracic radiographs alone.

Positive Contrast Esophagram—Preferably performed using videofluoroscopy. Helps to confirm the diagnosis and differentiate

between types I and II hiatal hernias. Can also diagnose associated gastroesophageal reflux and esophageal dysmotility. False-negative studies are common due to the highly intermittent and dynamic nature of hiatal herniation.

DIAGNOSTIC PROCEDURES

Upper gastrointestinal endoscopy—can document gastroesophageal reflux, esophageal strictures, esophagitis and hiatal hernia in some cases. Secondary evidence may only be detectable if herniation does not occur during the study.



TREATMENT

Not all dogs that have radiographic evidence require treatment. Conservative therapy can be successful in controlling clinical signs in dogs with mild hiatal herniation.

MEDICAL MANAGEMENT

- Can often be managed as an outpatient unless animal has severe aspiration pneumonia.
- Reduce gastric acid secretion (proton pump inhibitors are superior to H₂ receptor antagonists).
- Increase rate of gastric emptying and increase LES sphincter tone (prokinetic agents such as cisapride).
- Provide esophageal mucosal protection (sucralfate).
- Feed a low-fat diet in an elevated position.
- 30-day trial of medical management before surgery often recommended; not all patients require surgery.

SURGICAL MANAGEMENT

- Patients nonresponsive to medical therapy
- Treat with antacids and prokinetics prior to surgery
- Surgical procedures (used alone or in combination)
 - Phrenoplasty
 - Esophagopexy
 - Left-sided gastropexy



MEDICATIONS

DRUG(S)

- H₂ receptor antagonists/antacids—help to neutralize gastric pH and therefore reduce esophagitis secondary to GER
 - Famotidine 0.5–1 mg/kg PO, IV q12h
 - Ranitidine 1–2 mg/kg PO, IV, IM q8–12h
 - Proton pump inhibitors—are more potent than H₂ receptor antagonists
 - Omeprazole 0.7–1.5 mg/kg q24h PO
 - Pantoprazole 0.7–1.5 mg/kg q24h IV
 - Prokinetics—increase gastric emptying
 - Metoclopramide 0.2–0.5 mg/kg q6–8h PO or 1–2 mg/kg/24h as a CRI
 - Cisapride 0.5 mg/kg q8–12h PO
 - Mucosal protectants
 - Misoprostol 2–5 µg/kg q8h PO 1 h before or 2 h after food or other medications.



FOLLOW-UP

PATIENT MONITORING

- Long-term medical therapy may be indicated in both surgically and conservatively managed patients.
- Postoperative—monitor for dyspnea, worsening regurgitation (may require second surgery), abdominal distension that could result from overtightening of the hiatus resulting in an inability to eructate.

POSSIBLE COMPLICATIONS

Continuation of clinical signs, bloat episodes

EXPECTED COURSE AND PROGNOSIS

- Overall prognosis is good.
- Not all patients will necessarily need surgical intervention.
- When medical management fails, surgical intervention leads to a positive outcome in the majority of cases.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Often found in dogs with brachycephalic airway disease or other forms of upper airway obstructive diseases. Hypothesized that profound decreases in intrathoracic pressures generated in dogs with upper airway obstruction may act to pull the stomach into the thorax through the hiatus. Some evidence that gastroesophageal reflux can also worsen clinical signs of upper respiratory disease due to irritation of upper respiratory area with irritant gastric contents or associated bronchospasm of the lower airway.

ABBREVIATIONS

- GER = Gastroesophageal reflux
- LES = Lower esophageal sphincter

INTERNET RESOURCES

N/A

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Authors Kathryn A. Pitt and Philipp D. Mayhew
Consulting Editor Stanley L. Marks

HIP DYSPLASIA



BASICS

DEFINITION

A developmental syndrome resulting in osteoarthritis of the coxofemoral joints

PATHOPHYSIOLOGY

- Developmental defect initiated by a genetic predisposition to subluxation of the immature hip joint.
- Poor congruence between the femoral head and acetabulum; creates abnormal forces across the joint; interferes with normal development (leading to irregularly shaped acetabula and femoral heads); overloads the articular cartilage (causing microfractures and osteoarthritis).

SYSTEMS AFFECTED

Musculoskeletal

GENETICS

- Complicated, polygenic transmission.
- Expression is determined by an interaction of genetic and environmental factors.
- Heritability index—depends on breed.

INCIDENCE/PREVALENCE

- One of the most common skeletal diseases encountered clinically in dogs.
- Actual incidence—unknown; depends on breed.
- Incidence in cats is significantly lower than in dogs.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog, rarely cat

Breed Predilections

- Large-breed dogs—Saint Bernard, German shepherd, Labrador retriever, golden retriever, rottweiler.
- Smaller-breed dogs—may be affected; less likely to demonstrate clinical signs.
- Cats—more commonly affects purebred cats. Reportedly affects approximately 18% of Maine coon cats.

Mean Age and Range

- Begins in the immature dog. Onset of clinical signs varies with the severity of hip laxity in the immature dog and with worsening secondary OA in the mature dog.
- Clinical signs—may develop after 4 months of age in dogs with severe laxity; may also develop at any age after onset of secondary OA.

Predominant Sex

- Dogs—none
- Cats—more common in female cats

SIGNS

General Comments

- Severity of signs depends on the degree of joint laxity, degree of OA, and chronicity of the disease.

- Early—related to joint laxity.
- Later—related to OA.

Historical Findings

- Decreased activity.
- Difficulty rising.
- Reluctance to run, jump, or climb stairs.
- Intermittent or persistent hind limb lameness—often worse after exercise.
- Bunny-hopping or swaying gait.
- Narrow stance in the hind limbs.

Physical Examination Findings

- Pain on palpation or manipulation of the hip joint(s).
- Increased joint laxity (positive Ortolani sign)—characteristic of early disease; may not be a finding in chronic cases owing to periarthritis fibrosis.
- Crepitus.
- Decreased range of motion in the hip joints.
- Atrophy of thigh muscles.

CAUSES

- Genetic predisposition for hip laxity.
- Rapid weight gain, nutrition level, and pelvic muscle mass—fluence expression and progression.

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cranial cruciate ligament rupture: up to 1/3 of dogs referred for treatment of hip dysplasia are suffering from concurrent cranial cruciate rupture.
- Degenerative myelopathy.
- Lumbosacral instability.
- Unilateral or bilateral stifle disease.
- Panosteitis.
- Polyarthropathies.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

- Ventrodorsal hip-extended radiographs—commonly used for diagnosis; may need sedation or general anesthesia for accurate positioning.
- Early radiographic signs—subluxation of the hip joint with poor congruence between the femoral head and acetabulum; initially normally shaped acetabulum and femoral head; with disease progression, shallow acetabulum and flattened femoral head.
- Radiographic evidence of OA—flattening of the femoral head; shallow acetabulum; periarthritis osteophyte production; thickening of the femoral neck; sclerosis of the subchondral bone; periarthritis soft tissue fibrosis. Remodeling of the femoral neck is uncommon in cats.

- Distraction radiographs—quantify joint laxity; may accentuate the laxity for more accurate diagnosis.

- Dorsal acetabular rim view radiographs—evaluate acetabular rim; assess dorsal coverage of the femoral head.

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

- Early—normal femoral head and acetabulum; may note joint laxity and excess synovial fluid.
- With progression—malformed acetabulum and femoral head; synovitis; articular cartilage degeneration.
- Chronic—may note full-thickness cartilage erosion.

H



TREATMENT

APPROPRIATE HEALTH CARE

- May treat with conservative medical therapy or surgery.
- Depends on the patient's size, age, and intended function; severity of joint laxity; degree of OA; clinician's preference; and financial considerations of the owner.

NURSING CARE

- Physical therapy (passive joint motion)—decreases joint stiffness; helps maintain muscle integrity.
- Swimming (hydrotherapy)—excellent non-concussive form of physical therapy; encourages joint and muscle activity without exacerbating joint injury.

ACTIVITY

- As tolerated.
- Swimming—recommended to maintain joint mobility while minimizing weight-bearing activities.

DIET

- Weight control—important; decrease the load applied to the painful joint; minimize weight gain associated with reduced exercise.
- Supplementation with omega-3 fatty acids (in commercial diets or as a food additive) is beneficial to decrease pain and inflammation and improve function.

CLIENT EDUCATION

- Discuss the heritability of the disease.
- Explain that medical therapy is palliative, because the joint instability is not corrected.
- Warn the client that joint degeneration often progresses unless a corrective osteotomy procedure is performed early in the disease.
- Explain that surgical procedures can salvage joint function once severe joint degeneration occurs.

SURGICAL CONSIDERATIONS

Triple or Double Pelvic Osteotomy

- Corrective procedure; designed to reestablish congruity between the femoral head and the acetabulum.

HIP DYSPLASIA

(CONTINUED)

- Immature patient (6–12 months of age).
- Rotate acetabulum—improve dorsal coverage of the femoral head; correct the forces acting on the joint; minimize the progression of OA, but OA frequently progresses on radiographs even though progression is not clinically apparent in the dog.

Juvenile Pubic Symphysiodesis

- Pubic symphysis is fused at an early age (8–16 weeks) using electrocautery.
- Causes ventroversion of the acetabulum to better cover the femoral head.
- Improves joint congruence and stability—similar effects as TPO without surgical implants.
- Minimal morbidity; easy to perform—must be performed very early (ideally 3–4 months of age) to achieve effect; minimal effect achieved if performed after 5 months of age.

Total Hip Replacement

- Indicated to salvage function in mature dogs with severe degenerative disease that is unresponsive to medical therapy.
- Pain-free joint function—reported in > 90% of cases.
- Unilateral joint replacement—provides acceptable function in ~80% of cases.
- Staged bilateral joint replacement now chosen by 50% of owners.
- Complications—luxation; sciatic neuroparaxia; infection.

Excision Arthroplasty

- Removal of the femoral head and neck to eliminate joint pain.
- Extremely important to achieve a smooth osteotomy close to femoral shaft.
- Primarily a salvage procedure—for significant OA; when pain cannot be controlled medically; when total hip replacement is cost-prohibitive.
- Best results—small, light dogs (< 20 kg); patients with good hip musculature.
- Can provide good results in larger dogs.
- A slightly abnormal gait often persists.
- Postoperative muscle atrophy—common, particularly in large dogs.

Denervation Procedure

- Surgical procedure described in anecdotal literature to reduce pain associated with HD.
- Does not improve joint conformation or OA.
- Little objective scientific evidence exists for this procedure's effectiveness.
- Most recent studies suggest that the treatment does not improve the treated hip, but may slow the development of further clinical signs.



MEDICATIONS

DRUG(S) OF CHOICE

- Analgesics and anti-inflammatory drugs—minimize joint pain (and thus

stiffness and muscle atrophy caused by limited usage); decrease synovitis.

- Medical therapy—does not correct biomechanical abnormality; degenerative process likely to progress; often provides only temporary relief of signs.
- Agents—carprofen (2.2 mg/kg PO q12h or 4.4 mg/kg PO q24h); etodolac (10–15 mg/kg PO q24h); deracoxib (3–4 mg/kg PO q12h for 1 week, then 2 mg/kg PO q12h); firocoxib (4 mg/kg PO q24h).
- Diet supplementation with omega-3 fatty acids (fish oils) decreases joint inflammation and provides pain relief.

CONTRAINdications

Avoid corticosteroids—potential side effects; articular cartilage damage associated with long-term use.

PRECAUTIONS

- NSAIDs—gastrointestinal upset may preclude use in some patients.
- Carprofen—reported to cause acute hepatotoxicity in some dogs.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Polysulfated glycosaminoglycans, glucosamine, and chondroitin sulfate—may have a chondroprotective effect in OA, but recent evidence suggests they are not or are only minimally efficacious.



FOLLOW-UP

PATIENT MONITORING

- Clinical and radiographic monitoring—assess progression.
- Medical treatment—clinical deterioration suggests an alternative dosage or medication or surgical intervention.
- Triple pelvic osteotomy—monitored radiographically; assess healing, implant stability, joint congruence, and progression of OA.
- Hip replacement—monitored radiographically on an annual basis; assess implant stability.

PREVENTION/AVOIDANCE

- Best prevented by not breeding affected dogs.
- Pelvic radiographs—may help identify phenotypically abnormal dogs; may not identify all dogs carrying the disease.
- Do not repeat dam-sire breedings that result in affected offspring.
- Special diets designed for rapidly growing large-breed dogs—may decrease the severity.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

Joint degeneration usually progresses—most patients lead normal lives with proper medical or surgical management.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Do not breed affected dogs; added weight owing to pregnancy may exacerbate clinical signs.

ABBREVIATIONS

- HD = hip dysplasia
- OA = osteoarthritis
- NSAID = nonsteroidal anti-inflammatory drug
- TPO = triple pelvic osteotomy

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**Client Education Handout
available online**



BASICS

OVERVIEW

The histiocytic diseases encompass a wide spectrum of diseases characterized by a variety of biologic behaviors and include: canine cutaneous histiocytoma, cutaneous histiocytosis (CH), systemic histiocytosis (SH), histiocytic sarcoma (HS) and hemophagocytic histiocytic sarcoma (HHS). Subtypes are classified by the cell of origin (i.e., Langerhans dendritic cell, interstitial dendritic cell, monocyte/macrophage).

SIGNALMENT

Cutaneous Histiocytoma

- Common in dog, extremely rare in cat.
- More than 50% of affected dogs are < 2 years old.
- Commonly affected breeds include boxer, dachshund, cocker spaniel, American Staffordshire terrier, Great Dane, Boston terrier, Doberman pinscher, miniature schnauzer, Shetland sheepdog, Labrador retriever, West Highland white terrier, and bull terrier.
- No breed predilection in cats.
- No sex predilection in cats or dogs.

Cutaneous Histiocytosis (CH)

- Uncommon in dog and cat
- Younger dogs more commonly affected (range 2–11 years)
- No breed predilection
- Male predilection

Systemic Histiocytosis (SH)

- Uncommon in dog and cat
- Commonly affected breeds include Bernese mountain dog (BMD), rottweiler, golden retrievers, and Irish wolfhound
- Male predilection in the BMD
- Younger dogs more commonly affected (range 3–9 years)

Histiocytic Sarcoma (HS)

- Common in dogs, rare in cats
- Commonly affected breeds include BMD, flat-coated retrievers, rottweiler, golden retriever, Labrador retriever, and Pembroke Welsh corgi
- Middle-aged or older dogs
- Possible male predisposition

Hemophagocytic Histiocytic Sarcoma (HHS)

Similar signalment to HS

SIGNS

Cutaneous Histiocytoma

- Solitary “button-like,” raised, well-circumscribed, hairless dermal lesion that may be ulcerated.
- Often fast growing in first 1–4 weeks.
- Considered nonpainful.
- Common sites—head, ear pinna, and limbs.

Cutaneous Histiocytosis

- Cutaneous/subcutaneous nodules that may wax and wane, disappear with new lesions appearing at different sites.
- Limited to the skin, subcutis, and local draining lymph node(s); lack of systemic extension beyond peripheral lymph nodes is a distinguishing factor from SH.
- The head, pinna,

extremities (including footpad) and scrotum are commonly affected.

Systemic Histiocytosis

- Cutaneous/subcutaneous lesions may be similar to CH.
- Other common sites include lymph nodes, bone marrow, scrotum, spleen, liver, lung, and mucous membranes (nasal and ocular tissue).
- Clinical signs include depression, anorexia, weight loss, conjunctivitis and respiratory difficulty.

Histiocytic Sarcoma

- Lameness and a palpable mass (periarticular location) or lymphadenopathy often reported.
- Clinical signs vary depending on site(s) of involvement by the tumor, however, lethargy, anorexia, weight loss, respiratory signs, fever, vomiting, diarrhea, and lymphadenopathy are reported.
- Reported anatomic sites include lung, lymph node, liver, spleen, stomach, pancreas, mediastinum, skin, skeletal muscle, central nervous system, bone and bone marrow; the author has also seen cases with intranasal and ocular involvement.

Hemophagocytic Histiocytic Sarcoma

- Similar clinical signs to HS, however patients tend to be symptomatic (secondary to widespread disease).
- Rather than presenting as solid tumors, this subtype tends to present in a more infiltrative manner, causing hepatosplenomegaly and myelophthisis.

CAUSES & RISK FACTORS

- Histiocytoma is hypothesized to represent an atypical proliferation or reactive hyperplasia rather than a true cancer.
- SH has a possible familial causation in BMD.
- HS and HHS likely have a genetic origin due to breed predilections (specifically in the BMD).
- History of joint disease may be a predisposing factor in periarticular HS.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Differentiate from focal granulomatous inflammation, other sarcomas, other round cell tumors (transmissible venereal tumor, lymphoma, plasma cell tumor, mast cell tumor) and each distinctive subtype of the histiocytic disease.
- Differentiate HHS from immune-mediated anemia/thrombocytopenia and tick-borne diseases.

CBC/BIOCHEMISTRY/URINALYSIS

- *Histiocytoma/CH, SH:* Usually normal.
- *HS/HHS:* Anemia (regenerative), thrombocytopenia, leukocytosis, increased liver enzymes, hypoalbuminemia, hypcholesterolemia are commonly reported.

OTHER LABORATORY TESTS

- *Immunohistochemistry:* Differentiate HS from other sarcomas and round cell tumors.
- *Serum ferritin:* Hyperferritinemia has been

documented in dogs with HS and has potential as a biomarker for early screening.

IMAGING

SH

Thoracic radiographs: perihilar lymphadenopathy, focal pulmonary lesions.

HS, HHS

- Thoracic radiographs: diffuse interstitial infiltrate, patchy consolidated areas, focal or multifocal mass lesions. Sternal, cranial mediastinal or tracheobronchial lymphadenopathy may also be noted.
- Limb radiographs: periarticular soft tissue mass ± lytic lesions may be noted for periarticular HS.
- Ultrasonography: hepatosplenomegaly, splenic or hepatic mottling, masses in these organs and lymphadenopathy are the most commonly noted.

DIAGNOSTIC PROCEDURES

Cytology of Lesions

- *Cutaneous histiocytoma:* Characterized by sheets of pleomorphic round cells with abundant pale gray/blue cytoplasm, centrally located round to slightly indented nuclei, and inconspicuous nucleoli are noted. An inflammatory cell infiltrate (lymphocytes) may be present and often will precede spontaneous lesion regression.
- *CH/SH:* Characterized by mainly benign appearing histiocytes with occasional multinucleated giant cells. Lymphocytes, eosinophils and neutrophils can be interspersed.
- *HS/HHS:* Characterized by large, discrete, mononuclear cells often with marked anisocytosis and anisokaryosis. Nuclei are round, oval, or reniform with prominent nucleoli and cytoplasm is moderate to abundant, lightly basophilic, and vacuolated. Mitotic figures are common and erythrophagocytosis and/or multinucleated giant cells may be present.

Bone Marrow Cytology

In patients with cytopenias, tumor infiltrate and hemophagocytosis may be noted.

PATHOLOGIC FINDINGS

Cutaneous Histiocytoma

- Characterized by sheets of histiocytes infiltrating the dermis and subcutis, tracking hair follicles, and elevating the overlying hyperplastic and often ulcerated epithelium.
- Presence of lymphocyte infiltration and necrosis is often recognized in regressing lesions.
- A high mitotic index consistent with the rapid growth rate is a common feature of this tumor.

CH/SH

- Multicentric, nodular, perivascular histiocytic infiltrates within the deep dermis and subcutaneous tissue with variable lymphocyte, plasma cell, eosinophil and neutrophil infiltration.
- Blood and lymphatic vessel invasion is commonly noted, often accompanied by vascular wall degeneration, thrombosis and ischemic necrosis.
- **Note:** In CH the lesions are limited to the skin and

HISTIOCYTIC DISEASES

(CONTINUED)

draining lymph nodes while in SH, lesions are more widespread.

HS/HHS

- Lesions are composed of sheets of large, pleomorphic, mononuclear cells and multi-nucleated giant cells with numerous bizarre mitotic figures.
- Phagocytosis of red cells and leukocytes may be present in HS but is more typical of HHS where it is present to a high degree (spleen and liver).



TREATMENT

Cutaneous Histiocytoma

- Surgical excision or cryosurgery is generally curative.
- Cutaneous histiocytomas may spontaneously regress within 2–3 months, thus treatment is often not necessary. It is important to differentiate histiocytoma from a malignant tumor if client elects to monitor the lesion.

CH/SH

- Cutaneous lesions may wax and wane or spontaneously regress, but both diseases are usually progressive and require treatment.
- Rarely, dogs can present with localized lesions that can be surgically excised; however, most times disease is multifocal to widespread.
- Long-term aggressive immunosuppression is indicated for SH.

HS/HHS

- Localized (i.e., periarticular) HS can be successfully treated with surgical excision, usually requiring amputation. Radiation therapy can also be used as a palliative option for localized disease.
- Chemotherapy is indicated for multifocal and widespread systemic disease. Multiple agents have been evaluated, but lomustine (CCNU) has been the only drug with documented efficacy.



MEDICATIONS

DRUG(S)

- Lomustine (CCNU): 60–90 mg/m² q3 weeks
- Prednisone: 1–2 mg/kg/day continuously

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Lomustine can lead to severe myelosuppression and hepatotoxicity; prophylactic antibiotics and liver protectants

(Denamarin) are recommended with this drug.

ALTERNATIVE DRUG(S)

- Doxorubicin, vincristine, Doxil, paclitaxel, cyclophosphamide, mitoxantrone, dacarbazine and vinblastine have all been used with limited success.
- Immunomodulators such as leflunomide and cyclosporine have also been used and are most indicated for the reactive diseases (CH/SH).
- Bisphosphonates (pamidronate, zoledronate, liposomal clodronate) have been shown to have in vitro activity and synergy with certain chemotherapeutics in HS cell lines.



FOLLOW-UP

PATIENT MONITORING

Cutaneous Histiocytoma

Ensure the lesion is resolving within 2–3 months; if not, surgical excision is recommended.

CH/SH/HS/HHS

- Intensive scheduled monitoring occurs during treatment.
- Physical examination, complete blood count, serum chemistry panel, abdominal ultrasonography, and thoracic radiography every 2–3 months after completion of treatment.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Bleeding due to thrombocytopenia

EXPECTED COURSE AND PROGNOSIS

Cutaneous Histiocytoma

- Prognosis is considered excellent with surgical removal.
- Spontaneous regression is likely within 2–3 months.
- Cases with multiple histiocytomas may have a more lengthened clinical course, but spontaneous resolution is still possible.
- Metastatic histiocytomas (rare) have been reported.

CH/SH

- Both diseases are rarely fatal, but can negatively impact quality of life.
- Cutaneous lesions may wax and wane or spontaneously regress but are usually progressive and require treatment with immunomodulatory drugs or surgical excision (if localized).
- SH is associated with a poorer prognosis than CH because dogs are often ill from the disease and relapses are common, often prompting euthanasia.

HS/HHS

- Localized (periarticular) HS: Long-term (> 12 months) survival has been documented for dogs that undergo aggressive local and systemic therapy (surgery + CCNU).
- Disseminated HS: Reported response rates to CCNU are 40–50% for a median remission duration of 3–6 months.
- HHS is associated with rapid progression and a grave prognosis (median 7 weeks) even with treatment.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Chemotherapy drugs may be carcinogenic and mutagenic.

ABBREVIATIONS

- BMD = Bernese mountain dog
- CCNU = lomustine
- CH = cutaneous histiocytosis
- HHS = hemophagocytic histiocytic sarcoma
- HS = histiocytic sarcoma
- SH = systemic histiocytosis

Suggested Reading

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Authors Craig A. Clifford and Christine Mullin

Consulting Editor Timothy M. Fan

HISTOPLASMOSIS



BASICS

DEFINITION

A systemic fungal infection caused by *Histoplasma capsulatum*.

PATHOPHYSIOLOGY

- Soil-borne dimorphic fungus with the mycelial form growing best in bird manure or organically enriched soil. • Mycelium in the soil—produces infectious spores (microconidia); inhaled into the terminal airways.
- Spores—germinate in the lungs; develop into yeast form that reproduce by budding.
- Yeast are phagocytized by mononuclear phagocytes.
- Mononuclear phagocytes—distribute the organisms throughout the body.
- Ingested organisms may directly infect the intestinal tract.
- Immune response—determines whether disease develops; affected animals often develop transient, asymptomatic infection.

SYSTEMS AFFECTED

- Cats—respiratory tract main site of infection; bone, bone marrow, liver, spleen, skin, and lymph nodes also affected; intestinal tract, eyes, kidneys, adrenals, and brain less frequently involved.
- Dogs—intestinal tract most frequently involved site; liver, lung, spleen, and lymph nodes often involved; bones, bone marrow, kidneys, adrenals, oral cavity, tongue, eyes, and testes less frequently affected.

GENETICS

N/A

INCIDENCE/PREVALENCE

Prevalence of clinically relevant histoplasmosis relatively low in cats and dogs; an active practice, even in endemic areas, would see three to four cases a year.

GEOGRAPHIC DISTRIBUTION

- Endemic areas—Ohio, Missouri, Mississippi, Tennessee, and St. Lawrence river basins.
- Also seen in Texas, the southeastern United States, the Great Lakes region, and California.
- Has been isolated from the soil of 31 continental US states.

SIGNALMENT

Species

Dog and cat

Breed Predilections

N/A

Mean Age and Range

- Cats—predominantly young; many < 1 year of age; all ages can be infected.
- Dogs—most often young to middle-aged; all ages can be infected.

Predominant Sex

- Cats—females may be overrepresented.
- Dogs—none reported.

SIGNS

Historical Findings

Cat

- Insidious onset over days to weeks.
- Anorexia, weight loss, and dyspnea—most common.
- Coughing occasionally.
- Lameness.
- Ocular discharge.
- Diarrhea.

Dogs

- Weight loss, depression, and diarrhea with straining—most common.
- Coughing.
- Dyspnea.
- Exercise intolerance.
- Lymphadenopathy.
- Lameness and eye and skin changes—less common.

Physical Examination Findings

Cats

- Fever to 40°C (104°F).
- Increased respiratory effort and harsh lung sounds.
- Mucous membranes pale.
- Enlarged lymph nodes.
- Lameness, ocular changes, and skin lesions may be found.

Dogs

- Thin to emaciated.
- Fever to 40°C (104°F).
- Hepatosplenomegaly.
- Mucous membranes often pale.
- Icterus and ascites occasionally seen.
- Coughing and dyspnea associated with harsh lung sounds.
- Ocular and skin lesions less commonly noted.

CAUSE

H. capsulatum

RISK FACTORS

- Bird roosts where the soil is enriched with bird or bat droppings are high-risk environments; old chicken coops and caves have been implicated.
- Exposure to airborne dust contaminated with fungal spores coming from sites of fungal growth (especially indoor cats).
- Tissue samples from nearly half of stray dogs and cats from an endemic area were positive for *Histoplasma*, supporting the theory that many people and animals are infected but few develop clinically significant disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Cats

- Dyspnea from fungal pneumonia—differentiate from heart failure, feline asthma, lymphoma, pneumonia, pleural effusion, and other fungal pneumonias.
- Lameness—differentiate from trauma.
- Ocular changes—differentiate from lymphoma, toxoplasmosis, and feline infectious peritonitis.

Dogs

- Severe chronic diarrhea and weight loss—consider lymphocytic plasmacytic enteritis, eosinophilic enteritis, lymphoma, chronic parasitism, and pancreatic exocrine insufficiency.
- Diarrhea and anemia—consider severe inflammatory bowel disease, lymphoma or other intestinal neoplasia, and

parasitism (hookworm infection).

- Hepatosplenomegaly and peripheral lymphadenopathy—consistent with lymphoma.
- Respiratory signs—differentiate from infectious causes (distemper, bacterial, or other fungal pneumonia), chronic bronchitis, pleural effusion, heart failure, and pulmonary hypertension.

CBC/BIOCHEMISTRY/URINALYSIS

- Moderate to severe nonregenerative anemia common.
- Leukocyte counts—usually normal; some patients have a leukocytosis; patients with bone marrow involvement may be leukopenic.
- *Histoplasma* organisms—may be found in circulating neutrophils and monocytes; 2–4 µm round body with a basophilic center and lighter halo.
- Severe liver involvement—may see hyperbilirubinemia and high ALT activity.
- Dogs with severe intestinal histoplasmosis often have low total protein and exhibit panhypoproteinemia.

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OTHER LABORATORY TESTS

- AGID test—for antibodies; supports diagnosis; positive results indicate active disease; previous infections may produce false-positive results; many animals with active disease are negative on serology.
- Antigen testing—antigen excretion in urine may provide a more accurate assay for identifying infected animals, although little data available; has been found to be a sensitive assay in cats; resource: www.miravistalabs.com.
- Coombs' test—may be positive because antibodies to *Histoplasma* may cross-react with RBCs; steroid therapy contraindicated.

IMAGING

Thoracic Radiography

- Dogs—diffuse interstitial to nodular pneumonia; enlarged tracheobronchial lymph nodes compressing the tracheal bifurcation; old lung lesions may be calcified, coin-like opacities that suggest metastatic tumors.
- Cats—usually a diffuse interstitial pattern of lung involvement; calcification and tracheobronchial lymphadenopathy uncommon.

Abdominal and Bone Radiography

- Dogs—hepatosplenomegaly, mesenteric lymphadenopathy, and potentially ascites..
- Cats and less often dogs—bone lesions predominantly osteolytic and usually occur distal to the elbows and stifles.

DIAGNOSTIC PROCEDURES

- Identification of organisms on cytology, histopathology, or culture—definitive.
- Tissue samples—enlarged lymph nodes, liver, and spleen are higher yield sites; rectal scrapings may be rich in organisms; bone marrow; lung aspirates (when less invasive procedures are not diagnostic); tracheal washes inconsistent.
- Urine antigen assay has high sensitivity in initial report.

HISTOPLASMOSIS

(CONTINUED)

PATHOLOGIC FINDINGS

- Multifocal, granulomatous lesions in organs rich in reticuloendothelial cells (e.g., spleen, liver, lymph nodes, lungs, and bone marrow).
- Dogs—gut prime site of involvement; tracheobronchial lymph node enlargement common.
- Cats—predominantly respiratory involvement.



TREATMENT

APPROPRIATE HEALTH CARE

- Usually outpatient with oral itraconazole.
- Inpatient with intravenous amphotericin B—dogs with severe intestinal disease and malabsorption.

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NURSING CARE

- Dogs on amphotericin B therapy—keep well hydrated to decrease potential for nephrotoxicity.
- Emaciated animals with malabsorption—consider total parenteral nutrition until the intestinal disease is resolved enough for adequate food absorption.
- Animals with severe dyspnea—oxygen supplementation.

ACTIVITY

Dogs with dyspnea—reduce.

DIET

Good-quality, easily absorbed, palatable food.

CLIENT EDUCATION

- Discuss possible areas of exposure in the home environment.
- Inform client that both pets and family members may have been exposed to the same source but that the animal is not a hazard to the family.



MEDICATIONS

DRUG(S) OF CHOICE

Itraconazole

- Drug of choice if adequate intestinal function for drug absorption exists.
- Dogs and cats—5 mg/kg PO q12h; give with a high-fat meal.
- Be cautious about compounded itraconazole because absorption may not be acceptable.
- Duration depends on the clinical response; minimum treatment is 90 days.

Intravenous Amphotericin B

Dogs

- With severe inflammatory bowel disease and malabsorption—use until patient begins to gain weight; then start on itraconazole.
- Patient must be well hydrated before starting treatment; do not give amphotericin B in electrolyte solutions that may precipitate the drug.
- Usual dose—0.5–1.0 mg/kg IV q48h.
- Reconstitute in 5% dextrose and dilute for administration.
- Normal renal function—dilute in 60–120 mL 5% dextrose

and give over 2 hours.

- Some renal compromise—dilute in 0.5–1 L 5% dextrose and give over 3–4 hours to reduce renal toxicity.

Cats

- Use cautiously.
- Usual dose—0.25 mg/kg IV in 5% dextrose over 3–4 hours q48h.
- More sensitive to the drug than are dogs.

Fluconazole

- Eye and CNS involvement may best be treated with fluconazole that penetrates the blood-brain barrier.
- Use for dogs that cannot be given amphotericin B.
- Usual dose (intravenous form)—5 mg/kg IV q12h until intestinal absorption allows oral itraconazole treatment.

CONTRAINdications

Amphotericin B—caution with azotemic patients (in life-threatening situation, may still consider its use); monitor creatinine throughout therapy—elevation above normal or 20% greater than baseline is considered significant.

PRECAUTIONS

- Steroids—use with caution; allows proliferation of *Histoplasma*; life-threatening respiratory distress due to infiltrative lung disease or hilar lymphadenopathy justifies use of dexamethasone 0.1–0.2 mg/kg IV daily for 2–3 days.
- Itraconazole and fluconazole—hepatotoxicity; temporarily discontinue if patient becomes anorexic or if serum ALT activity > 300 U/L; restart at half-dose after appetite improves.

POSSIBLE INTERACTIONS

Itraconazole—inhibits cytochrome P450 system (CYP3A) and can increase concentrations of cyclosporine, digoxin, and midazolam in humans.

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

- Serum ALT—with itraconazole treatment; check monthly or if the patient becomes anorexic.
- Chest radiographs—with pulmonary involvement; check after 60 days of treatment to assess improvement; repeat at 30-day intervals and stop treatment when infiltrates are clear or remaining lung lesions fail to improve, indicating residual scarring; may be difficult to differentiate between residual fibrotic lesions and active disease; continue treatment for at least 1 month after all signs of active disease have resolved.
- Monitoring urinary antigen levels may be helpful.

PREVENTION/AVOIDANCE

- Avoid suspected areas of exposure (e.g., bird roosts).
- Recovered dogs are potentially immune.

POSSIBLE COMPLICATIONS

Recurrence possible; requires a second course of treatment.

EXPECTED COURSE AND PROGNOSIS

- Treatment—duration is usually about 4 months; drugs are expensive, especially for large dogs.
- Prognosis—good for stable patients without severe dyspnea; influenced by severity of lung involvement and debility of patient.



MISCELLANEOUS

ASSOCIATED CONDITIONS

No apparent predisposing conditions.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

- Yeast form is not spread from animals to humans.
- Care must be taken to avoid needlestick injury when collecting aspirates.
- Infection can occur from cuts when doing necropsies on infected animals.

PREGNANCY/FERTILITY/BREEDING

Itraconazole—no teratogenic effects in rats and mice at therapeutic doses; embryotoxicity found at high doses; no dog or cat studies; however, azole drugs can be teratogenic, use with caution in pregnant animals.

ABBREVIATIONS

- AGID = agar gel immunodiffusion
- ALT = alanine transaminase • RBC = red blood cell

Suggested Reading

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Author Daniel S. Foy

Consulting Editor Stephen C. Barr

Acknowledgment The author and editors acknowledge the prior contribution of Alfred M. Legendre.



Client Education Handout available online

HOOKWORMS (ANCYLOSTOMIASIS)



BASICS

OVERVIEW

- Nematode parasites of small intestine; *Ancylostoma caninum*, dogs; *A. tubaeforme*, cats; *A. braziliense* and *Uncinaria stenocephala*, dogs and cats. • *A. braziliense* in southern states; others also in temperate zone.
- Voracious blood-sucking adults and fourth-stage larvae of *A. caninum* and *A. tubaeforme* cause blood-loss anemia, enteritis; active worms leave bite sites with ongoing hemorrhage. • Disease can occur in peracute to chronic forms; peracute form in neonates results from transmammary infection; acute disease in older pups; in adults infection can be acute, chronic compensatory, or chronic non-compensatory in immunosuppressed or debilitated dog.
- *Uncinaria* is of little clinical concern.
- *A. braziliense* is major cause of CLM in humans. • Respiratory disease may result from larval migration in lungs. • *A. caninum* is transmitted via colostrum/milk to pups; all species are transmitted by ingestion of infective larvae in food, water, or transport hosts and by larval skin penetration.

SIGNALMENT

- Peracute to acute disease in young animals; asymptomatic or chronic in mature dogs and cats. • Clinical severity greater in dogs than cats.

SIGNS

Historical Findings

- Pale mucous membranes; dark, tarry stools (melena); diarrhea; constipation; loss of condition; poor appetite; dry cough.
- Sudden death.

Physical Examination Findings

- Poor body condition; ill-thrift, poor hair coat. • Pale mucous membranes.
- Erythematous, pruritic lesions, papules on feet, especially between toes.

CAUSES & RISK FACTORS

- Neonatal animals are at highest risk for clinical disease. • Infected bitch or queen.
- Environment contaminated with feces of hookworm-infected dog/cat. • Concurrent enteric infections. • Compromising conditions (e.g., pregnancy, malnutrition).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of erythrocyte destruction or blood loss resulting in anemia. • Ascariasis (large roundworm infection), coccidiosis, and strongyloidosis can cause similar signs without significant anemia. • Melena and mild anemia can also occur with physalopterosis.

CBC/BIOCHEMISTRY/URINALYSIS

- Eosinophilia. • Anemia usually acute normochromic, normocytic, and regenerative; can become microcytic, hypochromic due to chronic iron deficiency.

DIAGNOSTIC PROCEDURES

- Note that disease/death may occur prior to egg shedding by adult worms. • Fecal flotation to detect typical morulated strongylid eggs; minor size differences among species; eggs of *Uncinaria* slightly longer than *Ancylostoma* spp. • Necropsy of littermates that died with similar clinical signs.

PATHOLOGIC FINDINGS

- Gross: hookworms attached to small intestinal mucosa; multifocal hemorrhagic ulcerations ("bite sites") on mucosa; blood in intestinal lumen. • Microscopic: eosinophilic enteritis.



TREATMENT

- Peracute and severe acute cases treated as inpatients; anthelmintic plus fluid therapy, blood transfusion, supplemental oxygen as indicated by severity of anemia and clinical signs. • Peracute and severe acute cases: alert owner to possible sudden death in spite of treatment. • Chronic compensatory cases: anthelmintic; if non-compensatory, provide nutritional support (iron supplement).



MEDICATIONS

DRUG(S)

Adulcicide/Larvicide Anthelmintics

- Fenbendazole 50 mg/kg PO q24h for 3 consecutive days in dogs. • Milbemycin oxime 0.5 mg/kg (dogs) or 2 mg/kg (cats) PO q30 days. • Emodepside (3 mg/kg)/praziquantel (12 mg/kg) topically once in cats. • Moxidectin 0.17 mg/kg SC q6 months in dogs. • Moxidectin 2.5 mg/kg (dogs) or 1.0 mg/kg (cats)/imidoclopramide 10 mg/kg, topically q30 days. • Ivermectin 24 µg/kg PO q30 days in cats.

Adulcicide Activity

- Pyrantel pamoate, label dose in dogs; 10–20 mg/kg PO in cats (extra-label).
- Praziquantel/pyrantel pamoate/febantel, label dose for dogs. • Praziquantel/pyrantel pamoate, label dose for cats. • Ivermectin/pyrantel pamoate or ivermectin/pyrantel pamoate/praziquantel, label dose for dogs.
- Selamectin 6 mg/kg topically q30 days in cats.



FOLLOW-UP

Monitor fecal egg counts after treatment and hematocrit in anemic patients.

PREVENTION/AVOIDANCE

- Eliminate intestinal stages and activated dormant larvae in breeding bitch; fenbendazole at 50 mg/kg/day from day 40 of gestation to day 14 of lactation or ivermectin at 0.5 mg/kg 4–9 days prior to whelping and again 10 days later. • Begin biweekly anthelmintic treatment of pups at 2 weeks of age; continue until weaned, especially pups at high risk of infection from bitch or environment; treat monthly after weaned.
- Treat queen with adulticide/larvicide anthelmintic prior to breeding and after littering. • Begin anthelmintic treatment of kittens at 3–4 weeks of age; treat monthly thereafter. • Promptly remove and dispose of feces to prevent contamination of environment with larvae. • Prevent hunting and scavenging to prevent ingestion of potential transport hosts.

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EXPECTED COURSE AND PROGNOSIS

- Puppies with peracute or acute *A. caninum* infection may die in spite of treatment.
- Expect full recovery in cases with anthelmintic treatment and nutritional support. • Anthelmintic treatment of adult dogs with dormant larvae in their tissues can result in larval activation and repopulation of small intestine.



MISCELLANEOUS

AGE-RELATED FACTORS

- Disease more acute in young animals and chronic in adults. • Transmission of *A. caninum* larvae from bitch to offspring in colostrum/milk results in high rate of infection in pups.

ZOONOTIC POTENTIAL

- All hookworms, especially *A. braziliense*, cause CLM when infective larvae penetrate human skin. • *A. caninum* larvae can cause VLM or migrate to GI tract, causing abdominal pain and eosinophilia without becoming patent.

ABBREVIATIONS

- CLM = cutaneous larva migrans • GI = gastrointestinal • VLM= visceral larva migrans

INTERNET RESOURCES

- www.capcvet.org • www.cdc.gov

Suggested Reading

Bowman DD. Georgis' Parasitology for Veterinarians, 9th ed. St. Louis, MO: Saunders, 2008, pp. 179–185.

Author Matt Brewer

Consulting Editor Stephen C. Barr

HORNER'S SYNDROME



BASICS

OVERVIEW

- Sympathetic denervation to the eye.
- Anatomic pathway very important. • Affects the ophthalmic and nervous systems.

SIGNALMENT

- Idiopathic—one study suggests male golden retrievers 4–13 years of age at increased risk. Most of these localize to a postganglionic

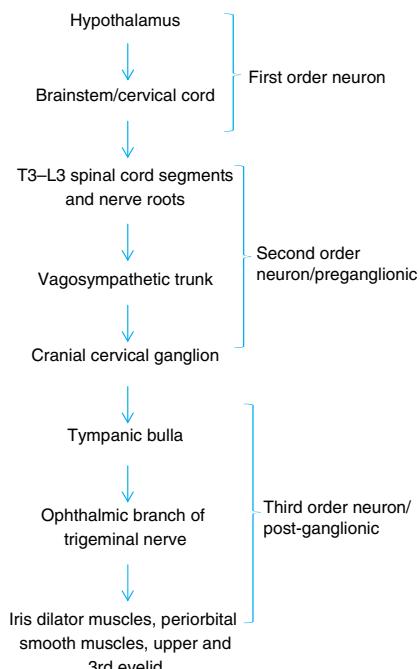


Figure 1.

lesion. • Idiopathic—dogs, 50–93%; cats, 45%. • Other causes—N/A.

SIGNS

- Miosis. • Protruding third eyelid. • Ptosis (drooping) of upper eyelid. • Enophthalmia.
- Other neurologic and non-neurologic signs dependent on the underlying cause.

CAUSES & RISK FACTORS

See Table 1.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Anterior uveitis—IOP usually low; aqueous flare.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

- See Table 1. • Thoracic radiographs—may reveal cause of injury to the sympathetic trunk (e.g., trauma and mediastinal tumor). • Skull radiographs—may reveal middle ear problem.
- MRI—may help identify brainstem lesion, retrobulbar mass, cervical spinal cord problem. • CT may help identify middle ear problem. • Ultrasonography—orbit; may reveal retrobulbar mass.

DIAGNOSTIC PROCEDURES

- See Table 1. • CSF tap—investigate brain and spinal cord disease. • Electromyography—look for brachial plexus avulsion.
- Pharmacologic testing—see Anisocoria.

TREATMENT

Treat underlying disease.



MEDICATIONS

DRUG(S)

- Depends on underlying disease
- Idiopathic—none

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Do not use drugs which alter the autonomic nervous system prior to referral for lesion localization.



FOLLOW-UP

- Depends on severity of underlying disease.
- Idiopathic—may take up to 4 months for a partial or complete recovery.

MISCELLANEOUS

ABBREVIATIONS

- CN = cranial nerve • CSF = cerebrospinal fluid • CT = computed tomography
- FCE = fibrocartilagenous embolism
- IVDH = intervertebral disc herniation
- MRI = magnetic resonance imaging

Suggested Reading

Cottrill NB. Differential diagnosis of anisocoria. In: Kirk's Current Veterinary Therapy, 14th ed. St Louis, MO: Saunders, 2009, pp. 1168–1174.

Author Heidi Barnes Heller

Consulting Editor Paul E. Miller

Acknowledgment The author and editors acknowledge the prior contribution of David Lipsitz.

Table 1

Summary of lesions resulting in Horner's syndrome.

Lesion location	Causes	Common concurrent neurologic abnormalities	Diagnostic plan
Brainstem	Neoplasia, encephalitis, vascular, trauma	Altered mental status, ipsilateral hemiparesis, ipsilateral postural reaction deficits	MRI; CSF analysis
C1–T3 spinal cord	IVDH, trauma, neoplasia, FCE	Ipsilateral or bilateral hemiparesis/plegia, ± reduced reflexes to thoracic limbs, normal mentation	MRI preferred, myelogram also may show lesion. CSF analysis
T1–T3 nerve roots	Brachial plexus avulsion, peripheral nerve tumor (lymphoma, nerve sheath tumor most common)	Ipsilateral loss of thoracil imb reflexes, ipsilateral loss of cutaneous trunci, ipsilateral monoparesis/plegia, absent postural reactions in affected thoracic limb only	MRI, electrodiagnostic testing
Sympathetic trunk, cranial cervical ganglion*	Trauma, iatrogenic following jugular venipuncture, mediastinal or thyroid neoplasia	Possibly laryngeal dysfunction	Neck ultrasound, MRI, thoracic radiographs
Tympanic bulla	Otitis media, polyp (cat), neoplasia, trauma	Ipsilateral vestibular disease, ipsilateral facial nerve paralysis	MRI, CT, bulla radiographs, myringotomy
Retrobulbar	Neoplasia, abscess, trauma	None, or dysfunction of CN II, III, IV, and VI.	MRI, orbital ultrasound



BASICS

DEFINITION

- Deposition of urine or feces outside the litter box.
- Urine housesoiling (also called periuria) includes inappropriate urination, a toileting behavior in which urine is typically found on horizontal surfaces outside the litter box, and urine marking, in which urine is sprayed on vertical surfaces as part of a ritualistic tail-up display.
- Fecal housesoiling includes both inappropriate defecation, a toileting behavior characterized by feces deposited outside the litter box, and fecal marking, called middening, characterized by feces deposited in prominent locations.
- Marking behavior serves a normal communicative function in cats.
- Housesoiling will negatively impact the human-animal bond and can lead to relegation outside, rehoming, relinquishment, or euthanasia.

PATOPHYSIOLOGY

- Inappropriate urination/defecation—may be a response to dissatisfaction with the litter box environment or preference for an alternative location or substrate, or may reflect an underlying pathophysiologic state such as a negative (pain) association with the litter box secondary to uroliths, constipation, or orthopedic pain.
- Urine marking—a normal behavior observed in free-ranging and confined cats; significant individual differences in the propensity to urine mark in a given environment. Cat density is correlated to probability of urine marking. Cats that urine mark also commonly use a litter box for toileting.
- Fecal marking (middening) is rarely observed; it should be a diagnosis of exclusion.
- Social or environmental stressors may contribute to housesoiling, primarily marking.

SYSTEMS AFFECTED

- Behavioral
- Endocrine
- Gastrointestinal
- Renal/Urologic

GENETICS

- Not specifically identified.
- Persians and Himalayans that exhibit inappropriate urination should be DNA tested for the genetic disorder polycystic kidney disease.

INCIDENCE/PREVALENCE

- Housesoiling is the most common behavioral problem for which cat owners seek veterinary advice and the second most common reason for relinquishment of cats to animal shelters.

- Inappropriate urination/defecation: in one survey, 11% of indoor cat owners reported inappropriate elimination as a problem.
- Urine marking: exhibited by approximately 10% of castrated male and 5% of ovarioectomized female house cats.

GEOGRAPHIC DISTRIBUTION

Housesoiling may be more problematic where cats are commonly restricted indoors.

SIGNALMENT

Species

Cat

Breed Predilections

Housesoiling may occur in any breed, although Persians, Himalayans, and relatives are overrepresented in some studies.

Mean Age and Range

Inappropriate urination/defecation can occur at any age. Marking behaviors are typically seen in cats > 6 months.

Predominant Sex

- Housesoiling can occur in either sex, intact or altered.
- Urine marking is more common in males (intact and neutered) than females (intact and neutered).

SIGNS

General Comments

Identify the Affected Cat in a Multi-Cat Household

- Direct observation, although if punished, cats may become secretive.
- Videotaping or video monitoring.
- Separate the cats to identify the culprit. Note that this protocol may alter the social milieu sufficiently to inhibit inappropriate elimination.
- Add a urine indicator. If urine is alkaline, administer the dye fluorescein (6 fluorescein test strips in a gel capsule PO or 10 mg/cat) sequentially to each cat. Urine outside the litter box will fluoresce under a Wood's light for approximately 24 hours; if negative after 36 hours, the test can be repeated on another cat. Negative results are common in households in which the frequency of urine housesoiling is low. Fluorescein may stain fabrics.

Identify the Locations of Housesoiling within the House

The owner should generate a map of the home, indicating the locations of urine and fecal housesoiling and locations of litter boxes. Location of the housesoiling can provide insight into the type of housesoiling and etiology.

Historical Findings

Inappropriate Urination/Defecation

- Abnormal pattern of urination (incontinence, polyuria, hematuria, dysuria) suggests an underlying congenital or medical problem.
- History of straining to defecate; vocalizing or running away when defecating; hard, dry,

or bulky feces suggest painful defecations that may lead to conditioned avoidance of the litter box for defecation.

- History of polydipsia, anorexia, vomiting, or diarrhea suggest an underlying medical etiology.

Urine Marking

- History of displacement, aggression, or avoidance behavior between cats in a multi-cat household.
- Observation of the posture of spraying urine: the cat orients caudally to a vertical surface, stiffens its posture, raises and quivers its tail, and directs a small burst of urine caudally.
- Observation of urine marks on vertical surfaces or puddled at the bottom of a wall.
- Urine marks can be found on prominent furniture or other objects, or urine sprayed on new objects brought into the house.
- Horizontal urine marks may be found on clothing or bedding associated with a particular person or in response to visitors or novel objects.

Fecal Marking

Feces deposited on prominent, conspicuous locations.

Physical Examination Findings

- Presence of abnormal physical findings depends on whether problem is pathophysiologic or behavioral.
- If strictly behavioral, physical examination will be normal.
- Apparently-neutered males that urine mark should be examined for the presence of penile spines, indicating the presence of endogenous testosterone, or quantify serum testosterone.

CAUSES

Medical Causes

- Any metabolic or GI condition that causes polyuria, diarrhea, or constipation
- Lower urinary tract disease, including idiopathic interstitial cystitis (may be associated with environmental stressors)
- Urolithiasis
- Diabetes mellitus
- Hyperthyroidism
- FeLV
- FIV
- Liver disease
- CNS disease/cognitive dysfunction (senility)
- Iatrogenic—administration of fluids, corticosteroids, diuretics
- Musculoskeletal pain that make entry/exit from the litter box or elimination postures difficult, can contribute to litterbox aversion
- Hormonal influences may contribute to urine marking

Behavioral Causes

Inappropriate Urination/Defecation

- Soiled litter box.
- Inadequate number of boxes or locations (one box per cat plus one is recommended).

HOUSESOILING—CATS

(CONTINUED)

- Box located in remote or unpleasant surroundings or subject to interference by dogs or children.
- Inappropriate type of box—a covered litter box, box too small to allow large cats to move around comfortably; or allows other cats, pet dogs, and young children to target the cat as it exits.
- Time factors—daily or weekly temporal patterns of inappropriate urination suggest an environmental cause; acute onset in a cat that has previously used the litter box suggests a medical or social problem.
- Substrate—unacceptable litter type; preference tests indicate that most cats prefer unscented, fine-grained (clumping) litter but individual variability; coincident change in litter box habits with new litter type suggests an association; a sudden shift from one substrate (e.g., litter) to an unusual substrate (e.g., porcelain sink) suggests a lower urinary tract disorder.
- Location—urination outside the litter box may suggest a location preference or influential social factors. Urination in the vicinity of the litter box may suggest dissatisfaction with qualities of the litter box, including litter box hygiene.
- Social dynamics—consider social conflicts between cats at the time the problem started (e.g., addition of a new cat).

Marking

- Marking is associated with arousal, anxiety, or territorial behavior.
- The probability of urine marking is directly proportional to the number of cats in the household.
- Marking can be a response to household disruption or another cat(s) in or outside the home. Urine marks around windows and doors to the outside suggest a response to the presence of an outdoor cat.
- Urine marking grocery bags or new furniture suggests arousal in response to new stimuli.

RISK FACTORS

Inappropriate Urination/Defecation

- Inadequate litter box hygiene
- Litter box features (litter type or scent, box size or style)

Urine Marking

- Male
- Sexually intact
- Multiple-cat household
- History of urine marking by a parent



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Must identify if a medical problem underlies the behavioral problem.

- If behavioral, must differentiate inappropriate urination from urine marking.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal when urine marking and inappropriate urination are strictly behavioral; urinalysis via cystocentesis is the minimum database in any cat examined because of inappropriate urination; collect serial samples from cats whose behavioral signs wax and wane; CBC and biochemistry are recommended prior to administration of medication and to evaluate medical status.

OTHER LABORATORY TESTS

Cats with refractory inappropriate urination or progressive signs should be tested for hyperthyroidism, FeLV, and FIV.

IMAGING

Abdominal ultrasonography, abdominal radiographs, and contrast studies if indicated to rule out urolithiasis as an underlying cause for inappropriate urination.

DIAGNOSTIC PROCEDURES

Helpful historical information: map of the house, with litter boxes and urine/fecal housesoiling identified; behavioral diary with daily frequency of urinations/defecations inside each litter box and outside the litter boxes. Requires daily household monitoring.

PATHOLOGIC FINDINGS

None, unless an underlying medical etiology.



TREATMENT

APPROPRIATE HEALTH CARE

- Treat any underlying medical condition.
- Use environmental and behavioral therapies before or concomitant with pharmacologic treatment.
- The environment for indoor cats should include safe resting places, separated resources, and positive and predictable human-cat interactions.
- Restrict the cat from rooms in which urine housesoiling occurs.
- For immediate management and in cases of agonistic relationships between cats in a multi-cat household, it may be necessary to confine the cat to one room in the owner's absence. Provide a litter box (see specifications below), water, food, and resting sites. The cat can be let out of the room when the owner returns and is available for strict supervision of the cat. Initiate other, more permanent treatments.
- Clean urine "accidents" with an enzymatic cleaner specific for this purpose.

Inappropriate Urination

- Scoop out the litter boxes daily. Clean out and wash litter box and refill regularly.
- Avoid deodorizers, scented litters, or other strong odors in the vicinity of the litter box.

- Move food bowls away from litter boxes.

- Provide one litter box per cat, plus one, distributed in more than one location; positioned away from high traffic or noisy areas.

- If the litter box is covered, provide an additional large, plain, uncovered litter box filled with unscented, fine-grained, clumping litter, with no liner and quantify cat use on a behavioral diary. Additional boxes may be provided ("litter box buffet") to reveal cat preference for litter box type and substrate.
- If one site in the home is preferred for inappropriate urination, place another litter box over this site. After it is in regular use, move it 2.5 cm per day to a site more acceptable to the owner.

Urine Marking

- If there are signs that the cat is marking in response to cats outside the home, use mechanical or olfactory products to deter outside animals, or trap and remove.
- Reduce cat numbers to reduce conflicts if possible.
- Synthesized feline facial pheromone (Feliway, Ceva Animal Health) is commercially available as a treatment for urine marking. The product is sprayed regularly or diffused in the environment and may reduce urine marking up to 75%.
- Litter box management, as described above, has been shown to decrease urine marking.
- Pharmacotherapy plays an important role in the control of urine marking.

NURSING CARE

N/A

ACTIVITY

Opportunities for active play that incorporate behavioral patterns of predatory stalking and pouncing should be provided daily.

DIET

No specific diet unless suggested by an underlying medical etiology, such as urolithiasis or constipation.

CLIENT EDUCATION

- Cats do not housesoil to be spiteful.
- Scolding and punishment are contraindicated, they may increase cat anxiety and will cause the cat to avoid the owner.
- Understanding the underlying motivation for housesoiling behavior is critical for treatment success.
- Creating a predictable environment will decrease anxiety and arousal that may contribute to housesoiling.
- Work to resolve cat conflicts within the home (see Aggression, Intercat Aggression).
- Meet cat needs for exercise, play, and safe elevated resting sites.

SURGICAL CONSIDERATIONS

Castration reduces urine marking in up to 90% of males and 95% of females.

(CONTINUED)

HOUSESOILING—CATS**Table 1**

Drugs and dosages used to manage feline urine marking.

<i>Drug</i>	<i>Drug Class</i>	<i>Oral Dosage in Cats</i>	<i>Frequency</i>	<i>Side Effects (Usually Transient)</i>
Fluoxetine	SSRI	0.5–1.0 mg/kg	q24h	Decreased appetite, sleepiness
Paroxetine	SSRI	0.25–0.50 mg/kg	q24h	Constipation
Clomipramine	TCA	0.2–0.50 mg/kg	q24h	Sleepiness
Amitriptyline	TCA	0.25–1.0 mg/kg	q24h	Sleepiness
Buspirone	Azaprione	0.5–1.0 mg/kg	q12h	GIT side effects (rare)

**MEDICATIONS****DRUG(S) OF CHOICE****Inappropriate Urination**

Psychotropic medication not usually indicated, except in treatment-resistant cases or when associated with generalized anxiety or heightened arousal.

Urine Marking

- Medication to decrease arousal is often needed for treatment success.
- Drugs from a number of drug classes may be used. All have the general effect of decreasing arousal and anxiety. Side effects can be sedation and/or altered social behavior (see Table 1). Drugs commonly used include fluoxetine, paroxetine, clomipramine, amitriptyline, buspirone.

Fecal Marking

Medication may be needed to decrease the arousal that drives this behavior.

CONTRAINDICATIONS

- Benzodiazepines—use cautiously or avoid because of rare reported cases of fatal idiopathic hepatic necrosis in cats receiving diazepam.
- Tricyclic antidepressants—cats with a history of cardiac conduction disturbances, urinary or fecal retention, megacolon, lower urinary tract blockages, seizures, and glaucoma.
- Transdermal route does not appear to consistently produce satisfactory drug levels.

PRECAUTIONS

All drugs listed are extra-label. Inform the client of extra-label use and potential side effects; document the discussion in the medical record or use a release form. Start psychotropic drugs when the owner is present to monitor the patient.

POSSIBLE INTERACTIONS

Do not use monoamine oxidase inhibitors (e.g. selegiline) concurrently with TCAs or SSRIs.

ALTERNATIVE DRUG(S)

- Synthetic progestins—the risk of serious side effects, including blood dyscrasias, pyometra, mammary hyperplasia, mammary carcinoma, diabetes mellitus, and obesity, has diminished their once-common use.
- Pheromone therapy (Feliway, Ceva Animal Health) may reduce urine spraying.
- L-theanine (Anxitane, Virbac Animal Health) or alpha-casozepine may reduce cat anxiety.

**FOLLOW-UP****PATIENT MONITORING**

- Regular follow-up is essential.
- The owner should keep a daily log of elimination patterns so that treatment success can be evaluated and appropriate adjustments in therapy can be made. Number the litter boxes and request that client count and record the number of urinations/defecations in each box and outside the litter boxes each day.
- For marking behavior, after 2 months of successful medication management, medication might be withdrawn gradually over 2 weeks. However, if the social features that underlie the behavior are still present, medication may need to be continued for treatment success.
- For medication monitoring, an annual CBC, chemistry profile, urinalysis, and physical examination are recommended at a minimum.

PREVENTION/AVOIDANCE

- Neuter cats.
- Restrict cat numbers to decrease the probability of urine marking.
- Counsel clients on appropriate litter box selection, location, and hygiene.
- Veterinary practitioners should inquire about housesoiling at each veterinary visit. Early identification and treatment optimize treatment success.

POSSIBLE COMPLICATIONS

Client expectations must be realistic. Immediate control of a long-standing

problem of housesoiling is unlikely; the goal is gradual improvement over time.

EXPECTED COURSE AND PROGNOSIS

- Prognosis for improvement is good if underlying etiology is identified and managed.
- Housesoiling is destructive to household belongings and erosive to the human-animal bond, which if not successfully controlled can lead to abandonment, relegation outside, relinquishment to an animal shelter, and euthanasia.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Aggression between cats may be associated with urine marking.

AGE-RELATED FACTORS

- Older cats might find litter box access difficult and seek alternative locations. Low-rise litter boxes can provide better access for these cats.
- Failure to use the litter box could be associated with age-related cognitive decline.

ZOONOTIC POTENTIAL

Pregnant women should avoid or take appropriate precautions when cleaning cat feces because of the risk of toxoplasmosis.

PREGNANCY/FERTILITY/BREEDING

Tricyclic antidepressants are contraindicated in animals used for breeding.

SYNOMYS

- General: feline housesoiling.
- Urine: feline inappropriate elimination, squat urination outside the litter box, urine marking, urine spraying, peruria.
- Feces: feline inappropriate defecation, defecation outside the litter box, fecal marking, middening.

SEE ALSO

- Aggression, Intercat Aggression
- Marking, Roaming, and Mounting Behavior—Cats
- Pediatric Behavior Problems—Cats

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HOUSESOILING—CATS

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ABBREVIATIONS

- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant

INTERNET RESOURCES

- Cornell University Feline Health Center, Feline Behavior Problems: House Soiling: http://www.vet.cornell.edu/FHC/health_resources/brochure_housesoiling.cfm
- Ohio State University Indoor Pet Initiative: <http://indoorpet.osu.edu/cats/problemsolving/sprayingmarking/index.cfm> and <http://indoorpet.osu.edu/cats/problemsolving/cleanupurine/index.cfm>

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Client Education Handout available online

HOUSESOLING—DOGS



BASICS

DEFINITION

Urination and/or defecation, for the means of eliminating or marking territory, in a location that owners consider inappropriate.

PATHOPHYSIOLOGY

- Improper or incomplete housetraining
- Submissive or excitement urination
- Testosterone, leading to marking behavior
- Marking behavior, due to territoriality, anxiety
- Anxiety (separation anxiety, noise phobia)
- Cognitive dysfunction

SYSTEMS AFFECTED

Behavioral—shelter relinquishment, leading to euthanasia or rehoming.

GENETICS

Some dog breeds appear to be more easily housetrained than others.

INCIDENCE/PREVALENCE

- Almost 20% of owners relinquishing a dog to a shelter did so because it soiled in the house.
- 37% of owners who reported talking to their veterinarian about a behavior problem reported that their dog was housesoiling.
- Housesoiling also represents a common reason that dogs are referred to a veterinary behaviorist.
- The incidence of inappropriate elimination, including marking behavior, in intact male dogs is almost 60%, higher than that seen in castrated male dogs and intact or spayed female dogs.

GEOGRAPHIC DISTRIBUTION

None described

SIGNALMENT

Species
Dogs

Breed Predilections

Potential genetic breed predisposition for ease of housetraining and submissive or excitement urination is anecdotally described. Dogs obtained from a commercial breeding establishment are more likely to urinate against household objects or display submissive urination than those obtained from a non-commercial breeder.

Mean Age and Range

- Inappropriate elimination due to improper or incomplete housetraining primarily seen in younger dogs.
- Submissive and excitement urination seen primarily in younger dogs.
- Urine marking begins to be displayed as the dog reaches sexual maturity.
- Housesoiling is a common complaint from owners of elderly dogs.

Predominant Sex

Intact male dogs are more likely to urine mark than female dogs and castrated male dogs.

SIGNS

General Comments

- Inappropriate elimination is the most common individual reason for relinquishment of a pet to a shelter.
- Proper housetraining must be discussed with clients from the very beginning.
- Housesoiling can be associated with medical problems such as endocrine disorders, urinary tract disorders, orthopedic disease, and metabolic disease.

Historical Findings

- History of urination and/or defecation in inappropriate areas.
- May be associated with signs of other behavioral disorders (such as separation anxiety).
- May be associated with lack of time spent by owner to properly teach housetraining.
- May be associated with punishment of a dog that has submissive urination.
- A complete medical and behavioral history will help determine potential triggers, including when, where, and how often the elimination occurs, and reliability of outdoor elimination.

Physical Examination Findings

- If examination findings and laboratory results are normal, housesoiling is probably due to a behavioral cause.
- There may have been an inciting medical cause that has since resolved but the animal has learned to eliminate indoors.

CAUSES

Canine inappropriate elimination can be primarily due to a behavioral problem or secondary to/concurrent with a medical disorder.

Behavioral

- Lack of, improper, or incomplete housetraining
- Marking behavior
- Submissive urination
- Excitement urination
- Separation anxiety
- Cognitive dysfunction syndrome
- Noise phobia
- Fear-induced
- Psychogenic polydipsia/polyuria

Medical Causes

Degenerative

- Osteoarthritis
- Renal failure

Anatomic

Ectopic ureters

Metabolic

- Incontinence
- Diabetes mellitus
- Diabetes insipidus
- Hepatic insufficiency
- Hyperadrenocorticism
- Hypoadrenocorticism
- Seizures

Neoplastic

- Genitourinary neoplasia
- Neurologic
- Other neoplastic diseases causing weakness

Infectious/Inflammatory

- Urinary tract infection or inflammation
- Crystalluria with cystitis
- Inflammatory bowel disorder
- Pancreatic disease
- Intestinal parasites

RISK FACTORS

- Intact male.
- Concurrent behavioral problem, such as separation anxiety.
- Owners

poorly informed or motivated to properly housetrain the dog.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiate behavioral causes of inappropriate elimination from medical causes with a proper medical workup.

CBC/BIOCHEMISTRY/URINALYSIS

- Indicated to rule out medical causes.
- Normal if inappropriate elimination is solely due to a behavioral cause.

IMAGING

Not indicated, other than to rule out medical causes, primarily urolithiasis or ectopic ureters.

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DIAGNOSTIC PROCEDURES

- Video recording when the owner is present to view household interactions with the dog.
- Journal to monitor potential causal factors, as well as to monitor improvement of the problem.
- Video recording the dog when the owner is gone from the home to rule in/out separation anxiety or other anxiety disorders.

PATHOLOGIC FINDINGS

None for behavioral causes



TREATMENT

APPROPRIATE HEALTH CARE

Appropriate measures to assure continued good health of the dog.

ACTIVITY

- Take dog outside often to ensure enough access to eliminate outside, or provide acceptable access to the outside, for example, via a dog door if the dog is trained properly.
- Increase activity level to help in the treatment of other problem behaviors, as well as to improve the dog's health.

DIET

- If the dog is inappropriately eliminating stool, feeding scheduled meals may help to maintain the dog on a schedule of elimination.
- Feeding a diet of higher caloric density may help decrease the urge to defecate as frequently.
- In general, water should not be withheld from the dog.

CLIENT EDUCATION

General Comments

- Counsel the owner as to the cause(s) of the inappropriate elimination, as well as the potential long-term management of the problem.
- Treat underlying/contributing medical problems.
- Treat other underlying/contributing behavioral problems.
- Counsel owners on proper housetraining techniques.
- Clean the soiled areas with an enzymatic cleaner to help eliminate any odor that may attract the dog to eliminate there again.
- If the

HOUSESOILING—DOGS

(CONTINUED)

soiled object is a piece of clothing or other smaller cloth object, such as a throw rug, wash it. • Punishment is inappropriate, as it may create anxiety, fear, and defensive aggression. • Do not use punishment to housetrain a dog, such as rub its nose in the soiled area, nor should they be verbally or physically reprimanded.

Incomplete Housetraining

- Keep the dog supervised at all times. If it is not supervised, keep confined unless confinement causes panic, destruction, and/or injury to the dog. • In some cases, tethering the dog to owners or nearby allows better supervision. Dogs should never be tethered without supervision. • Take the dog outside frequently to eliminate. • Accompany the pet to the appropriate elimination site and reward elimination as soon as it occurs. • Thoroughly clean soiled areas. • Use a consistent “key phrase” to help associate the act with the location and timing of elimination. • Feed on a set schedule, with water always available.

Submissive or Excitement Urination

- Do not punish the behavior, since this may make problem worse. • Owners should ignore the dog when they come into the house (no verbal or physical interactions or eye contact). • The dog should go outside to eliminate before it is greeted. • The dog should be greeted in a non-confrontational and quiet manner; do not lean over the dog or institute interactive play at the time of greeting. • Alternating activities at homecoming, such as asking for a toy or requesting a “Sit,” may help in mild cases.

Urine Marking Behavior

- Educate owners on effectiveness of neutering to decrease urine marking. • Determine any possible triggers to the behavior, including anxiety-provoking stimuli. • Address those triggers with desensitization and counter-conditioning and/or avoidance of the trigger as appropriate. • Prevent access to the preferred marking locations. • Make the areas that have been urine marked aversive to the dog by use of “booby traps” such as upside-down plastic carpet runners or foil. • Alternatively, the owner can change the significance of the area to a positive place, such as by feeding the dog in the marked area.

SURGICAL CONSIDERATIONS

Neutering intact male dogs decreases urine marking rapidly in 30% of dogs, with a gradual decline in 20% of dogs, and no change in 50% of them. The results are the same regardless of age of neutering.



MEDICATIONS

DRUG(S) OF CHOICE

- Behavioral modification used in conjunction with psychotropic medications.

- Negligible effect in animals not housetrained or if displaying submissive or excitement urination. Rarely effective when anxiety is not part of the problem behavior.
- If urine marking or inappropriate elimination is anxiety induced, medications may be helpful, in conjunction with behavior modification. • Selective serotonin reuptake inhibitors or tricyclic antidepressants/antianxiety medications may be helpful.
- SSRI: fluoxetine at 1–2 mg/kg PO q24h.
- TCA: clomipramine at 3 mg/kg PO q12h.
- The full onset of action of these medications can be 4–6 weeks after initiation of treatment; inform owners of time required for response to be noted. • Side effects of the SSRIs and TCAs can include nausea, vomiting, diarrhea, and lethargy. • Additional side effects of the TCAs can include potentiation of seizure activity.

CONTRAINDICATIONS

- Medication without concurrent behavior modification. • Tricyclic antianxiety medications are contraindicated in seizures and cardiac disease, and may interfere with thyroid medications.

PRECAUTIONS

Based on drug chosen

POSSIBLE INTERACTIONS

Do not use an SSRI and TCA together or in conjunction with an MAOI.

ALTERNATIVE DRUG(S)

- Pheromone products can potentially help decrease anxiety. • Some neutraceuticals such as alpha-casozepine and L-theanine may decrease anxiety.



FOLLOW-UP

PATIENT MONITORING

Monitor with owner by follow-up visits or telephone calls. The owner should keep a journal of incidents, inciting factors, and treatments instituted to have an objective view of improvement.

PREVENTION/AVOIDANCE

- Properly housetrain the dog. • Neuter male and female dogs. • Treat any underlying medical condition. • Treat any underlying behavioral condition.

POSSIBLE COMPLICATIONS

Recurrence if owner relapses in treatment, perhaps pet relinquishment.

EXPECTED COURSE AND PROGNOSIS

- Prognosis for any behavioral problem is highly dependent on the owner's ability to follow instructions. The following estimations of prognosis are based on the owner following your instructions for behavior modification.
- Prognosis for decreasing submissive and excitement urination is good. • Prognosis for managing incomplete housetraining is good.

- Prognosis for marking in previously intact male: 50% improve (30% quickly, 20% more slowly) with neutering, even without complementary behavior modification.
- Prognosis for managing urine marking in spayed or neutered dogs is good if the triggers are identified and managed with avoidance or other forms of behavior modification. • Some animals with a history of a medical cause of inappropriate elimination can still eliminate inappropriately after the medical cause has been treated.



MISCELLANEOUS

AGE-RELATED FACTORS

- Puppies are more likely to present for lack of or incomplete housetraining, as well as for submissive and excitement urination.
- Cognitive dysfunction becomes more likely as the dog ages.

ZOONOTIC POTENTIAL

Low unless potentially zoonotic organisms in the urine or feces.

SYNOMYMS

- Inappropriate defecation • Inappropriate elimination • Inappropriate urination • Urine marking

SEE ALSO

- Cognitive Dysfunction Syndrome
- Separation Distress Syndrome • Submissive and Excitement Urination—Dogs

ABBREVIATIONS

- MAOI = monoamine oxidase inhibitor
- SSRI = selected serotonin reuptake inhibitors • TCA = tricyclic antidepressant

INTERNET RESOURCES

- American College of Veterinary Behaviorists: www.dacvb.org. • American Veterinary Society of Animal Behavior: www.avsonline.org.

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Client Education Handout
available online

HYDROCEPHALUS



BASICS

DEFINITION

- Abnormal dilation of the ventricular system due to an increased volume of cerebrospinal fluid.
- May be symmetrical or asymmetrical.
- May involve the entire ventricular system or only elements proximal to a site of ventricular system obstruction.

PATHOPHYSIOLOGY

- Hydrocephalus is an active distension of the ventricular system—most commonly obstructive, rarely due to CSF overproduction.
- Obstructive—CSF accumulates in front of an obstruction along the normal CSF circulatory pattern (non-communicating) or at its resorption site by the meningeal arachnoid villi (communicating); depending on the balance between production of CSF (which is constant and independent of intracranial pressure) and the capacity for absorption of CSF, ICP may be high or normal; clinical signs may be noted in either case.
- Congenital obstruction—primary obstructive hydrocephalus; most common site is at the level of the mesencephalic aqueduct due to fusion of the rostral colliculi; prenatal infections (especially parainfluenza virus) may cause aqueductal stenosis with subsequent hydrocephalus; may result in considerable disruption of the architecture of the brain.
- Acquired obstruction—secondary obstructive hydrocephalus; sites include the interventricular foramina, mesencephalic aqueduct, or lateral apertures of the fourth ventricle.
- Overproduction of CSF (communicating)—rare; caused, for example, by a choroid plexus tumor.
- “Compensatory hydrocephalus”—condition wherein CSF fills the space where the neural parenchyma was destroyed; not true hydrocephalus; terminology obsolete.
- Clinical signs of neurologic dysfunction result from damage to neural parenchyma, which has a multifactorial etiology.

SYSTEMS AFFECTED

Nervous

GENETICS

Siamese cats—autosomal recessive

INCIDENCE/PREVALENCE

Unknown

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Congenital—small and brachycephalic dogs: bulldogs, Chihuahuas, Maltese, Pomeranians, toy poodles, Yorkshire terriers, Lhasa apsos, Cairn terriers, Boston terriers, Pug dogs, and Pekingese.
- Inherited—Siamese cats and Yorkshire terriers. High incidence of clinically asymptomatic

ventriculomegaly in normal adult beagles.

- Acquired—any breed of cat or dog.

Mean Age and Range

- Congenital—usually becomes apparent at a few weeks up to 1 year of age. Acute onset of signs can occur in dogs with previously undiagnosed congenital hydrocephalus. The exact cause of this decompensation is uncertain.
- Acquired—any age.

Predominant Sex

None

SIGNS

General Comments

- Congenital—may occur without clinical signs, especially in dogs of toy breeds; other malformations or anomalies of the CNS may be noted (e.g., malformations of the cerebellum or syringomyelia), which may further contribute to the constellation of signs.
- Acquired—signs attributable to the underlying disease may be as or more prominent than the signs attributable to the hydrocephalus.
- Severity of the clinical signs may not correspond to the degree of ventricular enlargement.

Historical Findings

- Behavioral—decreased awareness; lack of or loss of training ability (including house-training); excessive sleepiness; vocalization; sometimes hyperexcitability.
- Visual deficits including blindness.
- Seizures—may be noted.

Physical Examination Findings

- Head—may appear large and dome-shaped with an exaggerated “stop”; open sutures and/or persistent fontanelles often present, but these may be present without hydrocephalus and vice versa. Bilaterally divergent strabismus in some dogs with severe congenital hydrocephalus—due to malformation of the orbit or to brainstem dysfunction.

Neurologic Examination Findings

- Signs may be acute or gradual in onset, and may be static or progressive.
- A wide variety of signs of brain dysfunction can occur.
- Cerebral disease—abnormal behavior (dullness and sleepiness), cortical blindness (loss of vision with normal eyes and pupillary light reflexes), inappropriate vocalization, sometimes hyperexcitable, circling may be present in lateralized disease.
- Gait abnormalities—incoordination, ataxia, and decreased postural reactions.
- Seizures—may occur.
- Congenital form—malformation of the orbit during growth may result in a ventrolateral strabismus with normal oculocephalic movements; oculocephalic movements may be abnormal if brainstem dysfunction is the cause of strabismus.
- Severely increased ICP—stupor or coma, pinpoint or dilated fixed pupils, loss of normal oculocephalic movements (physiologic nystagmus), abnormal respiratory patterns,

decerebrate posture; may lead to fatal tentorial herniation.

- Severity of clinical signs may not correlate with ventricular size, although there is a tendency for worse clinical signs with greater enlargement of the ventricles.

CAUSES

- Congenital—numerous congenital malformations cause obstruction of the ventricular system and result in hydrocephalus; heritable malformation, prenatal infection (e.g., dogs: parainfluenza virus, cats: coronavirus), exposure to teratogens, brain hemorrhage secondary to dystocia, nutritional deficiency (vitamin A), other.
- Acquired—tumors, abscesses, and inflammatory diseases (including inflammation resulting from hemorrhage caused by traumatic injuries or other causes of bleeding).

RISK FACTORS

Animals with compensated hydrocephalus may decompensate in the face of an insult such as infection or trauma, resulting in development of clinical signs.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other congenital brain anomalies.
- Metabolic or toxic diseases resulting in cerebral dysfunction.
- Brain mass lesions or infectious diseases resulting in high intracranial pressure (hydrocephalus may coexist).
- Traumatic injury to the brain (hydrocephalus may coexist).

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

IMAGING

- Skull radiography (congenital)—enlarged domed cranium with open sutures and persistent fontanelles; cranial vault may have a ground-glass appearance; also may reveal calvarial thinning.
- CT and MRI—provide definite diagnosis.
- Ultrasonography through fontanelles may reveal enlarged ventricles.

DIAGNOSTIC PROCEDURES

- CSF—use caution when collecting sample if patient has high ICP (may lead to fatal brain herniation through the foramen magnum and/or beneath the tentorium cerebelli); composition normal if no other intracranial disease (e.g., neoplasia, inflammation), but frequently abnormal when acquired underlying disease is present.
- EEG—congenital: usually characteristic, including hypersynchrony, high amplitude (25–300 µV), and low frequency (1–7 Hz); acquired: varies.

PATHOLOGIC FINDINGS

- Brain—may be large with loss of the normal pattern of sulci and gyri; may see distortion of the parenchyma, including thinning of the

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H HYDROCEPHALUS

(CONTINUED)

cerebral cortex, rupture of the septum pellucidum, and atrophy of other adjacent structures; with severe disease, brain herniation may occur, either of the cerebrum and midbrain under the tentorium cerebelli or of the cerebellum and caudal medulla oblongata through the foramen magnum.

- Ventricular system—mildly to severely distended (either entirely or only the part rostral to the obstructive lesion); with non-communicating form, narrowing or blockage of the ventricular system due to inflammation or mass lesions.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—intensive care for patients with severe signs or when undergoing surgical therapy.
- Outpatient—patients with mild-to-moderate signs that can be treated medically.

NURSING CARE

Prevent secondary complications of recumbency for stuporous or comatose patients—avoid pressure sores; drying eyes; hypostatic lung congestion.

CLIENT EDUCATION

Advise client to observe for deterioration in mental alertness, vision, and behavior, which may signal worsening of the problem.

SURGICAL CONSIDERATIONS

- Surgical shunting of the CSF from the ventricles to the peritoneal cavity or right atrium—definitive treatment.
- Surgery should be considered only when medical management is ineffective or results in adverse side effects.
- Complications—shunt blockage occurs in up to 50% of patients; infection is less common; shunt revision commonly needed; over-shunting may result in severe and potentially fatal complications (collapse of the cerebral mantle).
- Clinical signs may not resolve completely; residual signs usually indicate irreversible brain damage.
- Surgery for a brain tumor or other mass lesion—consider if it is the underlying cause.



MEDICATIONS

DRUG(S) OF CHOICE

- Reduce CSF production. Data on the efficacy of corticosteroids in reducing CSF

production are conflicting, but beneficial clinical effects usually are seen (prednisone 0.25–0.5 mg/kg PO q12h or dexamethasone 0.1 mg/kg PO q12h); should be tapered to an alternate-day regimen and the dose lowered as far as possible. Carbonic anhydrase inhibitors: acetazolamide (10 mg/kg PO q8h) with or without furosemide (1 mg/kg q24h); electrolytes must be monitored frequently; long term use is unlikely to be beneficial and may lead to adverse consequences. Omeprazole has been reported to reduce CSF production in normal dogs in an experimental model, but no data is available on the usefulness of this drug in the clinical setting; anecdotal reports have been disappointing.

- Reduce ICP—osmotic diuretics: mannitol (1 g/kg slow IV infusion over 20 minutes; may repeat twice at 6-hour intervals); and/or loop diuretics: furosemide (dogs, 2–8 mg/kg IV, IM, SC q12h; cats, 1–2 mg/kg IV, IM, SC q12h). These are short-term treatments only, helpful for acute treatment of severe cases.
- Treat underlying cause—administer specific drugs when possible (e.g., antibiotics for bacterial infection, irradiation or surgery for neoplasia).

CONTRAINDICATIONS

Fluid therapy—use with caution with severe disease; do not overhydrate.

PRECAUTIONS

- Corticosteroids—long-term treatment may cause iatrogenic hyperadrenocorticism or hypoadrenocorticism if drug is suddenly withdrawn.
- Diuretics—may cause shock or electrolyte imbalances, especially hypokalemia with furosemide administration.



FOLLOW-UP

PATIENT MONITORING

Monitor for exacerbation of the hydrocephalus and for signs attributable to an underlying cause (e.g., intracranial neoplasia).

POSSIBLE COMPLICATIONS

- Brain herniation and death.
- Infection and blockage when ventriculo-peritoneal shunting is carried out; shunt revision and specific treatment for bacterial infection are then indicated.

EXPECTED COURSE AND PROGNOSIS

- Good to poor—depends on cause and severity.
- Mild congenital form—good prognosis; may require only occasional medical treatment.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Cerebellar hypoplasia in kittens congenitally infected with feline panleukopenia virus.

AGE-RELATED FACTORS

Congenital—usually seen in animals < 1 year old

SEE ALSO

Stupor and Coma

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- EEG = electroencephalogram
- ICP = intracranial pressure
- MRI = magnetic resonance imaging

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Client Education Handout
available online



BASICS

OVERVIEW

• Hydronephrosis causes progressive distention of the renal pelvis resulting in compression and atrophy of the renal parenchyma secondary to ureteral outflow tract obstruction and associated increased hydrostatic pressure. • Most often hydronephrosis is unilateral (~80–85%) and occurs secondary to complete or partial obstruction of the ureter by uroliths, ureteral strictures, ureteral or trigonal neoplasia, retroperitoneal disease causing extraluminal compression, spay stump granuloma, trauma, radiotherapy, and accidental ligation of the ureter during ovariohysterectomy, cryptorchectomy, or after ectopic ureter surgery. • Bilateral hydronephrosis is less common, resulting from ureteral stone disease, congenital ureteral strictures, trigonal neoplasia, or a urethral outflow obstruction. Severe hydronephrosis can also be seen in dogs with ectopic ureters (commonly males) associated with a ureterovesical junction (UVJ) stenosis.

SIGNALMENT

Dog and cat

SIGNS

Historical Findings

- Subclinical in some dogs/cats.
- Inappetence.
- Weight loss.
- Polydipsia and/or polyuria.
- Hematuria.
- Depression, diarrhea, vomiting associated with uremia in patients with bilateral hydronephrosis or with compromised function in the contralateral kidney.
- May be referable to the cause of the obstruction (e.g., abdominal pain).
- It is important to realize that most dogs and cats with a ureteral obstruction will continue to produce urine due to the unilateral nature of the condition or the presence of a partial, rather than complete, ureteral obstruction.

Physical Examination Findings

- Normal in some patients.
- Renomegaly.
- Big kidney–little kidney syndrome associated with a previous ureteral obstruction.
- Renal, abdominal, or lumbar pain.
- Abdominal mass—bladder or prostate.
- Trigonal, prostatic, vaginal, or urethral mass (including ureteroliths) palpable on rectal examination.

CAUSES & RISK FACTORS

Ureteral Diseases

- Ureteroliths
- Ureretal stricture ± circumcaecal ureter
- Neoplasia
- Ureteral fibrosis
- Ureteral ligation during ovariohysterectomy
- Secondary to congenital ectopic ureter
- Complication from previous ectopic ureter surgery

Lower Urogenital Tract Diseases

- Urinary bladder masses (e.g., transitional cell carcinoma)
- Prostatic disease (e.g., neoplasia)
- Vaginal mass
- Cryptorchectomy resulting in inadvertent prostatectomy

Retroperitoneal Disease

- Masses—granuloma, neoplasm, cyst, abscess, hematoma
- Perineal hernia
- Post-radiotherapy-induced fibrosis



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes for renal pelvic dilation—e.g., ureteral obstruction (stone, stricture, tumor), pyelonephritis, pyelonephrosis, IV fluid therapy, chronic kidney disease, PU/PD
- Other causes of renomegaly—e.g., neoplasia, cysts, and perinephric pseudocysts (cats)
- Other causes of abdominal pain—e.g., pancreatitis and peritonitis
- Intervertebral disc disease leading to lumbar pain.
- Other causes for azotemia—e.g., chronic kidney disease, dehydration, urethral obstruction

CBC/BIOCHEMISTRY/URINALYSIS

- Normal in some patients
- Loss of urine-concentrating ability (first abnormality detected), hematuria, pyuria
- Azotemia, hyperphosphatemia, hyperkalemia, and acidemia with either bilateral ureteral obstructions or concurrent renal parenchymal disease

IMAGING

- Abdominal radiographs may be normal or show nephroliths, ureteroliths, urocystoliths, urethroliths, renomegaly, prostatomegaly, reduced retroperitoneal contrast, ureteral distension, or urinary bladder distension.
- Ultrasonography reveals dilation of the renal pelvis and diverticula, with thinning of the renal parenchyma; dilation of one or both ureters is detected in some dogs/cats if the hydronephrosis is associated with a ureteral obstruction (most common cause). If ureteral dilation is present, evaluation for cause (UVJ tumor, stenosis; ureteral stones; ureteral stricture).
- Injection of radiographic contrast material via either excretory urography (not recommended) or by nephropelvocentesis and ureteropyelography may be required to determine the location and cause of obstruction.
- CT can be helpful. Most commonly ultrasound and radiographs will determine cause without the need for further contrast imaging.

DIAGNOSTIC PROCEDURES

Urethrocystoscopy or vaginoscopy may help determine the location and cause of lower urinary tract obstruction or presence of ureteral ectopia, UVJ stenosis.



TREATMENT

- Treat as an inpatient.
- Start supportive care (e.g., fluids, ± antibiotics) while performing diagnostic tests.
- Correct fluid and electrolyte deficits with intravenous fluid therapy over 12–24 hours, followed by maintenance fluids as needed. Patients with extreme polyuria may need higher maintenance fluid rates to maintain hydration.
- Pending reestablishment of urinary patency, relieve lower urinary tract obstruction by catheterization, serial cystocentesis, or tube cystostomy as soon as possible.
- Specific treatment (e.g., interventional or surgical) depends on the cause and whether there is concurrent kidney disease or other disease processes (e.g., bilateral uroliths affecting contralateral kidney and/or ureter, metastatic neoplasia, etc.).
- Emergency surgery often required for a ureteral obstruction; metabolic and electrolyte abnormalities should be corrected prior to surgery.
- Nephrectomy is rarely ever indicated (e.g., neoplasia). If a ureteral obstruction is present, traditional ureteral surgery (ureterotomy, ureteral re-implantation) or more novel interventional therapies such as subcutaneous ureteral bypass (cat) or endoscopic ureteral stent placement (dog) should be considered.
- Referral to an experienced clinician is mandatory for the best ultimate outcome.

H



MEDICATIONS

DRUG(S)

- For a ureteral obstruction caused by uroliths alpha-adrenergic blockade should be considered (prazosin 0.25 mg/cat q12h or 1 mg/15 kg dog q8–12h).
- IV fluid diuresis; being careful to avoid overhydration.
- Diuretics, e.g., mannitol (0.25 g/kg bolus over 30 minutes then 1 mg/kg/min constant rate infusion (CRI) for 24 hours).
- Hyperkalemia (mild to moderate) often resolves with fluid replacement and/or bicarbonate administration unless bilateral obstruction and/or oliguria is present. Severe, symptomatic hyperkalemia requires more aggressive medical or surgical management for emergent decompression (ie. calling for prompt action).

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Do not add or mix sodium bicarbonate with calcium-containing fluids.
- Do not give radiographic contrast material intravenously until the patient is rehydrated. Use radiographic contrast material with caution in azotemic patients.

HYDRONEPHROSIS

(CONTINUED)

SPECIAL CONSIDERATIONS

Patients with ureteral obstruction(s) should be considered an emergency and referred to colleagues who are highly experienced in managing this condition.



FOLLOW-UP

PATIENT MONITORING

- Ultrasonography—can repeat at 2- to 4-week intervals after relief of obstruction to assess improvement. Often some signs of resolution appear within days after relief of obstruction but can take up to 3 months.
- Monitor serum chemistries and electrolytes as needed. • After relief of obstruction—polyuria and post-obstructive diuresis may lead to hypokalemia, weight loss, dehydration, and possibly permanent renal injury so care should be taken to monitor these patients carefully.

POSSIBLE COMPLICATIONS

Rupture of the excretory system and irreversible renal damage. Decompression

should be considered when medical management fails to relieve obstruction.

EXPECTED COURSE AND PROGNOSIS

- Variable depending on the cause, duration of obstruction, and presence or absence of concurrent infection.
- Irreversible damage to the kidney usually begins 15–45 days after obstruction.
- If the obstruction is relieved within 2–4 weeks, some renal damage is reversible. If the obstruction is partial (over 80% of cases), the time before irreversible damage is prolonged.
- Concurrent infection accelerates the severity of renal damage. Antimicrobial therapy should be initiated when pyelonephritis is suspected.



MISCELLANEOUS

SEE ALSO

- Acidosis, metabolic • Hyperkalemia • Renal Failure, Acute • Renal Failure, Chronic

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Client Education Handout
available online

HYPERADRENOCORTICISM (CUSHING'S SYNDROME)—CATS



BASICS

OVERVIEW

Feline Cushing's (hyperadrenocorticism or HAC) syndrome is a disorder of excessive cortisol secretion by the adrenal glands.

PATHOPHYSIOLOGY

- Spontaneous FCS—caused by overproduction of cortisol by the adrenal glands.
- Approximately 85% of cats with FCS have bilateral adrenocortical hyperplasia resulting from pituitary hyperplasia or tumor. The remaining 15% have an adrenal tumor, half of which are benign and half malignant. Regardless of the cause, FCS is usually (80%) accompanied by diabetes mellitus.

SIGNALMENT

- Cat
- No known breed or sex predisposition
- Middle-aged to older cats

SIGNS

- Polyuria, polydipsia, polyphagia, fragile (bruising, tearing, thin) skin, weight loss, and muscle weakness are most common.
- Obesity, hepatomegaly, alopecia, diarrhea, vomiting, abdominal enlargement, curled ear tips, and unkempt appearance are also seen.
- Lethargy (dullness) has been reported due to muscle weakness or the effects of a pituitary mass.
- Excess sex hormones can cause signs such as penile barbs and behavioral changes (sexual behavior).

CAUSES & RISK FACTORS

- Pituitary adenoma with subsequent corticotrophic hyperplasia and excess adrenocortical cortisol secretion.
- Autonomously functioning benign adenoma (50%) or malignant adenocarcinoma (50%).
- Iatrogenic due to glucocorticoid administration is rare.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Diabetes mellitus
- Insulin resistance
- Acromegaly
- Hepatopathy
- Renal disease
- Sex hormone-secreting adrenal tumors
- Hypothyroidism

CBC/BIOCHEMISTRY/URINALYSIS

- Stress leukogram.
- Hyperglycemia, hypercholesterolemia, mild increased ALT due to poorly regulated concomitant diabetes mellitus.
- High serum alkaline phosphatase not common because cats do not have corticoid-induced isoenzyme.
- Elevated urine cortisol:creatinine ratio (UC:Cr) is common.
- Less common—azotemia, proteinuria, and hyperglobulinemia.

OTHER LABORATORY TESTS

Screening Tests

- UC:Cr—sensitive (useful for its negative

predictive value, i.e., if a normal UC:Cr is obtained, FCS is unlikely), inexpensive, and easy to perform and interpret. Home collection (non-stressed) of urine is preferred.

- Low-dose dexamethasone-suppression test (LDDST)—extremely sensitive. Requires ten times the dose used in dogs: 0.1 mg/kg IV. Plasma obtained for cortisol before and 4 and 8 hours after dexamethasone administration. Failure to suppress is consistent with FCS.
- ACTH stimulation test, mainly a test of adrenal reserve—requires little time, is easy to interpret, is relatively inexpensive, and is specific for FCS when results are abnormal.

Differentiating Tests

- High-dose dexamethasone-suppression test (HDDST)—1 mg/kg dexamethasone, protocol as with LDDST. An at-home version using multiple UC:Crs and oral dexamethasone is easier to perform and interpret than the in-hospital protocol.
- Plasma endogenous ACTH measurement is high normal or greater with PDH compared to low plasma ACTH levels with AT (< 10 pg/mL). The normal range for cats is 0–60 pg/mL. Blood is collected in EDTA, spun immediately, and the plasma transferred to plastic and frozen.
- “At home” dexamethasone-suppression protocol—have owners collect morning urine samples on days 1, 2, and 3. Give oral doses of dexamethasone (LDDST [0.1 mg/kg] or HDDST [1 mg/kg]) at 6-h intervals for 2 days. Submit all three urine samples for UC:Cr ratio. Days 1 and 2 are basal values. Day 3 suppression less than 50% is not seen in cats with AT but may be seen with PDH.

IMAGING

- Abdominal ultrasound preferred to visualize adrenal glands. Although subjective, ultrasonography can be an excellent tool to discern PDH from AT. Symmetric adrenal glands of normal or enlarged size are suggestive of PDH, whereas unilateral enlargement supports AT.
- CT and MRI allow visualization of pituitary macroadenomas.

DIAGNOSTIC PROCEDURES

Sex hormone panels or insulin-like growth factor-1 (IGF-1) obtained to rule-out differentials.



TREATMENT

- FCS is a debilitating disease. Compared to dogs, options with cats are more limited and not as successful.
- Medical pretreatment prior to surgery is beneficial to prevent complications from fragile skin, infections, and bruising.
- Pituitary cobalt radiation of PDH has the potential to become a part of FCS treatment.
- Unilateral adrenalectomy for AT and bilateral adrenalectomy for PDH (with medical management of

hypoadrenocorticism) appear to be the most successful treatment options.

- Desoxycorticosterone pivalate (DOCP) and depo-medrol may be required.
- Hypophysectomy (microsurgical transsphenoidal) is available at some institutions.



MEDICATIONS

DRUG(S)

- Mitotane (Lysodren; o,p'-DDD) causes selective destruction of cortisol-secreting adrenocortical cells. Doses of 50 mg/kg/day divided have been used, but even when doubled sometimes failed to demonstrate improvement.
- Trilostane reversibly inhibits 3- β -17-hydroxysteroid dehydrogenase, which blocks steroid synthesis. In a majority of cases of FCS with PDH, trilostane reduced clinical signs and improved endocrine test results. Doses up to 60 mg/cat PO q12h have been used.
- Other medications have been used with some limited success (ketoconazole, metyrapone, and aminoglutethimide).

H



FOLLOW-UP

- Clinical improvement with reduced signs of FCS is supportive of beneficial drug therapy.
- Repeated UC:Cr and ACTH stimulation tests can be beneficial.



MISCELLANEOUS

ABBREVIATIONS

- ACTH = adrenocortotropic hormone
- AT = adrenal tumor
- CT = computed tomography
- FCS = feline Cushing's syndrome
- HAC = hyperadrenocorticism
- HDDST = high-dose dexamethasone-suppression test
- LDDST = low-dose dexamethasone-suppression test
- MRI = magnetic resonance imaging
- PDH = pituitary-dependent hyperadrenocorticism
- UC:Cr = urine cortisol:creatinine ratio

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HYPERADRENOCORTICISM (CUSHING'S SYNDROME)—DOGS



BASICS

DEFINITION

- Spontaneous hyperadrenocorticism (HAC) is a disorder caused by excessive production of cortisol by the adrenal cortex.
- Iatrogenic HAC results from excessive exogenous administration of glucocorticoids of any form or by any route.
- In either instance, clinical signs are due to deleterious effects of elevated circulating glucocorticoid concentrations on multiple organ systems.

PATOPHYSIOLOGY

- Approximately 80–85% of cases of naturally occurring HAC are due to bilateral adrenocortical hyperplasia resulting from pituitary corticotroph tumors or hyperplasia with oversecretion of ACTH.
- In the remaining 15–20% of cases, cortisol-secreting adrenocortical neoplasia is present; approximately one-half of these are malignant.
- Rarely caused by ectopic ACTH secretion from a non-pituitary tumor.
- Iatrogenic HAC results from excessive administration of exogenous glucocorticoids.

SYSTEMS AFFECTED

- The degree to which each system is involved varies considerably; signs referable to one system may predominate or several systems may be involved to a comparable degree.
- Signs referable to the urinary tract or skin often predominate.
- Endocrine/Metabolic—hyperglycemia; diabetes mellitus occurs in 10%.
- Cardiovascular—hypertension (usually mild).
- Gastrointestinal—polyphagia.
- Hemic/Lymphatic/Immune—stress leukogram; immunosuppression; mild erythrocytosis and thrombocytosis.
- Hepatobiliary—hepatopathy due to glycogen deposition; increased serum ALP activity due to production of corticosteroid-induced isoenzyme.
- Neuromuscular—muscle weakness; CNS signs including anorexia, ataxia, disorientation and, uncommonly, seizures if pituitary macroadenoma present.
- Renal/Urologic—polyuria/polydipsia in 90% of cases; proteinuria; UTI common.
- Reproductive—testicular atrophy and anestrus.
- Respiratory—panting; pulmonary thromboembolism possible due to a hypercoagulable state.
- Skin—bilaterally symmetric alopecia common; comedones; hyperpigmentation; recurrent pyoderma.

GENETICS

No genetic basis known.

INCIDENCE/PREVALENCE

- No exact figures available.
- Considered one of most common endocrine disorders in dogs.

SIGNALMENT

Species

Dog

Breed Predilections

Poodle, dachshund, Boston terrier, German shepherd dog, and beagle.

Mean Age and Range

Generally a disorder of middle-aged to old animals; pituitary-dependent HAC (PDH) can very rarely be seen in dogs as young as 1 year.

Predominant Sex

No predilection for PDH in dogs; possible predilection for female dogs to have an adrenal tumor.

SIGNS

General Comments

- Severity varies greatly, depending on duration and severity of cortisol excess.
- In some cases, the physical presence of the neoplastic process (pituitary or adrenal) contributes.

Historical and Physical Examination Findings

Polyuria and polydipsia, polyphagia, pendulous abdomen, increased panting, hepatomegaly, hair loss, cutaneous hyperpigmentation, thin skin, muscle weakness, obesity, lethargy, muscle atrophy, comedones, bruising, testicular atrophy, anestrus, calcinosis cutis, facial nerve palsy.

CAUSES

- Pituitary-dependent—adenoma most common; adenocarcinomas rare; anterior pituitary involved in approximately 80% of cases, intermediate lobe in remaining cases; exact incidence of pituitary macroadenomas (i.e., > 1 cm diameter) unknown, may be 10–25%.
- Adrenal tumor—adenoma or carcinoma (50/50).
- Ectopic ACTH secretion—rare.
- Iatrogenic—due to glucocorticoid administration.

RISK FACTORS

- None known for spontaneous disease.
- Presence any condition that leads to exogenous glucocorticoid administration is a risk factor for iatrogenic HAC.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Depends on clinical and laboratory abnormalities displayed.
- Includes hypothyroidism, sex hormone dermatoses, Alopecia X, sex hormone-secreting tumors, acromegaly, diabetes mellitus, hepatopathies, renal disease, and other causes of polyuria/polydipsia.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram may show eosinopenia, lymphopenia, leukocytosis, neutrophilia, erythrocytosis and/or thrombocytosis.
- Serum chemistry may show high liver enzymes, cholesterol, and total CO₂; alkaline

phosphatase activity high in approximately 90% and ALP elevations are proportionately greater than that for ALT; hyperglycemia common but only about 10% of dogs with HAC have concurrent diabetes mellitus.

- Urinalysis may reveal low specific gravity, proteinuria, hematuria, pyuria and/or bacteriuria.

OTHER LABORATORY TESTS

- Endocrine testing required in dogs with history, clinical signs, and laboratory abnormalities suggestive of HAC.
- Do not perform testing for HAC in sick dogs unless clinical signs consistent with HAC are present.
- Screening tests are designed to determine if HAC is present or not.
- Once a diagnosis of HAC is made, a differentiation test should be performed to determine if PDH or AT is present; differentiation provides information crucial to therapeutic decisions and an accurate prognosis.
- Differentiation tests should never be performed before a diagnosis of HAC is made via screening tests.
- See Appendix II for table of endocrine test protocols.
- To convert cortisol concentration in nmol/L to µg/dL, divide by 27.6.
- All cortisol concentrations below used for illustration purposes; check with your own laboratory for its normal ranges and cut-off values.

Screening Tests

Urine Cortisol:Creatinine Ratio (UC:Cr)

- Urine cortisol excretion increases as a reflection of augmented adrenal secretion of the hormone, whether PDH or AT present.
- An elevated UC:Cr is a sensitive marker of HAC, present in 90–100% of affected dogs.
- Should be measured in a sample collected at home when the pet not stressed.
- False-positive results common; only about 20% of dogs with an elevated UC:Cr have HAC.
- A normal ratio makes the diagnosis of HAC very unlikely ($\leq 10\%$ chance).
- Elevated ratio consistent with a diagnosis of HAC, but since the chance of a false-positive result is great, an ACTH stimulation test or low-dose dexamethasone suppression test must always be done to confirm the presence of HAC.

Low-Dose Dexamethasone Suppression Test

- Lack of suppression 8 hours after an injection of a low dose of dexamethasone consistent with a diagnosis of HAC.
- Sensitivity approximately 95% in dogs.
- In dogs, there is a relatively high chance of a false-positive result, up to 50%, if non-adrenal illness is present.
- Lack of suppression at 4 hours but with full suppression at 8 hours is technically not consistent with HAC but is suspicious for its presence; further testing warranted.
- With certain results, the LDDST may also serve as a differentiation test; if the 8-hour sample is > 30 nmol/L, the result is consistent with HAC; if, in addition,

(CONTINUED) HYPERADRENOCORTICISM (CUSHING'S SYNDROME)—DOGS

there is suppression to < 30 nmol/L at 4 h post-dexamethasone (i.e., an “escape” at 8 hours post-dexamethasone) or the 4- and/or 8-h post-dexamethasone samples are < 50% of baseline, the results are consistent with PDH; if criteria for PDH not met, chances are still approximately 50/50 for PDH versus AT. • If baseline values close to 30 nmol/L or suppression just at 50%, presence of PDH should be confirmed by other means. • A protocol exists in Europe where a minimum of two morning urine samples are collected and then dexamethasone is administered (3 doses over 24 h) for differentiating purposes and another urine sample is collected. The protocol reportedly has high sensitivity and specificity. However, the cortisol assay used is proprietary and not commercially available. The accuracy of the protocol using cortisol assays commercially available in the United States has not been established, and, thus, the method is not recommended for use in the United States and Canada.

ACTH Stimulation Test

- A response greater than normal is consistent with a diagnosis of spontaneous HAC.
- Overall sensitivity of the test approximately 80%; for PDH, sensitivity is approximately 87%, while for HAC due to an AT, sensitivity is approximately 61%. • More specific in dogs than the LDDST (only 15% chance of a false-positive result with non-adrenal illness).
- Can never differentiate between PDH and AT. • Only test that can diagnose iatrogenic HAC; a diagnosis is made with a history of glucocorticoid exposure by any route, presence of consistent clinical signs and a post-ACTH cortisol concentration below the reference range. • Cortrosyn is the recommended form of ACTH to use; if using compounded ACTH, collect samples before and at 1 and 2 hours post-ACTH administration so peak response not missed.

Differentiating Tests**High-Dose Dexamethasone Suppression Test**

- Two responses consistent with PDH; if there is suppression to < 30 nmol/L at 4 and/or 8 hours post-dexamethasone or the 4-and/or 8-h post-dexamethasone samples are < 50% of baseline, PDH is present. • If baseline values close to 30 nmol/L or suppression just at 50%, presence of PDH should be confirmed by other means. • Can never confirm presence of an AT; if criteria for diagnosis of PDH not met, there is a 50/50 chance the patient has PDH or an AT.

Endogenous ACTH Concentration

- Requires only a single blood sample but special handling needed. • In patients with PDH, endogenous ACTH (eACTH) concentration is normal to increased; with AT, eACTH concentration is below normal.
- Can be used to confirm the presence of an AT. • A gray zone exists in the results; if the

patient's eACTH concentration falls into this zone, results not diagnostic. • With repeat testing when the original concentration measured is in the gray zone (about 15% chance), approximately 96% have definitive differentiation. • There is no way to predict when eACTH concentration will be in the gray zone.

IMAGING

- Abdominal radiographs may differentiate PDH from AT; approximately 40–50% of canine ATs are visualized; adrenal mineralization is highly suspicious for the presence of an AT. • Chest radiographs indicated in patients with an AT to check for metastases. • Ultrasonography, CT, and MRI—useful for differentiating PDH from AT and for staging AT; abdominal ultrasonography can never be used as a screening test as bilateral adrenal enlargement may be seen due to chronic non-adrenal illness; AT can be small and may be difficult to see with ultrasonography; vena caval, hepatic or renal invasion is an indicator of malignancy; adrenal atrophy can be difficult to determine with ultrasonography. • CT and MRI—often useful for demonstrating pituitary macroadenomas. • Since radiation therapy, a treatment modality required for a pituitary macroadenoma, is more effective for smaller tumors, some authors advocate routine pituitary imaging in all dogs when PDH diagnosed; follow-up and treatment recommendations vary depending on tumor size.

DIAGNOSTIC PROCEDURES

Adrenal biopsy (usually performed on AT obtained via adrenalectomy) often needed to differentiate benign vs. malignant tumor.

PATHOLOGIC FINDINGS

- PDH—gross examination reveals normal-to-enlarged pituitary and bilateral adrenocortical enlargement. • Microscopically, pituitary adenoma, adenocarcinoma, or corticotroph hyperplasia of pars distalis or pars intermedia and adrenocortical hyperplasia. • AT—gross examination reveals variable-sized adrenal mass, atrophy of contralateral gland (rarely bilateral tumors), and metastasis in some patients with adrenal carcinoma; invasion into vena cava or vena caval thrombosis may be seen with malignant tumors. • Microscopically, see adrenocortical adenoma or carcinoma.
- With any form HAC, general changes of cortisol excess may be seen such as cutaneous atrophy and glomerulopathy.

**TREATMENT****APPROPRIATE HEALTH CARE**

Dictated by severity of clinical signs, patient's overall condition, and any complicating

factors (e.g., diabetes mellitus, pulmonary thromboembolism).

NURSING CARE

Variable as above.

ACTIVITY

No alteration of activity necessary.

DIET

Usually no need to alter; use appropriate diet if diabetes mellitus concurrent.

CLIENT EDUCATION

- If using medical therapy, life-long therapy required. • If adverse reaction to mitotane or trilostane occurs—discontinue drug, give prednisone, and have veterinarian reevaluate next day; if no response to prednisone noted in a few hours, veterinarian should evaluate immediately.

SURGICAL CONSIDERATIONS

- Hypophysectomy—described, but generally not available in the United States. • Bilateral adrenalectomy not used for treatment of PDH in dogs • Surgery is the treatment of choice in dogs with adrenocortical adenomas and small carcinomas unless the patient is a poor surgical risk or the client refuses surgery.
- Appropriate personnel and facilities are required as adrenalectomy is a technically demanding surgery and intensive postoperative management is required.
- Removal of tumor and vena caval thrombi can be performed; surgery not expected to be curative in such cases, but long-term survival can be achieved, e.g., > 1 year. • Depending on patient status, medical control of HAC may be desirable prior to surgery, if possible.

**MEDICATIONS****DRUG(S) OF CHOICE****Mitotane**

- Mitotane (*o,p'*-DDD, Lysodren) is one of two main drugs used for medical management of PDH in dogs; selectively destroys glucocorticoid-secreting cells of the adrenal cortex; may be drug of choice for medical management of AT since it may destroy tumor cells as well as control cortisol secretion.
- PDH—give an initial loading dose of 40–50 mg/kg divided twice daily; evaluate efficacy with ACTH stimulation test after 8 days or sooner if decreased appetite, vomiting, diarrhea, listlessness or decreased water intake (< 60 mL/kg/day) noted; goal is for both basal and post-ACTH cortisol concentration to be in ideal range of 30–150 nmol/L; continue induction with repeat testing as necessary until adequate response seen, then initiate maintenance therapy at 50 mg/kg/week divided into two to three doses; dosage adjustments based on ACTH stimulation testing (maintain basal

HYPERADRENOCORTICISM (CUSHING'S SYNDROME)—DOGS (CONTINUED)

and post-ACTH cortisol levels within ideal range); if serum cortisol concentration pre- or post-ACTH < 30 nmol/L, stop administering mitotane and administer physiologic doses prednisone (0.1 mg/kg q12h); cannot administer prednisone within 12 hours before ACTH stimulation test; perform ACTH stimulation tests every 7–14 days initially; cortisol secretion usually recovers in weeks to a couple months but can take longer; once cortisol concentration is in ideal range, discontinue prednisone and begin maintenance therapy; if had been on maintenance therapy when became cortisol deficient, restart maintenance at 25% lower dose; if relapse occurs at any time while on maintenance therapy, as indicated by cortisol levels above ideal range, dose adjustment required; if post-ACTH serum cortisol concentration 150–300 nmol/L, increase maintenance dose 25% and reevaluate in 4 weeks; if post-ACTH serum cortisol concentration > 300 nmol/L, reload for 5–7 days and do an ACTH stimulation test; continue loading until cortisol concentration is in ideal range, then reinstitute weekly maintenance dose at approximately 50% higher dose.

- AT—goal of mitotane use is low-to-non-detectable (i.e., < 30 nmol/L) basal and post-ACTH cortisol concentrations; starting dose 50–75 mg/kg divided daily; perform ACTH stimulation test after 10–14 days to evaluate efficacy or sooner if decreased appetite, vomiting, diarrhea, listlessness or decreased water intake (< 60 mL/kg/day) noted; induction typically requires higher doses and is of longer duration than for treatment of PDH; dose should be increased by 50 mg/kg/day every 10–14 days if control has not been achieved as judged by an ACTH stimulation test; if adverse effects develop due to mitotane, administration should continue at highest tolerable dose; once control achieved, maintenance therapy should begin at 75–100 mg/kg/wk divided into 2–3 doses; if cortisol levels pre- and post-ACTH rise into normal resting range (i.e., 10–160 nmol/L), increase maintenance dose 50%; if cortisol levels rise above normal resting range pre- and post-ACTH, reload until control achieved and increase weekly maintenance dose approximately 50%; during induction and maintenance, since goal is to create glucocorticoid insufficiency, give prednisone at 0.2 mg/kg/day.
- Aldosterone deficiency possible secondary to mitotane therapy; if occurs, likely patient will have permanent complete adrenocortical insufficiency; treatment for hypoadrenocorticism should be initiated.

Trilostane

- Trilostane (Vetoryl) is approved for use in Europe and the United States; efficacy for treatment of PDH high, comparable to mitotane; survival of dogs with PDH is same

for dogs treated with mitotane or trilostane; inhibits adrenocortical enzyme 11- β -hydroxysteroid dehydrogenase and maybe others, thereby suppressing production of progesterone and its end-products, including cortisol and aldosterone.

- Initial dose is 2.2–6.7 mg/kg PO q24h or divided q12h; if minor side effects are seen (i.e., anorexia, vomiting, diarrhea), stop the drug for 3–5 days and then restart q48h for 1 week before continuing with initial dosing scheme; an ACTH stimulation test should be performed beginning 4–6 hours post-pill at 10–14 days, 30 days, and 90 days after being on a full dose; if at the 10–14 day recheck any improvement is seen, do not increase the dose even if cortisol concentrations above ideal but wait until the 30 day recheck and change the dose then if needed. If post-ACTH cortisol concentration is < 40 nmol/L and the patient feels well, stop the trilostane for 48–72 hours and then either restart at a lower dose, or, ideally, an ACTH stimulation test should be performed and trilostane not reinstated until cortisol secretion has recovered; if the post-ACTH cortisol concentration is 40–150 and clinical signs have resolved, the dose should continue as is; if the post-ACTH cortisol concentration is 150–250 nmol/L, increase the trilostane dose if clinical signs are present or, if the clinical signs have resolved, leave as is but monitor carefully for signs of recurrence; if the post-ACTH serum cortisol concentration is > 250 nmol/L, increase once-daily dose or twice-daily therapy should be used; the same dose given once-daily should be divided and given twice (e.g., if giving 60 mg once daily then give 30 mg q12h); if post-ACTH serum cortisol concentration is 40–150 nmol/L but clinical signs are continuing, use twice-daily therapy; once the dog's clinical condition and dose have stabilized, an ACTH stimulation test should be performed every 3–6 months and serum potassium concentration measured to check for hyperkalemia.
- Since trilostane can suppress aldosterone secretion, an Addisonian crisis can occur; adrenocortical necrosis secondary to trilostane administration may be more common than previously believed; hypocortisolemia secondary to trilostane administration usually resolves within 48–72 hours of discontinuation of drug administration, but temporary suppression of weeks to months and even permanent suppression can occur.
- Can be used to treat AT and will control clinical signs, at least transiently, but not the drug of choice; for AT, mitotane is the drug of choice as it is truly chemotherapeutic and may kill tumor cells.

I-Deprenyl

- I-Deprenyl (selegiline hydrochloride) FDA approved for treatment of PDH; decreases pituitary ACTH secretion by increasing dopaminergic tone in the hypothalamic-

pituitary axis, thus decreasing serum cortisol concentrations; indicated only for treating uncomplicated PDH; not recommended for dogs with concurrent illnesses such as diabetes mellitus; cannot be used to treat AT; initiate therapy with 1 mg/kg daily and increase to 2 mg/kg/day after 2 months if response inadequate; if higher dose also ineffective, give alternative therapy; no objective monitoring; assessment of efficacy based on subjective evaluation of remission of clinical signs.

- Efficacy questionable; one study found 20% efficacy and another judged L-deprenyl ineffective.

- Adverse effects such as anorexia, lethargy, vomiting, and diarrhea uncommon (< 5% of dogs) and usually mild; disadvantages include need for lifelong daily administration and medication expense.

Ketoconazole

Ketoconazole (10 mg/kg PO q12h initially; up to 20 mg/kg PO q12h in some dogs) inhibits enzymes responsible for cortisol synthesis; indicated for dogs unable to tolerate mitotane at doses necessary to control HAC; may be useful for palliation of clinical signs of HAC in dogs with AT; monitoring done by performance of ACTH stimulation tests with same goals as for mitotane; efficacy approximately 50% or less; adverse effects include anorexia, vomiting, diarrhea, lethargy, thrombocytopenia and idiosyncratic hepatopathy.

CONTRAINdications

- Do not use nonsteroidal anti-inflammatory agents in dogs with uncontrolled HAC.
- Drugs that increase blood pressure or coagulation should be used with caution.

PRECAUTIONS

- Side effects of mitotane not uncommon; mild in most dogs; include lethargy, weakness, anorexia, vomiting, diarrhea, ataxia, and iatrogenic hypoadrenocorticism. • Side effects more common in dogs with AT given high doses of mitotane. • For mitotane, use with caution in patients with renal insufficiency and primary hepatic disease. • Side effects of ketoconazole seem to be less common; include anorexia, vomiting, diarrhea, thrombocytopenia, and hepatopathy. • For ketoconazole, use with caution in patients with primary hepatic disease or thrombocytopenia; effect on breeding ability unknown. • Side effects of l-deprenyl uncommon. • Side effects of trilostane include anorexia, lethargy, vomiting and diarrhea; may occur in approximately 60% of patients; Addisonian crisis and adrenocortical necrosis have been reported. • For trilostane, use with caution in patients with renal insufficiency and primary hepatic disease; contraindicated in pregnancy. • For all drugs, if using on a diabetic patient, careful monitoring needed; insulin needs can decrease rapidly with control of HAC.

(CONTINUED) HYPERADRENOCORTICISM (CUSHING'S SYNDROME)—DOGS

ALTERNATIVE DRUG(S)

Radiation therapy required for animals with pituitary macroadenomas; ACTH levels may take several months to decrease; control HAC with above drugs in the interim.

**FOLLOW-UP****PATIENT MONITORING**

Response to therapy—use periodic ACTH stimulation testing to assess mitotane, ketoconazole, or trilostane efficacy (see above for details); once on maintenance mitotane therapy, test at 1, 3, and 6 months and every 3–6 months thereafter or if clinical signs of HAC recur; adequacy of any necessary mitotane reloading period is checked with an ACTH stimulation test before higher maintenance mitotane dose initiated; adequacy of ketoconazole or trilostane dose checked with an ACTH stimulation test after any dose alteration; with trilostane, ACTH stimulation test should be performed starting 4–6 hours post-pill, while with mitotane and ketoconazole, post-pill timing does not matter; clinical signs of HAC resolve several days to months after control achieved; evaluate efficacy of l-deprenyl therapy solely on the basis of resolution of clinical signs of HAC.

PREVENTION/AVOIDANCE

For prevention of recurrence, regular administration of medications with appropriate follow-up required.

POSSIBLE COMPLICATIONS

- Hypertension • Proteinuria • Recurrent infection • Urinary calculi (calcium oxalate)
- Diabetes mellitus • Pulmonary thromboembolism • Neurologic signs secondary to a pituitary macroadenoma

EXPECTED COURSE AND PROGNOSIS

- Untreated HAC—generally a progressive disorder with a poor prognosis. • Treated PDH—usually a good prognosis; median

survival time with mitotane or trilostane treatment approximately 2 years; at least 10% survive 4 years; dogs living longer than 6 months tend to die of causes unrelated to HAC. • Macroadenomas and neurologic signs—poor-to-grave prognosis; macroadenomas with no or mild neurologic signs—fair-to-good prognosis with radiation and medical therapy. • Adrenal adenomas—usually good-to-excellent prognosis; small carcinomas (not metastasized) fair-to-good prognosis overall, good-to-excellent with surgical resection. • Large carcinomas and AT with widespread metastasis—generally poor-to-fair prognosis, but impressive responses to high doses of mitotane occasionally seen.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Neurologic signs in dogs with large pituitary tumors; glucose intolerance or concurrent diabetes mellitus; pulmonary thromboembolism; increased incidence of infections, especially urinary tract and skin; hypertension; proteinuria/glomerulopathy.

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

Cushing's disease; Cushing's syndrome

SEE ALSO

Hyperadrenocorticism (Cushing's Syndrome)—Cats

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone
- ALP = alkaline phosphatase • ALT = alanine aminotransferase • AT = adrenal tumor • CNS = central nervous system
- CT = computed tomography • eACTH = endogenous ACTH • HAC = hyperadrenocorticism • HDDST = high-dose dexamethasone-suppression test • LDDST = low-dose dexamethasone-suppression test
- MRI = magnetic resonance imaging

- PDH = pituitary-dependent hyperadrenocorticism • UC:Cr = urine cortisol:creatinine ratio • UTI = urinary tract infection

INTERNET RESOURCES

www.dechra.com: good information on use of trilostane.

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Client Education Handout
available online

H

HYPERCALCEMIA



BASICS

DEFINITION

- Serum total calcium > 11.5 mg/dL (dogs).
- Serum total calcium > 10.5 mg/dL (cats).
- Serum ionized calcium > 1.45 mmol/L (dogs).
- Serum ionized calcium > 1.4 mmol/L (cats).
- Hypercalcemia must be confirmed by demonstration of increased concentrations of ionized calcium.
- Total calcium concentrations and correction formulas do not accurately predict ionized calcium.

H

PATHOPHYSIOLOGY

- Control of calcium is complex and is influenced by the actions of PTH and vitamin D and the interaction of these hormones with the gut, bone, kidneys, and parathyroid glands.
- Derangement in the function of these can lead to hypercalcemia.
- Secretory products of some neoplastic cells can also disturb calcium homeostasis.

SYSTEMS AFFECTED

- Cardiovascular—hypertension and altered cardiac contractility.
- Gastrointestinal—reduces excitability of smooth muscle and can alter gastrointestinal function.
- Neuromuscular—depressed skeletal muscle contractility causes weakness.
- Renal/Urologic—high levels of calcium are toxic to the renal tubules and can cause polyuria and polydipsia (PU/PD) and renal failure; can also lead to urolithiasis and associated lower urinary tract disease.

SIGNALMENT

- Dog and cat
- Primary hyperparathyroidism in the Keeshond and Siamese cat

SIGNS

General Comments

- Depend on the cause of hypercalcemia.
- Patients with underlying neoplasia, renal failure, or hypoadrenocorticism generally appear ill.
- Patients with primary hyperparathyroidism show mild clinical signs, if any, due solely to the effects of hypercalcemia.
- Signs become apparent when hypercalcemia is severe and chronic.

Historical Findings

- Many animals have no clinical signs.
- PU/PD—most common in dogs.
- Anorexia.
- Lethargy—most common in cats.
- Vomiting.
- Constipation.
- Weakness.
- Stupor and coma—severe cases.

- Lower urinary tract signs in animals with secondary calcium-containing uroliths.

Physical Examination Findings

- Lymphadenomegaly or abdominal organomegaly in patients with lymphoma.
- Usually unremarkable in dogs with primary hyperparathyroidism.
- Parathyroid gland adenoma—rarely palpable in dogs; often palpable in cats with primary hyperparathyroidism but can be confused with the thyroid gland.

CAUSES

- Neoplasia—lymphoma (most common in dogs, less common in cats), anal sac apocrine gland adenocarcinoma (dogs), multiple myeloma, lymphocytic leukemia, metastatic bone tumor, fibrosarcoma (cats), various types of carcinoma.
- Primary hyperparathyroidism.
- Renal failure—acute or chronic.
- Granulomatous diseases.
- Hypoadrenocorticism.
- Vitamin D rodenticide intoxication—no longer marketed in the United States.
- Vitamin D intoxication from plant or food sources.
- Osteolytic diseases.
- Aluminum toxicosis.
- Idiopathic hypercalcemia in cats.

RISK FACTORS

- Keeshond breed—hyperparathyroidism
- Renal failure
- Neoplasia
- Use of calcium supplements or calcium-containing intestinal phosphate binders
- Use of calcitriol or other vitamin D preparations



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- History should include exposure to exogenous vitamin D sources and any previous response to steroids.
- History of waxing/waning illness suggests hypoadrenocorticism.
- Complete lymph node, rectal, and abdominal palpation may raise index of suspicion for lymphoma and other neoplasia.
- Assessment of hydration status, renal palpation, and urinary history points toward lower urinary tract disease or renal failure.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

- Oxalate, citrate, and EDTA anticoagulants bind calcium and falsely lower calcium measurement.
- Vitamin D preparations and thiazide diuretics can raise serum calcium concentrations.

Disorders That May Alter Laboratory Results

- Hemolysis and lipemia can falsely raise calcium concentrations.
- Hypoalbuminemia can falsely lower total calcium concentration.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Serum calcium—total calcium concentration depends on binding proteins; adjusted (corrected) calcium can be estimated by the following formulas:

$$\text{Corrected Ca} = \text{Ca (mg/dL)} - \text{albumin (g/dL)} + 3.5$$

or

$$\text{Corrected Ca} = \text{Ca (mg/dL)} - [0.4 \times \text{total protein (g/dL)}] + 3.3$$

- (These formulas are not always indicative of true ionized calcium status in the dog, and have not been well evaluated in the cat.)
- Azotemia and isosthenuria help define degree of renal impairment.

- Serum phosphorus is usually low or low-normal in patients with primary hyperparathyroidism or hypercalcemia associated with malignancy.
- Hyperphosphatemia in the absence of azotemia suggests a non-parathyroid cause of hypercalcemia.
- Combination of hyperphosphatemia and azotemia is difficult to interpret because renal failure can be the cause or effect of hypercalcemia.
- Hyperkalemia and hyponatremia suggest hypoadrenocorticism.
- Hyperglobulinemia is associated with multiple myeloma.
- Cytopenias are seen in patients with myelophthisic disease.

OTHER LABORATORY TESTS

- Serum ionized calcium is high in patients with primary hyperparathyroidism or hypercalcemia associated with malignancy; usually normal in patients with hypercalcemia associated with renal failure.
- Serum PTH measurement—intact molecule and two-site assay methods have the greatest specificity; high-normal or high concentration suggests primary hyperparathyroidism; can be high in patients with chronic renal failure; low concentration makes neoplasia more likely.
- Serum PTH-rp measurement is often high in patients with hypercalcemia associated with malignancy.
- Vitamin D assays are not widely available.

IMAGING

- Radiography is useful for assessing renal size and shape, urolithiasis, bone lysis, and occult neoplasia.

(CONTINUED)

HYPERCALCEMIA

- Ultrasonography valuable for assessing renal architecture, abdominal lymphadenomegaly, parathyroid tumors, and urolithiasis.

DIAGNOSTIC PROCEDURES

- Cytologic examination of fine-needle aspirate of lymph nodes to confirm lymphoma.
- Examination of bone marrow aspirate to confirm occult hematopoietic neoplasia.
- ACTH stimulation testing to confirm hypoadrenocorticism.

**TREATMENT**

- Inpatient care because of the deleterious effects of hypercalcemia and the need for fluid therapy.
- Consider severe hypercalcemia a medical emergency.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Normal saline—fluid of choice.
- Avoid calcium-containing fluids.
- Diuretics (furosemide) and corticosteroids can be useful.

CONTRAINDICATIONS

- Do not use glucocorticoids until the diagnosis of lymphoma is excluded; they can obfuscate the diagnosis; if hypoadrenocorticism is suspected, do not give glucocorticoids until after ACTH stimulation testing.
- Thiazide diuretics can cause calcium retention.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

Avoid the use of calcium- or phosphorus-containing compounds; they can cause soft tissue mineralization in severely hypercalcemic and hyperphosphatemic patients.

ALTERNATIVE DRUG(S)

- Sodium bicarbonate (1–4 mEq/kg) may be useful in combination with other treatments.

- Mithramycin has been used in severe hypercalcemic crises; avoid its use if possible, because of associated nephrotoxicity and hepatotoxicity.
- Calcitonin may be useful in the treatment of hypervitaminosis D.
- Pamidronate has been used successfully for treatment of hypercalcemia of various causes in dogs and cats.

**FOLLOW-UP****PATIENT MONITORING**

- Serum calcium every 12 hours (ionized calcium if possible).
- Renal function tests—the first sign of tubular damage may be casts in the urine sediment.
- Must monitor urine output, particularly if oliguric renal failure is suspected, in which case urine output should be measured carefully; oliguria cannot be determined unless the patient is fully hydrated.
- Hydration status must be monitored; indicators of overhydration include increased body weight, increased central venous pressure, and edema (pulmonary or subcutaneous).

POSSIBLE COMPLICATIONS

- Irreversible renal failure
- Soft tissue mineralization

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Calcium-containing urolithiasis

AGE-RELATED FACTORS

- Mild elevations in calcium and phosphorus may be normal in growing animals.
- Middle-aged and older dogs and cats are at increased risk for cancer.

PREGNANCY/FERTILITY/BREEDING

A fetus is at the same risk as the dam; do not alter treatment because of pregnancy.

SEE ALSO

- Hyperparathyroidism
- Lymphoma—Dogs
- Paraneoplastic Syndromes
- Renal Failure, Acute
- Renal Failure, Chronic
- Vitamin D Toxicosis

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- Ca = calcium
- EDTA = ethylene diamine tetra-acetic acid
- PTH = parathyroid hormone
- PTH-rp = parathyroid hormone-related peptide
- PU/PD = polyuria and polydipsia

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**Client Education Handout
available online**

H

HYPERCAPNIA



BASICS

DEFINITION

- An increase in the partial pressure of carbon dioxide in arterial blood.
- Normal PaCO₂ values—35–45 mmHg.
- Hypercapnia is synonymous with hypoventilation.

PATHOPHYSIOLOGY

- CO₂—end product of aerobic cellular metabolism; considered the primary drive for ventilation by stimulation of central chemoreceptors in the medulla oblongata; carried in the blood in three forms: bicarbonate (65%), bound to hemoglobin (30%), and dissolved in plasma (5%; the source of PaCO₂ values); constantly being added to alveolar gas from the pulmonary circulation and removed by alveolar ventilation.
- Uncommonly encountered in non-anesthetized, clinically normal patient; result of alveolar hypoventilation.

SYSTEMS AFFECTED

- Cardiovascular—may result in endogenous catecholamine release, which may induce cardiac arrhythmias; may cause vasodilation leading to hypotension.
- Hemic/Lymphatic/Immune—may alter acid-base balance; acute increase results in production of excess hydrogen ions and a decrease in pH (respiratory acidosis).
- Nervous—the brain is primary affected organ; cerebral blood flow related to PaCO₂ in a linear fashion; hypercapnia results in increased cerebral blood flow and intracranial pressure; PaCO₂ > 90 mmHg may lead to CO₂ narcosis and unconsciousness.

SIGNALMENT

Any breed, age, and sex of dogs and cats

SIGNS

Historical Findings

- Abnormal breathing pattern.
- Weakness—secondary to concurrent hypoxemia or primary neuromuscular disease.

Physical Examination Findings

- Anesthetized patients—usually no obvious signs; severe condition may lead to tachypnea and tachycardia.
- Hypoventilation owing to muscle weakness or neuropathy—weak respiratory efforts; decreased thoracic excursion; excessive abdominal effort; exaggerated movement of facial muscles during inspiration; possibly generalized weakness as a result of primary neuromuscular disorder (myasthenia gravis, polyradiculoneuropathy).
- Upper airway obstruction—marked, prolonged inspiratory efforts with variable expirations, depending on whether the obstruction is fixed (e.g., mass) or non-fixed (e.g., laryngeal paralysis); stridor or stertor common.

- Pleural effusion—may have shallow rapid respirations; may note a marked abdominal component; lung sounds decreased in ventral thorax.
- Pulmonary parenchymal disease—increased bronchovesicular sounds; crackles (edema, infection, contusions).

CAUSES

- Hypoventilation can result from anesthesia, muscular paralysis, upper airway obstruction, air or fluid in the pleural space, restriction in movement of the thoracic cage, diaphragmatic hernia, pulmonary parenchymal disease, and CNS disease. Can occur in spontaneously breathing patients during inhalation anesthesia (isoflurane or sevoflurane).
- Increased inspired CO₂—rebreathing of expired gases because of accumulation of exhausted CO₂ absorbent in an anesthesia machine most common cause; also inadequate fresh gas flow in a non-rebreathing anesthesia circuit (e.g., Bain and Ayres T-piece).
- Exogenous administration of sodium bicarbonate, which dissociates into CO₂, with inadequate ventilation.

RISK FACTORS

- Use of inhalation agent (isoflurane or sevoflurane) as sole anesthetic, as inhalation anesthetics are potent respiratory depressants.
- Deep planes of inhalation anesthesia.
- Inadequate fresh flow of oxygen with non-rebreathing anesthesia circuits.
- Bronchial or alveolar disease.
- Upper airway obstruction.
- Pleural disease.
- Inadequate ventilation during administration of sodium bicarbonate.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Conscious patient—hyperthermia; hypoxemia; head trauma.
- Anesthetized patient—hypoxemia.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

N/A

Disorders That May Alter Laboratory Results

Air bubbles in the arterial blood sample and/or improper packaging of the arterial blood sample—falsely low PaCO₂ values after approximately 30 minutes.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

- Arterial blood gas analysis—diagnosis determined from a blood sample collected in an anaerobic manner, as follows: use enough heparin to coat the needle and the inside of

the syringe; obtain sample from femoral or dorsal pedal artery; place a rubber stopper on the needle or cover the hub of the syringe to prevent room air from entering the sample.

- Analyze sample within 15 minutes if left at room temperature; place sample on ice to extend time for safe and accurate analysis to 2–4 hours.
- Bedside or portable blood gas analyzers—several models available; make analysis more convenient.

IMAGING

Thoracic radiography—may reveal bronchial, alveolar, or pleural space disease. Cervical radiography can suggest a large airway obstruction.

OTHER DIAGNOSTIC PROCEDURES

- Upper airway endoscopy used to rule out laryngeal mass or paralysis.
- Alternative method of analysis—capnometer (see Figures 1 and 2).
- End-tidal gas is almost entirely alveolar gas and provides nearly the same value for CO₂ as PaCO₂, which closely approximates the mean value of perfused alveoli.
- Advantage of capnometry—can monitor PaCO₂ on a breath-by-breath basis, whereas a blood gas sample is a finite value at a finite time.
- Disadvantages—tachypnea and insufficient tidal volume will result in falsely low PetCO₂;

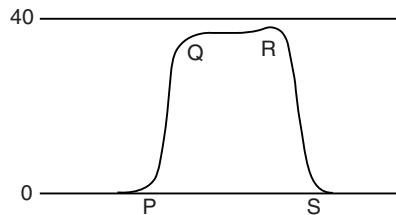


Figure 1.

Normal capnogram. The wave segment from P to Q is exhalation; Q to R is the plateau after exhalation, point R is the end tidal CO₂; R to S is inhalation.

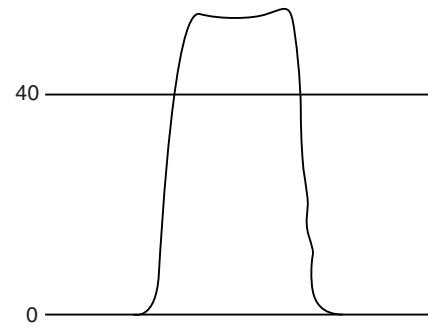


Figure 2.

Capnogram with hypercapnia. The plateau and end tidal CO₂ is above normal.

(CONTINUED)

HYPERCAPNIA

PaCO_2 much higher than PetCO_2 with pulmonary thromboembolism; open thoracic cavity (surgery) reports falsely low PetCO_2 due to excessive dead space.

**TREATMENT**

- Provide adequate alveolar ventilation.
- Anesthesia—ventilation accomplished manually or mechanically with anesthesia ventilator.
- Non-anesthetized patient with severe pulmonary or CNS disease—mechanical ventilation with critical care ventilator; generally requires heavy sedation.
- Supplemental oxygen—need determined by primary disease; providing supplemental oxygen without providing ventilation will likely not correct hypercapnia.
- Definitive treatment—treat primary cause; discontinue inhalation anesthesia or provide ventilation during anesthesia; diagnostics for neuromuscular disease.

**MEDICATIONS****DRUG(S) OF CHOICE**

Respiratory stimulants not indicated and rarely reverse hypoventilation.

CONTRAINDICATIONS

Anesthetic drugs or other respiratory depressants—contraindicated with CNS disease if adequate ventilatory support cannot

be provided; increased PaCO_2 may result in dangerous elevations of intracranial pressure and predispose patient to herniation of the brainstem.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

**FOLLOW-UP****PATIENT MONITORING**

- Assess effectiveness of supportive therapy (ventilation) and definitive treatment—should result in decreased respiratory effort.
- Reevaluate the arterial blood gas or capnometry—determine improvement; assess adequacy of ventilation.

POSSIBLE COMPLICATIONS

Concurrent CNS disease may cause high intracranial pressure and predispose the patient to herniation of the brainstem and death.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Hypercarbia
- Hypoventilation

SEE ALSO

- Dyspnea and Respiratory Distress
- Panting and Tachypnea

ABBREVIATIONS

- CNS = central nervous system
- PaCO_2 = partial pressure of carbon dioxide in arterial blood
- PetCO_2 = end-tidal carbon dioxide

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Author Thomas K. Day

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H

HYPERCHLOREMICA



BASICS

DEFINITION

Serum chloride concentration > 122 mEq/L in dogs and > 129 mEq/L in cats.

PATHOPHYSIOLOGY

- Chloride is the most abundant anion in the extracellular fluid.
- Hyperchloremia is associated with similar conditions to those that cause hypernatremia—water loss in excess of sodium and chloride or excessive NaCl intake.
- Chloride concentration varies inversely to bicarbonate concentration; high bicarbonate loss (i.e., GI or renal wasting), followed by low renal chloride resorption in excess of bicarbonate, can cause hyperchloremia.

SYSTEMS AFFECTED

Relates to underlying cause

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog and cat

SIGNS

General Comments

- Related to concurrent hypernatremia or the underlying disorder or both.
- Severity of neurologic signs is related to the degree of hypernatremia and the rate at which it develops.

Historical and Physical Examination Findings

- Polydipsia
- Disorientation
- Coma
- Seizures

CAUSES

High Total Body Chloride

- Oral ingestion—rare.
- NaCl administered IV during cardiovascular resuscitation.

Normal Total Body Chloride with Water Deficit

- Low intake (e.g., no access to water).
- High urinary water loss (e.g., diabetes insipidus).
- High insensible water loss (e.g., panting).

Low Total Body Chloride with Hypotonic Fluid Loss

Urinary loss—diabetes mellitus, osmotic diuresis, and diuresis after urinary obstruction.

Hyperchloremic Metabolic Acidosis

- Renal tubular acidosis—renal tubular disorders that cause renal wasting of bicarbonate or low hydrogen ion secretion.
- Diarrhea associated with gastrointestinal loss of bicarbonate and renal resorption of chloride.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Normal anion gap metabolic acidosis (e.g., renal tubular acidosis and gastrointestinal bicarbonate loss).
- Diabetes insipidus.
- Hypertonic dehydration.
- Severe forms of diabetes mellitus (e.g., diabetic ketoacidosis and hyperosmolar non-ketotic syndrome).
- Salt ingestion—rare.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

- A wide variety of drugs can interfere with renal capacity to concentrate urine, leading to water loss in excess of sodium, and high sodium and chloride concentrations; these drugs include lithium, demeclocycline, and amphotericin.
- Other drugs that may increase chloride concentration include acetazolamide, ammonium chloride, androgens, and cholestyramine.
- A falsely high chloride concentration can occur with a high serum concentration of iodide or bromide—most commonly seen in patients with epilepsy treated with potassium bromide.

Disorders That May Alter Laboratory Results

Hemoglobin and bilirubin cause falsely high chloride readings if colorimetric tests are used.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- High chloride, often coupled with high sodium.
- Diabetes insipidus—low urinary specific gravity, polyuria, and low urinary sodium.
- Diabetic ketoacidosis and hyperosmolar non-ketotic syndrome—high blood glucose.

- Hypertonic dehydration—low urinary sodium and high urinary specific gravity (usually > 1.030).

- Renal tubular acidosis—hyperchloremic acidosis, urine pH > 5.3, serum potassium often low, and other causes of metabolic acidosis have been ruled-out.

OTHER LABORATORY TESTS

- Renal tubular acidosis—response to NaHCO_3 or NH_4Cl
- Anion gap
- Blood gases

IMAGING

CT scan or MRI in patients with diabetes insipidus to rule out pituitary tumor.



TREATMENT

APPROPRIATE HEALTH CARE

Hyperchloremia with hypernatremia—hypotonic fluids (5% dextrose in water); decrease sodium by 0.5 mEq/h or by no more than 20 mEq/L/day.



MEDICATIONS

DRUG(S) OF CHOICE

- Hypovolemia—isotonic saline (normal saline or lactated Ringer's solution) or isotonic fluid (5% dextrose with half-normal saline).
- Central diabetes insipidus—DDAVP (1–2 drops in the conjunctival sac q12–24h).
- Nephrogenic diabetes insipidus—chlorothiazide (10–40 mg/kg PO q12h).
- Hyperchloremic metabolic acidosis—treat underlying cause; consider bicarbonate and potassium replacement if needed.

PRECAUTIONS

- Rapid correction of hyperchloremia with hypernatremia can cause pulmonary edema.
- Hypocalcemia may develop during correction of hyperchloremia.



FOLLOW-UP

PATIENT MONITORING

Electrolytes, body weight, and hydration status

(CONTINUED)

HYPERCHLOREMIA**PREVENTION/AVOIDANCE**

Make sure animals always have access to water.

POSSIBLE COMPLICATIONS

- Related to associated hypernatremia or the underlying disorder.
- Neurologic complications include CNS thrombosis or hemorrhage; seizures; and hyperactivity.

EXPECTED COURSE AND PROGNOSIS

Varies with underlying cause

**MISCELLANEOUS****SEE ALSO**

Hypernatremia

ABBREVIATIONS

- CNS = central nervous system
- DDAVP = brand name for desmopressin, a synthetic antidiuretic hormone preparation
- GI = gastrointestinal

Suggested Reading

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H

HYPERCOAGULABILITY



BASICS

OVERVIEW

- HC is an imbalance between procoagulants and anticoagulants leading to a predisposition for thrombosis.
- HC may result from platelet hyperaggregability; increased amounts or activation of clotting factors; reduced or inhibited anticoagulants (e.g., AT-III, protein C); or defective fibrinolysis.
- Thrombus formation depends on three major influences (Virchow's triad): endothelial injury, altered blood flow (stasis or turbulence), and HC. Only endothelial injury is likely to cause thrombosis independently.
- Common sites of thrombosis: pulmonary arteries, distal aorta, cranial vena cava, intestinal/mesenteric vessels, portal vein.

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SIGNS

- HC is symptomless. Progression to thrombosis may cause site-dependent signs.
- PTE—acute severe dyspnea and tachypnea or chronic labored breathing.
- ATE—acute paresis/paralysis, limb pain, decreased femoral pulse and cold limbs. Onset in dogs may be gradual vs. very acute in cats.
- DIC—initial TE followed by bleeding (see Disseminated Intravascular Coagulation).

CAUSES & RISK FACTORS

Thrombosis is most commonly associated with conditions acting through Virchow's triad (above):

- IMHA
- DIC
- PLN (or enteropathy)
- Hyperadrenocorticism or corticosteroid therapy
- Neoplasia
- Systemic inflammation (Parvovirus infection, pancreatitis)
- Sepsis
- Cardiac disease



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- PTE may mimic pulmonary diseases such as bacterial or fungal pneumonia, pulmonary edema, and dirofilariasis.
- Distal ATE—consider other causes of paraparesis and paraplegia; absence of femoral pulses and cold limbs support distal ATE.

CBC/BIOCHEMISTRY/URINALYSIS

Reflect underlying disease or effects of thrombosis in specific organs.

OTHER LABORATORY TESTS

- D-dimer—increases are very sensitive for fibrinolysis. Thrombosis unlikely if normal. Nonspecific for type/mechanism of thrombosis.
- AT decreases (60–75% of reference) increase risk of thrombosis.
- PT, APTT—shortened clotting times are unreliable marker for HC.
- TEG-reported to identify HC states in DIC, parvovirus, IMHA, PLN, etc.
- Arterial blood gas—hypoxemia seen in PTE.

IMAGING

- Thoracic radiography—often few abnormalities despite severe dyspnea in PTE
- Abdominal ultrasonography—may confirm distal aortic occlusion in ATE.
- Echocardiography—to identify intracardiac thrombi and assess for pulmonary hypertension associated with PTE (dilation or hypertrophy of right ventricle, enlarged main pulmonary artery, tricuspid valve regurgitation).

DIAGNOSTIC PROCEDURES

- Angiography—to localize and confirm TE.
- Nuclear perfusion scintigraphy—noninvasive study may support a diagnosis of PTE.



TREATMENT

- Inpatient—to initiate thrombosis management and anticoagulant therapy.
- Supportive care—ensure hydration, maintain perfusion, minimize vascular stasis, correct and monitor acid-base and electrolyte abnormalities, use venous catheters appropriately.
- Severely restrict activity.
- Oxygen therapy—often indicated in PTE.
- Analgesics for acute pain.
- Inform owners that there is a risk of future TE events, especially if the underlying disease remains.



MEDICATIONS

DRUG(S)

Anticoagulants

- Unfractionated heparin—most common choice for initial therapy. Starting doses: 150–200 IU/kg SC q6h (dogs) and 200 IU/kg q8h (cats); titrate to achieve a 1.5- to 2-fold increase in APTT; check APTT daily (2 hours post-heparin administration).
- Low molecular weight heparin (e.g., enoxaparin, dalteparin); (safer, expensive alternate for initial therapy) APTT typically unaltered; anti-Xa activity used for assessment; appropriate starting dose of enoxaparin: 1 mg/kg (1,000 U/kg) SC q12h.
- Warfarin—(chronic therapy) vitamin K antagonist; appropriate starting doses: 0.1–0.2 mg/kg PO q24h, adjust to prolong PT to about twice the baseline.

Platelet Inhibition

- Aspirin—for initial prophylaxis or to prevent rethrombosis; 0.5–5.0 mg/kg PO q12–24h (dogs); 5 mg/cat q72h.
- Clopidogrel—for initial prophylaxis or to prevent rethrombosis; 1 mg/kg PO q24h (dogs); 18.75 mg/cat q24h. More effective than aspirin in preventing recurrence of aortic thromboembolism in cats.

Thrombolysis

- Severe side effects possible. Feline reperfusion injury is common, often fatal.

Consider for cerebral, splanchnic or renal infarction where restoring blood flow is essential.

- Streptokinase: dogs/cats, 90,000 IU IV over 1 hour, then 45,000 IU/hour up to 12 hours
- Urokinase: dogs/cats, 4,400 IU/kg over 10 minutes, then 4,400 IU/kg/hour for 12 hours.

CONTRAINdications/POSSIBLE INTERACTIONS

- Do not treat with warfarin initially or exclusively; initial HC state possible; overlap with heparin therapy for 4 days.
- High rate of interaction between warfarin and other drugs; reassess PT with any changes in medication.
- Bleeding is the major risk with anticoagulation; discontinue anticoagulant and administer protamine (for heparin overdose) or vitamin K (warfarin) and plasma as necessary to treat bleeding.



FOLLOW-UP

PT—monitor daily for 4–5 days (8 hours post-dose) and discontinue heparin when appropriate PT is achieved; check PT 6–8 hours after last heparin dose as it may decrease; following discharge, check PT twice weekly, then weekly for several weeks, then every 2 months.



MISCELLANEOUS

SEE ALSO

- Amyloidosis
- Aortic Thromboembolism
- Disseminated Intravascular Coagulation
- Glomerulonephritis
- Nephrotic Syndrome
- Pulmonary Thromboembolism

ABBREVIATIONS

- APTT = activated partial thromboplastin time
- AT = antithrombin
- ATE = aortic thromboembolism
- DIC = disseminated intravascular coagulation
- HC = hypercoagulability
- IMHA = immune-mediated hemolytic anemia
- PLN = protein-losing nephropathy
- PT = prothrombin time
- PTE = pulmonary thromboembolism
- TE = thromboembolism
- TEG = thromboelastography

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Author John A. Christian

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HYPEREOSINOPHILIC SYNDROME (HES)



BASICS

OVERVIEW

- Idiopathic, persistent eosinophilia with infiltration of multiple organs causing dysfunction, often leading to death.
- Hypothesized to be caused by a severe reaction to an unidentified antigen or dysregulation of immunologic control of eosinophil production. • Organ damage caused by effects of eosinophil granule products and eosinophil-derived cytokines that are released in tissues from activated and/or necrotic cells.
- Common sites of infiltration: gastrointestinal tract (especially intestine and liver), spleen, bone marrow, lung (dogs mainly), and lymph nodes (especially mesenteric).
- Other sites of infiltration are reported less frequently.
- More common in cats than dogs, with rottweilers possibly being overrepresented.
- It is unclear whether this disease is a distinct entity from eosinophilic leukemia, or if it matters.
- Generally poor prognosis, especially in cats.

SIGNALMENT

- Cats—may occur more frequently in female, middle-aged domestic shorthair cats.
- Dogs—rare, but rottweilers may be predisposed.

SIGNS

- Lethargy • Anorexia • Intermittent vomiting and diarrhea • Hepatosplenomegaly
- Weight loss leading to emaciation
- Thickened (diffuse or segmental) intestine that is generally non-painful
- Mesenteric and possible peripheral lymphadenopathy
- Mass lesions caused by eosinophilic granulomatous inflammation and infiltration involving lymph nodes and/or organs
- Less frequently, fever, pruritus, and seizures

CAUSES & RISK FACTORS

- Unknown; however, believed to be a severe reaction to an underlying, yet unidentified antigenic stimulus.
- Cats—Eosinophilic enteritis may be an early form.
- A fusion gene, FIP1L1-PDGFR α , has been identified in humans with some forms of HES; no such gene has been identified in veterinary cases.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Reactive eosinophilia—parasitism, allergic/hypersensitivity reactions, infectious disease, immune-mediated disease, fungal infections and neoplasia; with these conditions, eosinophilia is usually limited in magnitude

and remains confined to a specific organ.

- Eosinophilic leukemia—differentiating criteria: eosinophilic leukemia tends to have (1) immature eosinophils seen in higher numbers in the circulation and constitute a higher percentage of the leukocyte differential, (2) anemia is more common and often more severe, (3) myeloid:erythroid (M:E) ratio in bone marrow is higher ($> 10:1$) with more immature/blast forms and disorderly maturation, (4) tissue infiltrates consist of immature eosinophils and may show a sinusoidal pattern in the liver without fibrosis, (5) in cats, chloroma-like masses in the kidneys are reported.

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis with marked eosinophilia, possibly with left shift in the eosinophil series (not routinely reported); mature eosinophil count range from 5,000 to $> 130,000/\mu\text{L}$.
- Basophilia.
- Mild anemia.
- With organ damage or dysfunction, appropriate CBC, biochemical and urinalysis abnormalities may be seen.

OTHER LABORATORY TESTS

Rule out identifiable causes of eosinophilia: fecal floatation, heartworm test, fungal visualization/culture, and biopsy.

IMAGING

- Intestinal mucosal irregularities and thickened intestine seen on radiographic contrast studies and ultrasound.
- Organ enlargement/infiltration may be visualized with survey radiographs and/or ultrasound.

DIAGNOSTIC PROCEDURES

- Bone marrow aspiration and/or core biopsy
- Biopsy of affected organ or mass

PATHOLOGIC FINDINGS

- Spleen—eosinophilic infiltrates in red pulp, sometimes in the white pulp.
- Gastrointestinal tract—mucosal and submucosal eosinophilic infiltrates in small intestine, sometimes in colon and stomach.
- Bone marrow—hypercellularity, eosinophilic hyperplasia (up to 40% of all nucleated cells are eosinophils), lack of morphologic abnormalities, orderly maturation and a high M:E ratio (mean 7.27:1).
- Lymph nodes—reactive hyperplasia and infiltration of cords and sinuses with eosinophils.
- Other (less frequent)—eosinophilic infiltrates in the skin, myocardium and endocardium, liver, lung, etc. or eosinophilic effusions.



TREATMENT

- Long-term maintenance therapy to control or reduce the eosinophilia and organ damage.

- Address specific organ dysfunction as indicated.
- High serum IgE concentration portends a good response to treatment with prednisone and a better prognosis.



MEDICATIONS

DRUGS

- Corticosteroids—prednisone, 1–3 mg/kg q24h initially, then taper to q48h if eosinophilia is suppressed; if eosinophilia returns, resume higher daily dose.
- Imatinib mesylate is approved in humans to treat chronic myelogenous leukemia as well as HES, used with possible efficacy in cats at 9.6 mg/kg PO q24h.
- Chemotherapeutic agents—try if eosinophilia is steroid resistant; paucity of case reports describing these therapies precludes recommending their use.
- Hydroxyurea—administer to reduce eosinophil count if not normal or near normal after 7–14 days of treatment with steroids; most likely would be used long-term if effective in conjunction with steroids.
- Cyclosporine A—suppresses production of eosinophilopoietic factors by T cells.
- Vincristine and alkylating agents such as chlorambucil, effective in human.
- Reduce dosage or discontinue drugs if bone marrow suppression or thrombocytopenia develops.

H

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Specific drug toxicities for each agent, most notably myelosuppression.
- Imatinib mesylate may lead to protein-losing nephropathy but this association is uncertain.



FOLLOW-UP

- Serial monitoring of eosinophil count (not always indicative of tissue infiltrates) and WBC count if myelotoxic drugs are used.
- Monitor signs (e.g., anorexia, lethargy, vomiting and diarrhea) and physical abnormalities.
- Other testing for specific organ function (e.g., bile acids).



MISCELLANEOUS

Suggested Reading

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Author Craig A. Thompson

Consulting Editor Alan H. Rebar

HYPERESTROGENISM (ESTROGEN TOXICITY)



BASICS

OVERVIEW

- A syndrome characterized by high serum concentration of estrogens (estradiol, estriol, or estrone).
- Can occur as a result of excessive estrogen secretion, accumulation or administration of exogenous estrogens, such as diethylstilbestrol or estriol.
- Sites of endogenous estrogen production include ovarian follicles, follicular ovarian cysts, Leydig cells, and the adrenal cortex (zona glomerulosa and fasciculata); can also occur as a result of peripheral conversion of excessive androgens.
- Endogenous estrogens in the female are responsible for normal sexual behavior and development and function of the female reproductive tract; in the male, estrogens are responsible for Leydig cell function.
- Estrogens potentiate the stimulatory effect of progesterone in the endometrium and permit cervical relaxation; these two effects increase the risk of cystic endometrial hyperplasia and pyometra. In the male, estrogens potentiate the action of androgens in the prostate. Estrogens also increase osteoblastic activity, retention of calcium and phosphorus, total body protein and metabolic rate.
- High serum concentration of estrogen provides a source of negative feedback in the hypothalamic-pituitary axis and results in suppression of gonadotropin secretion; interferes with stem cell differentiation in the bone marrow and erythrocyte iron metabolism.

SIGNALMENT

Endogenous Hyperestrogenism

- Older male dog (secondary to functional testicular tumors).
- Older female dog (secondary to granulosa cell tumors or other functional ovarian tumor types, follicular ovarian cysts).
- Young female dog (follicular ovarian cysts).

Exogenous Hyperestrogenism

- All breeds, genders, and ages in association with estrogen administration or exposure.
- Toy breed dogs are at increased risk when exposed to transdermal hormone replacement therapy.

SIGNS

Historical Findings

- Attractive to intact male dogs.
- Infertility.

- Prolonged proestrus and estrus (female).
- Decreased libido (male).
- Nymphomania (female).
- Variable vulvar bleeding and enlargement causing excessive vulvar licking.
- Epistaxis, hematuria if thrombocytopenic; lethargic, febrile if neutropenic; lethargic if anemic.

Physical Examination Findings

- Skin/Endocrine—non-pruritic, symmetric alopecia (endocrine alopecia), hyperpigmentation.
- Reproductive (male)—palpable testicular mass; testicular asymmetry (in association with a tumor mass and/or testicular atrophy); testicular atrophy: may be unilateral atrophy in the non-tumor-containing testicle, as seen in association with a functional estrogen-producing testicular tumor, or bilateral, as seen in association with exogenous hyperestrogenism; cryptorchidism (unilateral or bilateral) should be ruled out; prostatomegaly (secondary to squamous metaplasia); gynecomastia. The testicular tumor can replace most of the normal testicular tissue if advanced.
- Reproductive (female)—vulvar edema and enlargement; variable vulvar discharge depending on the presence of residual uterine tissue; gynecomastia.
- Hemic/Lymphatic/Immune—pale mucous membranes; thrombocytopenic hemorrhage; petechia; fever (due to secondary bacterial infection in association with neutropenia); depression.

CAUSES & RISK FACTORS

- Follicular ovarian cysts.
- Functional ovarian tumor (granulosa cell tumor and other ovarian tumors).
- Testicular tumor (specifically Sertoli cell tumor, but also may occur secondary to Leydig and interstitial cell tumors).
- Exogenous estrogen administration or exposure—iatrogenic.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Non-pruritic, Symmetric Alopecia (Endocrine Alopecia)

- Hypothyroidism—diagnosis based on appropriate clinical signs in conjunction with typical hematologic and biochemical abnormalities (normocytic normochromic non regenerative anemia, hypercholesterolemia) and thyroid function testing (total T₄, free T₄, cTSH).

- Hyperadrenocorticism—clinical signs usually include polyuria, polydipsia, and exercise intolerance; CBC may reveal leukocytosis and erythrocytosis; serum biochemistry abnormalities include elevated ALP, ALT, and cholesterol, and decreased BUN; additional testing includes urine cortisol creatinine ratio, ACTH stimulation, LDDS test (preferred), endogenous ACTH, abdominal ultrasonography.
- GH-responsive dermatosis.

Attractive to Male Dogs

- Vaginitis, perivulvar dermatitis—can be differentiated from hyperestrogenism via examination of vaginal cytology (lack of vaginal superficial epithelial cell predominance), lack of evidence of ovarian abnormalities, or confirmation of complete ovariectomy or ovariohysterectomy.
- Genitourinary tract infection, inflammation (foreign body) or neoplasia.

Infertility

- Testicular degeneration/atrophy/immune-mediated orchitis—diagnosis based on physical examination, lack of testicular or intra-abdominal masses, semen evaluation (azoospermia, teratospermia), and testicular FNA for cytology or testicular biopsy.
- Intersex abnormalities—uncommon; diagnosis supported by physical examination findings (abnormal external genitalia), abnormal karyotype, and histologic examination of the reproductive tract, where available.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—changes are extremely variable; if present, initial 2–3 weeks characterized by thrombocytopenia or thrombocytosis, progressive anemia, and leukocytosis (white cell counts may exceed 100,000 WBC/ μ L); after 3 weeks, pancytopenia and aplastic anemia may be noted; hematuria (secondary to thrombocytopenia).
- Chemistry panel and urinalysis usually unremarkable.

OTHER LABORATORY TESTS

- Serum estrogen (estradiol) concentrations—may be evaluated via radioimmunoassay; however, physiologic serum concentrations may be within normal limits due to accuracy of assay. Prolonged elevation (> 30 days) of estradiol at levels expected for proestrus or estrus is responsible for the clinical signs rather than the actual level.
- Vaginal/preputial cytology—extremely reliable as a bioassay for estrogen; under the

(CONTINUED)

HYPERESTROGENISM (ESTROGEN TOXICITY)

influence of estrogen, will reveal a predominance of superficial epithelial cells that are anuclear or have pyknotic nuclei.

- Evaluation for ovarian remnant syndrome (see Ovarian Remnant Syndrome).

IMAGING/ENDOSCOPY

- Ultrasonography of the abdomen, inguinal canal, and testes—to assess for testicular masses, cystic or enlarged ovarian structures, intra-abdominal masses, prostatomegaly (not appropriate for a neutered dog), and regional lymph node size and echogenicity.
- Vaginoscopy—can be completed to evaluate the vaginal mucosa; under the influence of estrogen, the vaginal mucosa should appear edematous and pink.

DIAGNOSTIC PROCEDURES

- Fine-needle aspiration for cytology of testicular masses—can provide a cytologic diagnosis prior to pursuing surgery.
- Percutaneous ultrasound-guided aspiration of large ovarian follicular cysts rarely results in clinical resolution, as the cystic structure persists. The cystic fluid obtained can be evaluated for hormone concentration.
- Three-view metastatic radiographic evaluation of the thoracic cavity—complete prior to any surgical intervention when neoplasia is suspected.
- Complete hemogram, serum chemistries, and urinalysis—always perform preoperatively for cytopenias, hepatic dysfunction (estrogen metabolism).
- Examination and biopsy of local lymph nodes—for evaluation of metastatic disease; can be completed, if indicated, at time of surgical exploration or performed with ultrasound guidance.
- Bone marrow core biopsy—can confirm the presence of myelosuppression.
- Laparoscopy or laparotomy—can be used to identify and remove intra-abdominal masses, ovarian tissue, or cryptorchid testicular tissue, followed with histopathology.
- Skin biopsy—may reveal nonspecific changes associated with endocrine alopecia such as orthokeratotic hyperkeratosis, epidermal atrophy and melanosis, follicular keratosis, telogen hair follicles, and sebaceous gland atrophy.

**TREATMENT**

- Treatment of choice for endogenous hyperestrogenism in the intact or partially neutered female and male is surgical neutering; the prognosis is good if residual or malignant gonadal tissue can be completely removed.

- Unilateral orchiectomy or ovariecomy of the affected neoplastic testicle or cystic or neoplastic ovary may be considered in valuable breeding animals. Use of testicular prosthetic devices is not advised and is not ethical. Contralateral testicular changes (male) or endometrial changes (female) secondary to prolonged estrogen exposure can occur and contribute to subfertility even if the abnormal gonad has been removed, making the prognosis for fertility guarded. Histopathology should always be performed to evaluate neoplastic changes and for local lymphatic metastasis.

- Discontinue exogenous estrogen exposure in cases of exogenous hyperestrogenism. Small dogs are at increased risk of exposure to transdermal hormone replacement therapy (often applied to the forearms) as a consequence of being held frequently. Discontinue or reduce the dose of exogenous estrogen if used therapeutically for sphincter incompetence in the ovariectomized bitch. Both have a good prognosis.

**MEDICATIONS****DRUG(S)**

- Supportive care—including administration of appropriate antimicrobial therapy and blood products.
- Synthetic erythropoietin, darbopoietin, G-CSF, GM-CSF—may be considered to stimulate erythroid and granulocytic production at the level of the bone marrow; lithium has reportedly been of benefit in cases of estrogen-induced bone marrow aplasia.
- GnRH—unlikely to induce ovulation in cases of follicular cysts.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Administration of chemotherapeutic agents for treatment of metastatic testicular or ovarian neoplasia should be pursued with caution due to increased risk of bone marrow suppression secondary to hyperestrogenism. Consult with a veterinary oncologist.

**FOLLOW-UP**

- Repeat serial CBC analysis if myelosuppression present—to evaluate response to therapy and progression of disease.
- Repeat serial bone marrow aspiration cytology—to evaluate bone marrow response and erythroid, myeloid, and megakaryocytic regeneration when myelosuppression is

chronic. Peripheral signs of regeneration may not occur for weeks to months after initial insult.

- Concurrent administration of iron dextran intramuscularly or multiple daily doses of oral iron to support erythrocyte regeneration.
- Use of erythropoietin, darbopoietin, G-CSF, GM-CSF—closely monitor erythrocyte and leukocyte regeneration.
- Clinical signs of male feminization syndrome should resolve within 2–6 weeks after testicular tumor removal.
- Lack of resolving pancytopenia and continued bone marrow hypoplasia 3 weeks after surgical removal of ovarian or testicular neoplasia or removal of follicular cysts—associated with a grave prognosis.

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**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Prostatomegaly metaplasia
- Cystic-endometrial hyperplasia and subfertility
- Hepatic insufficiency
- Infertility
- Bone marrow aplasia, pancytopenia
- Sepsis
- Ovarian remnant syndrome (see chapter)

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- ALP = alanine phosphatase
- ALT = alanine aminotransferase
- G-CSF = granulocyte colony-stimulating factor
- GH = growth hormone
- GM-CSF = granulocyte-macrophage colony-stimulating factor
- GnRH = gonadotropin-releasing hormone
- hCG = human chorionic gonadotropin
- LDDS = low-dose dexamethasone suppression
- T₄ = thyroxine
- TSH = thyroid-stimulating hormone
- WBC = white blood cell

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Authors Autumn P. Davidson and Sophie A. Grundy

Consulting Editor Deborah S. Greco



Client Education Handout available online

HYPERGLYCEMIA



BASICS

DEFINITION

Transient or persistently increased serum glucose concentrations.

PATHOPHYSIOLOGY

- Insulin resistance and pancreatic amyloidosis (type 2 DM in cats).
- Insulin resistance from endogenous hormones (growth hormone) or drugs (corticosteroids).
- Absolute or relative insulin deficiency (type 1 DM in dogs).
- Increased gluconeogenesis and increased glycogenolysis (epinephrine release from stress, type 2 DM).

H

SYSTEMS AFFECTED

- Endocrine/Metabolic—insulin resistance, hepatic glycogenolysis.
- Nervous—severe hyperglycemia may cause CNS dehydration from increasing serum osmolality. Hind limb weakness and plantigrade stance from diabetic neuropathy in cats.
- Ophthalmic—persistent hyperglycemia can cause cataracts in dogs.
- Renal/Urologic—osmotic diuresis from blood glucose exceeding the renal threshold (higher in the cat than dog) causes polyuria with secondary polydipsia.

SIGNALMENT

Cat and dog of any age or breed

SIGNS

General Comments

- Clinical signs vary and often reflect underlying disease.
- Some patients are asymptomatic, especially those with drug, stress-induced, and post-prandial hyperglycemia.

Historical Findings

- Variable by species and duration of hyperglycemia.
- May be normal.
- Dogs with diabetes: polydipsia, polyuria, depression, weight loss, obesity, polyphagia.
- Cats with diabetes: obesity, plantigrade stance, anorexia, vomiting, diarrhea, polydipsia/polyuria.
- CNS depression, coma—severe hyperglycemia with hyperosmolality.

Physical Examination Findings

- May be normal
- Obesity in cats with type 2 DM
- Plantigrade stance in cats
- Cataracts in dogs
- Emaciation in dogs with type 1 DM
- Hepatomegaly resulting from diabetic hepatopathy
- Chronic infections: respiratory, skin
- Poor hair coat

CAUSES

- Relative or absolute insulin deficiency—type 1 and type 2 DM.
- Insulin resistance—type 2 DM in cats, hyperadrenocorticism, pheochromocytoma, glucagonoma, hypersomatotropism, hyperthyroidism, high progesterone during diestrus (dogs), renal insufficiency, urinary tract infection.
- Physiologic—post-prandial fluctuation and stress (epinephrine-induced) in cats.
- Drugs—thiazide diuretics, morphine, dextrose-containing fluids, progestins (e.g., megestrol acetate), growth hormone, glucocorticoids, and ACTH.
- Regulation problems in treated diabetics—high carbohydrate diets (cats), insulin administration problems, insulin-induced hypoglycemic hyperglycemia (rare).
- Parenteral administration of nutritional solutions.
- Laboratory error.

RISK FACTORS

- Stress in cats
- Concurrent disease—hyperadrenocorticism, acromegaly, and acute pancreatitis
- Diabetogenic drugs—steroids, progestagens
- Dextrose-containing fluids



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Mild, transiently high blood glucose can be associated with stress.
- In patients with mild hyperglycemia and no history of polydipsia/polyuria, repeat blood glucose determination after 12-hour fast and perform serum fructosamine.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

High blood glucose concentration—glucocorticoids, ACTH, dextrose-containing fluids, epinephrine, asparaginase, $\alpha\beta\gamma\delta$ -adrenergic agonists, and diazoxide.

Disorders That May Alter Laboratory Results

- Lipemia, hemolysis, and icterus may interfere with spectrophotometric assays.
- Delayed serum separation artificially lowers glucose concentration; must separate serum within 1 hour of collection to prevent cellular glucose use.
- Use of human glucometers—may read 25% below actual blood glucose value, repeat with monitor validated in dog or cat whole blood.
- Blood glucose reagent strips require whole blood.
- Measure glucose concentration in whole blood within 30 minutes of collection.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Hyperglycemia may be the only abnormal finding.
- CBC—may be normal; possible inflammatory leukogram in patients with sepsis.
- Urinalysis—may be normal; glucosuria, pyuria, bacteruria, and ketonuria.
- Fasting hyperglycemia plus glucosuria suggests DM.
- Lipemia in patients with low lipoprotein lipase (miniature schnauzers), hyperadrenocorticism, acute pancreatitis, and post-prandial blood sampling.
- High amylase and lipase activity suggests acute pancreatitis, especially in non-azotemic patients.
- Increased plasma lipase immunoreactivity in patients with acute pancreatitis.
- High liver enzyme activity may accompany fatty infiltration with diabetes.

OTHER LABORATORY TESTS

- Fructosamine—normal values rule-out diabetes as cause of hyperglycemia.
- ACTH stimulation or low-dose dexamethasone-suppression test to rule-out hyperadrenocorticism.

IMAGING

N/A



TREATMENT

- Insulin therapy (dogs and some cats), oral hypoglycemic agents (cats).
- Discontinue diabetogenic drugs.
- Dextrose-free fluids.

DIET

- High-protein, low-carbohydrate diet in cats with diabetes mellitus.
- High soluble fiber, low-fat diet in dogs with diabetes mellitus.



MEDICATIONS

DRUG(S) OF CHOICE

- Insulin—regular (crystalline) insulin for diabetic ketoacidosis, Lente insulin (dogs).
- Insulin glargine or PZI insulin in cats with DM.
- Oral hypoglycemics such as glipizide (cats with type 2 DM).

CONTRAINDICATIONS

- Diabetogenic drugs (e.g., glucocorticoids)
- Dextrose-containing fluids

PRECAUTIONS

Avoid rapid and aggressive insulin therapy that lowers blood glucose abruptly and causes hypoglycemia or cerebral edema.

(CONTINUED)

HYPERGLYCEMIA**ALTERNATIVE DRUG(S)**

Acarbose 12.5 mg PO q12h; intestinal starch blocker

**FOLLOW-UP****PATIENT MONITORING**

- For return of clinical signs of diabetes such as polyuria, polydipsia, and polyphagia.
- Blood glucose after discontinuing diabetogenic drugs.
- Glycosylated hemoglobin and fructosamine on an outpatient basis to monitor long-term glucose control.

POSSIBLE COMPLICATIONS

- High incidence of sepsis (and infection).
- Severe hyperglycemia may be associated

with CNS depression and coma because of hyperosmolarity.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Hyperosmolarity
- Uremia may be associated with hyperglycemia

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

High blood sugar

SEE ALSO

- Diabetes Mellitus without Complications—Cats

- Diabetes Mellitus without Complications—Dogs

- Hyperosmolarity

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- CNS = central nervous system
- DM = diabetes mellitus

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Author Deborah S. Greco

Consulting Editor Deborah S. Greco

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H

H HYPERKALEMIA



BASICS

DEFINITION

Serum potassium concentration higher than the testing laboratory's upper limit of normal, generally > 5.7 mEq/L (mmol/L).

PATHOPHYSIOLOGY

- Potassium is primarily intracellular; serum concentrations do not accurately reflect tissue concentrations.
- Hyperkalemia is often associated with cellular injury (e.g., trauma and ischemia) and other causes of translocation of potassium out of the intracellular space (e.g., acidosis).
- Potassium is eliminated in the kidneys and elimination is enhanced by aldosterone; conditions that inhibit renal elimination of potassium will cause hyperkalemia.

SYSTEMS AFFECTED

- Cardiovascular**—potassium affects cardiac conduction, and changes are reflected on the ECG; as potassium rises, the T waves become tall and spiked with a narrow base, the QRS complexes widen, and the P-R intervals lengthen; the P waves become smaller and wider and, in animals with severe hyperkalemia, disappear (atrial standstill); higher concentrations of potassium cause fusion of the QRS-T, which causes a wide complex idioventricular rhythm followed by ventricular fibrillation or asystole; ECG changes in animals with hyperkalemia vary and are diminished by hypernatremia, hypercalcemia, and alkalosis.
- Nervous—neuromuscular function** affected.

SIGNALMENT

- Dog and cat
- Pseudohyperkalemia in certain East Asian dog breeds (e.g., Akita, Shiba, Jindo, and Chinese Shar-Pei)

SIGNS

Historical Findings

- Weakness
- Collapse
- Flaccid paralysis
- Death

Physical Examination Findings

In addition to historical findings, arrhythmias, especially bradycardia, in some animals.

CAUSES

- Pseudohyperkalemia**—some blood cells (i.e., RBCs [reported in East Asian dog breeds including Akita, Shiba, Jindo, and Chinese Shar-Pei] due to the presence of a Na-K pump in the mature RBC membrane in some animals], platelets, WBCs), contain high concentrations of potassium; if the blood sample is not analyzed or separated promptly, this intracellular potassium is released into the serum, causing the potassium concentration to be artificially high (pseudohyperkalemia).
- Low potassium elimination**—anuric or oliguric renal failure; renal hypoperfusion (complete AV block); urinary tract rupture or urethral obstruction; administration of

potassium-sparing diuretics, ACE inhibitors, trimethoprim, nonsteroidal anti-inflammatory drugs, or heparin (causing hypoaldosteronism); some gastrointestinal diseases (e.g., salmonellosis, trichuriasis, duodenal perforation). • Translocation of potassium—acidosis, reperfusion syndrome, thrombolysis in feline aortic thromboembolism, tumor lysis syndrome, muscle injury (trauma, phosphofructokinase deficiency), severe digitalis overdose, infusion of mannitol, and hyperglycemia causing hyperosmolality. • High potassium intake—oral or parenteral potassium supplements. Potassium bromide toxicosis

- Miscellaneous—pleural effusion and ascites.

RISK FACTORS

- Fluid therapy with potassium supplementation.
 - Parenteral nutrition.
 - Administration of potassium-sparing diuretics (e.g., spironolactone) and ACE inhibitors (e.g., enalapril, benazepril), primarily in patients with renal disease.
 - Conditions associated with acidosis.
 - Trauma.
 - Renal disease.
 - Lower urinary tract disease in male cats.
 - Cystic calculi in male dogs.
 - Thrombocytosis and leukemia.
 - Akita, Shiba, Jindo, and Chinese Shar-Pei—pseudohyperkalemia. Not all animals within a breed are at risk for pseudohyperkalemia.
- Approximately 20% of Akitas have the high potassium phenotype.
- Phosphofructokinase deficiency.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Waxing and waning history of gastrointestinal complaints, weakness, collapse—consider hypoadrenocorticism.
- Straining to urinate or low urine output—consider urinary obstruction or oliguric/anuric renal failure.

LABORATORY FINDINGS

Disorders That May Alter Laboratory Results

Thrombocytosis (> 1,000,000 cells/mm³), leukocytosis (> 200,000 cells/mm³), and abnormal (leukemic) leukocytes can cause release of large amounts of potassium into the serum if not separated quickly.

CBC/BIOCHEMISTRY/URINALYSIS

- In patients with Na:K ratio < 27, consider hypoadrenocorticism; some patients with diarrhea and metabolic acidosis, ascites, chylothorax, or pregnancy may also have a low Na:K ratio.
- In patients with azotemia, consider hypoadrenocorticism, anuric or oliguric renal failure, and ruptured or obstructed urinary tract.
- In patients with high creatine kinase, aspartate aminotransferase, and lactic dehydrogenase, consider muscle injury.
- In patients with

severe thrombocytosis or leukocytosis or if the patient is an East Asian dog breed, consider pseudohyperkalemia.

OTHER LABORATORY TESTS

ACTH response test to rule out hypoadrenocorticism.

IMAGING

Radiographic contrast studies or ultrasound to rule out urinary tract rupture or obstruction.



TREATMENT

- Varies, depending on the underlying cause of hyperkalemia.
- Aggressiveness is dictated by patient's appearance and severity of ECG abnormalities.
- Initiate supportive measures to lower potassium while pursuing definitive diagnosis.
- Saline (0.9%) is the fluid of choice for lowering potassium concentrations and blunting the effects of hyperkalemia on cardiac conduction; if the patient is dehydrated or hypotensive, fluids can be administered rapidly (dogs, up to 90 mL/kg/h; cats, 60 mL/kg/h or faster with monitoring of central venous pressure).
- Reduced potassium diet in animals with hyperkalemia secondary to chronic renal disease.



MEDICATIONS

DRUG(S) OF CHOICE

- Can administer sodium bicarbonate to patients with severe hyperkalemia to induce translocation of potassium into cells; if blood pH and base deficit cannot be determined, administer 1–2 mEq/kg slowly IV; to calculate bicarbonate dose more accurately:
 - Dogs, 0.3 × body weight (kg) × (21 – patient's HCO₃⁻)
 - Cats, 0.3 × body weight (kg) × (19 – patient's HCO₃⁻)
- Administer half of dose and reevaluate.
- Can administer dextrose and regular insulin to patients with severe hyperkalemia to induce translocation of potassium into cells (regular insulin, 0.5 U/kg IV with 50% dextrose, 1 g/kg IV); dextrose can also be used without insulin.
- For patients with life-threatening hyperkalemia, administer calcium gluconate 10% (0.5–1 mL/kg slowly IV over 10 minutes) while monitoring the ECG; calcium antagonizes the effect of potassium on the conduction system without lowering the potassium concentration.

CONTRAINdications

- Avoid potassium-containing fluids and fluids that cause hyponatremia, acidosis, or hypocalcemia.
- Avoid drugs that contain potassium or interfere with potassium elimination (e.g., ACE inhibitors, trimethoprim antibiotics, and potassium-sparing diuretics).

(CONTINUED)

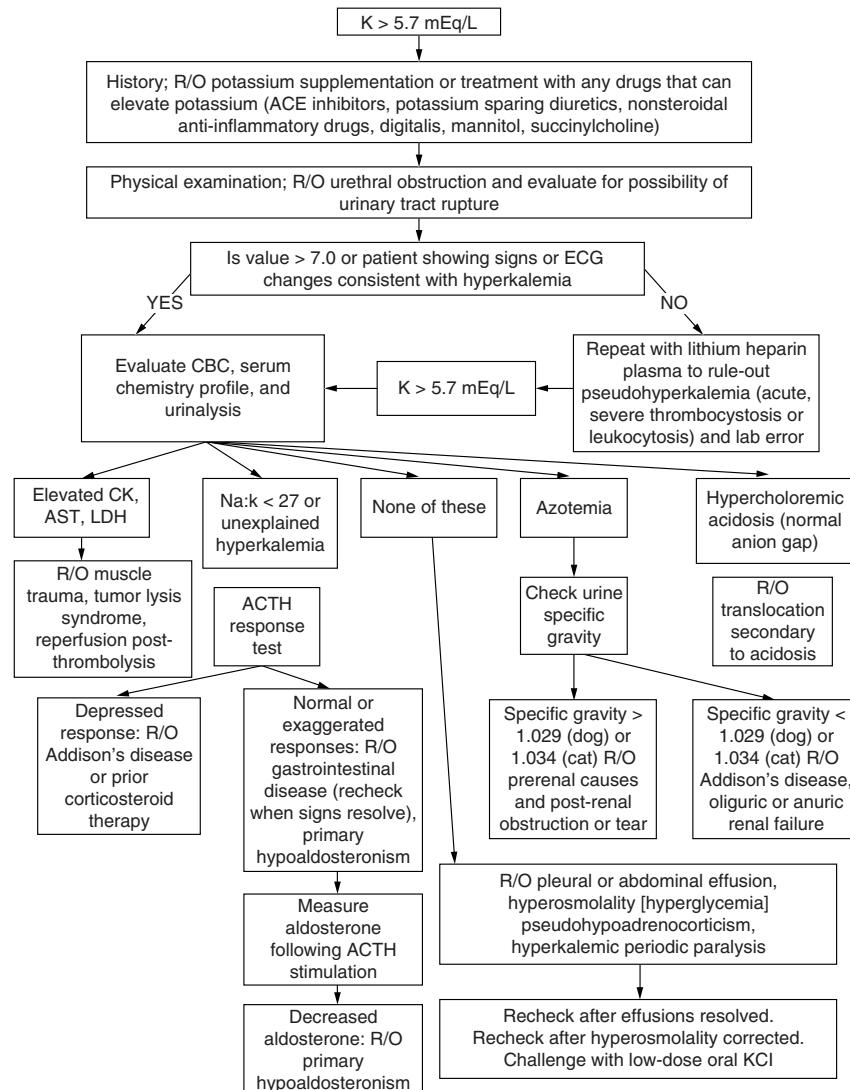
H HYPERKALEMIA

Figure 1.

Algorithm for diagnosing hyperkalemia.

PRECAUTIONS

- Kayexalate and sodium bicarbonate cause a sodium load that may lead to fluid retention in patients with cardiac or renal failure.
- Sodium bicarbonate lowers ionized calcium levels. Use cautiously in hypocalcemic patients.

ALTERNATIVE DRUG(S)

Sodium polystyrene sulfonate (Kayexalate) per os or per rectum binds potassium within the intestinal tract, limiting absorption and reabsorption; rarely used in veterinary practice.

**FOLLOW-UP****PATIENT MONITORING**

- Recheck potassium at frequency dictated by

the underlying disease. • Check ECG frequently until rhythm disturbances resolve.

PREVENTION/AVOIDANCE

- Monitor potassium in patients receiving drugs that alter potassium elimination.
- Administer IV potassium at a rate less than 0.5 mEq/kg/h.

POSSIBLE COMPLICATIONS

Death of animals with severe hyperkalemia

**MISCELLANEOUS****PREGNANCY/FERTILITY/BREEDING**

Combined hyperkalemia and hyponatremia reported in several pregnant dogs.

SEE ALSO

- Acidosis, Metabolic • Atrial Standstill

- Hypoadrenocorticism (Addison's Disease)
- Phosphofructokinase Deficiency • Renal Failure, Acute • Urinary Tract Obstruction

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- ACTH = adrenocorticotropic hormone
- ECG = electrocardiogram/electrocardiography
- RBC = red blood cell
- WBC = white blood cell

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Author Francis W.K. Smith, Jr.

Consulting Editor Deborah S. Greco

HYPERLIPIDEMIA



BASICS

DEFINITION

- Increased concentration of lipid in the blood of a fasted (> 12 hours) patient; includes hypercholesterolemia, hypertriglyceridemia, or both.
- Lipemic—serum or plasma separated from blood that contains an excess concentration of triglycerides (> 200 mg/dL).
- Lactescence—opaque, milk-like appearance of serum or plasma that contains an even higher concentration of triglycerides (> 1,000 mg/dL) than lipemic serum.

H PATHOPHYSIOLOGY

Primary Hyperlipidemia

- Primary (idiopathic) hyperlipidemia—defect in lipid metabolism causing hypertriglyceridemia with or without hyperchylomicronemia; likely hereditary in miniature schnauzer but the genetic defect has yet to be determined.
- Idiopathic hyperchylomicronemia in cats—familial, autosomal recessive defect in lipoprotein lipase activity.
- Primary hypercholesterolemia—occurs in some families of briard, rough collie, Shetland sheepdog, Doberman pinscher, and rottweiler; LDL cholesterol is high.

Secondary Hyperlipidemia

- Postprandial—absorption of chylomicrons from the gastrointestinal tract occurs 30–60 minutes after ingestion of a meal containing fat; may increase serum triglycerides for up to 12 hours.
- Diabetes mellitus—low lipoprotein lipase activity; high synthesis of very-low-density lipoprotein by the liver.
- Hypothyroidism—low LPL activity and lipolytic activity by other hormones (e.g., catecholamines); reduced hepatic degradation of cholesterol to bile acids.
- Hyperadrenocorticism—increased synthesis of VLDL by the liver and low LPL activity causes both hypercholesterolemia and hypertriglyceridemia.
- Liver disease—hypercholesterolemia caused by reduced excretion of cholesterol in the bile; cholestasis.
- Nephrotic syndrome—common synthetic pathway for albumin and cholesterol and possibly low oncotic pressure lead to increased cholesterol synthesis.
- Pancreatitis—associated with hypertriglyceridemia in dogs, but causal relationship not established.
- Obesity—excessive hepatic synthesis of VLDL.

Drug-Induced Hyperlipidemia

- Glucocorticoids
- Megestrol acetate (cat)

SYSTEMS AFFECTED

- Endocrine/Metabolic

- Gastrointestinal
- Hepatobiliary
- Nervous
- Ophthalmic

SIGNALMENT

- Dog and cat.
- Variable, depending on the cause.
- Hereditary hyperlipidemias—age of onset is > 8 months in cats and > 4 years in predisposed breeds of dog such as the miniature schnauzer.

SIGNS

Historical Findings

- Asymptomatic
- Recent ingestion of a meal
- Seizures, neurologic signs
- Abdominal pain and distress
- Neuropathies

Physical Examination Findings

- Lipemia retinalis
- Lipemic aqueous
- Neuropathy
- Cutaneous xanthomata
- Lipid granulomas in abdominal organs

CAUSES

Increased Absorption of Triglycerides or Cholesterol

Postprandial

Increased Production of Triglycerides or Cholesterol

- Idiopathic
- Nephrotic syndrome
- Pregnancy
- Defects in lipid clearance enzymes or lipid carrier proteins
- Idiopathic hyperchylomicronemia
- Hyperchylomicronemia in cats

Decreased Clearance of Triglycerides or Cholesterol

- Hypothyroidism
- Hyperadrenocorticism
- Diabetes mellitus
- Pancreatitis
- Cholestasis

RISK FACTORS

- Obesity
- High dietary intake of fats
- Genetic predisposition in miniature schnauzer and Himalayan cat
- Idiopathic hypercholesterolemia observed in families of briard, rough collie, Shetland sheepdog, Doberman pinscher, and rottweiler



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Fasting Hyperlipidemia

Rule out postprandial lipemia with a 12-hour fast.

Primary Hyperlipoproteinemia

- Idiopathic hyperlipidemia is observed most commonly in the miniature schnauzer breed.
- Hyperchylomicronemia in cats often manifests as polyneuropathies and lipogranulomas.
- Idiopathic hypercholesterolemia is observed in a variety of breeds; animals are often asymptomatic.

Secondary Hyperlipidemia

- Diabetes mellitus—signs include polyphagia, weight loss, polydipsia, and polyuria; glycosuria and fasting hyperglycemia confirm the diagnosis.
- Hypothyroidism—signs include lethargy, hypothermia, heat-seeking, and dermatologic changes (e.g., alopecia and hyperpigmentation).
- Pancreatitis—signs include abdominal pain, vomiting, diarrhea, and anorexia; often hyperlipidemia is accompanied by high liver enzyme activities and high lipase and amylase.
- Hyperadrenocorticism—signs include polydipsia, polyuria, polyphagia, dermatologic changes (e.g., alopecia and thin skin), and hepatomegaly; hypercholesterolemia often is attended by high ALP enzyme activity.
- Hepatic disease and cholestatic disorders—signs include anorexia, weight loss, and icterus.
- Nephrotic syndrome—signs include ascites and peripheral edema; hypercholesterolemia is observed in conjunction with hypoproteinemia and proteinuria.

LABORATORY FINDINGS

Sample Handling

- Submit serum.
- Lipemia causes hemolysis if serum remains in RBC for a long time; inquire about the laboratory method of clearing lipemic samples before submission.
- Two samples may be submitted: one for biochemical analysis, which may be cleared, and one for triglycerides and cholesterol concentrations.

Drugs That May Alter Laboratory Results

- Corticosteroids
- Phenytoin
- Prochlorperazine.
- Thiazides
- Phenothiazines

Disorders That May Alter Laboratory Results

- Falsely high cholesterol
- Non-fasted samples (< 12 hours)
- Icterus—spectrophotometric techniques
- Fluoride and oxalate anticoagulants—enzymatic techniques
- Lipemia

Valid If Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Results of hemogram usually normal.

(CONTINUED)

- Hyperadrenocorticism—elevated ALP activity, polycythemia, nucleated RBCs.
- Hypothyroidism—mild normocytic, normochromic anemia.
- High triglycerides—dogs, > 150 mg/dL; cats, > 100 mg/dL.
- High cholesterol—dogs, > 300 mg/dL; cats, > 200 mg/dL.
- Nephrotic syndrome—low albumin, proteinuria.
- Diabetes mellitus—high fasted serum glucose, glycosuria.
- Pancreatitis—high PLI (species-specific), hypocalcemia.
- Results of urinalysis often normal.

OTHER LABORATORY TESTS

- HDL and LDL determinations—used in human medicine; values reported for HDL and LDL in dogs and cats cannot be assumed to be reliable.
- Chylomicron test—obtain serum sample after a 12-hour fast and refrigerate for 12–14 hours; do not freeze; chylomicrons rise to the surface and form a creamy layer.
- Lipoprotein electrophoresis—separates LDL, VLDL, HDL1, and HDL2.
- LPL activity—collect serum for triglycerides and cholesterol concentrations and lipoprotein electrophoresis before and 15 minutes after IV administration of heparin (90 IU/kg); if there is no change in values before and after heparin administration, a defective LPL enzyme system should be suspected.
- T₄, free T₄, and TSH determinations indicated if hypothyroidism is suspected.
- Adrenocorticotropic hormone (ACTH) stimulation test or low-dose dexamethasone-suppression test (LDDS) indicated if hyperadrenocorticism is suspected.

**TREATMENT**

Diet should contain < 10% fat (e.g., Waltham Royal Canin Low Fat, Hill's Prescription Diet r/d or w/d, Iams Restricted Calorie, Purina OM).

**MEDICATIONS****DRUG(S) OF CHOICE**

- Initial management is dietary.
- See “Alternative Drug(s)” if diet fails to control hyperlipidemia.

ALTERNATIVE DRUG(S)

- Gemfibrozil 7.5 mg/kg PO q12h; 200 mg/dog/day
- Fish oils—omega-3 polyunsaturated fat, 50–300 mg/kg PO q24h
- Niacin 25–100 mg/dog/day (slow release)

**FOLLOW-UP****PATIENT MONITORING**

- Keep triglyceride concentrations < 500 mg/dL to avoid possibly fatal episodes of acute pancreatitis.
- Checking cholesterol often is not necessary because hypercholesterolemia is not associated with clinical signs.

POSSIBLE COMPLICATIONS

- Pancreatitis and seizures are common complications of hyperlipidemia in the miniature schnauzer.
- In cats with hereditary chylomicronemia, xanthoma formation, lipemia retinalis, and neuropathies have been reported; peripheral neuropathies usually resolve 2–3 months after institution of a low-fat diet.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Pancreatitis
- Seizures
- Neuropathies

AGE-RELATED FACTORS

None

PREGNANCY/FERTILITY/BREEDING

Potential cause of high cholesterol

SYNONYMS

- Lipemia—turbid serum or plasma secondary to significant hypertriglyceridemia
- Hyperlipoproteinemia—increased blood concentration of lipoproteins

SEE ALSO

Under “Causes”

ABBREVIATIONS

- ALP = alkaline phosphatase
- HDL = high-density lipoprotein
- LDL = low-density lipoprotein
- LPL = lipoprotein lipase
- PLI = pancreatic lipase immunoreactivity
- RBC = red blood cell
- T₄ = thyroxine
- TSH = thyroid stimulating hormone
- VLDL = very-low-density lipoprotein

H

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Client Education Handout
available online

HYPERMAGNESEMIA



BASICS

DEFINITION

- Dogs—serum magnesium > 2.5 mg/dL
- Cats—serum magnesium > 2.3 mg/dL

PATOPHYSIOLOGY

- Hypermagnesemia is less clinically significant than low total body magnesium in veterinary patients.
- Magnesium is second only to potassium as the most abundant intracellular cation; is found primarily in bone and muscle; is required for many metabolic functions.
- Serum magnesium is present in three forms: protein-bound form (approximately 25–30%) and chelated and ionized forms (together account for 70–75%).
- Magnesium absorption occurs primarily in the ileum. Absorption also occurs in the jejunum and colon.
- Magnesium is an important cofactor in the sodium-potassium ATPase pump that maintains electrical gradients across membranes.
- Interference with the electrical gradient can change resting membrane potentials; repolarization disturbances result in neuromuscular and cardiac abnormalities.
- The kidneys maintain magnesium balance with 10–15% reabsorbed in the proximal tubule, 60–70% in the thick ascending limb of the loop of Henle, and 10–15% reabsorbed in the distal convoluted tubule. Reabsorption within the distal convoluted tubule is under hormonal and neurohormonal control and determines the final urine concentration of magnesium.
- Any condition that severely lowers the glomerular filtration rate can elicit hypermagnesemia because magnesium homeostasis is largely controlled by renal elimination.
- High magnesium concentration impairs transmission of nerve impulses and decreases post-synaptic responses at the neuromuscular junction. When magnesium was given to anesthetized dogs at 0.12 mEq/kg/min, cardiovascular effects were not noted until plasma levels exceeded 12.2 mEq/L. The total dose of magnesium required to reach that level was 1–2 mEq/kg. It took cumulative doses of 5.9–10.9 mEq/kg to cause fatal cardiac arrhythmias (ventricular fibrillation).
- Magnesium has been called nature's calcium blocker; the most serious complications of hypermagnesemia result from calcium antagonism in the cardiac conduction system.

SYSTEMS AFFECTED

- Cardiovascular
- Musculoskeletal
- Nervous

INCIDENCE/PREVALENCE

Hypermagnesemia was found in 18% of hospitalized cats and 13% of hospitalized

dogs. Most of these patients also had renal insufficiency or post-renal azotemia.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat

Breed Predilections

N/A

SIGNS

General Comments

- Usually caused by renal failure; clinical signs might be referable to azotemia and renal insufficiency. Clinical hypermagnesemia is reported most often in patients with preexisting renal disease that are oversupplemented with parenteral magnesium salts.
- Characterized by progressive loss of neuromuscular, respiratory, and cardiovascular function.

Historical and Physical Examination Findings

- Nausea, vomiting, weakness, bradycardia, flaccid paralysis, mental depression, and hyporeflexia.
- Hypotension and ECG changes, including delayed intraventricular conduction and prolonged QT interval, occur with increased serum magnesium.
- Atrioventricular block, respiratory depression, coma, and cardiac arrest have been observed in humans with serum magnesium concentrations > 16 mg/dL.

CAUSES

- Renal failure.
- Intestinal hypomotility disorders and constipation.
- Endocrine disorders including hypoadrenocorticism, hypothyroidism, and hyperparathyroidism.
- Combined angiotensin-converting enzyme inhibitors and spironolactone administration.
- Excessive magnesium administration from magnesium-containing cathartic solutions given in conjunction with activated charcoal, magnesium-containing laxatives, and excess magnesium in peritoneal dialysis solutions.
- Iatrogenic oversupplementation in patients with concurrent renal disease.

RISK FACTORS

- Renal disease
- Intestinal hypomotility
- Massive hemolysis
- Hypoadrenocorticism
- Hyperparathyroidism
- Patients receiving angiotensin-converting enzyme inhibitors and spironolactone concurrently
- Excessive use of magnesium-containing cathartic solutions, especially in patients with renal insufficiency



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Signs are most similar to those of hypocalcemia, which often occurs simultaneously.
- Bradycardia can be caused by neurologic disease, hyperkalemia, hypertension, hypothyroidism, sick sinus syndrome, and various drugs.

LABORATORY FINDINGS

Note: 12 mg of magnesium = 1 mEq of magnesium; to convert from mg/dL to mEq/L, divide by 1.2.

Drugs That May Alter Laboratory Results

- Serum is favored over plasma because the anticoagulant used for plasma samples can contain citrate or other ions that can bind magnesium.
- EDTA, sodium fluoride-oxalate, sodium citrate, and intravenous calcium gluconate can cause falsely low serum magnesium values.

Disorders That May Alter Laboratory Results

- Hemolysis can result in falsely increased serum magnesium; the magnesium concentration in erythrocytes is approximately three times that in serum.
- Storage of serum or urine in metal containers can falsely elevate magnesium values.
- Hyperbilirubinemia can cause falsely decreased serum magnesium.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Serum magnesium—dogs, > 2.5 mg/dL; cats, > 2.3 mg/dL
- Hypocalcemia is common
- Azotemia in some patients

OTHER LABORATORY TESTS

Ionized magnesium can be measured with an ion-selective electrode or by ultrafiltration of plasma; alternative methods of evaluating magnesium status include mononuclear blood cell magnesium levels or quantifying retention from a loading dose.

DIAGNOSTIC PROCEDURES

Electrodiagnostics (e.g., electromyography and electrocardiography) reveal effects of hypermagnesemia but do not differentiate the cause.



TREATMENT

APPROPRIATE HEALTH CARE

- Management involves enhancing elimination from the body and symptomatic therapy.

(CONTINUED)

- Discontinue all magnesium-containing medications and nutritional supplements.
- Saline diuresis and loop diuretics enhance renal clearance of magnesium.
- Fluid therapy with 0.9% NaCl provides fluid volume to address hypovolemia, hypotension and azotemia.
- Patients with oliguria might require peritoneal dialysis to treat severe hypermagnesemia.
- Parenteral calcium supplementation directly antagonizes the effects of magnesium, reversing respiratory depression, cardiac arrhythmias, and hypotension; calcium also enhances magnesium excretion.
- Hypermagnesemia associated with combined angiotensin-converting enzyme inhibitors and spironolactone is rare, mild, and unlikely to be clinically significant.

NURSING CARE

Patients with neurologic manifestations of hypermagnesemia might require intensive nursing care to prevent aspiration pneumonitis, pulmonary atelectasis, pressure necrosis (bed sores), and urine and fecal scalding.

DIET

Any magnesium supplementation should be discontinued.

CLIENT EDUCATION

Clients should be advised if preexisting conditions contributed to hypermagnesemia.

ACTIVITY

Patient activity is dependent on underlying conditions and response to therapy.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Furosemide promotes renal excretion of magnesium by decreasing absorption of magnesium in the loop of Henle.

- Enteral and parenteral calcium administration helps reverse clinical manifestations of hypermagnesemia and correct concurrent hypocalcemia; oral supplementation with any preparation can be given at a dosage of 25–50 mg/kg/day; severe hypermagnesemia can be treated with 10% calcium gluconate: 1–2 mL/kg (diluted 1:1 with saline) IV or SC q8h, administered slowly.

CONTRAINdications

Magnesium-containing compounds and fluids

PRECAUTIONS

Monitor ECG during calcium infusion

**FOLLOW-UP****PATIENT MONITORING**

- Serum magnesium and calcium concentrations
- Renal function—azotemia and urine output
- Continuous electrocardiogram if possible

PREVENTION/AVOIDANCE

Magnesium supplementation should be approached cautiously in patients with renal insufficiency.

POSSIBLE COMPLICATIONS

- Severe hypermagnesemia and hypocalcemia can be fatal.
- Hypermagnesemic dogs were 2.6 times less likely to survive their illness than patients with normal serum magnesium levels.

EXPECTED COURSE AND PROGNOSIS

Veterinary patients with iatrogenic overdose can have a good outcome with prompt recognition and supportive care.

HYPERMAGNESEMIA**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Hypocalcemia
- Hyperphosphatemia
- Azotemia

PREGNANCY/FERTILITY/BREEDING

Effects on the fetus are identical to effects on the dam.

SEE ALSO

Hypocalcemia

ABBREVIATIONS

- ECG = electrocardiogram
- Mg = magnesium

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Author Timothy B. Hackett

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H

HYPERMETRIA AND DYSMETRIA



BASICS

OVERVIEW

- Dysmetria—incoordination of the limbs during voluntary movement characterized by an inability to judge the rate, range, and force of movements.
- Hypermetria—overreaching limb movements giving a characteristic goose-stepping gait. The term dysmetria includes both hypo- and hypermetria.
- The cerebellum plays a central role in generating skilled movements and maintaining muscle tone and body posture. It does not initiate but coordinates and smoothes out movements.
- Damage to the cerebellum results in inaccurate gauging of voluntary movements. Motor strength is preserved; conscious proprioception is unaffected.
- Rarely, compression of the spinocerebellar tracts in spinal cord disorders can produce dysmetria. This is more likely to occur with dorsally located lesions.
- The hereditary ataxias are an important cause of cerebellar disease in dogs.

SIGNALMENT

Dog and cat of any age, breed, or sex

SIGNS

Other signs of cerebellar disease that may be present include truncal sway, intention tremor, wide-based stance, head tilt, loss of menace response with normal vision, and anisocoria.

CAUSES

Cerebellar

- Dogs—hypoplasia (inherited or secondary to infection with canine herpesvirus in the perinatal period); hereditary ataxia (cerebellar abiotrophy or cerebellar cortical degeneration); lysosomal storage diseases; CDV; protozoal infections (*Toxoplasma gondii* and *Neospora caninum*); rickettsial infections (*Ehrlichia canis* and Rocky Mountain spotted fever); *Cryptococcus* and other fungal infections; granulomatous meningoencephalitis; meningoencephalitis of unknown etiology; steroid-responsive shaker/tremor syndrome; neoplasia; trauma; infarct; hemorrhage; metronidazole toxicity.
- Cats—hypoplasia secondary to *in utero* infection with feline panleukopenia virus; lysosomal storage diseases; FIP, FeLV, FIV (associated immunosuppression predisposes to other encephalitides and to neoplasia); toxoplasmosis; *Cryptococcus* and other fungal infections; neoplasia; hemorrhage; trauma.

Spinal

- While there are many causes of spinal cord disease, centrodorsally located cervical lesions are more likely to produce hypermetria.

- Dogs—subarachnoid diverticula; neoplasia; vertebral malformation (atlantoaxial subluxation); and calcinosis circumscripta.

RISK FACTORS

Cerebellar

- Hereditary ataxia reported in Gordon and Irish setters, Kerry blue terriers, Airedale terriers, Finnish harriers and hounds, Samoyeds, Bern running dogs, cocker spaniels, cairn terriers, Australian kelpies, bull mastiffs, Italian spinones, the terrier group, Old English sheepdogs, Rhodesian ridgebacks, border and rough-coated collies, Brittany spaniels, beagles and Scottish terriers.
- Cerebellar hypoplasia has been reported in chow chows, Irish setters, and wire fox terriers.
- Lysosomal storage diseases causing dysmetria have been reported in Siamese, Balinese, Persian, and domestic shorthair cats, and in English springer spaniels, American Staffordshire terriers, Portuguese water dogs, German shorthaired pointers, Australian silky terriers, schipperkes, English setters, border collies, salukis, Chihuahuas, Queensland blue heelers, dachshunds, Yugoslavian shepherds, and Tibetan terriers.
- Small-breed white dogs, such as Maltese and West Highland white terriers, are predisposed to steroid-responsive (idiopathic) tremor syndrome.
- Metronidazole at dosages > 60 mg/kg/day can induce cerebello-vestibular signs in dogs. Signs are induced in some dogs at lower doses.
- Vascular events, both thromboembolic and hemorrhagic, can cause cerebellar signs, typically due to thrombosis of the rostral cerebellar artery. Disorders that cause hypercoagulable state (such as hyperadrenocorticism) or hypertension (such as hyperthyroidism in cats, or chronic renal disease) can predispose to stroke. Hypothyroidism has also been associated with cerebellar stroke. Thrombosis of the rostral cerebellar artery occurs in older dogs; an underlying cause is not always identified.

Spinal

- Giant-breed dogs are predisposed to vertebral malformation and instability.
- Young large-breed dogs are predisposed to subarachnoid diverticula and calcinosis circumscripta.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Some dogs, especially small breeds, have a high-stepping gait in their thoracic limbs as a normal finding. If there are no other signs of cerebellar disease, establish whether a high-stepping thoracic limb gait is normal for the dog.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC may reflect infectious/inflammatory disease.
- Storage products may be present in leukocytes in some lysosomal storage diseases.

OTHER LABORATORY TESTS

- Acute and convalescent serologic titers—to diagnose rickettsial, protozoal, fungal, and viral diseases.
- CSF antibody or antigen (*Cryptococcus*) titers—for some infections (e.g., *Toxoplasma*, *Cryptococcus*), measure in addition to serologic titers.
- PCR on CSF and serum—to diagnose rickettsial, bacterial, protozoal, fungal, and viral diseases; sensitive and specific if the infectious agent is present in the CSF or serum.
- Genetic tests available for hereditary ataxia in beagles, Finnish hounds, Italian spinone, Gordon setter, Old English sheepdog and the terrier group (Jack and Parson Russell terriers).

IMAGING

- Thoracic radiography—to identify metastatic disease in older patients.
- Abdominal ultrasonography—if intra-abdominal neoplasia is suspected.
- Brain CT or MRI—to diagnose neoplasia, vascular disease, encephalitis, cerebellar atrophy due to hypoplasia or abiotrophy; MRI is the preferred modality for evaluating the caudal fossa.
- Survey spinal radiography—if spinal cord disease is suspected; may be helpful in identifying vertebral malformations and calcinosis circumscripta.
- Spinal MRI—non-invasive and informative about spinal cord parenchyma.

DIAGNOSTIC PROCEDURES

- Fundic examination—to identify chorioretinitis (evidence of infectious/inflammatory disease) and vascular lesions associated with vasculitis or hypertension.
- CSF—to diagnose encephalitis; storage products may be present in CSF leukocytes in some lysosomal storage diseases.
- Liver biopsy—may be helpful in diagnosing certain lysosomal storage diseases in animals with hepatomegaly.



TREATMENT

APPROPRIATE HEALTH CARE

- Severe and/or rapidly progressive clinical signs—hospitalization for diagnostic workup and treatment.
- Mild and slowly progressive clinical signs—outpatient, but diagnostic tests requiring anesthesia necessitate hospitalization.

(CONTINUED)

HYPERMETRIA AND DYSMETRIA

- Patients should be restricted to areas and activities where they are unlikely to fall and injure themselves.
- Appropriate treatment of the underlying cause should be undertaken once a diagnosis has been established.

SURGICAL CONSIDERATIONS

Surgical decompression of the spinal cord indicated for compressive myelopathies.

**MEDICATIONS****DRUG(S) OF CHOICE**

Discontinue metronidazole, regardless of the dose rate, to see if signs improve.

**FOLLOW-UP****PATIENT MONITORING**

- Periodic repeat neurologic examinations.
- Additional monitoring will depend on the underlying cause (e.g., serial monitoring of blood pressure in hypertensive patients).

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

Fungal infections can be zoonotic.

ABBREVIATIONS

- CDV = canine distemper virus
- CSF = cerebrospinal fluid
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- PCR = polymerase chain reaction

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H

HYPERNATREMIA



BASICS

DEFINITION

Serum sodium concentration > 158 mEq/L in dogs or > 165 mEq/L in cats.

PATHOPHYSIOLOGY

- Sodium is the most abundant cation in the extracellular fluid, so hypernatremia usually reflects hyperosmolality.
- Hypernatremia can be caused by excessive water loss, increased intake of sodium, or a combination of both.
- Common causes of hypernatremia include renal or gastrointestinal loss of water in excess of sodium loss and low water intake.

H

SYSTEMS AFFECTED

- Endocrine/Metabolic
- Nervous

SIGNALMENT

Dog and cat

SIGNS

- Polydipsia
- Disorientation
- Coma
- Seizures
- Other findings depend on underlying cause
- Severity of signs usually correlates to the degree of hypernatremia

CAUSES

- Total body sodium high—oral ingestion (rare); IV administration of NaCl during cardiovascular resuscitation; hyperaldosteronism (rare); hyperadrenocorticism (may cause mild changes).
- Total body sodium normal plus water deficit—low water intake (e.g., no access to water and adipsia or hypodipsia); high urinary water loss (e.g., diabetes insipidus); high insensible water loss (e.g., panting and hyperthermia).
- Total body sodium low and hypotonic fluid loss (i.e., loss of fluid containing sodium without adequate water replacement)—urinary loss (e.g., diabetes mellitus, osmotic diuresis, and diuresis after acute urinary obstruction); gastrointestinal sodium loss (e.g., administration of osmotic cathartic, vomiting, and diarrhea).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Diabetes insipidus
- Hyperosmolar non-ketotic syndrome
- Hypertonic dehydration
- Alterations in thirst reaction pathway: rare
- Salt ingestion—rare

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

A wide variety of drugs interfere with renal capacity to concentrate urine, leading to water loss in excess of sodium and high serum sodium concentration; these drugs include lithium, demeclocycline, and amphotericin.

Disorders That May Alter Laboratory Results

Lipemia or hyperproteinemia (> 11 g/dL) can artificially raise sodium concentration when the flame photometry method is used.

Valid if Run in a Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- High serum sodium concentration.
- Diabetes insipidus—polyuria, low urinary specific gravity, and low urinary sodium concentration.
- Hyperosmolar non-ketotic syndrome—high blood glucose, low urine output, and high urinary specific gravity (usually > 1.025).
- Hypertonic dehydration—low urinary sodium concentration and high urinary specific gravity (usually > 1.030).

OTHER LABORATORY TESTS

- Modified water deprivation test (see Appendix II for test protocol) to differentiate diabetes insipidus from other causes of polyuria and polydipsia; performed after results of CBC, biochemical analysis, urinalysis, and endocrine testing are evaluated to rule-out hyperadrenocorticism.
- After water restriction, patients with diabetes insipidus have little or no increase in urinary specific gravity or osmolality.
- After ADH or DDAVP administration, patients with nephrogenic diabetes insipidus have < 10% increase in urinary specific gravity; those with central diabetes insipidus have a 10–800% increase.

IMAGING

CT scan or MRI in patients with diabetes insipidus to rule out pituitary tumor.



TREATMENT

- After resolution of the hypernatremia, consider a sodium-restricted diet (especially in patients with nephrogenic diabetes insipidus).
- Water must be available at all times for patients with diabetes insipidus.



MEDICATIONS

DRUG(S) OF CHOICE

- If hypovolemia is severe—replace volume with isotonic saline (i.e., lactated Ringer's or normal saline) or isotonic fluids (i.e., 5% dextrose with half-normal saline).
- Hypernatremia—administer hypotonic fluids (e.g., 5% dextrose in water) to reduce serum sodium by 0.5 mEq/h or by no more than 20 mEq/L/day; supplement with potassium and phosphate if needed.
- Central diabetes insipidus—DDAVP (one to two drops in subconjunctival sac q12–24h).
- Nephrogenic diabetes insipidus—hydrochlorothiazide (2–4 mg/kg PO q12h).

CONTRAINDICATIONS

Refer to manufacturer's literature

PRECAUTIONS

- Rapid correction of hypernatremia can cause pulmonary edema.
- Hypocalcemia may develop during correction of hypernatremia.



FOLLOW-UP

PATIENT MONITORING

- Acute setting—electrolytes, urine output, and body weight
- Diabetes insipidus—water intake

(CONTINUED)

HYPERNATREMIA**POSSIBLE COMPLICATIONS**

- CNS thrombosis or hemorrhage.
- Hyperactivity.
- Seizures.
- Serum sodium > 180 mEq/L often associated with residual CNS damage.
- Many patients recover, but possibility of neurologic damage is high.

**MISCELLANEOUS****AGE-RELATED FACTORS**

None

SYNOMYS

None

SEE ALSO

- Diabetes Insipidus
- Hyposthenuria

ABBREVIATIONS

- ADH = antidiuretic hormone
- CNS = central nervous system
- CT = computed tomography
- DDAVP = brand name of desmopressin, a synthetic antidiuretic hormone preparation
- MRI = magnetic resonance imaging

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H

HYPEROSMOLARITY



BASICS

DEFINITION

- Osmolarity—expressed in mOsm/L; represents the number of solute particles per liter of solution.
- Osmolality—expressed in mOsm/kg; represents the number of solute particles per kilogram of solution.
- Hyperosmolarity—a high concentration of solute particles per liter of solution.
- Serum concentrations > 310 mOsm/L in dogs and > 330 mOsm/L in cats are usually considered hyperosmolar.
- Morbidity from hyperosmolarity is related more to rapid changes in osmolarity than to the actual amount of change.

H

PATOPHYSIOLOGY

- Serum sodium is responsible for most of the osmotically active particles that contribute to serum osmolarity; serum glucose and urea also contribute to serum osmolarity.
- Anything that causes water loss increases concentrations of solutes in plasma or serum, thereby increasing serum osmolarity.
- Blood volume, hydration status, and ADH are intimately involved in controlling extracellular fluid volume.
- Low circulating blood volume stimulates carotid and aortic baroreceptors to respond to changes in blood pressure, causing ADH secretion.
- Hyperosmolarity affects the osmoreceptors in the hypothalamus and stimulates ADH secretion from the neurohypophysis; the hypothalamic thirst center is also stimulated and causes an increase in water consumption to counteract serum hyperosmolarity by solute dilution.
- Rapid increases in serum osmolarity cause water movement along its concentration gradient from intracellular to extracellular spaces, resulting in neuronal dehydration, cell shrinkage, and cell death; cerebral vessels may weaken and hemorrhage.

SYSTEMS AFFECTED

- Cardiovascular—hypotension and decreased ventricular contractility.
- Nervous—excessive thirst may be the first sign of hyperosmolarity. Central nervous system depression may lead to coma.
- Renal/Urologic—low urine output.

SIGNALMENT

- Dog and cat.
- Hypodipsia and hyperosmolarity have been reported in young female miniature schnauzers.

SIGNS

General Comments

- Primarily neurologic or behavioral.
- Severity is related more to how quickly hyperosmolarity occurs than to the absolute magnitude of change.
- Most likely to occur if serum osmolarity is > 350 mOsm/L and usually severe if > 375 mOsm/L.

Historical Findings

Anorexia, lethargy, vomiting, weakness, disorientation, ataxia, seizures, and coma; polydipsia followed by hypodipsia.

Physical Examination Findings

- Normal, or abnormalities may reflect underlying disease.
- In addition to historical findings, dehydration, tachycardia, hypotension, weak pulses, and fever may be detected.

CAUSES

Increased Solutes

Hypernatremia, hyperglycemia, severe azotemia, ethylene glycol toxicosis, salt poisoning, sodium phosphate enemas in cats and small dogs, mannitol, radiographic contrast solution, administration of ethanol, aspirin toxicosis, shock, lactate in patients with lactic acidosis, acetoacetate and β -hydroxybutyrate in patients with ketoacidosis, liquid enteral nutrition, and parenteral nutrition solutions.

Decreased Extracellular Fluid Volume

Dehydration—gastrointestinal loss, cutaneous loss, third space loss, low water consumption, and polyuria without adequate compensatory polydipsia.

RISK FACTORS

- Medical conditions that predispose—renal failure, diabetes insipidus, diabetes mellitus, hyperadrenocorticism, hyperaldosteronism, and heat stroke.
- Therapeutic hyperosmolar solutions—hypertonic saline, sodium bicarbonate, sodium phosphate enemas in cats and small dogs, mannitol, and parenteral nutrition solutions.
- High environmental temperatures.
- Fever.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Primary CNS disease and neoplasia may be characterized by altered mentation, but serum osmolarity is usually normal.
- Physical evidence or history of injury usually helps to rule out CNS depression caused by cranial trauma.
- Perform a thorough physical examination to assess hydration status and obtain information regarding previous therapy that may have included sodium-containing fluids or hyperosmolar solutions.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

Excessive administration of sodium-containing fluids or hyperosmolar solutions increase serum osmolarity.

Disorders That May Alter Laboratory Results

N/A

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- High PCV, hemoglobin, and plasma proteins in dehydrated patients; serum electrolytes may also be increased.
- Hyperosmolarity is an indication to evaluate serum sodium and glucose concentrations.
- Without the presence of excessive unmeasured osmoles, estimated serum osmolarity may be calculated from serum chemistries as follows:

$$\frac{2(\text{Na}^+ + \text{K}^+) + \text{glucose}/18 + \text{BUN}/2.8}{\text{mOsm/L}}$$

- Normally, calculated osmolarity should not exceed measured osmolarity; if it does, consider laboratory error.
- If measured osmolarity exceeds the calculated osmolarity, determine the osmolar gap.
- Osmolar gap = measured osmolarity – calculated osmolarity.
- High measured osmolarity and normal calculated osmolarity with a high osmolar gap indicate the presence of unmeasured solutes (not Na, K, glucose, BUN).
- High measured osmolarity and high calculated osmolarity with a normal osmolar gap usually indicate that the hyperosmolarity is caused by hyperglycemia or hypernatremia.
- Serum sodium concentration may be artificially low in patients with severe hyperglycemia and hyperosmolarity.
- Fasting hyperglycemia and glucosuria support a diagnosis of diabetes mellitus.
- Numerous calcium oxalate crystals in the urine suggest ethylene glycol toxicosis.
- High urinary specific gravity rules out diabetes insipidus.
- Low urinary specific gravity, especially hyposthenuria, suggests diabetes insipidus.

OTHER LABORATORY TESTS

Urinary osmolarity lower than serum osmolarity suggests diabetes insipidus; concentrated urine rules out diabetes insipidus.

IMAGING

Renal ultrasonography may reveal bright hyperechoic kidneys in patients with ethylene glycol toxicosis.



TREATMENT

- Mild hyperosmolarity without clinical signs may not warrant specific treatment, but diagnose and treat underlying diseases.
- Hospitalize patients with moderate-to-high osmolarity (> 350 mOsm/L) and patients exhibiting clinical signs and gradually lower serum osmolarity with intravenous fluids while a definitive diagnosis is pursued.
- Administer D5W or 0.45% saline slowly IV.
- Free water deficit can be calculated by the following formula:

$$\text{Free water deficit} = 0.4 \times \text{lean body weight in kg} \times [(\text{Plasma Na}/140) - 1]$$

(CONTINUED)

- The goal is to not drop sodium more than 15 mEq/L in an 8-hour period; that is, the ultimate goal is to not drop the sodium by more than 2 mEq/L/hour.
- Initially, 0.9% saline may be used to restore normal hemodynamics and replace dehydration deficits; replace one-half of dehydration deficits over 12 hours and the remainder over 24 hours; then switch to D₅W or 0.45% saline.



MEDICATIONS

DRUG(S) OF CHOICE

Seizures can be controlled with diazepam, phenobarbital, propofol, or pentobarbital.

CONTRAINDICATIONS

Hypertonic saline and hyperosmolar solutions

PRECAUTIONS

- May use normal saline initially, but rapid administration may worsen neurologic signs.
- Rapid administration of hypotonic fluids (e.g., D₅W and 0.45% saline) may also cause cerebral edema and worsen neurologic signs.

ALTERNATIVE DRUG(S)

Regular insulin 0.1 unit/kg IM or IV can be administered if a hyperglycemic crisis occurs secondary to parenteral nutrition administration.



FOLLOW-UP

PATIENT MONITORING

- Hydration status; avoid overhydration.
- Bladder size, urine output, and breathing patterns during IV fluid administration.
- Anuria, irregular breathing patterns, worsening depression, coma, or seizures may be signs of deterioration.

POSSIBLE COMPLICATIONS

Altered consciousness and abnormal behavior



MISCELLANEOUS

ASSOCIATED CONDITIONS

Hypernatremia and hyperglycemia

AGE-RELATED FACTORS

None

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Diabetes Mellitus with Hyperosmolar Coma
- Hyperglycemia
- Hypernatremia

ABBREVIATIONS

- ADH = antidiuretic hormone
- CNS = central nervous system
- PCV = packed cell volume

HYPEROSMOLARITY

Suggested Reading

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Author Melinda Fleming

Consulting Editor Deborah S. Greco

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HYPERPARATHYROIDISM



BASICS

DEFINITION

A pathologic, sustained, high, circulating concentration of PTH.

PATHOPHYSIOLOGY

- PTH—secreted by the parathyroid glands in response to changes in the concentration of ionized calcium in the serum; raises the serum calcium concentration through its effects on bone and renal tubular calcium resorption and vitamin D-dependent intestinal calcium absorption.
- Can develop as a primary condition or be secondary to a disorder of calcium homeostasis; primary hyperparathyroidism is associated with benign (usually) adenoma of the parathyroid gland(s); secondary hyperparathyroidism can be caused by a deficiency of calcium and vitamin D associated with malnutrition or chronic renal disease.

SYSTEMS AFFECTED

- Cardiovascular
- Gastrointestinal
- Neuromuscular
- Renal/Urologic

GENETICS

- None known for primary hyperparathyroidism, but its association with certain breeds suggests a possible hereditary basis in some cases.
- Secondary hyperparathyroidism can develop in association with hereditary nephropathy, but is not inherited per se.

INCIDENCE/PREVALENCE

- Prevalence of primary form is unknown.
- More commonly diagnosed in dogs than in cats.
- Fairly common among causes of hypercalcemia, but much less common than hypercalcemia of malignancy in dogs.
- Nutritional secondary hyperparathyroidism is decreasing in prevalence as the public becomes more educated in pet nutrition.
- Chronic renal failure with secondary hyperparathyroidism is extremely common, more so in cats than in dogs.

SIGNALMENT

Species

Cat and dog

Breed Predilections

- Keeshonden
- Siamese cats

Mean Age and Range

- Cats—mean age, 13 years; range 8–15 years
- Dogs—mean age, 10 years; range 5–15 years

Predominant Sex

None

SIGNS

General Comments

- Most dogs and cats with primary hyperparathyroidism do not appear ill.
- Signs are usually mild and are due solely to the effects of hypercalcemia.
- Signs become apparent when hypercalcemia is severe and chronic.

Historical Findings

- Polyuria
- Polydipsia
- Anorexia
- Lethargy
- Vomiting
- Weakness
- Urolithiasis
- Stupor and coma

Physical Examination Findings

- Often unremarkable.
- Parathyroid adenoma is not palpable in dogs but often is in cats.
- Nutritional secondary disease is sometimes associated with pathologic bone fractures and general poor body condition.

CAUSES

- Primary hyperparathyroidism—PTH-secreting adenoma of the parathyroid gland. In most cases only one gland is adenomatous. Malignant tumors of the parathyroid glands are uncommon and usually non-invasive.
- Renal secondary hyperparathyroidism—renal calcium loss and reduced gut absorption of calcium due to deficiency in calcitriol production by the renal tubular cells.
- Nutritional secondary hyperparathyroidism—a nutritional deficiency of calcium and vitamin D.

RISK FACTORS

- Primary hyperparathyroidism—unknown.
- Secondary hyperparathyroidism—coexisting renal tubular disease or calcium/vitamin D malnutrition.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- The differential list includes causes of hypercalcemia.
- Lymphoma—common in dogs, rare in cats.
- Anal sac apocrine gland adenocarcinoma—dogs.
- Other miscellaneous carcinomas—dogs and cats.
- Myeloproliferative disease—cats.
- Fibrosarcoma—cats.
- Chronic renal failure.
- Hypoadrenocorticism.
- Vitamin D intoxication—rodenticides are not currently marketed in the United States, but exposure can come from plant sources and vitamin supplements.

- Granulomatous diseases.
- Idiopathic hypercalcemia in cats.

CBC/BIOCHEMISTRY/URINALYSIS

- High serum calcium concentration.
- Low or low-normal serum phosphorus concentration in primary hyperparathyroidism.
- Hyperphosphatemia in secondary hyperparathyroidism or hypervitaminosis D.
- BUN and creatinine concentrations are usually normal in patients with primary hyperparathyroidism, except those with hypercalcemia-induced renal failure.

OTHER LABORATORY TESTS

- Serum ionized calcium determination is often normal in patients with chronic renal failure and high in patients with primary hyperparathyroidism or hypercalcemia associated with malignancy.
- High serum PTH concentration is diagnostic for primary hyperparathyroidism in the absence of azotemia; assays that measure the intact PTH molecule are most useful. A normal serum PTH concentration in an animal with hypercalcemia may be considered abnormal and can signal parathyroid-dependent hypercalcemia.

IMAGING

- Radiography can be useful to assess urolithiasis, renal morphology, and bone density and to identify occult neoplasia.
- Ultrasonography of the ventral cervical area sometimes reveals a parathyroid gland adenoma.
- Ultrasound of the abdomen can reveal lymphadenomegaly, urolithiasis, or renal morphologic abnormalities.

DIAGNOSTIC PROCEDURES

Surgical exploration of the ventral cervical area

PATHOLOGIC FINDINGS

- Parathyroid adenoma is usually a solitary, small (= 1 cm), round, light brown or reddish mass located in the proximity of the thyroid gland.
- Occasionally multiple adenomas are found.
- The histologic distinctions between adenomas, hyperplasia, and carcinomas of the parathyroid gland are often unclear.



TREATMENT

APPROPRIATE HEALTH CARE

- Primary hyperparathyroidism generally requires inpatient care and surgery.
- Nutritional or renal secondary hyperparathyroidism in non-critical patients can be managed on an outpatient basis.

ACTIVITY

No alterations recommended

(CONTINUED)

HYPERPARATHYROIDISM**DIET**

Calcium supplementation for secondary forms

CLIENT EDUCATION

Explain signs referable to changes in calcium status, because hypocalcemia is a potential complication of parathyroidectomy.

SURGICAL CONSIDERATIONS

- Surgery is the treatment of choice for primary hyperparathyroidism and is often important in establishing the diagnosis.
- Percutaneous ultrasound-guided heat ablation has been used successfully for treatment of parathyroid adenoma, and may be recommended if available.
- Percutaneous ultrasound-guided ethanol ablation has been reported to be less successful than surgery or heat ablation.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Normal saline is the fluid of choice for treatment of hypercalcemia.
- Diuretics (furosemide) and corticosteroids can be useful in treating hypercalcemia.
- No medical treatment exists for primary hyperparathyroidism per se.
- Renal secondary hyperparathyroidism is sometimes treated with calcitriol, but its use has not gained wide acceptance.
- A new class of calcimimetic drugs is being used to treat renal secondary hyperparathyroidism in human patients, but studies of these drugs in dogs and cats have not been reported.

CONTRAINDICATIONS

- Do not use glucocorticoids until the diagnosis of lymphoma has been excluded; they can obfuscate the diagnosis.
- Avoid calcium-containing fluids.

PRECAUTIONS

Use furosemide only in patients with adequate hydration.

ALTERNATIVE DRUG(S)

Pamidronate has been used to treat hypercalcemia of various causes in dogs and cats.

**FOLLOW-UP****PATIENT MONITORING**

- Postoperative hypocalcemia is relatively common after treatment of primary hyperparathyroidism. Recent studies have shown that preoperative ionized calcium and PTH concentrations are poor predictors of post-surgical hypocalcemia, so monitoring is essential in all cases.
- Postoperative hypocalcemia requires treatment with vitamin D (calcitriol is recommended) and calcium supplements (see treatment of hypoparathyroidism), and ionized calcium should be monitored to guide dosage adjustments.
- In patients with renal impairment, check serum concentrations of urea nitrogen and creatinine.

PREVENTION/AVOIDANCE

- No strategies exist for prevention of primary hyperparathyroidism.
- Nutritional secondary hyperparathyroidism is prevented by proper nutrition.

POSSIBLE COMPLICATIONS

Irreversible renal failure secondary to hypercalcemia.

EXPECTED COURSE AND PROGNOSIS

- Untreated disease usually progresses to end-stage kidney or neurologic disease.
- Prognosis for treatment of parathyroid adenoma is excellent.
- Recurrence is seen in a small percentage of cases.
- In animals that develop postoperative hypoparathyroidism, the return of normal parathyroid function is unpredictable and can take weeks to months.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Calcium-containing urolithiasis

AGE-RELATED FACTORS

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Hypercalcemia
- Hyperparathyroidism, Renal Secondary
- Renal Failure, Chronic

ABBREVIATION

PTH = parathyroid hormone

Suggested Reading

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Client Education Handout
available online

HYPERPARATHYROIDISM, RENAL SECONDARY



BASICS

OVERVIEW

- Clinical syndrome characterized by a high concentration of biologically active PTH secondary to chronic kidney disease; results from impaired renal excretion of phosphorus leading to elevated levels of fibroblastic growth factor-23 (FGF-23) and associated suppression of renal calcitriol synthesis; low concentrations of ionized calcium and hyperphosphatemia also contribute.
- Hyperphosphatemia secondary to declining renal function is associated with an increase in phosphatonin FGF-23 which enhances renal phosphaturia and reduces the activity of 1- α -hydroxylase in the kidney, which in turn reduces production of calcitriol (1,25-dihydroxycholecalciferol). In more advanced CKD, reduced renal tubular mass also contributes to reduced calcitriol synthesis. Normal calcitriol concentrations exert a negative effect on PTH synthesis within the parathyroid gland nucleus. Low calcitriol and serum ionized calcium concentrations and hyperphosphatemia result in increased PTH production and parathyroid gland hyperplasia.
- PTH may act as a uremic toxin and may promote nephrocalcinosis and progression of chronic renal failure.

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SIGNALMENT

Dog and cat. See Renal Failure, Chronic, for age and breed predilections.

SIGNS

- Those associated with underlying chronic kidney disease are the usual reason for examination.
- Severe renal osteodystrophy or "rubber jaw" occurs in some patients, most commonly young dogs with severe renal secondary hyperparathyroidism.
- Pain around the head or bone pain—sometimes very marked.

CAUSES & RISK FACTORS

- Any disease that causes chronic kidney disease
- Excess consumption of dietary phosphorus



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hypercalcemic nephropathy—renal disease (or failure) caused by ionized hypercalcemia; can be difficult to differentiate from long-standing renal secondary hyperparathyroidism in which hyperplasia of the parathyroid glands limits their ability to stop releasing PTH in

the face of high concentrations of ionized calcium (tertiary hyperparathyroidism).

- The total serum calcium concentration is usually higher in patients with hypercalcemic nephropathy than in those with renal secondary hyperparathyroidism; the ionized serum calcium concentration is usually low or normal with renal secondary hyperparathyroidism, but high with hypercalcemic nephropathy.
- Serum PTH concentration is low and PTHrP high in animals with hypercalcemia of malignancy; may detect underlying causes of hypercalcemia such as lymphoma or apocrine gland adenocarcinoma of the anal sac.
- Primary hyperparathyroidism—initially characterized by hypercalcemia (ionized and total), normal or low serum phosphorus concentration, and high PTH concentration; renal function is initially normal but may become compromised later in the course of disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Azotemia.
- Hyperphosphatemia.
- Urine specific gravity < 1.030 in dogs and < 1.035 in cats.
- Total serum calcium concentration may be low, normal, or slightly increased; see Renal Failure, Chronic.

OTHER LABORATORY TESTS

- Definitive diagnosis and therapeutic monitoring of renal secondary hyperparathyroidism require measurement of serum PTH concentration; an immunoassay for PTH directed against the amino-terminal or intact PTH molecule and validated for dogs or cats is necessary for reproducible and meaningful results.
- A low-to-normal ionized serum calcium concentration is useful to differentiate renal secondary hyperparathyroidism from other causes of hypercalcemia.

IMAGING

Radiographs may reveal low bone density, loss of the lamina dura around the teeth, and soft-tissue mineralization of the gastric mucosa or other tissues.



TREATMENT

- See Renal Failure, Chronic, for general treatment principles.
- Minimize serum phosphorus concentration by feeding a diet low in phosphorus content (preferably formulated for dogs or cats with CKD) and, if indicated, intestinal phosphate binders.
- Provide free access to fresh water to maintain hydration.



MEDICATIONS

DRUG(S)

Intestinal Phosphate Binders

- Prescribe if dietary management does not return phosphorus concentration to recommended levels: serum phosphate < 4.5 mg/dL for dogs and cats in IRIS CKD stage 2; < 5.0 mg/dL in IRIS CKD stage 3; and < 6.0 mg/dL in IRIS CKD stage 4.
- Aluminum hydroxide (30–90 mg/kg/day PO with meals), calcium carbonate (90–150 mg/kg/day PO with meals), calcium acetate (60–90 mg/kg/day PO with meals), or lanthanum carbonate (same dosing as aluminum hydroxide). Dose to effect to achieve stated serum phosphorus concentration target, but do not exceed recommended dosage.
- Hypercalcemia may develop when a calcium-containing phosphate binder is combined with calcitriol; calcium-containing phosphate binders should be avoided with calcitriol therapy. Chemically different phosphate binders can be used in combination to reduce the dosage of each and minimize the risk of hypercalcemia or aluminum toxicity.

Calcitriol

- Low-dose calcitriol (2.0–3.5 ng/kg PO q24h)—may use after initiation of dietary phosphorus restriction and oral phosphate binders; note that this dose is in ng/kg rather than mg/kg; a pharmacy that specializes in reformulation of calcitriol into low doses is needed to provide this prescription. Calcitriol should be administered on an empty stomach and before bedtime (i.e., no food for 6–8 hours after administration).
- Maintain serum phosphorus concentration within the target range before and during calcitriol therapy: serum phosphorus < 4.5 mg/dL in CKD stage 2; < 5.0 mg/dL in CKD stage 3; and < 6.0 mg/dL in CKD stage 4.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Calcitriol administration may result in hypercalcemia, especially if combined with a calcium-containing intestinal phosphate binder. Increased total calcium concentration sometimes develops in patients with long-standing chronic kidney disease but is not related to calcitriol treatment. In these instances, ionized calcium concentration is normal or low, and hypercalcemia does not resolve when calcitriol treatment is discontinued.
- Do not use calcium-containing intestinal phosphate binders in patients with a calcium × phosphorus product > 70. Use

(CONTINUED)

aluminum-containing or lanthanum-containing intestinal phosphate binders initially to correct hyperphosphatemia. Calcium-containing intestinal phosphate binders can be reconsidered once the serum phosphorus concentration is within the target range.



FOLLOW-UP

PATIENT MONITORING

- Initially and in unstable patients, serum concentrations of calcium, phosphorus, creatinine, and urea nitrogen—monitor weekly to monthly depending on therapy and the severity of chronic kidney disease.
- Patients receiving calcitriol should be monitored for hypercalcemia and/or hyperphosphatemia weekly for 4 weeks, then monthly if the patient is stable, and then every 3–4 months.
- Serial evaluations of PTH concentration—most dogs and cats treated with low doses of calcitriol achieve near-normal levels of PTH within 3 months; it may be necessary to increase the dose in those with severe parathyroid gland hyperplasia.

HYPERPARATHYROIDISM, RENAL SECONDARY

- If hypercalcemia develops, discontinue use of calcitriol. Measurement of ionized calcium is recommended since some animals with chronic kidney disease develop non-ionized hypercalcemia that is unrelated to calcitriol treatment. If hypercalcemia is due to calcitriol treatment (high-ionized calcium), it should abate within 5 days. Intermittent-dose calcitriol treatment at twice the dose every other day may alleviate a mild degree of hypercalcemia. Patients with more severe hypercalcemia may benefit from 3.5 times the normal dose given every 3.5 days. These effects on reduction in hypercalcemia are due to decreased programming of intestinal epithelial cells for calcium absorption.

PREVENTION/AVOIDANCE

Dietary phosphorus restriction in patients with chronic kidney disease may delay the onset of renal secondary hyperparathyroidism.

POSSIBLE COMPLICATIONS

Renal osteodystrophy and pathologic fractures (rare)

EXPECTED COURSE AND PROGNOSIS

- Progression of the underlying chronic kidney disease may be slowed by minimizing phosphorus retention and renal secondary hyperparathyroidism.

- Long-term prognosis is guarded to poor for patients with chronic kidney disease and renal secondary hyperparathyroidism.



MISCELLANEOUS

AGE-RELATED FACTORS

Young animals can develop severe renal osteodystrophy and may benefit from treatment with calcitriol.

ABBREVIATIONS

- CKD = chronic kidney disease
- PTH = parathyroid hormone

Suggested Reading

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H

HYPERPHOSPHATEMIA



BASICS

DEFINITION

- Serum total phosphorus > 5.5 mg/dL (dogs)
- Serum total phosphorus > 6 mg/dL (cats)

PATHOPHYSIOLOGY

- Control of phosphorus is complex and is influenced by the actions of PTH and vitamin D and the interaction of these hormones with the gut, bone, kidneys, and parathyroid glands.
- High serum phosphorus results from excessive gastrointestinal absorption of phosphorus, excessive bone resorption of phosphorus, and reduced renal excretion of phosphorus.

SYSTEMS AFFECTED

- Endocrine
- Metabolic
- Renal

SIGNALMENT

- Dogs and cats.
- Any age, but commonly young, growing animals or old animals with renal insufficiency.

SIGNS

Historical Findings

- Depends on the underlying cause of hyperphosphatemia.
- No specific signs directly attributable to hyperphosphatemia
- Acute hyperphosphatemia causes hypocalcemic tetany and/or vascular collapse.

Physical Examination Findings

Chronic hyperphosphatemia causes calcification of soft tissues, resulting in chronic renal failure and tumoral calcinosis.

CAUSES

- Reduced glomerular filtration rate
- Prerenal azotemia
- Renal azotemia
- Post-renal azotemia
- Hyperphosphatemia secondary to excessive bone resorption or muscle breakdown
- Young growing dogs
- Hypoparathyroidism
- Hypersomatotropism
- Hyperphosphatemia caused by excessive gastrointestinal absorption of phosphorus
- Osteolysis
- Disease osteoporosis
- Osseous neoplasia
- Hyperthyroidism
- Phosphorus-containing enemas
- Vitamin D toxicosis
- Phosphorus dietary supplementation
- Nutritional secondary hyperparathyroidism

RISK FACTORS

- Renal disease
- Use of phosphorus-containing enemas in small animals such as cats



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hypoparathyroidism—also characterized by clinical signs of hypocalcemia such as seizures and tetany.
- Prerenal azotemia as a cause of hyperphosphatemia—associated with disease states that result in low cardiac output such as congestive heart failure, dehydration, hypoadrenocorticism, and shock.
- Renal insufficiency, either acute or chronic renal failure—attended by azotemia and abnormal findings on urinalysis (low urinary specific gravity).
- Young, growing animals—can have serum phosphorus concentrations twice those of adults.
- Vitamin D intoxication—history of vitamin D supplementation or ingestion of rodenticides (e.g., Rampage).
- Nutritional secondary hyperparathyroidism—history of dietary calcium-phosphorus imbalance.
- Hyperthyroidism in cats—clinical signs of weight loss, polyphagia, and polydipsia and polyuria.
- Hypersomatotropism—attended by a history of progesterone administration in dogs and insulin-resistant diabetes mellitus in cats.
- Non-azotemia tumoral calcinosis—observed in human beings as an autosomal dominant disorder; rare cause of hyperphosphatemia associated with large bone lesions.
- Jasmine toxicity—history of plant ingestion.
- Factitious.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

- Phosphorus-containing enemas
- Intravenous potassium phosphate
- Anabolic steroids
- Furosemide
- Hydrochlorothiazide
- Minocycline

Disorders That May Alter Laboratory Results

- Hemolysis and lipemia can falsely raise phosphorus concentrations.
- Collection in citrate, oxalate, or EDTA.

Valid If Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Serum phosphorus > 6 mg/dL.
- Low serum calcium in patients with primary hypoparathyroidism.
- High serum calcium in patients with vitamin D intoxication.
- Azotemia and isosthenuria help define degree of renal impairment.

- Hyperkalemia and hyponatremia suggest hypoadrenocorticism.

OTHER LABORATORY TESTS

- Serum PTH measurement—intact molecule and two-site assay methods have the greatest specificity; high-normal or high concentrations suggest primary hyperparathyroidism; low concentrations suggest neoplasia.
- Thyroxine concentrations—indicated in cats with hyperphosphatemia and clinical signs consistent with hyperthyroidism.
- Insulin-like growth factor 1 concentrations—indicated in dogs or cats with unexplained hyperphosphatemia and clinical signs consistent with acromegaly; IGF-1 concentrations are elevated in animals with hypersomatotropism.
- Vitamin D assays are not readily available.
- ACTH stimulation testing to confirm hypoadrenocorticism.

IMAGING

- Abdominal radiography to assess renal size and symmetry
- Renal ultrasonography to detect soft-tissue mineralization
- Thyroid scan to rule out hyperthyroidism
- Radiography of long bones to detect osteoporosis or neoplasia

DIAGNOSTIC PROCEDURES

Renal biopsy



TREATMENT

- Inpatient, because of the deleterious effects of hyperphosphatemia and the need for fluid therapy; consider severe hyperphosphatemia a medical emergency.
- Restrict dietary phosphorus.
- Normal saline is the fluid of choice.



MEDICATIONS

DRUG(S) OF CHOICE

Acute Hyperphosphatemia

- Dextrose (1 g/kg IV) and insulin (0.5 U/kg IV).
- Avoid phosphorus-containing fluids.

Chronic Hyperphosphatemia

- Oral administration of phosphorus binders (e.g., aluminum hydroxide or aluminum carbonate, 30–100 mg/kg/day PO with meals).

CONTRAINdications

N/A

ALTERNATIVE DRUG(S)

N/A

(CONTINUED)



FOLLOW-UP

PATIENT MONITORING

- Serum calcium every 12 hours.
- Renal function tests—urine output must be monitored, particularly if oliguric renal failure is suspected, in which case urine output should be measured carefully; oliguria cannot be determined unless the patient is fully hydrated.
- Hydration status—indicators of overhydration include increased body weight, increased central venous pressure, and edema (pulmonary or subcutaneous).

POSSIBLE COMPLICATIONS

- Hypophosphatemia resulting in hemolysis
- Soft tissue mineralization



MISCELLANEOUS

ASSOCIATED CONDITIONS

Hypocalcemia

AGE-RELATED FACTORS

Mild elevations in phosphorus may be normal in growing animals.

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Hypoparathyroidism
- Renal Failure, Acute
- Renal Failure, Chronic

HYPERPHOSPHATEMIA

ABBREVIATIONS

- ACTH = adrenocorticotropin
- EDTA = ethylene diamine tetra-acetic acid
- IGF-1 = insulin-like growth factor I
- PTH = parathyroid hormone

Suggested Reading

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H

HYPERTENSION, PORTAL



BASICS

DEFINITION

Portal pressure > 13 cm H₂O or 10 mm Hg

PATHOPHYSIOLOGY

- Causes—increased portal blood flow (arterialized system); increased resistance to portal blood flow, or a combination of factors.
- Portal vein—lacks valves; blood follows a path of least resistance.
- Increased Portal Flow—arterialization of portal circulation occurs in AV malformation or subsequent to increased hepatic resistance; causing retrograde blood flow into the valveless splanchnic portal circulation.
- Hepatofugal—portal splanchnic circulation away from the liver.

Increased Resistance Relative to the Liver

- Prehepatic: abdominal portion of portal vein.
- Hepatic: within the liver.
- Posthepatic: cranial to the liver: terminal hepatic veins, vena cava, heart, pericardium.

Intrahepatic Increase in Resistance

- Presinusoidal: within the portal tract.
- Sinusoidal: within sinusoid or space of Disse.
- Postsinusoidal: hepatic venular outflow tract causing a sinusoidal occlusion or Budd Chiari syndrome.
- Consequences—development of multiple acquired portosystemic shunts (APSS), abdominal effusion due to increased lymph formation, and predisposition to HE.
- APSS—collaterals connect the extrahepatic portal system to the caudal vena cava allowing hepatofugal flow in the valveless portal vein; develop within 1–2 months of acquired portal hypertension (PH).

Effusion Protein Content

- Hepatic causes—pure transudate reflects concurrent PH and hypoalbuminemia (protein < 1.5 g/dL).
- Posthepatic causes—modified transudate (protein > 2.5 g/dL).
- Prehepatic causes—often short-lived, pure or modified transudate, low cellularity reflects splanchnic lymph.

SYSTEMS AFFECTED

- Hepatobiliary disorders—obstructed blood flow in any zone or diffusely across sinusoids causes intrahepatic PH, splanchnic PH, ± passive splenic congestion (splenomegaly).
- Posthepatic disorders—hepatic passive congestion, hepatomegaly, and variable PH; APSS usually absent because of a lack of pressure differential between splanchnic portal vein and vena cava.
- Prehepatic disorders—cause splanchnic PH, splenic congestion (splenomegaly) and APSS; portal venous thrombi, stenosis, stricture, entrapment within porta hepatis (e.g., pancreatitis, neoplasia), mass compression (pancreatic inflammation; neoplasia).
- Nervous—HE due to APSS.

- Cardiovascular—APSS and ascites may develop with vena caval/hepatic vein obstruction (at the level of the diaphragm), but not with congestive heart failure or pericardial tamponade as these dually increase hydrostatic pressure in both hepatic and vena caval systems.
- Portal thrombi—caused by gastrointestinal inflammation/necrosis and splanchnic vasculitis, neoplasia, DIC, loss of anticoagulants, accelerated thrombosis.
- Gastrointestinal—splanchnic hypertension can provoke enteric edema, increased gut wall permeability provoking transmural bacterial translocation (endotoxemia, bacteremia), hypertensive enteric vasculopathy (enteric bleeding, ulceration), diapedesis blood loss, and protein malassimilation.

GENETICS

- Vascular malformations causing portal atresia (intrahepatic, prehepatic) are congenital and represent a severe phenotype of polygenic portal venous malformations in small-breed dogs (see Portosystemic Vascular Anomaly, Congenital).
- Ductal plate malformation (DPM): congenital hepatic fibrosis (CHF) phenotype causes APSS; these represent dysfunction of primary cilia; occur in numerous dog breeds and Persian related cats; increased frequency in Boxers; genetic cause and heritability not specifically studied in dogs; feline polycystin-1 precursor mutation has 15% occurrence.
- Non-cirrhotic PH: adult-onset diminution of tertiary portal branches, affects individual dogs of many breeds, described in Doberman pinschers (rare).
- Acquired sinusoidal PH due to necroinflammatory liver injury—immune-mediated chronic hepatitis (anecdotal in some breeds).
- Copper associated hepatopathy—Bedlington terrier *COMMD1* mutation, predisposition for copper associated hepatopathy in Labrador retrievers, Dalmatian, Doberman pinscher, and numerous other dogs may reflect pharmacogenetic breed differences in copper transporters (see Copper Associated Hepatopathy).

SIGNALMENT

Species

Dog > cat

Breed Predilections

Familial hepatic vascular disorders—Doberman pinschers (non-cirrhotic PH); Saint Bernard (AV malformation); Cocker spaniel hepatopathy; copper associated hepatopathy: Bedlington terriers, Doberman pinschers, Labrador retriever, others; ductal plate malformation (DPM)—congenital hepatic fibrosis (CHF) phenotype: Boxers predisposed, any large or small dog breed, and cats.

Mean Age and Range

- Juveniles—herited or congenital disorders; vena caval and cardiac malformations.
- Young dogs and cats < 1.5 years of age—

congenital hepatic vascular malformations with portal venous atresia: lack of microscopic portal vein tributaries or splanchnic portal vascular atresia, if PSVA are intolerant to surgical ligation and develop APSS; may be more common in Yorkshire terriers, Maltese, pugs, and cats.

- Juvenile and young adult dogs and cats—DPM with CHF phenotype.
- Young dogs and cats—hepatic AV malformations (rare), onset of signs < 1.5 years of age.
- Middle-aged and older animals—acquired hepatobiliary disorders and portal thrombi.

Predominant Sex

N/A

SIGNS

General Comments

- Depends on site, degree, and rate of onset of PH and causal factors.
- Acquired disorders—slowly progressive and chronic in onset.

Historical Findings

- Portal thromboembolism may acutely appear but remain unnoticed until APSS form; vague GI signs at occurrence including bloody diarrhea, ileus, abdominal pain, lethargy, and inappetence.
- Abdominal distention: ascites.
- HE—secondary to APSS.
- Cardiac disorders or pericardial restriction—cough; exercise intolerance; dyspnea, jugular pulse, weak femoral pulses or pulsus alternans, reduced heart sounds on auscultation.

Physical Examination Findings

- Abdominal effusion
- Hepatomegaly—posthepatic causes only
- Splenomegaly—reflects splanchnic congestion or venous thrombi, inconsistent
- Jugular vein distention—posthepatic cardiac or pericardial causes
- Muffled heart sounds—pericardial or pleural effusion
- Cardiac arrhythmias or murmur—cardiac disease
- Pulmonary “crackles” (edema)—cardiac or pericardial causes
- Confusion, stupor, coma, blindness, other neurobehavioral abnormalities—HE
- Jaundice—hepatic causes
- Hepatic bruit (hepatic AV malformation) (see Arteriovenous Malformation of Liver)
- Signs consequent to surgical ligation of PSVA (see Portosystemic Vascular Anomaly, Congenital)

CAUSES

Prehepatic

- Portal vein thrombosis, stenosis, or neoplasia
- Portal vein compression—large lymph nodes; neoplasia, granuloma; abscess; pancreatitis, entrapment in diaphragmatic hernia
- Postoperative complication of PSVA ligation, especially with ameroid constrictor
- Congenital portal vein atresia

Intrahepatic

- Hepatic fibrosis/cirrhosis
- Chronic inflammatory liver disease
- Chronic EHBDO > 6 weeks
- DPM: CHF phenotype
- Hepatic neoplasia—porta hepatis location
- Liver entrapment—in diaphragmatic hernia

(CONTINUED)

- Sinusoidal occlusion syndrome
- Veno-occlusive disease (zone 3 lesion), Budd-Chiari syndrome
- Non-cirrhotic portal hypertension
- Portal vein atresia (intra- or extrahepatic)
- Hepatic AV malformation

Posthepatic

- Right-sided congestive heart failure
- Heartworm disease
- Pericardial tamponade
- Pericarditis—restrictive or constrictive
- Cardiac neoplasia
- Cor triatriatum dexter
- Pulmonary TE
- Disorders affecting the supradiaphragmatic caudal vena cava—thrombosis; congenital kink or web; heartworm vena cava syndrome; occlusion by neoplasia; entrapment in diaphragmatic hernia

RISK FACTORS

Depend on underlying cause

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- Physicochemical analysis of abdominal effusion—helps narrow diagnoses
- Pure transudate—hypoalbuminemia secondary to PLE, PLN, liver failure
- Modified transudate with normal or low albumin—PLE, PLN, liver failure (chronic effusion), neoplasia, splanchnic TE, liver (visceral) entrapment in diaphragmatic hernia
- Modified transudate with large liver and jugular distention—cardiac or pericardial abnormalities; heartworm; right atrial tumor
- Modified transudate with large liver without jugular distention, muffled heart, or pulmonary edema—kinked vena cava; Budd-Chiari-like or sinusoidal occlusion syndrome
- HE—liver fibrosis; cirrhosis; CHF; hepatic AV malformation; any cause of APSS
- Jaundice—chronic hepatitis, cholangitis; EHBD0; infiltrative hepatic neoplasm
- Bloody diarrhea, abdominal pain, ileus, signs of endotoxemia—acute splanchnic portal TE

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—schistocytes with TE; RBC microcytosis with PSVA or APSS; icteric plasma with liver disease or microangiopathic shearing anemia (also show schistocytes).
- Biochemistry—liver disease associated with variable liver enzymes, low BUN, creatinine, cholesterol, and/or glucose concentrations, hyperbilirubinemia, and coagulation abnormalities; Posthepatic disorders associated with high liver enzymes, \pm azotemia, and normal plasma color.
- Urinalysis—ammonium biurate crystalluria with APSS; may note granular casts with TE affecting renal perfusion; may note proteinuria with heartworm disease.

OTHER LABORATORY TESTS

- TSBA—variable fasting and high 2-h postprandial concentrations with APSS or hepatobiliary disease; shunting pattern

(normal fasting and markedly high postprandial values) common.

- Blood ammonia—hyperammonemia with APSS or inferred by finding ammonium biurate crystalluria; ammonia tolerance testing and ammonia measurement less convenient and reliable compared to TSBA.

- Physicochemical characterization of abdominal effusion—high serum:effusion albumin ratio (> 1.1) consistent with PH.

IMAGING**Radiography**

- Thoracic radiography—may reveal cause of posthepatic PH (e.g., kinked vena cava, pericardial effusion, pulmonary disease, pleural effusion, diaphragmatic hernia).
- Abdominal radiography—may reveal effusion, splenomegaly, hepatomegaly (e.g., congestion, infiltrative neoplasia, or hepatic AV malformation); microhepatia in most hepatic disorders causing APSS and hepatic portal malformation associated with APSS (portal atresia).

Abdominal Ultrasonography

- Identify abnormalities involving the abdominal or extrahepatic portal vein: atresia, stricture, thrombi, occlusive lesions in porta hepatis.
- Identify lobe(s) containing AV malformations.
- Inspect splanchnic circulation using Doppler color flow; document hepatofugal circulation, identify portal thrombi (filling defects, abrupt flow termination), APSS (caudal to left kidney), or PSVA (interrogate vena cava for turbulent flow).
- Evaluate echogenicity of nonhepatic viscera; identify lymphadenomegaly, mass lesions (neoplasia), adhesions.
- Estimate hepatic venous distention—extrahepatic and supradiaphragmatic segments; may identify posthepatic causes of PH and sinusoidal occlusion syndrome.

Echocardiography

Detects congenital and acquired cardiac and pericardial disorders, neoplasia, thrombi, heartworms, pleural effusion, malformed or thrombosed vena cava, diaphragmatic hernia.

Angiography and Nuclear Imaging

- Colorectal or splenoportal scintigraphy—confirms PSS but not anatomic details.
- Radiographic angiography—celiac trunk and hepatic artery contrast studies confirm hepatic AV malformation; nonselective or selective studies—congenital cardiac disease, TE, hepatic vein disorders, AV malformation.
- Portovenography—confirm APSS.
- Multisector CT—high-quality characterization of regional vasculature; non-invasive; displays arterial and venous phases.

ADDITIONAL DIAGNOSTICS

- Electrocardiography and central venous pressure—with cardiac disease, cranial mediastinal obstructions.
- Liver biopsy—required for diagnosis of hepatobiliary

HYPERTENSION, PORTAL

disorders.

- Portal pressure—although may be measured during laparotomy is not recommended; unreliable in deducing underlying causes; PH blunted by APSS PH adequately confirmed with imaging studies and on gross inspection.

**TREATMENT****APPROPRIATE HEALTH CARE**

Inpatient—for severe HE, amelioration of tense ascites by therapeutic abdominocentesis, supportive care for acute TE.

NURSING CARE

- Fluid therapy—with all causes, restrict sodium concentration (avoid 0.9% NaCl); high likelihood of total-body sodium loading. Avoid iatrogenic pulmonary edema during fluid therapy (**caution:** if hypoalbuminemia).
- Monitor body weight and condition, girth circumference, plasma proteins, and PCV—assess hydration status, volume of abdominal effusion, and IV fluid tolerance.
- Low oncotic pressure—may require plasma or colloid administration (plasma preferred for liver patient); Voloven or VetStarch (6%; 130 MW/0.4 molar substitution) 10–20 mL/kg/day IV CRI) may be necessary for acute adjustments; avoid Hetastarch as can reduce platelet function.
- Glucose supplementation—with hepatic dysfunction and hypoglycemia; 2.5–5.0% dextrose with half-strength polyionic fluids initially; titrate dextrose concentration to achieve euglycemia (avoid hyperglycemia).

MOBILIZATION OF ASCITES

- *Abdominal effusion*—sequentially assess: body weight, girth, and body condition score; initially exercise restrict (improves renal perfusion, sodium and water elimination); enforce dietary sodium restriction.
- *Conventional diuretics*: combine furosemide and spironolactone; furosemide (0.5–2 mg/kg PO q12–24h) and spironolactone (0.5–2 mg/kg PO q12h, use a single doubled dose for loading one time): dose titrations based on response q4 days; adjust using incremental 25–50% dose increase. Spironolactone: potassium sparing; less potent than furosemide. Furosemide: potassium wasting, diuresis induces RAAS response. Serum:effusion albumin ratio (> 1.1) may predict response to diuretics.
- *Vasopressin V₂ antagonists* (aquaretics) may assist with management of diuretic resistant ascites. Tolvaptan successful in dogs with experimentally induced (rapid pacing) congestive heart failure. Human dose in cirrhosis is 7.5 mg/day; Tolvaptan is metabolized exclusively in the liver primarily by cytochrome P450; dose undetermined in dogs with liver disease.
- *Telmisartan*: angiotensin receptor blocker (ARB), nephro-protective in diabetes and renal injury

H

HYPERTENSION, PORTAL

(CONTINUED)

H in humans, also prevents effects of drug-induced hepatotoxicity and hepatic fibrosis) is an alternative diuretic worthy of consideration. ARBs selectively antagonize angiotensin-1 receptor bypassing intermediary activation steps within the RAAS cascade. Telmisartan administration PO in at 1.0 mg/kg/day significantly increased urine volume and sodium excretion in healthy dogs. • Taper diuretic dose after initial positive response; individualize chronic treatment to response; diuretics may be used intermittently to mobilize recurring ascites • Avoid dehydration as this can lead to HE. • Avoid hypokalemia as this can provoke HE. • If cardiac disease is the cause of ascites: treatment involves sodium restriction, enalapril, furosemide, newer diuretics described above. *Diuretic-resistant ascites*—large volume (therapeutic) abdominocentesis if ascites resistant to medical intervention or compromises food intake, ventilation, or sleep: requires aseptic technique, fluid removal over 45–90 minutes, concurrent polyionic fluid and/or colloids reduces risk for post-centesis hypotension and acute renal failure (ARF). Repeated large-volume fluid removal may result in: hypovolemia, hypoproteinemia, electrolyte depletion; iatrogenic infection; *postcentesis hypovolemia/hyperperfusion syndrome and ARF* (rapid redistribution of fluid into abdominal cavity). Use aseptic technique and concurrently provide polyionic fluids in moderation with colloids. General rule in humans: provide 4–8 g of albumin per L of ascites removed (consider colloids, discussed above). • If ascites fails to mobilize, consider measuring urine sodium output vs. sodium intake (dietary) to determine whether intake requires restriction or diuretics upward titration. Urine output should be measured over a minimum of 12 hours.

ACTIVITY

Depends on cause, restrict activity if ascites

DIET

• Ascites—restrict dietary sodium < 100 mg/100 kcal. • If HE—restrict dietary protein (see Hepatic Encephalopathy); **caution:** only restrict protein if nitrogen intolerance suspected.

CLIENT EDUCATION

Inform client that definitive diagnosis requires logical diagnostic strategies and no prediction for cure or chronic amelioration until definitive diagnosis is ascertained.

SURGICAL CONSIDERATIONS

• Ligation of APSS or vena caval banding strongly contraindicated. • If acute symptomatic PH after surgical ligation of PSVA—ligature removal imperative (see Portosystemic Vascular Anomaly,

Congenital). • Embolectomy of thrombi not recommended; emboli may recanalize with supportive care; clot dissolution (streptokinase, TPA) complicated, expensive, requires ICU hospitalization and monitoring, and warrants a grave prognosis. • LMW heparin (see Coagulopathy of Liver Disease). • Correction of chronic diaphragmatic hernia—release of entrapped viscera may provoke perioperative/postoperative endotoxemia, hypotension, shock, ARF. • Surgical correction and cure of cor triatriatum and kinked vena cava are possible. • Pericardectomy—pericardial restriction or tamponade; thoracoscopic procedure least invasive, with lowest mortality and best outcome. • Removal of tumor or fibrous adhesions causing hepatic vein occlusion may be difficult. • Removal (lobectomy) or embolization (acrylamide) of hepatic AV malformation may not be curative as microscopic intrahepatic AV shunting usually continues PH and APSS.



MEDICATIONS

DRUG(S) OF CHOICE

Treatment of abdominal effusion—sodium restriction (see above, “Diet”); combined diuretic therapy (spironolactone and furosemide), consider tolvaptan or telmisartan (see above), use large-volume paracentesis sparingly.

DIURETICS

(see above; mobilization of ascites)

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

• Avoid drugs relying on first-pass hepatic extraction, biotransformation, or hepatic elimination; if not possible, adjust dosage based on available information. • Reduce dose of highly protein-bound drugs if patient hypoalbuminemic. • Avoid NSAIDs: these are metabolized in the P450 cytochrome-rich centrilobular regions where toxic adducts may provoke cell injury augmented by hypoxia, poor perfusion, sinusoidal occlusion, copper accumulation; NSAIDs may provoke ARF, sodium retention, and enteric bleeding that may augment HE.

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Sequentially monitor body weight, condition, and abdominal girth.

- Sequentially assess hydration, electrolytes, acid-base, and blood pressure as necessary.
- Monitor: albumin and glucose—with liver disease or APSS. • Monitor lung sounds, pulse oximetry, and ventilatory effort—in cardiovascular disorders.

POSSIBLE COMPLICATIONS

- Thrombosis • Endotoxemia • Hypotension
- Hepatic encephalopathy • Acute renal failure

EXPECTED COURSE AND PROGNOSIS

Depends on cause



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Chronic liver disease • Numerous disorders may cause prehepatic or posthepatic portal hypertension.

PREGNANCY/FERTILITY/BREEDING

Affects uterine perfusion and likely leads to abortion or stillbirths.

SEE ALSO

- Ascites • Cirrhosis and Fibrosis of the Liver
- Congestive Heart Failure, Right-Sided
- Hepatic Encephalopathy • Pericarditis
- Portosystemic Shunt, Acquired
- Portosystemic Vascular Anomaly, Congenital

ABBREVIATIONS

- ARF = acute renal failure • APSS = acquired portosystemic shunt(s) • ARB = angiotensin receptor blocker • AV = arteriovenous • CRI = constant rate infusion
- EHBDO = extrahepatic bile duct obstruction • HE = hepatic encephalopathy
- PH = portal hypertension • PLE = protein-losing enteropathy • PLN = protein-losing nephropathy • PSS = portosystemic shunting • PSVA = portosystemic venous anomaly • TE = thromboembolism • TPA = tissue plasminogen activator • TSBA = total serum bile acids

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HYPERTENSION, PULMONARY



BASICS

DEFINITION

Peak systolic pulmonary artery (PA) pressure > 30 mmHg and/or peak diastolic PA pressure > 15 mmHg

PATOPHYSIOLOGY

- Causes of elevated PA pressure:
 - (1) pulmonary arterial vasoconstriction,
 - (2) pulmonary arterial obstruction, (3) high left atrial pressure with resultant pulmonary venous and arterial hypertension, (4) excessive pulmonary blood flow.
 • As a result of pulmonary hypertension (PHTN) right heart pressures increase to maintain pulmonary blood flow. May result in right ventricular dysfunction and decreased pulmonary blood flow. Decreased pulmonary blood flow interferes with filling of the left heart which can lead to decreased cardiac output. High right heart pressures can cause venous congestion, tricuspid regurgitation, and R-CHF.

SYSTEMS AFFECTED

- Cardiovascular—see Pathophysiology
- Hepatobiliary—R-CHF may cause hepatic congestion and dysfunction
- Respiratory—Associated pulmonary disease; R-CHF may cause pleural effusion.

GENETICS

- No specific genetic basis found.
- Causes of primary disease (congenital heart disease—CHD, left heart disease, pulmonary disease) may have a genetic basis.

GEOGRAPHIC DISTRIBUTION

Unknown; likely higher prevalence in heartworm-endemic areas and at high altitudes.

SIGNALMENT

Species

Dogs and cats

Breed Predilections

- Possibly based on underlying cause of PHTN
- Increased incidence in the terrier breeds has been suggested.

Predominant Sex

Increased incidence in female is reported

SIGNS

General Comments

Signs due to hypoxia and cardiac dysfunction

Historical Findings

- Exercise intolerance
- Dyspnea/tachypnea
- Coughing/hemoptysis
- Syncope
- Abdominal distention
- Weight loss
- Lethargy
- Sudden death

Physical Examination Findings

- Dyspnea/tachypnea
- Coughing
- Hemoptysis
- Loud and/or split-second heart sound
- Pulmonary crackles and/or harsh bronchovesicular sounds
- Cyanosis

- Heart murmur
- Abdominal distention
- Jugular distention
- Subcutaneous edema
- Weight loss

CAUSES

Primary/Idiopathic/Familial PHTN

Etiology

- Primary congenital disorders of the pulmonary vasculature identified in humans.
- Abnormalities in endothelial derived vasodilatory/vasoconstrictor substances result in vascular obstruction and vasoconstriction.
- Not reported in companion animals.

Pulmonary Parenchymal Disease

Etiology

- *Vascular obstruction*—resulting from pulmonary lesions (e.g. fibrosis, neoplasia), vascular hypertrophy/inflammation
- *Vasoconstriction*—reactive vascular constriction secondary to hypoxia and acidemia
- *Causes:*
 - Pneumonia (bacterial, viral, fungal, parasitic)
 - Chronic bronchitis
 - Pulmonary fibrosis
 - Eosinophilic bronchitis
 - Pulmonary neoplasia
 - Acute respiratory distress syndrome

Pulmonary Thromboembolism (PTE)

Etiology

- *Vascular obstruction*—secondary to thrombus
- *Vasoconstriction*—secondary to hypoxia and vasoconstrictive substances released from the thrombus
- *Causes:*
 - Hyperadrenocorticism
 - Protein-losing nephropathy/enteropathy
 - Sepsis
 - Immune-mediated hemolytic anemia
 - Neoplasia
 - Pancreatitis
 - Endocarditis
 - Disseminated intravascular coagulation
 - Primary cardiac disease (typically right heart disease)

Heartworm Disease (HWD)

Etiology

- *Vascular obstruction*—vascular hypertrophy, inflammation, thromboembolism, and presence of heartworms
- *Vasoconstriction*—secondary to hypoxia/thrombi

Congenital Heart Disease (CHD) with Left-to-Right Shunting

Etiology

- *Excessive pulmonary blood flow* due to left-to-right shunting results in damage to pulmonary vasculature
- *Vasoconstriction/vascular obstruction*—result of vascular damage and vascular hypertrophy
- *Causes:*
 - Patent ductus arteriosus
 - Ventricular septal defect
 - Atrial septal defect

Left Heart Disease

Etiology

- *High left atrial pressure*—results in pulmonary venous and arterial hypertension
- *Vasoconstriction/vascular obstruction*—result of elevated pressure and vascular hypertrophy
- *Causes:*
 - Mitral regurgitation
 - Cardiomyopathy (dilated, hypertrophic, restrictive, unclassified)
 - Mitral stenosis
 - Congenital pulmonary venous obstruction (e.g., cor triatriatum sinister)
 - Left atrial tumors

Extrapulmonary Causes of Chronic Hypoxia

Etiology

- *Vasoconstriction*—some environmental/extrapulmonary factors result in hypoxia and acidemia leading to pulmonary vasoconstriction and secondary vascular hypertrophy
- *Causes:*
 - Hypoventilation (Pickwickian syndrome, neuromuscular disorders)
 - High altitude disease

RISK FACTORS

- Cardiac and pulmonary disease
- Heartworm disease
- Diseases causing hypercoagulability
- Obesity
- High altitude



DIAGNOSIS

H

DIFFERENTIAL DIAGNOSIS

- Left-sided congestive heart failure (L-CHF)*
- Collapsing trachea
- R-CHF*
- Primary pulmonary disease*
- HWD*
- Pneumothorax
- Pleural effusion (pyothorax, chylothorax, hemothorax, hydrothorax)
- Laryngeal paralysis/disease *without concurrent PHTN

CBC/BIOCHEMISTRY/URINALYSIS

- Polycythemia can be seen due to hypoxemia
- Leukocytosis seen with infectious lung disease
- Possible evidence of hypercoagulability

OTHER LABORATORY TESTS

- Arterial blood gases (hypoxemia)
- Occult heartworm test
- Workup for causes of PTE (urine protein:creatinine ratio, antithrombin III level, D-dimer, coagulation profile, urine cortisol:creatinine ratio, ACTH stimulation test, dexamethasone suppression test)
- Cytology of effusions

IMAGING

Radiography

- Dilated pulmonary artery and/or tortuous pulmonary vessels
- Right ventricle and atrial enlargement
- Dilated caudal vena cava
- Pleural effusion
- Hepatomegaly
- Ascites
- Evidence of primary pulmonary disease, PTE, or HWD

Echocardiography

- RV concentric/eccentric hypertrophy
- Flattening of the interventricular septum and/or paradoxical septal motion
- RA dilation
- PA dilation
- Pleural/pericardial effusion
- Evidence of left heart disease, HWD, CHD, or PTE
- Asymmetric and notched pulmonary outflow envelope/tracing

Echocardiographic Assessment of PHTN Severity

- Tricuspid valve regurgitation (TR): if present without pulmonic stenosis or pulmonary artery stenosis, the TR gradient estimates systolic PHTN severity.
- *Systolic pressure gradient* between the RV and RA: estimated with spectral Doppler using the

HYPERTENSION, PULMONARY

(CONTINUED)

modified Bernoulli equation: $4 \times (\text{peak TR velocity})^2$. • Pressure gradient > 35 mmHg (TR velocity $\geq 3.0 \text{ m/s}$) suggestive of PHTN. • Gradient determines severity: mild: 35–50 mmHg, moderate: 51–80 mmHg, severe > 80 mmHg. • Pulmonary valve insufficiency (PI): if PI is present without pulmonary artery stenosis the PI gradient estimates diastolic PHTN severity. • *Diastolic pressure gradient* between the pulmonary artery and the RV: estimated with spectral Doppler using the modified Bernoulli equation: $4 \times (\text{peak PI velocity})^2$. • Pressure gradient > 15 mmHg (PI velocity > 2.0 m/s) suggestive of PHTN.

CT Scan/MRI

May be of diagnostic value if pulmonary neoplasia or other infiltrative diseases

DIAGNOSTIC PROCEDURES

Transtracheal wash, bronchoscopy/bronchoalveolar lavage, or lung aspirate/biopsy may be of value if evidence of primary pulmonary disease

Electrocardiography

- Right mean electrical axis deviation
- Deep S waves leads I, II, III, and aVF
- Widening of QRS complex
- P-pulmonale
- ST segment depression/elevation
- Hypoxia-induced arrhythmias (VPCs)

Cardiac Catheterization and Pulmonary Angiography

- The gold standard of diagnosis
- Uncommonly performed due to risk and usefulness of echocardiography
- Indicated if necessary to confirm diagnosis or cause

PATHOLOGIC FINDINGS

- Dependent on underlying disease and severity:
 - Primary pulmonary lesions
 - PTE
 - Dilated PA/RV/RA/vena cava
 - Heartworms
 - Pleural/pericardial/abdominal effusions
 - Medial hypertrophy, intimal proliferation, and sclerosis of pulmonary vasculature
 - Necrotizing arteritis



TREATMENT

APPROPRIATE HEALTH CARE

- Hospitalize patients in severe respiratory distress
- Medical therapy as described below
- Perform diagnostics based on patient stability

NURSING CARE

- Judicious fluid therapy may be of benefit to improve pulmonary bloodflow
- Risk of CHF must be considered
- Maintain low-stress environment

CLIENT EDUCATION

- Prognosis varies with reversibility of the underlying disease, but generally very guarded
- Avoid environments that may predispose to respiratory distress—heat/humidity extremes, second-hand smoke, high altitudes

SURGICAL CONSIDERATIONS

Surgical heartworm extraction is a consideration in patients with severe infestation



MEDICATIONS

DRUG(S) OF CHOICE

- Treat the primary underlying disease process whenever possible
- The ideal therapeutic agent for PHTN causes pulmonary vasodilation without causing significant systemic hypotension

Oxygen

- Treatment of choice, but long-term administration not feasible
- Useful in acute setting to correct hypoxia and cause vasodilation

Phosphodiesterase Type V Inhibitor (PDE5 inhibitor)

- Inhibit the breakdown of cGMP causing increased nitric oxide and pulmonary vasodilation
- Avoid other drugs with similar effects (nitrates)
- Sildenafil—drug of choice for most causes of PHTN in dogs
- Tadalafil—one published study suggests benefit in dogs
- Vardenafil—not evaluated in companion animals

Other Vasodilators

- Limited benefit due to concurrent systemic vasodilation and hypotension
- Important in management of PHTN resulting from left heart disease
- ACE inhibitors, hydralazine, and calcium channel blockers

Phosphodiesterase Type III Inhibitor (PDE3 inhibitor)

- Pimobendan
- Causes pulmonary and systemic vasodilation
- Indicated if PHTN secondary to left heart disease
- Unclear if useful with other causes of PHTN

Bronchodilators

- May benefit patients with pulmonary disease
- Sympathomimetics (e.g., terbutaline) and methylxanthines (e.g., theophylline)
- Methylxanthines may also cause mild pulmonary arterial vasodilation

Anticoagulant Therapy

- In humans, common therapy for all causes of PHTN due to primary and/or secondary thromboembolism
- Use in companion animals unclear except in patients with PTE

Thrombolytic Therapy

- Streptokinase and t-PA indications and effectiveness debated in companion animals
- Likely only indicated if acute PTE with significant cardiac compromise

Anti-inflammatory and Antibiotic Therapy

- Steroids may be of benefit if cause of the PHTN has an inflammatory component (e.g., heartworm disease, some cases of primary pulmonary disease)
- Antibiotics indicated if suspect bacterial component

CONTRAINDICATIONS

- Respiratory depressants
- Cardiac myocardial depressants (e.g., beta-blockers)
- Bronchoconstrictors (e.g., nonspecific beta-blockers)
- Vasoconstrictors

PRECAUTIONS

- Vasodilators can cause systemic hypotension
- Bronchodilators can cause tachycardia and hyperexcitability
- Hypovolemia may result in depressed pulmonary blood flow



FOLLOW-UP

PATIENT MONITORING

- Serial echocardiography to assess improvement/progression
- Repeat thoracic radiographs, ECG, laboratory work, blood pressure as needed

POSSIBLE COMPLICATIONS

- Right-sided heart failure
- Syncope
- Arrhythmias
- Sudden death

EXPECTED COURSE AND PROGNOSIS

- Based on ability to reverse underlying disease
- In general, very guarded prognosis



MISCELLANEOUS

ABBREVIATIONS

- ACE = angiotensin-converting enzyme
- ACTH = adrenocorticotrophic hormone
- CHD = congenital heart disease
- CT = computed tomography
- ECG = electrocardiogram
- HWD = heartworm disease
- L-CHF = left-sided congestive heart failure
- MRI = magnetic resonance imaging
- PA = pulmonary artery
- PHTN = pulmonary hypertension
- PI = pulmonary valve insufficiency
- PTE = pulmonary thromboembolism
- RA = right atrium
- R-CHF = right-sided congestive heart failure
- RV = right ventricle
- TR = tricuspid valve regurgitation

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Client Education Handout available online



BASICS

DEFINITION

Sustained elevation in systolic or diastolic (or both) arterial blood pressure. In dogs and cats, systolic BP > 160 mmHg or diastolic BP > 120 mmHg obtained by any method is considered abnormal. BP elevation may be transient and related to measurement artifact (stress-induced or white-coat effect), or sustained and pathologic. In veterinary patients, HT is usually due to another disease process and is termed secondary hypertension. If an underlying disease is not present or cannot be determined, the terms primary, essential or idiopathic HT are used.

PATHOPHYSIOLOGY

- Arterial BP is the product of cardiac output and systemic vascular resistance; cardiac output is determined by HR and stroke volume.
- BP regulation depends on integration of complex mechanisms within the central and peripheral nervous systems, renal and cardiac tissues, and humoral factors, which synergistically affect cardiac output and vascular resistance.
- Baroreceptors in the carotid sinus and aortic arch respond to changes in BP; a fall in BP increases sympathetic discharge, causing vasoconstriction and increased cardiac contractility and HR.
- Humoral substances that modulate BP include catecholamines, vasopressin, kinins, renin, angiotensin, aldosterone, prostaglandins, and atrial natriuretic peptide.
- Primary HT is not fully understood in veterinary patients, but some cases have a hereditary component.
- Secondary HT is most commonly associated with chronic kidney disease and endocrinopathies in dogs and cats.
- HT may also occur secondary to fluid therapy, vasoconstricting drugs, steroid administration, or erythropoietin therapy.
- Persistent elevation of BP causes tissue injury and is termed target organ damage (TOD).

SYSTEMS AFFECTED

- Cardiovascular
- Nervous
- Ophthalmic
- Renal/Urologic

GENETICS

Colonies of hypertensive dogs have been produced by mating dogs with essential HT; mode of inheritance not known.

INCIDENCE/PREVALENCE

- Varies with criteria for HT and method of measurement.
- Dogs: prevalence of HT in chronic kidney disease (9–93%; most studies support a rate of 25%), hyperadrenocorticism (73–80%), diabetes mellitus (24–46%).
- Cats: prevalence of HT in chronic kidney disease (19–65%), hyperthyroidism (9–23%).

SIGNALMENT

Species

Dog and cat

Breed Predilections

None

Mean Age and Range

- Usually older dogs and cats.
- Younger animals may be affected if renal disease due to infection (e.g., leptospirosis) or heritable disease (e.g., polycystic renal disease, dysplasia).

CLINICAL SIGNS AND FINDINGS

- Ocular: acute blindness, intraocular hemorrhage, dilated pupils, exudative retinal detachment, retinal vessel tortuosity, retinal perivasculär edema, papilledema, retinal degeneration (late).
- Neurologic: depression, head tilt, seizures, nystagmus, paresis, ataxia, circling, disorientation.
- Renal: polyuria/polydipsia associated with progression of chronic renal disease, hematuria, proteinuria.
- Cardiovascular: murmur, gallop rhythm, cardiomegaly, rarely CHF, epistaxis.

CAUSES

Primary or Essential

Not known; familial in some dogs

Secondary

- Accounts for most cases in dogs and cats
- Renal disease—tubulointerstitial or glomerular disease, amyloidosis, polycystic kidney disease, dysplasia
- Hyperadrenocorticism
- Hyperthyroidism
- Diabetes mellitus—less common
- Pheochromocytoma—less common
- Hyperaldosteronism—less common
- Central nervous system disease—less common

RISK FACTORS

Underlying renal disease or endocrinopathy



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cardiovascular—hypertrophic cardiomyopathy, thyrotoxic heart disease, aortic stenosis, arterial thromboembolic disease.
- Ophthalmic—ocular trauma, systemic infections (bacterial, fungal, viral), coagulopathies, vasculopathy.
- Neurologic—primary brain, spinal cord, or peripheral nerve disease.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC: usually normal; decreased PCV with severe chronic renal disease; increased PCV with hyperadrenocorticism.
- Biochemistry profile: azotemia, hyperphosphatemia, hypokalemia (renal insufficiency); hyperglycemia (diabetes mellitus); high ALP (hyperadrenocorticism); increased ALT (hyperthyroidism); hypokalemia (hyperaldosteronism).
- Urinalysis: proteinuria (glomerulonephritis, amyloidosis, hyperadrenocorticism); hematuria; poor urine concentrating ability (renal insufficiency,

hyperadrenocorticism); glucosuria (diabetes mellitus).

OTHER LABORATORY TESTS

- Glomerulonephropathy—increased urine protein:urine creatinine ratio (> 0.5 in dogs, > 0.4 in cats), decreased creatinine clearance.
- Renal dysfunction—decreased creatinine clearance.
- Hyperadrenocorticism—exaggerated ACTH response test, failure to suppress with dexamethasone, increased urine cortisol:creatinine ratio.
- Hyperthyroidism (cats)—increased T₄, inadequate suppression with a T₃ suppression test.
- Hypothyroidism (dogs)—decreased T₃, T₄, free T₃, free T₄; possibly increased T₃ and T₄ auto-antibodies, increased endogenous TSH.
- Pheochromocytoma—increased urinary catecholamine metabolites.
- Hyperaldosteronism—increased plasma aldosterone.

IMAGING

- Echocardiography to evaluate hypertensive heart disease (findings include left ventricular free wall and/or interventricular septal hypertrophy, diastolic dysfunction, or normal structure and function).
- Thoracic radiography to evaluate secondary cardiac changes (typically mild cardiomegaly without CHF).
- Abdominal radiography to evaluate liver, adrenals, and kidneys.
- Abdominal ultrasonography to evaluate kidneys, liver, adrenal glands, and bladder.
- CT or MRI scan if brain tumor, hemorrhage, hyperadrenocorticism suspected.
- Thyroid scintigraphy to evaluate hyperthyroidism.

DIAGNOSTIC PROCEDURES

Definitive diagnosis of HT requires documentation of high arterial BP via direct or indirect methods in the population at risk. There is no evidence that BP should be measured in all animals. Although correlation with direct BP measurements may vary, indirect measurements in the appropriate clinical population are invaluable in the treatment of HT and prevention of TOD.

Direct (Invasive)

Considered the gold standard, but seldom performed on an outpatient basis in awake animals; reserved for intraoperative monitoring or emergency management of severe HT.

Indirect (Non-invasive)

- Indirect BP measurement is easily performed in a clinical setting, and are most commonly obtained with oscillometric or Doppler techniques, depending on the size of the animal.
- An inflatable cuff is wrapped around an extremity; the width of the cuff should be approximately 30–40% (cats) or 40% (dogs) of the circumference of the limb or tail at the site of placement. The cuff should be at or near the level of heart when

HYPERTENSION, SYSTEMIC

(CONTINUED)

measuring BP. • A cuff that is too small will result in a falsely high BP measurement, while too large a cuff will result in a falsely low measurement. • An average of 5–7 measurements should be obtained for the BP session; discard the first measurement. • A permanent record of the BP measurement session should include: technique used, cuff size, limb used, time of day, time of medication, animal's disposition, and operator name. • Consistent techniques yield more reliable results. Interpret results in light of the animal's excitement level during the procedure and repeat if results are questionable.

Oscillometric Technique

- Oscillometric technique (Cardell, Memoprint, PetMap) detects pulse pressure oscillations beneath the cuff bladder that result from changes in arterial diameter.
- Place the animal in lateral or sternal recumbency in a calm environment. Place the artery arrow marker on the cuff on the caudomedial aspect of forearm (or proximal to the carpus with arrow pointed medially), over the dorsomedial metatarsal region (or distal to the tarsus) or on the ventral aspect of the tail in a snug position. The machine can inflate the cuff automatically with display of systolic, diastolic, and mean BP and the heart rate.
- The oscillometric technique is not as reliable as the Doppler method for animals with fast heart rates, very small arteries, or muscle tremors. However, a recent study showed that high definition oscillometry is accurate in cats. In both cats and dogs, the oscillometric devices tend to underestimate BP by increasing amounts as pressure increases.

Doppler Technique

- Doppler flow meters (Parks, Vet-Dop, Jorgensen) detect blood flow as a change in the frequency of reflected sound (Doppler shift) due to the motion of underlying red blood cells. For measurements taken from the front limb, a pneumatic cuff is wrapped snugly around the forearm above the carpus. An aneroid manometer connects to the occluding cuff. The Doppler transducer is placed over the median artery on the ventral aspect of the forepaw, between the metacarpal and carpal pads (distal to the cuff). The hair between the pads should be moistened to remove air pockets prior to applying the transducer with gel. Shaving the area is not necessary. • After inflating the cuff to 30–40 mmHg higher than the expected systolic pressure, the cuff is deflated at approximately 3–4 mmHg/sec. An audible blood flow signal is heard by the operator and denotes systolic BP. • The major limitation of the Doppler technique is the imprecise discrimination of the sounds designating the diastolic, and therefore mean, pressures. • The Doppler technique is the preferred method of BP measurement in cats.

PATHOLOGIC FINDINGS

- Arteriolar hypertrophy, tunica media vasorum hyperplasia, and destruction of the internal elastic lamina layer; vascular damage in the eye, kidney, cardiovascular and nervous system tissues leads to hemorrhage, thrombosis, edema, and necrosis.
- Ventricular hypertrophy develops in response to an increased workload.



TREATMENT

Treatment Guidelines for Dogs and Cats

- In order to reduce the risk of TOD, BP should ideally be reduced to a systolic BP < 150 mmHg and a diastolic BP < 100 mmHg. • The ACVIM Hypertension Consensus Panel and International Renal Interest Society have recommended that treatment for high BP be based on classifications of the patient which depends upon both reliable BP measurements and knowledge of TOD. • Antihypertensive treatment is indicated in any dog or cat with a sustained systolic BP > 200 mmHg or a diastolic BP > 120 mmHg, regardless of other clinical findings. • In both species, any animal with clear evidence of ongoing TOD generally should be considered a candidate for antihypertensive therapy. • Animals with no clinical signs and mildly elevated BP should not be treated.

APPROPRIATE HEALTH CARE

Usually managed on an outpatient basis. Inpatient care may be necessary depending upon the underlying condition (e.g., fluid therapy with renal failure) or serious complications related to HT (e.g., neurologic signs or acute retinal hemorrhage).

ACTIVITY

No restrictions unless acute blindness present

DIET

- Influenced by underlying cause; sodium restriction is controversial since it will activate the renin-angiotensin aldosterone axis. Sodium restriction alone is unlikely to lower BP. • Avoid high salt intake.

CLIENT EDUCATION

- Unless underlying cause is curable (e.g., hyperthyroidism) or controllable (e.g., hyperadrenocorticism), the patient is likely to be on antihypertensive medication for life.
- Alert owners to TOD of uncontrolled HT (e.g., retinal hemorrhage, retinal detachment, progressive renal impairment, cardiac disease, neurologic signs).

SURGICAL CONSIDERATIONS

May be indicated for hyperthyroidism, pheochromocytoma, hyperaldosteronism, and some forms of hyperadrenocorticism.



MEDICATIONS

DRUG(S) OF CHOICE

- Treat underlying cause if possible, although HT may persist even if underlying disease is well controlled.
- Cats—amlodipine is first-line oral drug, with an ACE inhibitor added if proteinuria (UPC > 0.4) is present.
- Dogs—ACE inhibitor (e.g., enalapril, benazepril) is first-line drug due to frequency of underlying proteinuria (UPC > 0.5), with amlodipine added as second drug if necessary.
- Spironolactone and hydralazine may be added to the antihypertensive regime if ACE inhibitors and amlodipine are ineffective in lowering BP to < 150 mmHg.
- In a hypertensive emergency, parenteral hydralazine, sodium nitroprusside, or labetolol can be used. Continuous direct BP monitoring is necessary.

Dihydropyridine Calcium Channel Blockers

- Lower peripheral vascular resistance by vasodilation.
- T_{1/2} of amlodipine is 30 hours in dogs, so this is a drug for chronic, not acute, management of HT.
- Amlodipine—dogs, 0.1–0.5 mg/kg PO q24h; cats, 0.625–1.25 mg/cat PO q24h.

ACE Inhibitors

- Lower peripheral vascular resistance and stroke volume by blocking the conversion of angiotensin I to angiotensin II; renoprotection; decrease vascular remodeling.
- Enalapril—dogs, 0.5 mg/kg PO q12h; cats, 0.25–0.5 mg/kg PO q12h.
- Benazepril—dogs and cats, 0.5 mg/kg PO q12h.

Angiotensin Receptor Blockers (ARBs)

- Blocks the activation of angiotensin II AT₁ receptors and directly causes vasodilation, reduces secretion of vasopressin, and reduces production and secretion of aldosterone.
- Telmisartan—dogs, 1.0 mg/kg PO q24h.

Direct-Acting Vasodilators

- Lower peripheral vascular resistance.
- Hydralazine—dogs, 0.5 mg/kg PO q12h, with a stepwise increase to 3 mg/kg PO q12h if needed. Caution if high-dose amlodipine also used.

Alpha-Receptor Antagonists

- Most commonly used with beta-receptor antagonists in cases of pheochromocytoma.
- Phenoxybenzamine—dogs, 0.25 mg/kg PO q12h; cats, 2.5 mg/cat PO q12h.

Diuretics

- Spironolactone—dogs and cats, 1–2 mg/kg PO q12h; primarily used for antialdosterone effects to limit fibrosis; weak diuretic.
- Furosemide—dogs, 2–4 mg/kg PO q12h; cats, 1–2 mg/kg PO q12h; not routinely used in antihypertensive therapy.

(CONTINUED)

Beta-Receptor Antagonists

- Lower HR and cardiac output and suppress renin secretion.
- Blocks the effects of excess thyroid hormone, although additional drugs are needed to control BP.
- Rarely used in dogs unless pheochromocytoma present.
- Propranolol—dogs, 0.2–1 mg/kg PO q8h; cats, 2.5–5 mg/cat PO q8–12h.
- Atenolol—dogs, 0.25–1 mg/kg PO q12h; cats, 6.25–12.5 mg/cat PO q12h.

CONTRAINDICATIONS

Taper or discontinue steroids, vasoconstricting drugs (e.g., phenylpropanolamine).

PRECAUTIONS

- Arterial vasodilators can cause reflex tachycardia; rapidly acting drugs and multiple vasodilators used together increase the risk of hypotension and acute renal failure.
- Beta blockers may worsen bronchiolar disease, CHF, conduction disturbances (e.g., second- and third-degree AV block).
- High volume IV fluid therapy increases BP.

POSSIBLE INTERACTIONS

- Combinations of drugs increase risk of hypotension.
- Hyperkalemia may result from ACE inhibitors and spironolactone, especially with underlying renal disease.

ALTERNATIVE DRUG(S)

In a hypertensive emergency, hydralazine (0.2 mg/kg SC or IM), sodium nitroprusside (1–5 µg/kg/min up to 10 µg/kg/min CRI), or labetolol (0.25 µg/kg q10min; 20–30 µg/kg/min CRI) can be used. Continuous direct BP monitoring is necessary.

**FOLLOW-UP****PATIENT MONITORING**

- BP measurements of < 150/100 are the treatment goal, although systolic BP < 160 mmHg is reasonable and will minimize risk of TOD.
- BP and hypertensive complications (especially retinopathy) should be checked weekly until BP is controlled.

- Laboratory tests to measure side effects of medications and clinical disease response (e.g., proteinuria, hematuria, anemia, thrombocytopenia, potassium balance, sodium balance, azotemia, albumin).

POSSIBLE COMPLICATIONS

- CHF (rare).
- Glomerulonephropathy (proteinuria, hematuria).
- Renal failure.
- Retinopathy (hemorrhage, detached retina).
- Cerebral vascular accident (various central nervous system signs).
- Gingival hyperplasia may develop with amlodipine treatment in dogs.

EXPECTED COURSE AND PROGNOSIS

- Dictated by underlying cause of HT.
- BP can be controlled with appropriate/combined therapy in most patients, but antihypertensive therapy does not necessarily improve survival time.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Chronic renal disease, endocrinopathies

ZOONOTIC POTENTIAL

None, unless Leptosirosis determined to cause renal disease and HT

PREGNANCY/FERTILITY/BREEDING

Pregnancy is a high volume state, and would be expected to make HT more severe.

AGE-RELATED FACTORS

Chronic renal disease, hyperthyroidism, and hyperadrenocorticism—more common in older animals.

SYNONYMS

- High blood pressure
- Systemic arterial hypertension

SEE ALSO

- Diabetes Mellitus without Complication—Cats
- Diabetes Mellitus without Complication—Dogs
- Glomerulonephritis
- Hyperadrenocorticism (Cushing's Syndrome)—Cats
- Hyperadrenocorticism (Cushing's Syndrome)—Dogs
- Hyperthyroidism
- Pheochromocytoma

HYPERTENSION, SYSTEMIC

- Renal Failure, Acute
- Renal Failure, Chronic

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- ACTH = adrenocorticotropic hormone
- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- ARBs = angiotensin receptor blockers
- AV = atrioventricular
- BP = blood pressure
- CBC = complete blood count
- CHF = congestive heart failure
- CT = computed tomography
- HR = heart rate
- HT = systemic hypertension
- MRI = magnetic resonance imaging
- PCV = packed cell volume
- T₃ = triiodothyronine
- T₄ = thyroxine
- TOD = target organ damage
- TSH = thyroid stimulating hormone

INTERNET RESOURCES

<http://www.vin.com/proceedings/Proceedings.plx?CID=WALTHAMOSU2002&PID=2989>
<http://www3.interscience.wiley.com/cgi-bin/fulltext/120715479/PDFSTART?CRETRY=1&SRETRY=0>

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**Client Education Handout
available online**

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HYPERTHYROIDISM



BASICS

DEFINITION

A pathologic, sustained, high overall metabolism caused by high circulating concentrations of thyroid hormones.

PATHOPHYSIOLOGY

- Hyperthyroidism in cats is most often caused by autonomously hyperfunctioning nodules of the thyroid gland that secrete T_4 and T_3 , uncontrolled by normal physiologic influences (e.g., TSH secretion); one or both lobes of the thyroid gland can be affected.
- Rare cases of feline hyperthyroidism (1–2%) are caused by hyperfunctioning thyroid carcinoma. • Extremely uncommon in dogs, it has been seen in some dogs with thyroid carcinoma (most dogs with thyroid gland neoplasia are euthyroid) and in dogs with oversupplementation of exogenous thyroid hormone.

SYSTEMS AFFECTED

- Behavioral. • Cardiovascular—myocardial hypertrophy and hypertension.
- Gastrointestinal—chronic cellular malnutrition, decreased gastrointestinal transit time, malabsorption, and hepatocellular damage. • Musculoskeletal—cachexia.
- Nervous. • Renal/Urologic—high GFR may mask underlying chronic renal failure, possible hyperfiltration injury, and decreased urine-concentrating ability.

GENETICS

No known genetic predisposition

INCIDENCE/PREVALENCE

- Most common endocrine disease of cats; one of the most common diseases in late middle-aged and old cats; true incidence is unknown, but diagnosis of the disease is increasing. In the United Kingdom, overall prevalence is 2–3%, with 9% prevalence in cats over 10 years old. • Rare in dogs.

SIGNALMENT

Species

Cat and (rarely) dog

Mean Age and Range

Mean age in cats, approximately 13 years; range 4–22 years. Uncommon in cats less than 6 years old.

SIGNS

General Comments

- Multisystemic; reflect the increase in metabolism. • Less than 10% of patients are referred to as “apathetic”; these cats exhibit atypical signs (e.g., poor appetite, anorexia, depression, and weakness).

Historical Findings

- Weight loss • Polyphagia • Vomiting
- Diarrhea • Polydipsia • Tachypnea
- Hyperactivity • Dyspnea • Aggression

Physical Examination Findings

- Large thyroid gland—70% of patients are affected bilaterally
- Poor body condition
- Heart murmur • Tachycardia • Gallop rhythm
- Unkempt appearance • Thickened nails

CAUSES

- Cats—autonomously hyperfunctioning nodules; rarely, thyroid carcinoma.
- Dogs— T_4 or T_3 secretion by a thyroid carcinoma or iatrogenic due to oversupplementation of thyroxine.

RISK FACTORS

- Some reports have linked feline hyperthyroidism to canned food diets.
- Recent studies have implicated endocrine disruptor toxins (e.g., PBDEs) as possible causes of feline hyperthyroidism, but this has not been proven. • Advancing age increases risk. • Risk may be decreased in purebred cats.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

The clinical signs of feline hyperthyroidism can overlap with those of chronic renal failure, chronic liver disease, and neoplasia (especially intestinal lymphoma); they can be excluded based on routine laboratory findings and thyroid function tests.

CBC/BIOCHEMISTRY/URINALYSIS

- Erythrocytosis (mild) and, less commonly, leukocytosis, lymphopenia, and eosinopenia—stress response associated with high T_3 and T_4 . • High ALT activity—common. • High ALP, LDH, AST, BUN, creatinine, glucose, phosphorus, and bilirubin—less common; caused by more severe complications of hyperthyroidism.

OTHER LABORATORY TESTS

- Serum total T_4 concentration (TT_4)—measures protein-bound and free (unbound) T_4 ; high resting concentration confirms the diagnosis of hyperthyroidism. • Serum total T_3 concentration—not reliable. • Free T_4 (FT_4) by equilibrium dialysis—sometimes useful to diagnose mild or early hyperthyroidism in cats with normal resting serum TT_4 concentrations. • In theory, FT_4 more accurately reflects true thyroid gland secretory status, but some cats with non-thyroidal illness exhibit unexplained elevations in FT_4 ; do not use FT_4 alone as a screening test. • T_3 suppression test—useful to diagnose mild hyperthyroidism (see Appendix II for protocol and interpretation).
- TRH stimulation test—useful to diagnose mild hyperthyroidism (see Appendix II for protocol and interpretation).

IMAGING

- Thoracic radiography and echocardiography may be useful in assessing the severity of

myocardial disease. • Dogs—thoracic radiography to detect pulmonary metastasis. • Cats—abdominal ultrasound may be useful to explore underlying renal disease. • Thyroid gland scintigraphy can be used to diagnose hyperthyroidism (thyroid-to-salivary gland ratio is increased in most cases) and to determine the location of abnormal thyroid tissue (mediastinal or sublingual ectopic disease is found in nearly 4% of cases).

DIAGNOSTIC PROCEDURES

- Treatment of hyperthyroidism can significantly decrease renal function; pursue any abnormal value revealed by CBC, serum biochemical testing, or urinalysis by bacterial culture of the urine, abdominal radiography, and ultrasonography of the urinary tract.
- Can measure GFR by plasma disappearance of iohexol or ^{99m}Tc -DTPA in cats with suspected underlying renal disease. Contrary to some reports, concentrated urine (specific gravity > 1.035) does not decrease the risk of post-treatment renal insufficiency. • Indirect blood pressure measurement may be useful in pretreatment assessment and monitoring of therapy.

PATHOLOGIC FINDINGS

- Adenomatous hyperplasia of one or both lobes of the thyroid gland • Carcinoma in dogs and 1–2% of cats



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient management usually suffices for cats, if antithyroid drugs are used.
- Radioiodine treatment and surgical thyroidectomy require inpatient treatment and monitoring. • Rare cases of overt congestive heart failure require emergency inpatient intensive care.

ACTIVITY

No alterations recommended

DIET

- Resolution of thyrotoxicosis obviates the need for modifications. • Poor absorption of many nutrients and high metabolism suggest the need for a highly digestible diet with high bioavailability of protein in untreated hyperthyroidism. • A commercial iodine-deficient diet (Hill's y/d) has been advocated for treatment of hyperthyroidism, but studies of disease control and long-term outcomes are lacking.

CLIENT EDUCATION

- Inform clients of adverse effects of antithyroid drugs (see below) and surgical complications. • Clients should be aware of possible (rare) recurrence after treatment.

SURGICAL CONSIDERATIONS

- Surgical thyroidectomy is one recommended treatment for hyperthyroidism

(CONTINUED)

in cats. • Surgical treatment of thyroid carcinoma (dogs and cats) is usually not curative, but can be palliative.



MEDICATIONS

DRUG(S) OF CHOICE

• Radioiodine therapy is arguably the safest and most effective treatment. • Methimazole (Tapazole) is most often recommended (5–15 mg/day divided q8–12h). • Methimazole can be given transdermally (compounded in PLO gel). Resolution of thyrotoxicosis takes longer with transdermal than with oral methimazole. • β -adrenergic blocking drugs—sometimes used to treat some of the cardiovascular and neurologic effects of excess thyroid hormone; can be used in combination with methimazole; mainly used to prepare the patient for surgical thyroidectomy or radioiodine therapy. Atenolol is useful for controlling tachycardia.

PRECAUTIONS

- Antithyroid drugs have several side effects.
- Anorexia and vomiting are common side effects of methimazole; rare side effects include self-induced excoriation of the face, thrombocytopenia, bleeding diathesis, agranulocytosis, serum antinuclear antibodies, and hepatopathy. • Side effects usually develop within the first 3 months of treatment and may or may not necessitate drug cessation and alternative treatment (depending on severity). • Bleeding, jaundice, and agranulocytosis necessitate immediate withdrawal of the drug. • With the exception of vomiting, side effects can occur with transdermal methimazole as well.

ALTERNATIVE DRUG(S)

- Carbimazole—another useful antithyroid drug; not available in the United States.
- Propylthiouracil—can be useful if methimazole is unavailable; adverse effects may be more common and more severe than with methimazole. • Iopodate—a radiographic contrast agent; can be used at 15 mg/kg PO q12h to treat some cases of mild hyperthyroidism, but not effective in most hyperthyroid patients; long-term effectiveness has not been established.



FOLLOW-UP

PATIENT MONITORING

- Methimazole (and other antithyroid drugs)—physical examination, CBC (with platelet count), serum biochemical analysis, and serum T_4 determination every 2–3 weeks for the initial 3 months of treatment; adjust the dosage to maintain serum T_4 concentration in the low-normal range.

- Surgical thyroidectomy—watch for development of hypocalcemia and/or laryngeal paralysis during the initial postoperative period; measure serum T_4 concentrations in the first week of surgery and every 3–6 months thereafter to check for recurrence. • Radioiodine—measure serum T_4 concentrations 2 weeks after treatment and every 3–6 months subsequently. • Renal function—GFR declines following treatment in most patients; therefore, perform a physical examination, serum biochemistry, and urinalysis 1 month after treatment and then as indicated by the clinical history.

POSSIBLE COMPLICATIONS

- Untreated disease can lead to congestive heart failure, intractable diarrhea, renal damage, retinal detachment (as a result of hypertension), and death. • Complications of surgical treatment include hypoparathyroidism, hypothyroidism, and laryngeal paralysis.
- Hypothyroidism can occur following radioiodine therapy and during treatment with antithyroid drugs. Evidence suggests that iatrogenic hypothyroidism is associated with decreased renal function and decreased survival.

EXPECTED COURSE AND PROGNOSIS

- Uncomplicated disease—prognosis is excellent; recurrence is possible and is most commonly associated with poor owner compliance with medical management; regrowth of hyperthyroid tissue is possible but uncommon after surgical thyroidectomy or radioiodine treatment. • Reported mean survival time in cats treated with radioiodine is 4 years; mean survival time with methimazole is 2 years; mean survival time of cats treated with radioiodine and methimazole is 5.3 years. • Cats with pre-existing renal disease have a poorer prognosis. Renal failure is the most common cause of death in hyperthyroid cats. • Dogs or cats with thyroid carcinoma—prognosis is poor; treatment with radioiodine, surgery, or both is usually followed by recurrence of disease; adjuvant chemotherapy is of questionable benefit.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- In cats with underlying renal disease (either secondary to chronic hypertension or unrelated to thyroid disease), the prognosis is less favorable. • Renal insufficiency may not become apparent until euthyroidism has been established; for this reason, a reversible form of treatment (i.e., antithyroid drugs) is recommended if renal disease is suspected in a cat with hyperthyroidism. Recent studies show the most significant post-treatment decline in GFR occurs during the first month post-treatment, so 30 days should be sufficient

HYPERTHYROIDISM

time for a trial with antithyroid drugs prior to use of a more permanent treatment for hyperthyroidism. • In some patients, hyperthyroidism might be best left untreated.

SYNOMYNS

- Multinodular toxic goiter • Plummer's disease • Thyrotoxicosis

SEE ALSO

- Cardiomyopathy, Hypertrophic—Cats
- Congestive Heart Failure, Left-Sided
- Hypertension, Systemic
- Hypoparathyroidism

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- ALP = alkaline phosphatase • ALT = alanine aminotransferase • AST = aspartate transaminase • FT₄ = free thyroxine
- GFR = glomerular filtration rate
- LDH = lactate dehydrogenase • T₃ = triiodothyronine • T₄ = thyroxine • TRH = thyrotropin-releasing hormone • TSH = thyroid-stimulating hormone • TT₄ = total thyroxine

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Client Education Handout
available online

HYPERTROPHIC OSTEODYSTROPHY



BASICS

DEFINITION

An inflammatory disease of bone that affects rapidly growing giant- and largebreed puppies.

PATHOPHYSIOLOGY

- Characterized by non-septic, suppurative inflammation within metaphyseal trabeculae of long bones.
- Rapidly growing bones more severely affected (distal radius, ulna, and tibia).
- Metaphyses—widened owing to perimetaphyseal swelling and bone deposition.
- Trabecular microfracture and metaphyseal separation—occur adjacent and parallel to the physis.
- Bone formation defective.
- Ossifying periostitis—may be extensive.
- Etiology unknown.

SYSTEMS AFFECTED

- Gastrointestinal—diarrhea.
- Musculoskeletal—symmetrical distribution; distal forelimbs most severely affected; may note soft tissue mineralization in other organs; widened costochondral junctions.
- Respiratory—interstitial pneumonia.

GENETICS

Suspect hyperreactivity to immune stimulation (vaccination)

INCIDENCE/PREVALENCE

Low

GEOGRAPHIC DISTRIBUTION

Northeastern United States—highest in fall; lowest in winter

SIGNALMENT

Species

Dog

Breed Predilections

- Large- and giant- breeds.
- Great Danes; Weimaraners—most common.
- Reported—Irish wolfhounds; Saint Bernards; Kuvaszes; Irish setters; Doberman pinschers; German shepherds; Labrador retrievers; boxers; Chesapeake Bay retriever; golden retriever; Irish setter; others.

Mean Age and Range

- Affects puppies 3–6 months old
- Range of onset—2–8 months of age

Predominant Sex

Males 2.3 times more than females

SIGNS

General Comments

Lameness—may be episodic; degree varies from mild to non-weight-bearing; initial episode may resolve with or without relapse.

Historical Findings

- Depend on severity of the episode.
- Owners often describe a depressed puppy that is reluctant to move.
- Inappetence—common.
- Painful.
- Shifting leg lameness.

Physical Examination Findings

- Lameness—symmetrical, more severe in forelimbs
- Metaphyses—painful; warm; swollen distal metaphyses of radius, ulna, and tibia
- Pyrexia—as high as 41.1°C (106°F)
- Inappetence
- Depression
- Weight loss
- Dehydration
- Diarrhea
- Cachexia
- Debilitation
- Manifestations of systemic illness—respiratory or gastrointestinal
- Foot pad hyperkeratosis
- Anemia

CAUSES

Unknown; the following hypotheses have been proposed.

Metabolic

- Hypovitaminosis C—discounted; may be seen as a result of overuse of available vitamin C in hyperactive bone formation.
- Hypocuprosis—in rats but not in dogs.

Nutritional

- Overnutrition and oversupplementation—association inconsistent.
- Incomplete occurrence in litters.
- Correcting diet does not always alter the course of the disease or eliminate relapses.

Infectious

- Bacterial or fungal organisms—may be secondary when found.
- Not transmissible.
- Temporal association with canine distemper virus vaccination.
- Secondary development may depend on the timing of the neonate's exposure.

RISK FACTORS

Vaccination against canine distemper virus may precipitate an uncontrolled inflammatory reaction in the osteogenic centers.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Panosteitis—no metaphyseal swelling; cottony intramedullary densities in long bones on radiographs.
- Septic metaphysitis/epiphysitis—radiographs of the extremities not typical of hypertrophic osteodystrophy; asymmetrical; may note septic suppurative inflammation on needle aspiration of metaphyseal/epiphyseal

lesions; hematologic findings implicate bacterial infection (neutrophilia plus left shift).

- Elbow dysplasia—no metaphyseal swelling; no fever; pain localized to the elbow(s); typical radiographic signs.
- Osteochondritis dissecans—no metaphyseal swelling or fever; pain localized to shoulder or elbow; subchondral defects on radiographs.
- Septic polyarthritis—septic suppurative inflammation on arthrocentesis; culture.
- Non-septic polyarthritis—non-septic suppurative inflammation on arthrocentesis.

CBC/BIOCHEMISTRY/URINALYSIS

- Do not positively contribute to diagnosis
- Stress leukogram
- Normal serum parameters
- Hypocalcemia uncommon

OTHER LABORATORY TESTS

N/A

IMAGING

- Distal extremity radiographs—irregular radiolucent zones within metaphyses, parallel and adjacent to physes; flared metaphyses; extraperiosteal new bone extending up the diaphyses; mineralization of peri-metaphyseal soft tissues; asynchronous growth in paired bones; cranial bowing; valgus deformity; usually bilaterally symmetric.
- Vertebrae, metacarpal bones, metatarsal bones, ribs, scapula, humerus, and mandible—rarely affected.
- Thoracic radiographs—may reveal interstitial infiltrates.

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

- Distal metaphyses of the radius and ulna—most severe changes; similar abnormalities in all long bones.
- Gross—wide metaphyses; peripheral mineralization; soft tissue swelling.

Histologic

- Non-septic suppurative inflammation of the metaphysis (osteochondritis), especially adjacent to growth plates.
- Necrosis and probable secondary failure of osseous tissue deposition onto the calcified cartilage lattice of the primary spongiosa.
- Trabecular microfractures and impaction.
- Mineralization of peri-metaphyseal soft tissues and soft tissues in other regions of the body.
- Interstitial pneumonia.



TREATMENT

APPROPRIATE HEALTH CARE

- None specific.
- Supportive—from none to intensive care for severely affected puppies.

(CONTINUED)

- Depends on the severity of the episode, pyrexia, and the patient's ability to maintain normal hydration and willingness to eat.

NURSING CARE

- Some patients will not stand or move—prone to develop pressure sores; turn every 2–4 hours to prevent sores and hypostatic congestion of the dependent lung.
- Intravenous fluid therapy—for dehydration; maintenance fluid thereafter.

ACTIVITY

- Restricted—running and jumping may exacerbate metaphyseal injury and result in further inflammation.
- Confine to a small well-padded area—recommended.
- Leash-walking only.

DIET

- Normal commercial puppy ration
- Avoid supplements

CLIENT EDUCATION

- Warn the client of the disease's relapsing nature.
- Inform client that bony deformities will remodel to some degree with time but that bowing and valgus deformations are permanent.
- Warn client that the more severe the disease, the more severe the bowing deformity.

SURGICAL CONSIDERATIONS

- None specific.
- May implement surgical methods of alimentation (pharyngostomy tube, esophagostomy tube, gastrostomy tube)—in debilitated puppies that will not eat or drink and have frequently relapsing episodes of acute clinical signs.
- Corrective osteotomy if growth deformity develops from physeal disruption.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Anti-inflammatory drugs—for pain and antipyretic effects; may try:
 - Aspirin (10 mg/kg PO q12h)
 - Carprofen (2.2 mg/kg IM or PO q12h)
 - Firocoxib (5 mg/kg PO q24h)
 - Etodolac (10–15 mg/kg PO q24h)
 - Deracoxib (1–2 mg/kg PO q24h)
(3–4 mg/kg PO q24h, 7-day limit)
 - Meloxicam (dogs, load 0.2 mg/kg PO, then 0.1 mg/kg PO q24h; cats, 0.1 mg/kg PO q24h—liquid)
 - Tepoxalin (load 20 mg/kg, then 10 mg/kg PO q24h).
- Analgesics—can be used in conjunction with anti-inflammatory medication.

- Tramadol (1–4 mg/kg PO q8–12h)
- Prednisone 0.5–1 mg/kg PO q24h); may cause physeal growth disturbances.
- Opiates may be needed in severe cases.

CONTRAINdications

Vitamin C—may be contraindicated; may accelerate dystrophic calcification and decrease bone remodeling.

PRECAUTIONS

- Avoid immunosuppressive drugs if secondary infection is present.
- NSAIDs—may cause gastric ulceration; watch for hematemesis or melena; NEVER use in conjunction with other NSAIDs or steroids.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None

**FOLLOW-UP****PATIENT MONITORING**

Signs of improvement—less metaphyseal sensitivity; patient gets up; appetite improves; pyrexia resolves.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Cachexia
- Permanent bowing deformities
- Secondary bacterial infection
- Pressure sores
- Muscle fasciculations, seizure—with hypocalcemia
- May see secondary septicemia
- Recurrence
- Death

EXPECTED COURSE AND PROGNOSIS

- Course—days to weeks.
- Most patients—one or two episodes and recover.
- Some patients—seem to have intractable relapsing episodes of pain and pyrexia; rarely die or are euthanized.
- Prognosis—usually good; guarded with multiple relapses or complicating secondary problems.
- Persistent bowing deformity—eliminates many purebred puppies from the show ring.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

None proven

AGE-RELATED FACTORS

Vaccination (canine distemper virus)

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Occurs only in juveniles

SYNOMYS

- Metaphyseal osteopathy
- Vitamin C deficiency
- Scurvy
- Moller Barlow's disease
- Osteodystrophy II

SEE ALSO

- Elbow Dysplasia
- Osteochondrosis
- Panosteitis

ABBREVIATION

NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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Client Education Handout
available online

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HYPERTROPHIC OSTEOPATHY



BASICS

OVERVIEW

- Disease of the distal extremities resulting from peripheral blood flow changes which stimulate an overgrowth of vascular connective tissue and subsequent periosteal proliferation.
- Pathogenesis—speculative; Increased blood circulation in the limb due to neural or humoral mechanisms are likely secondary to an underlying disease process—most notably intra-thoracic or intra-abdominal neoplasia. Predominately affects the diaphyseal region of long bones and distal extremities (distal phalanges, metacarpals, and metatarsals).
- A primary form occurs in humans (Marie's disease).

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SIGNALMENT

- More common in dog than cat.
- Age of highest frequency—8 years; coincides with the peak incidence of neoplasia.
- Mean age—5.6 years; dogs with non-neoplastic lung lesions.

SIGNS

Historical Findings

- Chronically or acutely lame and painful in one or more limbs.
- Reluctance to move.
- Enlargement of the distal portion of the extremities.
- Respiratory clinical signs if intrathoracic disease present (rare).

Physical Examination Findings

- Lame, sore, and pain noted in distal extremities.
- Distal extremities—enlarged, firm, taut, thickened; not edematous.
- Firm swelling may extend proximally with progression of disease.

CAUSES & RISK FACTORS

- Primary and metastatic neoplasia: lung tumors, esophageal sarcoma, rhabdomyosarcoma, adenocarcinoma of the adrenal gland, liver or prostate, nephroblastoma, renal cell carcinoma, thoracic and abdominal mesotheliomas.
- Non-neoplastic conditions: pneumonia, lung abscess/granulomas, dirofilariasis; congenital or acquired heart disease, bronchial foreign bodies; *Spirocercus lupi* infestation of the esophagus; focal lung atelectasis.
- Obscure toxins, hypertension, hyperestrogenism, congenital idiopathic megaesophagus.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Osteomyelitis—asymmetrical; generally edematous; lytic bone lesions; history of penetrating trauma or systemic infection.
- Metastatic neoplasia—asymmetrical.
- Hypervitaminosis A (feline)—asymmetrical; generally involves joint surface.

- Hypertrophic osteodystrophy—metaphyseal abnormality, young dogs.
- Multiple cartilaginous exostosis—metaphyseal abnormality, young dogs.
- Degenerative joint disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Depends on the underlying cause.
- Serum ALP—nonspecific elevation

OTHER LABORATORY TESTS

- Fecal examination—rule out gastrointestinal and respiratory parasitism.
- Ultrasound—helps identify and differentiate primary lesions.

IMAGING

- Radiographs of affected long bones—bilaterally symmetric extensive, aggressive or nonaggressive periosteal new bone formation on diaphyseal regions; periosteal reaction project outward from the cortex and perpendicular to the long axis (palisade-like); periosteal new bone forms around the entire circumference of the bone; joints not affected.
- Radiographs of the thoracic and abdominal cavities—identify underlying cause.
- Abdominal ultrasound—identify underlying cause.

DIAGNOSTIC PROCEDURES

Bone biopsy and culture (bacterial and fungal)—necessary only in atypical cases to rule out neoplasia and osteomyelitis.



TREATMENT

- Directed at underlying primary cause—may involve surgical resection of mass or treatment of underlying primary condition.
- Options in selected cases—unilateral vagotomy on the side of a lung lesion or bilateral cervical vagotomy; incising through parietal pleura; subperiosteal rib resection.



MEDICATIONS

DRUG(S)

- Depends on underlying cause.
- Analgesics—as needed.



FOLLOW-UP

PATIENT MONITORING

Condition indicates other disease processes—important to identify the primary cause.

EXPECTED COURSE AND PROGNOSIS

- Clinical signs may resolve with treatment of underlying disease.
- Bony changes may take several months to regress.

- Prognosis—guarded to poor due to the common occurrence of neoplastic causes.
- Tumor recurrence or metastasis may occur and osteopathy may return.
- No relationship between size, site, or histologic type of primary lesion and the development of or recurrence of hypertrophic osteopathy postoperatively.



MISCELLANEOUS

SYNOMYMS

- Hypertrophic pulmonary osteopathy/osteoarthropathy (HPO/HPOA)
- Hypertrophic osteoarthropathy (HOA)

ABBREVIATION

- ALP = alkaline phosphatase

Suggested Reading

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HYPERTROPHIC PYLORIC GASTROPATHY, CHRONIC



BASICS

DEFINITION

Pyloric stenosis or chronic hypertrophic pyloric gastropathy is an obstructive narrowing of the pyloric canal resulting from varying degrees of muscular hypertrophy or mucosal hyperplasia.

PATHOPHYSIOLOGY

- Can result from a congenital lesion composed primarily of hypertrophy of the smooth muscle or be one of three types of acquired form—primarily circular muscle hypertrophy (type 1), a combination of muscular hypertrophy and mucosal hyperplasia (type 2), or primarily mucosal hyperplasia (type 3).
- The cause is unknown; proposed factors include increased gastrin concentrations (which have a trophic effect on the muscle and mucosa) or changes in the myenteric plexus that lead to chronic antral distension and its associated effects.

SYSTEMS AFFECTED

- Gastrointestinal—chronic intermittent vomiting; regurgitation has also been reported.
- Musculoskeletal—weight loss.
- Respiratory—possible aspiration pneumonia.

GENETICS

Inheritance pattern unknown

INCIDENCE/PREVALENCE

Uncommon

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

- More common in dog
- Rare in cat

Breed Predilections

- Congenital—brachycephalic breeds (boxer, Boston terrier, bulldog); Siamese cats
- Acquired—Lhasa apso, Shih Tzu, Pekingese, poodle

Mean Age and Range

- Congenital—shortly after weaning (introduction of solid food) and up to 1 year of age.
- Acquired—9.8 years of age.

Predominant Sex

Twice as many males as females

SIGNS

General Comments

- Clinical signs are related to the degree of pyloric narrowing.
- Projectile vomiting is generally not a presenting complaint. Animals are generally in good body condition.

Historical Findings

- Chronic intermittent vomiting of undigested or partially digested food (rarely containing bile) often several hours after eating.
- Congenital lesions associated with clinical signs shortly after weaning.
- Frequency of vomiting increases with time.
- Lack of response to antiemetic agents or motility modifying agents.
- Occasional anorexia with weight loss.
- Regurgitation.

Physical Examination Findings

Most dogs are generally in good physical condition.

CAUSES

- Congenital or acquired
- May be influenced by infiltrative mural diseases
- Chronic elevations in gastrin concentrations
- Neuroendocrine factors may play a role

RISK FACTORS

Chronic stress, inflammatory disorders, chronic gastritis, gastric ulcers, and genetic predispositions influence the disease process in humans and may play a role in small animals.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Gastric neoplasia
- Gastric foreign body
- Granulomatous fungal disease (e.g., pythiosis)
- Eosinophilic granuloma
- Motility disorders
- Cranial abdominal mass—pancreatic or duodenal

CBC/BIOCHEMISTRY/URINALYSIS

- Findings vary, depending on the degree and chronicity of obstruction.
- Hypochloremic metabolic alkalosis (characteristic of pyloric outflow obstruction) or metabolic acidosis (or mixed acid-base imbalance).
- Hypokalemia.
- Anemia—if concurrent GI ulceration.
- Prerenal azotemia—if dehydration present.

OTHER LABORATORY TESTS

N/A

IMAGING

Abdominal Radiographs

Normal to markedly distended stomach.

Upper GI Barium Contrast Study

- May display a “beak” sign created by pyloric narrowing, allowing minimal barium to pass into the pyloric antrum.
- Retention of most of the barium in the stomach after 6 hours indicates delayed gastric emptying.

- Intraluminal filling defects or pyloric wall thickening.

Fluoroscopy

- Normal gastric contractility.
- Delayed passage of barium through the pylorus.

Abdominal Ultrasound

Measurable thickening of the wall of the pylorus and antrum.

DIAGNOSTIC PROCEDURES

Endoscopy—allows evaluation of the mucosa for ulceration, hyperplasia, and mass lesions; specimens can be obtained for histopathologic evaluation.

PATHOLOGIC FINDINGS

- Include focal to multifocal mucosal polyps, diffuse mucosal thickening, and pyloric wall thickening, with variable degree of pyloric narrowing.
- Changes range from hypertrophy of the circular smooth muscle to hyperplasia of the mucosa and associated glandular structures; a wide spectrum of inflammatory cell infiltration exists.

H



TREATMENT

APPROPRIATE HEALTH CARE

- Depends on severity of clinical signs.
- Patients should be evaluated and surgery scheduled at the earliest convenience.

NURSING CARE

- Appropriate parenteral fluids to correct any electrolyte imbalances and metabolic alkalosis or acidosis.
- Isotonic saline (with potassium supplementation) is the fluid of choice for hypochloremic metabolic alkalosis.
- Consideration of postoperative nutritional support is important.
- In severe cases treated with gastroduodenostomy or gastrojejunostomy, surgical placement of a jejunostomy tube for enteral nutrition may be advantageous.

ACTIVITY

Restrict

DIET

Highly digestible, low-fat—until surgical intervention is feasible.

CLIENT EDUCATION

- Surgical treatment is highly successful.
- If clinical signs recur postoperatively, more aggressive surgical procedures may be indicated.

SURGICAL CONSIDERATIONS

- Surgical intervention is the treatment of choice.
- Goals involve establishing a diagnosis with histopathologic samples, excising abnormal tissue, and restoring GI function with the least-invasive procedure.

HYPERTROPHIC PYLORIC GASTROPATHY, CHRONIC

(CONTINUED)

- Surgical procedures depend on the extent of obstruction—pyloromyotomy (Freder-Ramstedt), pyloroplasty (Heineke-Mikulicz or antral advancement flap), gastroduodenostomy (Billroth 1), gastrojejunostomy (Billroth 2).

**MEDICATIONS****DRUG(S) OF CHOICE**

- Antiemetics and motility modifiers are generally ineffective.
- H_2 -antagonists and proton pump inhibitors may provide symptomatic relief.

H**CONTRAINDICATIONS**

- Evidence of complete pyloric obstruction precludes the use of promotility drugs.
- Avoid anticholinergic agents because of their inhibitory effects on GI motility.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

Postoperatively for recurrence of clinical signs because of poor choice of surgical procedure.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Postoperative surgical complications include recurrence of clinical signs, gastric ulceration, pancreatitis, bile duct obstruction, and incisional dehiscence with peritonitis.

EXPECTED COURSE AND PROGNOSIS

- 85% of dogs show good-to-excellent results with resolution of clinical signs upon proper surgical intervention.
- Poor prognosis if gastric neoplasia (especially adenocarcinoma) is an underlying cause.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Gastric ulceration

AGE-RELATED FACTORS

Intermittent vomiting in young brachycephalic breeds upon weaning is suggestive of congenital stenosis.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

High gastrin concentrations in pregnant females may predispose to development of the syndrome.

SYNONYMS

- Chronic hypertrophic antral gastropathy
- Hypertrophic gastritis
- Acquired antral pyloric hypertrophy
- Congenital pyloric stenosis

ABBREVIATION

GI = gastrointestinal

Suggested Reading

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HYPERVISCOSITY SYNDROME



BASICS

OVERVIEW

- An assortment of clinical signs caused by high blood viscosity.
- Typically results from markedly high concentration of plasma proteins, although can result (rarely) from extremely high erythrocyte (polycythemia) or white blood cell count (leukemia).
- Most frequently seen as a paraneoplastic syndrome, often associated with multiple myeloma and other lymphoid tumors or leukemia.
- Total plasma protein may exceed 10 g/dL, with serum protein electrophoresis showing monoclonal gammopathy.
- Clinical signs caused by reduced blood flow through smaller vessels, high plasma volume, and associated coagulopathy.
- Systems affected include hemic/lymphatic/immune, ophthalmic, and nervous. In rare cases, pulmonary thromboembolism may occur.

SIGNALMENT

- Dogs more frequently affected than cats.
- No sex or breed predilections.
- More common in older animals due to increased incidence of malignancy.

SIGNS

Historical Findings

- No consistent signs
- Anorexia
- Lethargy
- Depression
- Polyuria and polydipsia
- Blindness, ataxia, and seizures
- Bleeding tendencies
- Respiratory distress

Physical Examination Findings

- Neurologic deficits, including seizures and disorientation.
- Tachycardia and tachypnea if congestive heart failure present owing to volume overload or pulmonary thromboembolism.
- Epistaxis or other mucosal bleeding.
- Hepatomegaly/splenomegaly/lymphadenopathy.
- Visual deficits associated with engorged retinal vessels, retinal hemorrhage or detachment, and papilledema.

CAUSES & RISK FACTORS

- Multiple myeloma and plasma cell tumors ($\text{IgM} > \text{IgA} > \text{IgG}$).
- Lymphocytic leukemia or lymphoma.
- Marked polycythemia ($\text{HCT} > 65\%$).

- Chronic atypical inflammation with monoclonal gammopathy (e.g., ehrlichiosis in dogs).
- Chronic autoimmune disease (e.g., systemic lupus erythematosus and rheumatoid arthritis)—very rare.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other unexplained neurologic disease or bleeding disorders.
- Hyperviscosity is a syndrome, not a final diagnosis.

CBC/BIOCHEMISTRY/URINALYSIS

- Nonregenerative anemia (in patients without polycythemia as a cause of hyperviscosity), thrombocytopenia, or leukopenia.
- Hyperproteinemia (total plasma protein $> 9 \text{ g/dL}$) and hyperglobulinemia ($> 5 \text{ g/dL}$).
- Azotemia and hypercalcemia if hyperviscosity caused by a paraneoplastic syndrome.
- Isosthenuria and marked proteinuria.

OTHER LABORATORY TESTS

- High concentration of IgG, IgA, or IgM, as detected by radial immunodiffusion.
- High plasma or serum viscosity (> 3 relative to water).
- Prolonged prothrombin time or activated partial thromboplastin time.
- Other testing as indicated by primary disease; polycythemia may be relative or absolute, and if absolute, due to hypoxemia (e.g., right to left cardiac shunt) or primary (polycythemia vera).

IMAGING

Hepatosplenomegaly, cardiomegaly, and osteolytic lesions (in association with multiple myeloma) are possible.

DIAGNOSTIC PROCEDURES

- Plasma cell or lymphoid infiltrate revealed by bone marrow biopsy.
- Bence-Jones proteinuria in patients with multiple myeloma.



TREATMENT

APPROPRIATE HEALTH CARE

- Generally treat as inpatient
- Treat underlying disease
- Phlebotomy (15–20 mL/kg) with crystalloid fluid volume replacement
- Plasmapheresis, either manual or automated

NURSING CARE

As dictated by underlying disease



MEDICATIONS

DRUG(S)

- Provide treatment for underlying neoplastic or inflammatory condition.
- See other chapters for drug therapy for the underlying cause (e.g., plasma cell tumor, lymphocytic leukemia, lymphoma, ehrlichiosis, and polycythemia).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Avoid use of medications that might increase vascular volume, including synthetic colloids (e.g., hetastarch); do not try to correct compensatory low albumin.
- Avoid medications that alter platelet function (e.g., NSAIDs).

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FOLLOW-UP

- Monitor serum or plasma proteins frequently as a marker of treatment efficacy.
- CBC, biochemistry panel, and urinalysis to monitor other laboratory abnormalities.



MISCELLANEOUS

SEE ALSO

- Ehrlichiosis (Anaplasma)
- Leukemia, Chronic Lymphocytic
- Lymphoma—Cats
- Lymphoma—Dogs
- Multiple Myeloma
- Plasmacytoma, Mucocutaneous
- Polycythemia

ABBREVIATIONS

- HCT = hematocrit
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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Consulting Editor Alan H. Rebar

HYPHEMA



BASICS

DEFINITION

Blood inside the anterior chamber in the form of a blood clot, settled blood in the ventral anterior chamber, or red blood cells suspended throughout the aqueous, giving a "cherry Kool-Aid" appearance to the aqueous.

PATHOPHYSIOLOGY

- Breakdown of the blood-aqueous barrier and/or direct injury to the iris and ciliary body blood vessels. Causes include direct tissue trauma to the cornea or anterior uvea (iris and ciliary body); prostaglandin release from tissue trauma or inflammatory mediators such as infectious agents; and direct damage to blood vessel walls, as with systemic hypertension, antigen-antibody complexes, or circulating infectious organisms or neoplastic cells.
- Abnormal hemostasis due to a clotting deficiency or thrombocytopenia.
- Bleeding from abnormal vessels within the eye. This is most commonly due to pre-iridal fibrovascular membranes (PIFMs), which form in response to chronic intraocular disease (uveitis, retinal detachment, glaucoma, neoplasia). Rarely, abnormal congenital blood vessels in the eye such as persistent pupillary membranes, tunica vasculosa lentis, or hyaloid artery may bleed, causing hyphema.

SYSTEMS AFFECTED

Ophthalmic

INCIDENCE/PREVALENCE

Not an uncommon ophthalmic finding and one that is important to recognize, as it may be the presenting clinical sign for a serious underlying systemic disease.

SIGNALMENT

Species

Dog and cat

Breed Predilections

Collies with collie eye anomaly

SIGNS

Historical Findings—Primary Ophthalmic Causes

- Usually a unilateral presentation in an otherwise systemically normal patient.
- Blunt globe trauma will often have a history of hit by a car, periocular dog bite, or exposure to cattle or horses.
- Corneal perforation may have a history of a corneal ulcer with subsequent perforation; or preceding encounter with a cat resulting in a cat claw laceration, especially in puppies.

Historical Findings—Systemic Causes

- Unilateral or bilateral presentation; bilateral presentation is strongly supportive of a systemic etiology.
- Weight loss, anorexia, lethargy, and decreased vision or loss of vision may accompany some systemic causes.
- Ocular pain usually accompanies infectious and neoplastic causes due to the accompanying uveitis.

Physical Examination Findings—Primary Ophthalmic Causes

- Except in cases of generalized trauma (hit by car), the physical exam will be unremarkable with abnormalities restricted to the globe and periorbital soft tissues.
- Blunt trauma will have painful periorbital soft tissue swelling and uncommonly orbital rim fractures; there is often total hyphema obscuring other intraocular structures.
- Perforating trauma is associated with severe pain, a bloody or clear (aqueous) ocular discharge, varying degrees of hyphema, miosis, and anterior synechia, and a shallow anterior chamber; corneal edema will surround the perforation site and an iris prolapse may be present through the perforation.
- Hyphema due to PIFMs, retinal detachment, neoplasia, or congenital vasculature are usually non-painful with very

little intraocular inflammation (aqueous flare, miosis).

- Hypermature cataract supports the development of either PIFM or retinal detachment as a cause of the hyphema.

Physical Examination

Findings—Systemic Disease Causes

- When an underlying systemic disease is suspected, a thorough physical exam is warranted; depending on the systemic disease the physical exam may be unremarkable or have significant findings such as lymphadenopathy.
- Ophthalmic examination findings will vary depending on the etiology of the hyphema.
- Non-inflammatory etiologies such as hypertension, thrombocytopenia, and clotting disorders will usually have minimal discomfort and uveitis (trace or no aqueous flare, no miosis, no conjunctival hyperemia). Hypertension is almost always associated with retinal involvement such as retinal hemorrhages and/or retinal detachment.
- Clotting deficiencies may have bleeding elsewhere, including the subconjunctival tissue and retrobulbar space; thrombocytopenia may have petechia on the palpebral or nictitans conjunctiva. Infectious and neoplastic etiologies will often have significant pain, anterior uveitis (miosis, aqueous flare, fibrin, iridal hyperemia and swelling), chorioretinitis with retinal detachment, and possible secondary glaucoma.

CAUSES

See Table 1.

RISK FACTORS

- Ophthalmic: hypermature cataract, retinal detachment, chronic anterior uveitis.
- Systemic: any disease, disorder, or geographic location predisposing to the systemic diseases known to cause uveitis or direct vascular damage (e.g., chronic renal disease or hyperthyroidism predisposing to systemic hypertension).

Table 1

Causes of hyphema.	
Primary Ophthalmic Etiologies	Systemic Disease Etiologies
Trauma (blunt or perforating)	Hypertension
Extraocular vascular compression (choking, chest compression)	Hyperviscosity syndrome
Preiridal fibrovascular membrane	Thrombocytopenia
Retinal detachment	Clotting disorder
Primary intraocular neoplasia (iris melanoma, ciliary body adenoma/adenocarcinoma)	Metastatic neoplasia (especially lymphoma)
Golden retriever pigmentary uveitis	Rickettsial disease
Patent anomalous congenital blood vessels (persistent pupillary membranes, tunica vasculosa lentis, hyaloid artery)	FIP
	Fungal disease
	Prototheca
	Parasitic (aberrant intraocular larval migration)

(CONTINUED)

HYPHEMA**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

Deep corneal vascularization, along the ventral limbus, can be mistaken for hyphema.

CBC/BIOCHEMISTRY/URINALYSIS

Abnormal findings may help support a systemic disease.

OTHER LABORATORY TESTS

Based on history and physical examination findings, clotting profile and serology (rickettsial, fungal) may be indicated if systemic disease is suspected.

IMAGING

- Ocular ultrasound is indicated to evaluate for retinal detachment or uveal tumors when not visible on the ophthalmic examination.
- Based on history and physical examination findings, thoracic radiographs, abdominal radiographs, and abdominal ultrasound may be indicated if systemic disease is suspected.

DIAGNOSTIC PROCEDURES

- Doppler blood pressure measurement if hypertension is suspected.
- Lymph node aspirates if lymphadenopathy is present or if neoplasia or fungal disease is suspected.

PATHOLOGIC FINDINGS

Gross hemorrhage in the anterior chamber.

**TREATMENT****APPROPRIATE HEALTH CARE**

Outpatient medical care is appropriate unless an underlying systemic disease is identified that requires hospitalization.

ACTIVITY

No restricted activity is required unless the patient is blind (restrict environment to fenced yards, no in-ground pools, leash walks, etc.) or the hyphema is due to thrombocytopenia or clotting disorder (avoid rough play, unrestricted running, etc.).

CLIENT EDUCATION

- Hyphema itself, although it appears dramatic, is not painful.
- It is very important to identify the underlying cause of the hyphema, as some etiologies pose a serious health threat.

- Ophthalmic treatment is important to initiate immediately to try to prevent painful and sometimes irreversible and blinding sequela like glaucoma.

SURGICAL CONSIDERATIONS

- Hyphema secondary to a perforating corneal laceration or ulceration should be surgically repaired by direct suturing of the cornea (laceration) or corneal graft (perforated ulcer) when a visual outcome is expected. For a severe perforation with extensive iris prolapse and loss of the pupil, enucleation is recommended.
- Permanently blind and painful eyes should be enucleated (with histopathology) for permanent comfort.
- Surgical irrigation/removal of the hyphema is not successful, as the trauma of the surgery results in exacerbation of the hyphema and intraocular inflammation.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Topical prednisolone acetate 1% or dexamethasone 0.1% q4–8h to help stabilize the blood-aqueous barrier; *do not use if a corneal ulcer or perforation is present*.
- Atropine 1% q6–24h to help prevent posterior synechia; *atropine is contraindicated if secondary glaucoma is present*.
- Systemic NSAID (carprofen, meloxicam, deracoxib) with perforating trauma for analgesia and to help stabilize the blood-aqueous barrier.
- Systemic prednisone/prednisolone with known or suspected choroidal/retinal involvement, *depending on the underlying cause*; anti-inflammatory dose (0.5–1.0 mg/kg PO q24h) can be used for blunt trauma, FIP, and rickettsial and fungal disease with proper antimicrobial therapy.
- Topical carbonic anhydrase inhibitors (dorzolamide 2%, brinzolamide 1%) q8h, beta-blocker (timolol 0.5%) q8–12h, and/or sympathomimetic (dipivefrin 0.1%) q8–12h can be used if secondary glaucoma is present.

CONTRAINDICATIONS

- Topical NSAIDs (e.g., flurbiprofen, diclofenac, ketorolac,) are generally considered contraindicated with hyphema.
- Topical prostaglandin analogues (latanoprost, travoprost, bimatoprost) are contraindicated in secondary glaucomas.

**FOLLOW-UP****PATIENT MONITORING**

- Tonometry should be used to monitor for secondary glaucoma, which lowers the prognosis for a visual outcome.
- Perform tonometry every 1–2 days if the IOP is high normal or greater, or if risk factors such as fibrin and/or posterior synechia are present.
- Perform tonometry weekly if the IOP is low, or if the hyphema and anterior uveitis are mild-moderate in severity.
- Tonometry is contraindicated with a corneal perforation.*

POSSIBLE COMPLICATIONS

Secondary glaucoma, posterior synechia/dyscoria, cataract formation, loss of vision, possible loss of the eye if the eye becomes permanently blind and painful.

EXPECTED COURSE AND PROGNOSIS

- If the underlying cause of the hyphema can be successfully treated, such as repair of a corneal laceration or control of hypertension, and intraocular damage is not extensive, the prognosis is good for complete resolution of the hyphema.
- If trauma to the eye is severe or if the underlying disease is not controlled, the hyphema will persist and blindness can result; no improvement in hyphema after 2 weeks following blunt trauma has a poor prognosis for return of vision.
- Hyphema caused by bleeding from PIFMs usually does not resolve or will resolve and recur.
- If the eye is painful due to a perforated globe or secondary glaucoma, with no reasonable hope of regaining vision, enucleation is recommended.

**MISCELLANEOUS****ABBREVIATIONS**

- CEA = collie eye anomaly
 - FIP = feline infectious peritonitis
 - IOP = intraocular pressure
 - NSAID = nonsteroidal anti-inflammatory drug
 - PIFM = pre-iridal fibrovascular membrane
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HYPOADRENOCORTICISM (ADDISON'S DISEASE)



BASICS

DEFINITION

- Hypoadrenocorticism is an endocrine disorder resulting from deficient production of glucocorticoids and/or mineralocorticoids.
- Primary hypoadrenocorticism is due to destruction of the adrenal cortices, typically resulting in glucocorticoid and mineralocorticoid deficiency.
- Addison's disease refers to a deficiency of both glucocorticoids and mineralocorticoids resulting from idiopathic (immune-mediated) primary hypoadrenocorticism.
- The term atypical hypoadrenocorticism has been applied to the subset of dogs with primary hypoadrenocorticism that present with normal electrolytes. Recent work, however, has demonstrated that most of these dogs are mineralocorticoid deficient and thereby may not be so atypical.
- Secondary hypoadrenocorticism results from pituitary ACTH insufficiency, resulting in inadequate glucocorticoid production by the adrenal cortices.

PATOPHYSIOLOGY

- Mineralocorticoid (aldosterone) deficiency results in a diminished ability to excrete potassium and retain sodium, disrupting sodium and potassium balance in the body.
- Sodium deficiency leads to diminished effective circulating volume. This then contributes to pathophysiologic changes and clinical abnormalities including prerenal azotemia, hypotension, dehydration, weakness, and depression.
- Hyperkalemia can contribute to clinical abnormalities including weakness, lethargy and anorexia. In combination with other electrolyte and metabolic derangements, it may result in myocardial toxicity as evidenced by bradycardia and various arrhythmias.
- Glucocorticoid (cortisol) deficiency contributes to the occurrence of anorexia, vomiting, diarrhea, melena, lethargy, and weight loss. Due to its role in glucose homeostasis hypocortisolemia predisposes to hypoglycemia. In addition, free water excretion is impaired.

SYSTEMS AFFECTED

- Gastrointestinal
- Musculoskeletal
- Cardiovascular
- Renal/Urologic
- Skin

GENETICS

A genetic basis has been determined in standard poodles, bearded collies and Leonbergers.

INCIDENCE/PREVALENCE

No exact figures available; considered uncommon to rare in dogs and very rare in cats.

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Great Danes, rottweilers, Portuguese water dogs, standard poodles, bearded collies, Leonbergers, West Highland white terriers, Nova Scotia duck tolling retrievers and Wheaten terriers have increased relative risk. Golden retrievers and Chihuahuas have decreased relative risk.
- No predilection in cats.

Mean Age and Range

- Dogs—range, < 1 to > 12 years; median, 4 years; most are young to middle-aged
- Cats—range, 1–9 years; most are middle-aged

Predominant Sex

Female dogs are at an increased relative risk; no predilection in cats.

SIGNS

General Comments

Signs vary from mild and few in some patients with chronic hypoadrenocorticism to severe and life-threatening in an acute Addisonian crisis. Multiple organ systems may be involved; type and extent of involvement varies from case to case.

Historical Findings

- Dogs—lethargy, anorexia, vomiting, weakness, weight loss, diarrhea, waxing/waning course, previous response to therapy, shaking, PU/PD, melena
- Cats—lethargy, anorexia, weight loss, vomiting, waxing/waning course, previous response to therapy, PU/PD

Physical Examination Findings

- Dogs—depression, weakness, dehydration, collapse, hypothermia, slow CRT, melena, weak pulse, bradycardia, painful abdomen, hair loss
- Cats—dehydration, weakness, hypothermia, slow CRT, depression, weak pulse, bradycardia, colapse

CAUSES

- Primary hypoadrenocorticism—idiopathic (immune-mediated), mitotane overdose, trilostane overdose, granulomatous disease, metastatic tumors, fungal disease, coagulopathy
- Secondary hypoadrenocorticism—iatrogenic following withdrawal of long-term glucocorticoid administration, isolated ACTH deficiency, panhypopituitarism, pituitary or hypothalamic lesions

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Signs are nonspecific and are seen in other, more common medical disorders, particularly gastrointestinal and renal diseases.
- Although no signs are pathognomonic, a waxing and waning course and previous response to nonspecific medical intervention ("fluids and steroids") should alert the clinician to consider the diagnosis.

CBC/BIOCHEMISTRY/URINALYSIS

- Hematologic abnormalities may include anemia, eosinophilia, and lymphocytosis.
- The absence of a stress (glucocorticoid influence) leukogram in a patient that has been ill for a few days should prompt consideration of hypoadrenocorticism.
- Serum biochemical findings may include hyperkalemia, azotemia, hyponatremia, hypochloremia, decreased total CO₂, hyperphosphatemia, hypercalcemia, increased ALT, increased serum alkaline phosphatase, and hypoglycemia.
- Urinalysis often reveals impaired urine-concentrating ability and in some cases isothenuria. Some patients with isothenuria are also azotemic, potentially causing confusion with primary renal disease.
- Some patients with hypoadrenocorticism exhibit normal electrolyte levels (so-called atypical hypoadrenocorticism).

OTHER LABORATORY TESTS

- Definitive diagnosis is by demonstration of undetectable-to-low baseline serum cortisol concentrations that fail to increase appropriately following ACTH administration. We prefer to determine cortisol concentrations before and 1 hour after administration of synthetic ACTH IV (5 µg/kg in dogs, 0.125 mg in cats). Alternatively, ACTH gel can be given IM (2 U/kg in dogs, 10 U in cats). ACTH gel (usually 40 U/mL) is available from several compounding pharmacies. Based on a recent study performed in normal dogs, it was recommended determine serum cortisol concentrations at both 1 and 2 hours post-ACTH administration when using a compounded ACTH gel.
- In hypovolemic dehydrated animals, use synthetic ACTH IV or delay testing until after initial fluid administration is completed and tissue perfusion restored.
- If IV synthetic ACTH is used, the ACTH stimulation test can be performed during initial stabilization and treatment if dexamethasone is used since it does not cross-react with the cortisol assay.
- If prednisone, prednisolone, or hydrocortisone have been administered, these treatments must be discontinued, and the

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HYPOADRENOCORTICISM (ADDISON'S DISEASE)

ACTH stimulation test performed at least 24 hours after changing the glucocorticoid to dexamethasone.

- A recent study demonstrated that a resting cortisol concentration above 2 µg/dL would make hypoadrenocorticism very unlikely in a dog that had not recently received glucocorticoids. Please note that this cutoff is a guideline and may vary a little based on methodology of the cortisol assay used, as well as from laboratory to laboratory using the same methodology. Also, a low resting cortisol does not confirm hypoadrenocorticism; an ACTH stimulation test is required. Determine the plasma ACTH concentration in patients with normal electrolyte levels to differentiate primary from secondary hypoadrenocorticism; must collect sample before initiating therapy, especially glucocorticoids. Carefully follow sample handling instructions from the laboratory being used. Plasma ACTH concentrations are high with primary hypoadrenocorticism and undetectable-to-low with secondary hypoadrenocorticism.

IMAGING

Radiographs may reveal microcardia, narrowed vena cava or descending aorta, hypoperfused lung fields, less commonly microhepatica, and very rarely megaesophagus. Abdominal ultrasound may reveal small adrenal glands.

PATHOLOGIC FINDINGS

- Gross examination—atrophy of the adrenal glands.
- Microscopically—lymphocytic-plasmacytic adrenalitis and/or adrenocortical atrophy. Other abnormalities may be present depending on etiology (neoplasia, fungal disease, etc.).

**TREATMENT****APPROPRIATE HEALTH CARE**

- An acute Addisonian crisis is a medical emergency requiring intensive therapy and 24 hour observation and care. The diagnostic workup is performed while initial treatment and stabilization are ongoing. Cats often respond more slowly than dogs.
- The intensity of treatment for patients with chronic hypoadrenocorticism depends on the severity of clinical signs; usually initial stabilization and therapy are conducted on an inpatient basis.

NURSING CARE

- Treat acute Addisonian crisis with rapid correction of hypovolemia and restoration of volume status using isotonic fluids (preferably 0.9% NaCl).
- Monitor hydration status, blood pressure, urine output, temperature and heart rate and rhythm.

ACTIVITY

Avoid unnecessary stress and exertion during an Addisonian crisis.

DIET

No need to alter

CLIENT EDUCATION

- Life-long glucocorticoid and/or mineralocorticoid replacement therapy is required.
- Increased dosages of glucocorticoid (above maintenance requirements) are required during periods of stress such as travel, boarding, hospitalization, and surgery.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Chronic primary hypoadrenocorticism—most patients will need daily glucocorticoid replacement (prednisone, 0.1–0.2 mg/kg/day), as well as mineralocorticoid replacement (DOCP, Percorten, 2.2 mg/kg IM or SC typically given monthly, and adjusted as needed on the basis of serial electrolyte determinations). The initial monthly DOCP dose for an average size cat is 12.5 mg. Though not preferred, an alternative means of administering glucocorticoid replacement to cats is Depo-Medrol (10 mg IM monthly).
- Alternatively an oral mineralocorticoid replacement can be used (fludrocortisone acetate, Florinef, 5–10 µg/kg q12h, adjusted by 0.05- to 0.1-mg increments on the basis of serial electrolyte determinations). Fludrocortisone acetate has some glucocorticoid activity and the maintenance dose of prednisone for patients receiving fludrocortisone may be lower than for dogs receiving DOCP. A few dogs develop PU/PD and/or polyphagia on fludrocortisone acetate.
- In an Addisonian crisis, parenteral administration of a rapidly acting glucocorticoid such as dexamethasone sodium phosphate or prednisolone sodium succinate is indicated; dexamethasone sodium phosphate is preferred because prednisolone cross-reacts with cortisol assays. Dexamethasone sodium phosphate is given at a dose of 2–4 mg/kg IV; this dose can be repeated in 2–6 hours if necessary. Glucocorticoid is gradually tapered as the condition improves. If prednisone, prednisolone, or hydrocortisone have been given, ACTH stimulation testing will need to be delayed until the glucocorticoid has been switched to dexamethasone for at least 24 hours.
- Fluid therapy with 0.9% NaCl as needed based on the patient's hydration, volume status and blood pressure. In an Addisonian crisis, fluids are typically initiated at a rate of 60–80 mL/kg/h for the first 1–2 hours, then tapered based on the clinical status and

discontinued when appropriate. If severe hyponatremia is noted on preliminary lab work, correct no quicker than 10–12 mEq/L per day over the first 48 hours of therapy.

- If necessary a colloid also can be given to help treat hypotension and hypovolemia.
- Treat hypoglycemia if present with IV dextrose.
- Sodium bicarbonate therapy is rarely needed; reserve for severe acidosis.
- Treat hyperkalemic myocardial toxicity with an intravenous insulin and glucose protocol. Alternatively use intravenous calcium chloride or calcium gluconate (cardioprotective only).
- Patients with confirmed secondary hypoadrenocorticism require only glucocorticoid supplementation (prednisone, 0.1–0.2 mg/kg/day).

PRECAUTIONS

N/A

ALTERNATIVE DRUG(S)

- See Hyperkalemia chapter for specific recommendations for emergency management of severe hyperkalemia.
- See Hyponatremia chapter for specific recommendations for emergency management of severe hyponatremia.

**FOLLOW-UP****PATIENT MONITORING**

- Depending on their clinical presentation, patients hospitalized for treatment of hypoadrenocorticism may require intensive monitoring and frequent laboratory evaluations. Monitor clinical status, urine output, CBC, blood chemistry, and ECG as needed. Blood glucose and electrolytes may need to be evaluated several times daily during initial therapy. Determine blood gas status when necessary.
- After the first 2 injections of DOCP, ideally measure electrolyte levels at 2, 3, and 4 weeks to determine the duration of effect; thereafter, check electrolyte levels at the time of injection for the next 3–6 months (and adjust the dosage of DOCP if necessary) and then every 6 months.
- DOCP is usually required at monthly intervals; rare patients need injections as often as every 2 or 3 weeks. On the other hand, an occasional dog will require DOCP as infrequently as every 6 weeks. Less than 5% of dogs require a dose of DOCP higher than 2.2 mg/kg per injection.
- The large majority of dogs with hypoadrenocorticism will be well controlled on a maintenance DOCP dose of 2.2 mg/kg/injection every month. If necessary, the DOCP dosage can be sequentially decreased based on electrolyte determinations as some dogs can be controlled on a monthly dosage that is significantly less

HYPOADRENOCORTICISM (ADDISON'S DISEASE)

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than 2.2 mg/kg. Alternatively, the interval between injections can be increased while monitoring electrolyte concentrations.

- Adjust the daily dose of fludrocortisone by 0.05- to 0.1-mg increments as needed, based on serial electrolyte determinations; following initiation of therapy, check electrolyte levels weekly until they stabilize in the normal range; thereafter, check electrolyte concentrations monthly for the first 3–6 months and then every 3–12 months.
- In many dogs given fludrocortisone, the daily dose required to control the disorder increases incrementally, usually during the first 6–24 months of therapy; in most dogs, the final fludrocortisone dosage needed is 20–30 µg/kg/day; very few can be controlled on 10 µg/kg/day or less.
- In patients that were initially azotemic, monitor creatinine concentrations as needed following discharge from the hospital.

PREVENTION/AVOIDANCE

- Continue hormonal replacement therapy for the lifetime of the patient.
- Increase the dosage of replacement glucocorticoid during periods of stress such as travel, boarding, hospitalization, and surgery.

POSSIBLE COMPLICATIONS

- PU/PD may occur from prednisone administration, necessitating decreasing or discontinuing the drug or trying an alternative glucocorticoid.
- PU/PD may occur from fludrocortisone administration, necessitating a change to DOCP therapy.

- Side effects from DOCP are very uncommon; rarely weight gain is seen and very rarely PU/PD.

EXPECTED COURSE AND PROGNOSIS

Except for patients with primary hypoadrenocorticism caused by granulomatous or metastatic disease and secondary hypoadrenocorticism caused by a pituitary mass, the vast majority of patients carry a good to excellent prognosis following with proper stabilization, treatment, and monitoring.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Concurrent endocrine gland failure occurs in up to 5% of dogs—hypothyroidism, diabetes mellitus, and/or hypoparathyroidism.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

None

SYNOMYS

Addison's disease (primary hypoadrenocorticism)

SEE ALSO

- Hyperkalemia
- Hyponatremia

ABBREVIATION

PU/PD = polyuria/polydipsia

INTERNET RESOURCES

None

Suggested Reading

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BASICS

DEFINITION

Hypoalbuminemia defined as measured value less than the reference range.

PATHOPHYSIOLOGY

- Albumin—constitutive protein exclusively synthesized in the liver. • Provides 75–80% of plasma colloid oncotic pressure. • Low oncotic pressure due to serum albumin < 1.5 g/dL may permit fluid extravasation into interstitial and potential third-space compartments, causing edema and body cavity effusion. • Albumin of 1.5–2.5 g/dL does not cause edema or effusion unless other factors (e.g., increased hydrostatic pressure [venous occlusion, vascular bed hypertension, renal water or sodium retention, fluid overload], increased vascular permeability [vasculitis]) are present.

SYSTEMS AFFECTED

- Cardiovascular and respiratory—transudative effusions (e.g., pleural effusion, ascites); peripheral edema; pulmonary edema.

INCIDENCE/PREVALENCE

Accompanies many primary diseases processes: primary necroinflammatory liver disorders, protein losing enteropathy (PLE), protein losing nephropathy (PLN), enteric hemorrhage, negative acute phase response in chronic disease.

SIGNALMENT

Species

Dog and cat

Breed Predilections

Numerous disease or syndromes may have propensity for breed specificity.

Mean Age and Range

Varies with syndrome association.

Predominant Sex

N/A

SIGNS

General Comments

- Reflects primary disease or syndrome leading to hypoalbuminemia. • Development of hypoalbuminemia influences: metabolite and xenobiotic protein binding, plasma oncotic pressure, third space fluid distribution, acid base balance, and ability to maintain intravascular perfusion pressure.

HISTORICAL FINDINGS

- Varies with the underlying primary disease or syndrome causing hypoalbuminemia.
- May demonstrate increased drug related effects due to reduced protein binding.

PHYSICAL EXAMINATION FINDINGS

- Varies with the underlying primary disease or syndrome causing hypoalbuminemia.
- Severe hypoalbuminemia (< 1.5 g/dL) associated with anasarca and increased

propensity for third-space fluid distribution with altered Starling forces.

CAUSES

Decreased Albumin Production

- Chronic hepatic insufficiency—chronic hepatitis; cirrhosis; idiopathic hepatic fibrosis; granulomatous hepatitis; congenital portosystemic shunt (dogs). • Inadequate nutritional intake/absorption

EXTRACORPOREAL ALBUMIN LOSS

- PLN—amyloidosis; glomerulonephritis
- PLE—lymphangiectasia; lymphoma; severe inflammatory bowel disease; histoplasmosis; pythiosis; chronic intussusception
- Severely exudative cutaneous lesions
- Chronic severe blood loss—usually enteric
- Repeated large volume paracentesis—abdominal or pleural effusion

Sequestration: Body Cavities/Tissues

- Inflammatory effusions—pancreatitis; septic or aseptic peritoneal or pleural effusions; chylous effusions.
- Vasculopathies—immune-mediated (SLE); infectious (Ehrlichia, Rocky Mountain spotted fever); sepsis syndrome; other.

Miscellaneous

- Downregulated albumin synthesis—hyperglobulinemia, negative acute-phase response, negative nitrogen intake, catabolism.
- Loss—hypoalbuminocorticism.

RISK FACTORS

- Diseases of the liver, kidney, intestines, and blood vessels
- Negative nitrogen balance; poor nutrition



DIAGNOSIS

DIFFERENTIAL DIAGNOSES

- Severe hepatic disease—may see jaundice; HE; polyuria—polydipsia; or ascites
- PLE—diarrhea common but inconsistent
- Cutaneous lesions—must be severe and exudative (e.g., burns, TEN, vasculitis, tumors, trauma)
- External blood loss—pallor due to anemia; evidence of extracorporeal blood loss (enteric, urinary, other)
- Malnutrition—causes mild hypoalbuminemia
- Aggressive fluid therapy (especially colloids)—exacerbates low albumin, may cause transient abnormality.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Depends on underlying disease
- Severe hepatic disease—RBC microcytosis (occasional) suggests portosystemic shunting
- Severe blood loss—regenerative anemia or microcytic/hypochromic anemia

Biochemistry

- Fractionation of total protein not helpful.
- Chronic hepatic disease—low albumin; normal to high globulin.
- PLE—low albumin; low to high globulin.
- PLN—low

HYPOALBUMINEMIA

albumin; globulin usually normal but may be low with non-selective proteinuria (severe PLN).

- Exudative losses—low albumin; variable globulin.
- Malnutrition—low albumin; normal globulin.
- Severe blood loss—low albumin; low to normal globulin.
- Cholesterol—low with chronic hepatic disease, severe PLE, Addison's disease, and severe malnutrition; high with PLN and pancreatitis.
- Hepatic enzymes—ALT may be high with chronic hepatitis, inflammatory bowel disease causing PLE; high ALP often seen with systemic inflammation.

- Bilirubin—sometimes high with chronic hepatic disease.
- BUN—often low with hepatic insufficiency or patients undergoing diuresis; high with reduced renal function or dehydration.
- Hyperkalemia and hyponatremia—suggest hypoalbuminocorticism, third-space effusions, or gut-associated pseudohypoalbuminocorticism.
- Spurious hypocalcemia—due to low protein.

Urinalysis

- Rules out PLN and urologic blood loss.
- Obtain urine by cystocentesis to avoid lower-tract contamination; **caution:** beware cystocentesis-induced microhematuria.
- Proteinuria—confirm dipstick detection with chemical determination.
- Urine protein:creatinine (UP:UCr) ratio—important; > 3.0 compatible with nephrotic range proteinuria; must evaluate urine sediment—spurious positive values with active sediment (i.e., substantial pyuria or macroscopic hematuria); many dogs with glomerulonephritis have hyaline, waxy, or granular casts.
- Microalbuminuria: not helpful; need UP:UCr.
- Ammonium biurate crystalluria—hepatic insufficiency, congenital or APSS.

OTHER LABORATORY TESTS

- TSBA—usually high with severe hepatic disease; sometimes spurious low values with PLE (fat malabsorption).
- Physicochemical evaluation of effusion—transudate (usually pure) if hypoalbuminemia is a major causal factor.
- Antithrombin (AT)—anticoagulant with molecular weight similar to albumin and synthesized largely in liver; may be low with PLE, PLN, and hepatic synthetic failure.
- Protein C (PC)—anticoagulant; may be low with severe hepatic disease/failure, portosystemic shunting, sepsis.

IMAGING

- Thoracic radiography—pleural effusion; pulmonary edema.
- May reveal lymphadenopathy, metastatic disease, cardiac or pulmonary disorders.
- Abdominal radiographs—effusion; altered hepatic size; mass lesions; quadrant signs of pancreatic disease.
- Abdominal ultrasonography—helps identify visceral abnormalities (e.g., small liver, lymphangiectasia in intestinal wall/mucosa), mass lesions, fluid pockets, altered portal blood flow, mesenteric

Hypoalbuminemia

(CONTINUED)

lymphadenopathy, and biliary tree abnormalities.

DIAGNOSTIC PROCEDURES

- Hepatic biopsy—after evaluating coagulation (mucosal bleeding time, PIVKA, PT, APTT, platelet count) status; request hepatic staining panel (H&E, rhodanine, Prussian blue, reticulin, Mason's trichrome staining).
- Renal biopsy—differentiates amyloidosis from glomerulonephritis; submit samples for special renal panel staining and ultrastructure studies otherwise biopsy features unlikely to influence treatment.
- Intestinal biopsy—endoscopic or surgical; severe hypoalbuminemia may cause post-laparotomy delay wound healing and seroma formation.

PATHOLOGIC FINDINGS

Diverse depending on underlying causal disease.



TREATMENT

APPROPRIATE HEALTH CARE

- Diverse, depends on cause.
- Pleural effusion restricting ventilation—perform thoracentesis, may require chest tube.

NURSING CARE

Provide physical therapy and walk patient to improve mobilization of peripheral edema.

DIET

- Achieve positive energy and nitrogen balance.
- Hepatic encephalopathy—restrict protein intake (see Hepatic Encephalopathy).
- Effusions or edema due to hypoalbuminemia—restrict sodium.
- PLE associated with lymphangiectasia—feed ultra-low-fat diet.

SURGICAL CONSIDERATIONS

Severe hypoalbuminemia may complicate healing rate, anesthetic drug metabolism, body cavity effusions may complicate drug dosing and dispersal, surgical approach, patient ventilation.



MEDICATIONS

DRUG(S) OF CHOICE

- Depends on underlying disease.
- Glucocorticoids—for some types of chronic hepatitis and some PLE's; prednisolone is preferred if it is effective; dexamethasone lacks mineralocorticoid effects which lessens sodium and water retention, but has greater potential for ulceration/erosion.
- Diuretics—assist in mobilization and excretion of excess body water and sodium; furosemide (1–4 mg/kg IV, IM, or PO q4–12h) in combination with spironolactone (1–4 mg/kg

q12h) in patients with hepatic or cardiac disease, use judiciously to avoid intravascular volume contraction. For body cavity effusion mobilization, taper diuretic dose after initial positive response; individualize chronic treatment to response; diuretics may be used intermittently to mobilize recurring ascites.

- Antithrombotic treatment (low AT, PC, evidence of thrombi)—clopidogrel (0.5–1.0 mg/kg PO q24h) especially in PLN.
- Enalapril (0.5 mg/kg PO q12–24h)—for dogs with PLN; alternative is benazepril or telmisartan: angiotensin receptor blocker (ARB), is an alternative diuretic worthy of consideration.

CONTRAINdications

Synthetic colloids—avoid with anuria, renal failure, congestive heart failure, severe coagulopathy, or von Willebrand disease.

PRECAUTIONS

- Fluid therapy—large doses of synthetic colloids given to patients with severe hypoalbuminemia may cause volume overload with acute worsening of effusions and coagulopathy; avoid over-dosing crystalloid fluids when administered with synthetic colloids as these are rapidly distributed into interstitial spaces (70% volume within 1 hour) aggravating antecedent pulmonary or limb edema, and body cavity effusions; restrict maintenance fluid volume of crystalloids to one-third normal (depending on contemporary losses) when used with colloids.
- Transfusion of canine plasma or human albumin—may be complicated by transfusion or allergic reactions; plasma and albumin transfusions of dubious value if severe contemporary extra-corporeal albumin loss (e.g. PLN, PLE, vasculitis).
- Diuretic therapy—may cause serious volume contraction leading to azotemia, hypotension, and electrolyte and acid-base derangements.
- Unanticipated drug side effects—owing to reduced albumin drug binding.
- Use of DDAVP for bleeding—may aggravate fluid retention and associated complications.
- Glucocorticoids—mineralocorticoid effects of some drugs may worsen fluid accumulation, necessitating use of synthetic glucocorticoids without mineralocorticoid effects.

POSSIBLE INTERACTIONS

Inadvertent overdosing of drugs with high-protein binding



FOLLOW-UP

PATIENT MONITORING

- Body weight—especially during fluid therapy; monitors fluid retention.
- Vital signs, thoracic auscultation for crackles—monitor for pulmonary edema.
- Sequential

serum albumin concentrations.

- Blood pressure—monitors vascular expansion.

- Abdominal girth—monitors ascites.
- Central venous pressure—unreliable; monitors fluid balance; avoid central venous catheters in patients with bleeding or thrombotic tendencies.

PREVENTION/AVOIDANCE

- Limit glucocorticoid exposure.
- Use alternate-day therapy with prednisolone; titrate to lowest effective dose; use alternative medications to control primary illness.

POSSIBLE COMPLICATIONS

- PLN—may be complicated by thromboembolism; minimize IV catheterization and trauma.
- Hypovolemia—in dehydration, Addisonian crisis, blood loss, or diuretic over-dose can predispose to acute renal failure, DIC or HE.

EXPECTED COURSE AND PROGNOSIS

Depends on underlying cause.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Numerous diverse diseases or syndromes

PREGNANCY/FERTILITY/BREEDING

Condition complicates pregnancy

SEE ALSO

- Amyloidosis
- Cirrhosis and Fibrosis of the Liver
- Glomerulonephritis
- Ductal Plate Malformation (Congenital Hepatic Fibrosis)
- Lymphangiectasia
- Portosystemic Shunting, Acquired
- Portosystemic Vascular Anomaly, Congenital
- Protein-Losing Enteropathy

ABBREVIATIONS

- ADH = antidiuretic hormone
- APTT = activated partial thromboplastin time
- AT = antithrombin
- DDAVP = 1 desamino-8-d-arginine vasopressin
- H&E = hematoxylin and eosin
- HE = hepatic encephalopathy
- PC = protein C
- PIVKA = proteins invoked by vitamin K absence or antagonism
- PLE = protein-losing enteropathy
- PLN = protein-losing nephropathy
- SLE = systemic lupus erythematosus
- TEN = toxic epidermal necrolysis
- TSBA = total serum bile acids
- UP:UCr = urine protein:urine creatinine ratio

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BASICS

DEFINITION

Low total and ionized serum calcium concentration

PATHOPHYSIOLOGY

- Of the total circulating serum calcium, 40–50% is protein-bound, 40–50% is ionized, and 10% is complexed with other substances. Protein-bound and complexed calcium are unavailable for use by tissues. Only ionized calcium is available to tissues and is responsible for clinical problems (hypocalcemia and hypercalcemia). Routine measurement of ionized calcium is difficult; many biochemical profiles record only total serum calcium, but some blood analyzers can measure ionized calcium. Mechanisms of hypocalcemia include: Low concentrations of binding proteins—hypoalbuminemia • Reduced intestinal absorption—deficient vitamin D (renal disease, severe intestinal disease, rickets, chronic glucocorticoid treatment) • Reduced renal and bone resorption—hypoparathyroidism • Inadequate dietary intake • Excessive loss—lactation (eclampsia)
- Sequestration—saponification (acute pancreatitis) • Binding/complexing with administered, ingested, or endogenous chemicals—phosphate-containing enemas, citrate toxicosis (multiple citrate-containing anticoagulant transfusions), ethylene glycol toxicosis, oxalate toxicosis, low calcium/high phosphorus diet (nutritional secondary hyperparathyroidism), acute tumor lysis syndrome (hyperphosphatemia from cancer therapy-induced rapid destruction of tumor cells) • Impaired synthesis or refractoriness to PTH—hypomagnesemia • Target organ calcitriol (vitamin D) resistance (vitamin D-dependent rickets type 2) • Multifactorial—ionized hypocalcemia in the critically patient

SYSTEMS AFFECTED

- Cardiovascular—ECG changes and bradycardia • Gastrointestinal—anorexia and vomiting (especially cats) • Nervous/Neuromuscular—seizures, tetany, ataxia, and weakness • Ophthalmic—posterior lenticonal cataracts • Respiratory—panting

SIGNALMENT

Species

Dog and cat

Breed Predilections

Varies depending on the underlying cause

Mean Age and Range

Varies depending on the underlying cause

Predominant Sex

Varies depending on the underlying cause

SIGNS

General Comments

Signs of the underlying disease may be seen without clinical signs of hypocalcemia,

because the latter do not occur until total serum calcium falls below 6.7 mg/dL.

Historical Findings

- Seizures • Muscle trembling, twitching, or fasciculations • Ataxia or stiff gait • Weakness • Panting • Facial rubbing • Vomiting • Anorexia

Physical Examination Findings

- Ataxia, stiff gait, weakness, muscle fasciculation, trembling, twitching. • Fever.
- Posterior lenticonal cataracts in patients with primary hypoparathyroidism.

CAUSES

Non-pathologic Hypocalcemia

- Laboratory error—repeat serum calcium determinations to confirm true hypocalcemia, especially if significant hypocalcemia despite absence of clinical signs.
- Hypoalbuminemia—most common cause; accounts for more than 50% of patients; reduction of protein-bound calcium without affecting ionized calcium; not associated with clinical signs. • Alkalosis—causes a reduction in both ionized and total measured calcium; not associated with clinical signs unless in cases of borderline low serum ionized calcium concentrations.

Pathologic Hypocalcemia

- Primary hypoparathyroidism.
- Hypoparathyroidism secondary to bilateral thyroidectomy (or other corrective hyperthyroid therapies, such as ultrasound-guided thyroid gland ethanol injection or thyroid gland radiofrequency heat ablation) and parathyroid damage.
- Hypoparathyroidism secondary to ultrasound-guided parathyroid gland radiofrequency heat ablation (for hyperparathyroidism/parathyroid masses) and parathyroid damage. • Renal failure—acute or chronic. • Ethylene glycol toxicosis.
- Oxalate toxicosis (lily, philodendron, etc.).
- Acute pancreatitis. • Puerperal tetany—eclampsia. • Phosphate-containing enemas.
- Nutritional secondary hyperparathyroidism.
- Puerperal tetany (eclampsia).
- Hypomagnesemia. • Intestinal malabsorption. • Citrate toxicosis—multiple blood transfusions or improper citrate-blood ratio. • Post-hyperparathyroid correction due to prolonged negative feedback-induced hypofunction of normal parathyroid glands.
- Rickets – rare in dogs and cats (hypovitaminosis D, decreased plasma calcitriol) or vitamin D-dependent rickets type 2 (target organ calcitriol receptor resistance). • Acute tumor lysis syndrome.
- Ionized hypocalcemia in the critically ill patient. Multifactorial: parathyroid dysfunction; cytokine suppression of parathyroid function; vitamin D deficiency; hypomagnesemia; calcium chelation; accumulation of calcium in soft tissues, body fluids, and cells.

RISK FACTORS

- Puerperal tetany (eclampsia)—small-breed bitches during first 21 days of nursing, but can rarely affect large breeds and can rarely occur preparturient. Preparturient eclampsia has also been reported in cats. • Post-corrective procedures for hyperthyroidism and hyperparathyroidism (parathyroid damage or prolonged negative feedback-induced hypofunction of normal parathyroid glands).



DIAGNOSIS

H

DIFFERENTIAL DIAGNOSIS

- Clinical signs of hypocalcemia—rule-out primary hypoparathyroidism, hypoparathyroidism secondary to corrective hyperthyroid and hyperparathyroid therapy and parathyroid damage, puerperal tetany (eclampsia), and intoxication leading to rapid calcium binding/complexing (e.g., phosphate-containing enemas, ethylene glycol); other causes rarely lower the serum calcium enough to cause clinical signs. • Polyuria and polydipsia—rule-out renal failure.
- Neurologic signs—rule-out ethylene glycol toxicosis. • Vomiting and diarrhea—rule-out acute pancreatitis, intestinal malabsorption, renal failure, and ethylene glycol toxicosis. • Bone pain or fractures—rule-out nutritional secondary hyperparathyroidism.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

- Sodium bicarbonate may cause alkalosis and lower the serum calcium concentration.
- Samples collected in EDTA tubes may have a falsely low serum calcium concentration because of calcium chelation.

Disorders That May Alter Laboratory Results

- Lipemia can raise the serum calcium significantly. • Hypoalbuminemia can falsely lower the serum calcium (see causes of non-pathogenic hypocalcemia).

CBC/BIOCHEMISTRY/URINALYSIS

- Low calcium. • Mild-to-moderate anemia possible with chronic renal failure, nutritional secondary hyperparathyroidism, or intestinal malabsorption. • Leukocytosis possible with acute pancreatitis. • Hypoalbuminemia with hypoproteinemia-induced hypocalcemia—intestinal malabsorption, protein-losing nephropathy, other causes. • High total CO₂ with alkalosis-induced hypocalcemia. • High BUN and creatinine with acute and chronic kidney injury, ethylene glycol toxicosis, or oxalate toxicosis. • High phosphorus with acute and chronic kidney injury, ethylene glycol toxicosis, oxalate toxicosis, primary hypoparathyroidism, hypoparathyroidism secondary to hyperthyroid or hyperparathyroid corrective procedures and parathyroid

HYPOCALCEMIA

(CONTINUED)

damage, acute tumor lysis syndrome, or in patients receiving phosphate-containing enemas. • High amylase and lipase in many, but not all, patients with acute pancreatitis.

- Isosthenuria with chronic kidney injury, moderate-to-advanced acute kidney injury, ethylene glycol toxicosis, or oxalate toxicosis.
- Glucosuria in some patients with acute kidney injury, ethylene glycol toxicosis, or oxalate toxicosis.

OTHER LABORATORY TESTS

- Ionized calcium—helps determine if clinical signs are due to hypocalcemia as this is the active form of calcium.
- Ethylene glycol test—indicated in patients suspected of ingesting ethylene glycol within the previous 12–16 hours (questionable reliability).
- Pancreatic lipase immunoreactivity—indicated in patients suspected of having acute pancreatitis.
- PTH assay—indicated when primary hypoparathyroidism is suspected.
- Serum magnesium concentration—hypomagnesemia is a rare cause of hypocalcemia.
- Plasma calcitriol (vitamin D, 1,25 dihydroxycholecalciferol) concentration—indicated to screen for rickets or vitamin D—dependent rickets type 2 (rare).

IMAGING

- Radiography usually normal.
- Possibly, small kidneys with chronic renal disease and large kidneys with acute kidney injury, hyperechoic renal parenchyma on ultrasound with ethylene glycol toxicosis, or oxalate toxicosis.
- Possibly, osteopenia and pathologic fractures with nutritional secondary hyperparathyroidism.
- Possibly, mild pleural effusion and decreased anterior abdominal detail from effusion with pancreatitis.

DIAGNOSTIC PROCEDURES

ECG changes include prolongation of the ST and QT segments; sinus bradycardia and wide T waves or T wave alternans in some patients.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient treatment for clinical hypocalcemia.
- Emergency treatment is usually only needed with primary hypoparathyroidism, hypoparathyroidism secondary to hyperthyroid or hyperparathyroid corrective procedures and parathyroid damage, puerperal tetany (eclampsia), recent phosphate-containing enema administration, citrate toxicosis (rare), and ethylene glycol toxicosis.
- Long-term and short-term treatments are usually needed only to treat primary hypoparathyroidism and puerperal tetany (eclampsia), respectively.
- Puerperal tetany (eclampsia)—remove puppies from bitch and hand-nurse until weaned.

DIET

Diet change recommended for nutritional secondary hyperparathyroidism (to a balanced diet) and renal failure (see Renal Failure, Chronic).



MEDICATIONS

DRUG(S) OF CHOICE

Emergency Treatment

- Calcium gluconate 10% solution—5–15 mg/kg (0.5–1.5 mL/kg) give IV slowly to effect over a 10-minute period; monitor heart rate and stop temporarily if bradycardia occurs; if ECG monitoring is possible, QT interval shortening is an indication to temporarily stop administration.
- Calcium chloride 10% solution—also effective; extremely caustic if administered extravascularly, and three times more potent than calcium gluconate; the mg/kg dosage is the same as for calcium gluconate (5–15 mg/kg), but only one-third the volume is needed (0.15–0.5 mL/kg).

Short-Term Treatment Immediately After Correction of Tetany for Hypoparathyroidism

- With calcium gluconate 10% solution, relapse of clinical signs after emergency treatment can be prevented by use of constant-rate IV infusion of 60–90 mg/kg/day (6.5–9.75 mL/kg/day) added to fluids that do not contain bicarbonate. This follow-up treatment is rarely necessary for postparturient eclampsia.
- Subcutaneous calcium gluconate 10% diluted 2–4 times with saline can be administered 3 or 4 times daily for initial control of tetany (reported to be safe in most patients but there have been reports of marked inflammatory calcinosis cutis associated with the subcutaneous treatment option).

Long-Term Treatment

See Hypoparathyroidism.

CONTRAINDICATIONS

Avoid bicarbonate as alkalinization may further decrease serum calcium levels.

POSSIBLE INTERACTIONS

- Calcium salts may precipitate if added to solutions containing bicarbonate, lactate, acetate, or phosphates. • See Hypoparathyroidism.



FOLLOW-UP

PATIENT MONITORING

- For patients requiring long-term hypocalcemia therapy, serum calcium should be assessed 4–7 days following initial treatment, then (if normocalcemic) monthly

for the first 6 months, then every 2–4 months.

- Goal is to maintain serum calcium concentration between 8 and 10 mg/dL.

EXPECTED COURSE AND PROGNOSIS

- Varies depending on the underlying cause.
- Recurrence of hypocalcemia following calcium administration is common; monitoring is advised.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

- Hypocalcemia can lead to weakness and dystocia.
- Puerperal tetany (eclampsia) usually is seen in small-breed bitches during the first 21 days of nursing a litter.

SEE ALSO

- Eclampsia • Ethylene Glycol Toxicosis
- Hypoalbuminemia • Hypomagnesemia
- Hypoparathyroidism • Lily Toxicosis
- Pancreatitis • Renal Failure, Acute • Renal Failure, Chronic

ABBREVIATIONS

- Ca = calcium • ECG = electrocardiogram
- EDTA = ethylene diamine tetraacetic acid
- PTH = parathyroid hormone

INTERNET RESOURCES

<http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/endocrinology/hypocalcemia/>

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Client Education Handout
available online

HYPOTHOLOREMIA



BASICS

DEFINITION

Serum chloride concentration below the lower limit of normal—dogs, < 105 mEq/L; cats, < 117 mEq/L (values may vary from laboratory to laboratory).

PATHOPHYSIOLOGY

- Chloride is the most abundant anion in the extracellular fluid.
- Chloride concentration is controlled by electrochemical gradients resulting from the active transport of sodium.
- In general, chloride concentration varies directly with sodium concentration and inversely with bicarbonate concentration.

SYSTEMS AFFECTED

Depends on underlying disorder

GENETICS

N/A

INCIDENCE/PREVALENCE

N/A

SIGNALMENT

Species

Dog and cat

Breed Predilections

N/A

Predominant Sex

N/A

SIGNS

Depends on underlying disorder

CAUSES

- Gastric vomiting
- Hypoadrenocorticism
- Metabolic alkalosis
- Chronic respiratory acidosis
- Salt-losing nephropathy
- Diuretic therapy

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

If the degree of hypochloremia exceeds that of hyponatremia, it suggests selective chloride loss as seen in patients with gastric vomiting.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

Furosemide, thiazides, bicarbonate, and laxatives lower the serum concentration.

Disorders That May Alter Laboratory Results

Lipemia and hyperproteinemia can falsely lower chloride concentration if ion-specific electrodes are not used.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Low chloride.
- Other abnormalities depend on underlying disorder, possibly hyponatremia, hyperkalemia, and high bicarbonate concentration

OTHER LABORATORY TESTS

- Measurement of urine fractional excretion of chloride may demonstrate high excretion.
- Blood gas measurement may reveal metabolic alkalosis.

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

N/A



TREATMENT

APPROPRIATE HEALTH CARE

- Depends on underlying disorder
- Use 0.9% NaCl if fluid administration is indicated

NURSING CARE

N/A

DIET

No need to alter

CLIENT EDUCATION

Depends on underlying disorder

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

Other fluid therapy and medication as dictated by underlying cause

PRECAUTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

Serum electrolyte concentrations as needed to ensure appropriate response.

POSSIBLE COMPLICATIONS

Depends on underlying disorder

PREVENTION/AVOIDANCE

Depends on underlying disorder

EXPECTED COURSE AND PROGNOSIS

Depends on underlying cause

H



MISCELLANEOUS

ASSOCIATED CONDITIONS

Often accompanied by hyponatremia

AGE-RELATED FACTORS

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

Hyponatremia

Suggested Reading

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Author Melinda Fleming

Consulting Editor Deborah S. Greco

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HYPOGLYCEMIA



BASICS

DEFINITION

Abnormally low blood glucose concentration

PATHOPHYSIOLOGY

- Mechanisms responsible for hypoglycemia:
- Excess insulin or insulin-like factors (e.g., insulinoma, extrapancreatic paraneoplasia (IGF2), xylitol toxicosis, and iatrogenic insulin overdose)
- Reduced hepatic gluconeogenesis and glycogenolysis (e.g., hepatic disease, glycogen storage diseases, hypoadrenocorticism, and sepsis)
- Excessive metabolic use of glucose (e.g., in hunting dogs, pregnancy, neoplasia, polycythemia, and sepsis)
- Reduced intake or underproduction of glucose (e.g., in puppies and kittens, toy breeds, glycogen storage disease, and severe malnutrition or starvation).

SYSTEMS AFFECTED

- Musculoskeletal
- Nervous

SIGNALMENT

- Dog and cat
- Variable, depending on the underlying cause

SIGNS

- Seizures
- Posterior paresis
- Weakness
- Collapse
- Muscle fasciculations
- Abnormal behavior
- Lethargy and depression
- Ataxia
- Polyphagia
- Weight gain
- PU/PD
- Exercise intolerance
- Some animals appear normal aside from findings associated with underlying disease
- Many animals have episodic signs
- Polyneuropathy

CAUSES

Endocrine

- Insulinoma
- Extrapancreatic paraneoplasia associated with insulin-like growth factor overproduction (e.g., hepatocellular carcinoma, hepatocellular adenoma, intestinal leiomyoma, intestinal leiomyosarcoma)
- Iatrogenic insulin overdose
- Hypoadrenocorticism

Hepatic Disease

- Portosystemic shunt
- Cirrhosis
- Severe hepatitis (e.g., toxic and inflammatory)
- Glycogen storage diseases

Overuse

- Hunting dog hypoglycemia
- Pregnancy
- Polycythemia
- Neoplasia
- Sepsis—increased glucose utilization induced by increased cytokine production in macrophage-rich tissues

Reduced Intake/Underproduction

- Young puppies and kittens
- Toy-breed dogs
- Severe malnutrition or starvation
- In sepsis there is also cytokine-induced inhibition of gluconeogenesis in the setting of nutritional glycogen depletion

Toxicosis

- Iatrogenic insulin overdose
- Xylitol toxicosis
- Antihyperglycemic agent toxicosis (e.g., sulfonylureas)

RISK FACTORS

- Low energy intake predisposes to hypoglycemia in patients with conditions causing overuse and underproduction.
- Fasting, excitement, exercise, and eating may or may not increase the risk of hypoglycemic episodes in patients with insulinoma.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Patients with hyperinsulinism—signs of hypoglycemia or a normal physical examination
- Patients with hypoadrenocorticism—waxing, waning, nonspecific signs (e.g., vomiting, diarrhea, melena, and weakness); Addisonian patients that present in a crisis usually display hypovolemia and hyperkalemia rather than hypoglycemia (e.g., shock, bradycardia, and dehydration)
- Patients with portosystemic shunts—usually young to middle-aged; often thin or appear to have stunted growth; rarely, they have ascites or edema
- Patients with cirrhosis and severe hepatitis usually have other signs of their disease (e.g., gastrointestinal signs, icterus, and ascites or edema)
- Patients with sepsis—critical; usually in shock; pyrexia or hypothermia revealed by examination; may have gastrointestinal signs
- Glycogen storage diseases—rare; usually seen in animals < 1 year old
- Extrapancreatic paraneoplasia and large neoplastic processes that cause hypoglycemia can often be detected by physical examination

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

None

Disorders That May Alter Laboratory Results

Delayed separation of serum causes falsely low serum glucose values; if blood cannot be centrifuged and the serum separated within 30 minutes of collection, it should be collected in a sodium fluoride tube

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Patients with hyperinsulinism may have normal results
- Patients with hypoadrenocorticism may have hypocholesterolemia, hypoalbuminemia, lymphocytosis, eosinophilia, hyperkalemia, hyponatremia, azotemia, or hypercalcemia
- Patients with congenital portosystemic shunts may have microcytosis

hypoalbuminemia, low BUN, mildly high liver enzyme activities, ammonium biurate crystals, and low urinary specific gravity. Serum bilirubin concentration sometimes increased. • Patients with cirrhosis, severe hepatitis, and hepatic neoplasia may have anemia associated with chronic disease, high liver enzyme activities, hyperbilirubinemia, hypoalbuminemia, bilirubinuria, and low urinary specific gravity. • Patients with polycythemia have a PCV > 65. • Patients with xylitol toxicosis may have hypokalemia, high liver enzyme activities, and hyperbilirubinemia.

OTHER LABORATORY TESTS

- Simultaneous fasting glucose/insulin determination—indicated when insulinoma is suspected; high plasma insulin in the face of hypoglycemia suggests insulinoma
- AIGR—indicated when insulinoma is suspected:

$$\text{AIGR} = \frac{\text{plasma insulin } [\mu\text{U/mL}] \times 100}{\text{plasma glucose } [\text{mg/dL}] - 30}$$

- Use 1 as denominator if glucose is < 30; AIGR > 30 suggests an insulinoma; AIGR = 19–30 is a gray zone—repeat test; AIGR < 19 indicates insulinoma is unlikely. (Note: false-positive results are possible, especially when the blood glucose concentration is < 40 mg/dL.)
- ACTH stimulation test—indicated when hypoadrenocorticism is suspected
- Fasting and postprandial serum bile acids—indicated when portosystemic shunt or functional hepatic disease is suspected (results uninterpretable if serum bilirubin is elevated)
- Bacterial culture of blood—indicated when sepsis is suspected
- Fructosamine—chronic hypoglycemia will result in low fructosamine concentrations

IMAGING

- Abdominal radiography and ultrasonography—useful in patients with extrapancreatic paraneoplasia and large neoplastic processes (may see organomegaly or masses), as well as portosystemic shunt (microhepatitis), cirrhosis (microhepatitis, hyperechogenicity), and severe hepatitis (hepatomegaly). Not very sensitive nor specific for detecting insulinoma. Abdominal computed tomography (CT) more accurately detects pancreatic endocrine tumors
- Ultrasound-guided, laparoscopic, or surgical hepatic biopsy—useful to evaluate for cirrhosis, hepatitis, and glycogen storage diseases
- Technetium-99m per rectal quantitative hepatic scintigraphy—useful to detect portosystemic shunt
- Mesenteric portography—useful to detect portosystemic shunt (requires surgery)

DIAGNOSTIC PROCEDURES

- ECG—useful to evaluate bradycardia in patients with hypoadrenocorticism

(CONTINUED)

- Ultrasound-guided or surgical tissue biopsy—useful to evaluate for cirrhosis, hepatitis, glycogen storage diseases, and extrapancreatic neoplasia.



TREATMENT

- Treat animals with clinical hypoglycemia whose underlying disease needs support as inpatients. • If able to eat (i.e., responsive, no vomiting), feeding should be part or all of initial treatment. • If unable to eat, start continuous fluid therapy with 2.5% dextrose; if clinical signs persist, use a 5% dextrose solution. • Surgery is indicated if a portosystemic shunt or insulin secreting neoplasia is the cause of hypoglycemia.



MEDICATIONS

DRUG(S) OF CHOICE

Emergency/Acute Treatment

- In hospital—administer 50% dextrose, 1 mL/kg (0.5 g/kg) IV slow bolus (1–3 minutes). Glucagon IM or IV at 0.03 mg/kg usually effective in cases of insulin-secreting tumors. • At home—do not attempt to have the client administer medication orally during a seizure; hypoglycemic seizures usually abate within 1–2 minutes; if a seizure is prolonged, recommend transportation to hospital; if a short seizure has ended or other signs of a hypoglycemic crisis exist, recommend rubbing corn syrup or 50% dextrose on the buccal mucosa, followed by 2 mL/kg of the same solution orally once the patient can swallow; then seek immediate attention.
- Owners of diabetic animals can be taught to inject prescribed glucagon IM. • Initiate frequent feeding of a diet low in simple sugars or, if patient is unable to eat, continuous fluid therapy with 2.5% dextrose.

Long-Term Treatment

- See Insulinoma for treatment of insulinoma and extrapancreatic paraneoplasia. • Hunting dog hypoglycemia—feed moderate meal of fat, protein, and complex carbohydrates a few hours before hunting; can feed snacks (e.g., dog biscuits) every 3–5 hours during the hunt. • Toy-breed hypoglycemia—increase the frequency of feeding. • Puppy and kitten hypoglycemia—increase the frequency of feeding (nursing or hand-feeding). • Other causes of hypoglycemia require treating the underlying disease and do not usually need long-term treatment.

CONTRAINDICATIONS

- Insulin. • Barbiturates and diazepam in patients with hypoglycemic seizures—they do

not treat the cause of the seizure and they may potentially worsen hepatoencephalopathy in patients with portosystemic shunt, cirrhosis, or xylitol toxicosis—induced hepatic failure.

PRECAUTIONS

- 50% dextrose causes tissue necrosis and sloughing if given extravascularly; never give dextrose in concentrations over 5% without confirmed vascular access. • Administering a dextrose bolus without following with frequent feedings or continuous IV fluids with dextrose can predispose to subsequent hypoglycemic episodes.

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- At home—for return or progression of clinical signs of hypoglycemia; assess serum glucose if signs recur. • Single, intermittent serum glucose determinations may not truly reflect the glycemic status of the patient because of normal production of counterregulatory hormones. • Other monitoring is based on the underlying disease. • If due to insulin overdose in the diabetic, reassess response to insulin with a blood glucose curve and adjust the insulin dose accordingly.

POSSIBLE COMPLICATIONS

Recurrent, progressive episodes of hypoglycemia



MISCELLANEOUS

ASSOCIATED CONDITIONS

Prolonged hypoglycemia can cause transient (hours to days) to permanent dementia and blindness from laminar and pseudolaminar necrosis involving many areas of the cerebral cortex. The cerebellum and brainstem nuclei can also be adversely affected.

AGE-RELATED FACTORS

Neonatal animals have poor glycogen storage capacity and a reduced ability to perform gluconeogenesis; thus, short periods of fasting (6–12 hours) can cause hypoglycemia.

Important to remember when fasting young patients prior to anesthesia.

PREGNANCY/FERTILITY/BREEDING

- Hypoglycemia can lead to weakness and dystocia. • Pregnancy coupled with fasting causes hypoglycemia in rare instances.

SEE ALSO

- Cirrhosis and Fibrosis of the Liver
- Glycogen Storage Disease • Hepatocellular Adenoma • Hepatocellular Carcinoma
- Hypoadrenocorticism (Addison's Disease)
- Insulinoma • Leiomyoma, Stomach, Small and Large Intestine • Leiomyosarcoma, Stomach, Small and Large Intestine
- Paraneoplastic Syndrome • Polycythemia
- Portosystemic Shunting, Acquired
- Portosystemic Vascular Anomaly, Congenital • Sepsis and Bacteremia • Xylitol Toxicosis

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone
- AIGR = amended insulin:glucose ratio
- ECG = electrocardiogram • PCV = packed cell volume • PU/PD = polyuria and polydipsia

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Client Education Handout
available online

HYPOKALEMIA



BASICS

DEFINITION

Serum potassium concentration < 3.5 mEq/L (normal range: 3.5–5.5 mEq/L).

PATHOPHYSIOLOGY

- Potassium is primarily an intracellular electrolyte (98% of total body potassium is intracellular); serum levels, however, may not accurately reflect total body concentrations.
- It is predominantly responsible for the maintenance of intracellular fluid volume and required for normal function of many enzymes.
- The resting cellular membrane potential is determined by the ratio of intracellular to extracellular potassium concentration and maintained by the Na^+ , K^+ -ATPase pump. Conduction disturbances in susceptible tissues (cardiac, nerve, and muscle) are caused by rapid shifts in this ratio causing myoneural membrane hyperpolarization.
- Hypokalemia can be caused by decreased intake, loss (via the gastrointestinal tract or kidneys), or translocation of potassium from the extracellular to the intracellular fluid space.

SYSTEMS AFFECTED

- Neuromuscular—muscle weakness, including skeletal and muscles of respiration.
- Cardiac—electrocardiac changes and arrhythmias.
- Renal—hyposthenuria, nephropathy, and renal failure.
- Metabolic—acid-base balance (metabolic alkalosis); glucose homeostasis.

SIGNALMENT

- Dogs and cats with predispositions to increased potassium loss, translocation of potassium, or decreased intake of potassium.
- Young Burmese cats with recurrent hypokalemic periodic paralysis episodes.

SIGNS

- Generalized muscle weakness or paralysis
- Muscle cramps
- Lethargy and confusion
- Vomiting
- Anorexia
- Carbohydrate intolerance and weight loss
- Polyuria
- Polydipsia
- Decreased bowel motility (humans; maybe dogs and cats)
- Hyposthenuria
- Ventroflexion of the neck (cats and dogs)
- Respiratory muscle failure

CAUSES

Decreased Intake

- Anorexia or starvation
- Administration of potassium-deficient or potassium-free intravenous fluids

- Bentonite clay ingestion (e.g., clumping cat litter)

Gastrointestinal Loss

- Vomiting
- Diarrhea
- Both upper and lower gastrointestinal obstruction; especially pyloric outflow obstruction

Urinary Loss

- Chronic renal disease
- Renal tubular acidosis
- Hypokalemic nephropathy
- Post-obstructive diuresis
- Dialysis (hemodialysis or peritoneal)
- Intravenous fluid diuresis
- Hyperaldosteronism
- Hypocholeremia
- Drugs (loop diuretics, amphotericin B, penicillins, rattlesnake envenomation)

Translocation (Extracellular to Intracellular Fluid)

- Glucose administration
- Insulin administration
- Sodium bicarbonate administration
- Catecholamines
- Alkalemia
- β_2 -adrenergic agonist overdose (e.g., albuterol)
- Hypokalemic periodic paralysis (Burmese cats)
- Rattlesnake envenomation (mechanism unknown)

RISK FACTORS

- Acidifying diets with negligible potassium
- Diuresis or dialysis with potassium-deficient fluids
- Chronic illness (sustained anorexia and muscle wasting)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- PU/PD, hyperglycemia, and glucosuria—rule out diabetes mellitus.
- PU/PD, azotemia, and isosthenuria—rule out chronic renal failure and nephropathy.
- Vomiting, metabolic alkalosis, and hypocholeremia—rule out upper gastrointestinal obstruction.
- Metabolic acidosis with urine pH > 6.5—rule out renal tubular acidosis.
- Urethral obstruction—rule out post-obstructive diuresis.
- Young Burmese cat with episodic muscle weakness—rule out hypokalemic periodic paralysis.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

Falsely elevated potassium measurement can be caused by excessive K_3EDTA relative to the blood sample, as found in “purple-stoppered”

blood tube for hematology; not a problem with “red-stoppered” tubes for serum).

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Hyperglycemia, glucosuria, \pm ketonuria, \pm ketoacidosis in patients with diabetes mellitus.
- Normocytic, normochromic, nonregenerative anemia in patients with chronic renal failure.
- Elevated BUN and creatinine, with isosthenuria in patients with chronic renal failure or hypokalemic nephropathy.
- Low total CO_2 or HCO_3^- in patients with renal tubular acidosis (RTA) or renal failure.
- Normal anion gap metabolic acidosis in RTA.
- Urine pH > 6.5 in patients with distal tubular acidosis.
- High total CO_2 or HCO_3^- in patients with metabolic alkalosis.

OTHER LABORATORY TESTS

- Increased aldosterone and decreased renin in patients with primary hyperaldosteronism.
- Elevated urinary fractional excretion of potassium in patients with chronic renal failure or hypokalemic nephropathy.
- ACTH stimulation tests are used to diagnose adrenal gland disorders.

IMAGING

- Radiography, ultrasonography are helpful to diagnose gastrointestinal tract obstructions (mass or foreign bodies), pancreatitis, chronic renal failure workup, adrenal gland diseases (hyperadrenocorticism, hyperaldosteronism, and adrenal tumors).
- Upper gastrointestinal barium study to additionally diagnose gastrointestinal obstructions (anatomic or functional).
- Computed tomography or magnetic resonance imaging to further diagnose adrenal gland diseases.

OTHER DIAGNOSTIC PROCEDURES

Upper gastrointestinal endoscopy to diagnose upper gastrointestinal disorders.



TREATMENT

- Mild hypokalemia (3.0–3.5 mEq/L) can be treated by oral supplementation.
- Moderate hypokalemia (2.5–3.0 mEq/L) is best treated by inpatient administration of oral \pm intravenous supplementation and carefully monitored.
- Severe hypokalemia (< 2.5 mEq/L) should be hospitalized for intensive intravenous potassium supplementation. Patients, especially cats, should be carefully monitored for cardiac arrhythmias and impaired ventilation.

(CONTINUED)

HYPOKALEMIA**Table 1**

Patient's K ⁺ Concentration	KCl/L (mEq)
3.5–4.5	20
3.0–3.5	30
2.5–3.0	40
2.0–2.5	60
<2.0	80

Note: do not exceed an intravenous supplementation rate or 0.5 mEq/kg/h unless continually monitoring and on the verge of ventilator muscle failure. With severe life threatening hypokalemia (serum potassium < 2.0), potassium chloride can be administered at a rate of 1.0–1.5 mEq/kg/h with ECG monitoring.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Oral supplementation with potassium gluconate (e.g., Tumil-K) is effective in mildly affected patients. The initial dosage is 1/4 teaspoon (2 mEq) per 4.5 kg body weight in food twice daily.
- Parenteral supplementation is required in anorectic or vomiting patients or in patients with moderate-to-severe hypokalemia (<3.0). Potassium chloride is added to intravenous fluids according to Table 1, best delivered via infusion pump or with a pediatric fluid administration set (60 drops/mL/minute). Monitor and taper accordingly.

CONTRAINDICATIONS

- Glucose supplementation
- Insulin administration
- Sodium bicarbonate administration
- Untreated hypoadrenocorticism

- Hyperkalemia
- Renal failure or severe renal impairment
- Acute dehydration
- Severe hemolytic reactions
- Impaired gastrointestinal motility

PRECAUTIONS

Administer with caution, avoid oversupplementation, monitor frequently.

POSSIBLE INTERACTIONS

Concurrent potassium supplementation with ACE inhibitors (e.g., enalapril), potassium-sparing diuretics (e.g., spironolactone), prostaglandin inhibitors (e.g., nonsteroidal anti-inflammatory drugs), beta-blockers (e.g., atenolol), or cardiac glycosides (e.g., digoxin) can cause adverse effects.

ALTERNATIVE DRUG(S)

Potassium phosphate can be used in patients with concurrent hypophosphatemia where one-half of the potassium dose is administered in the form of potassium phosphate solution.

**FOLLOW-UP****PATIENT MONITORING**

Check serum potassium every 6–24 hours based on severity of hypokalemia.

POSSIBLE COMPLICATIONS

Electrolyte disturbances and arrhythmias. It is essential to close the IV fluid outflow valve and thoroughly mix the fluid contents while adding potassium chloride solution to the parenteral fluid bag.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Hypokalemic nephropathy
- Hypophosphatemia
- Hypomagnesemia
- Metabolic alkalosis

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Alkalosis, Metabolic
- Diarrhea chapters
- Hypochloremia
- Renal Failure, Chronic
- Renal Tubular Acidosis
- Vomiting, Chronic

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- ACTH = adrenocorticotropic hormone
- ATPase = adenosine triphosphate
- CO₂ = carbon dioxide
- HCO₃⁻ = bicarbonate
- K⁺ = potassium
- Na⁺ = sodium
- PU/PD = polyuria/polydipsia

H**Suggested Reading**

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HYPOMAGNESEMIA



BASICS

DEFINITION

- Dogs—serum magnesium < 1.89 mg/dL
- Cats—serum magnesium < 1.8 mg/dL

PATHOPHYSIOLOGY

• Magnesium is second only to potassium as the most abundant intracellular cation; is found primarily in bone (60%) and soft tissue (38%), with most soft tissue magnesium residing in skeletal muscle and liver; is required for many metabolic functions; is an activator or catalyst for more than 300 enzyme systems including phosphatases and enzymes that involve ATP. • Serum magnesium is present in three forms: protein-bound form (approximately 25–30%) and chelated and ionized forms (together account for 70–75%). • Because only 1–2% of total magnesium resides in the extracellular compartment, serum magnesium concentration does not always reflect the whole-body magnesium status. • Magnesium absorption occurs primarily in the ileum. Absorption also occurs in the jejunum and colon. • The kidneys maintain magnesium balance with 10–15% reabsorbed in the proximal tubule, 60–70% in the thick ascending limb of the loop of Henle, and 10–15% reabsorbed in the distal convoluted tubule. Reabsorption within the distal convoluted tubule is under hormonal and neurohormonal control and determines the final urine concentration of magnesium. • Hypomagnesemia has many causes; incidence rates > 50% have been reported in critically ill humans. • Magnesium is an important cofactor in the sodium-potassium ATPase pump that maintains an electrical gradient across membranes. Magnesium is also important in the production and elimination of acetylcholine; a low concentration of magnesium in the extracellular fluid can increase concentrations of acetylcholine at motor endplates and cause tetany. • Interference with the electrical gradient can change resting membrane potentials and repolarization disturbances, resulting in neuromuscular and cardiac abnormalities. • Magnesium regulates calcium movement into smooth muscle cells and is important to contractile strength and peripheral vascular tone. • Hypomagnesemia can alter the functions of the skeletal muscles, resulting in tetany and a variety of myopathies observed in patients receiving cisplatin and other nephrotoxic drugs. • Magnesium regulates calcium movement into cardiac muscle cells and is important in cardiac conduction, excitability, and contraction. • Magnesium depletion can affect the membrane pump on cardiac cell membranes, resulting in the depolarization of cardiac cells and tachyarrhythmias; cardiac arrhythmias

associated with hypomagnesemia include ventricular arrhythmias, torsades de pointes, QT prolongation, ST segment shortening, and widening of T waves; hypomagnesemia increases the risk of digoxin toxicity because both inhibit the membrane pump.

- Hypomagnesemia causes resistance to the effects of PTH and can increase the uptake of calcium into bone.

SYSTEMS AFFECTED

- Multiple organ systems
- Cardiovascular
- Endocrine
- Gastrointestinal
- Neuromuscular
- Renal

SIGNALMENT

Dog and cat

INCIDENCE/PREVALENCE

Hypomagnesemia has been reported in 28–54% of critically ill dogs and cats.

SIGNS

- Hypomagnesemia occurs with a variety of diseases with diverse signs:
 - Weakness
 - Muscle fibrillation
 - Ataxia and depression
 - Hyperreflexia
 - Tetany
 - Behavior changes
 - Arrhythmias

CAUSES

- There are four general causes—gastrointestinal, renal, endocrine, and miscellaneous. • Severe malnutrition or significant malabsorptive intestinal diseases can lead to hypomagnesemia; hypomagnesemia can occur after excessive loss of body fluids (e.g., severe, prolonged diarrhea); magnesium is found in high concentrations in the lower gastrointestinal tract, so secretory diarrhea in humans has been associated with profound hypomagnesemia; this has been reported in a dog with protein-losing enteropathy.
- Magnesium homeostasis is regulated by the kidney; renal control of tubular reabsorption takes place primarily in the ascending limb of the loop of Henle; renal magnesium loss can be due to nephrotoxic drugs, including cisplatin, aminoglycosides, and amphotericin B; magnesium reabsorption can also be impaired with osmotic diuresis (diabetes mellitus), loop diuretics, hypercalcuria, and tubular acidosis. Hypomagnesemia associated with diuretic administration is a significant problem in human heart failure patients and has been noted experimentally in mice.
- Hypomagnesemia develops during chronic thiazide diuretic therapy by downregulation of the epithelial Mg²⁺ channel transient receptor and accompanying Na⁺-Cl⁻ cotransporter inhibition or inactivation. Endocrine problems associated with hypomagnesemia include hypercalcemia, hyperthyroidism, and hyperparathyroidism.
- Lactation can cause excessive magnesium loss. • Magnesium can be redistributed by refeeding after starvation, insulin therapy in diabetic patients, following parathyroidectomy, with the use of a total parenteral nutrition formulation with inadequate magnesium

content, and in patients with acute pancreatitis or conditions of catecholamine excess.

- Causes of hypomagnesemia in the critically ill include decreased intake, lack of magnesium in parenteral fluids in patients receiving long-term fluid therapy or dialysis, excessive gastrointestinal loss, redistribution, and sequestration. • Hypomagnesemia is associated with diabetes mellitus in humans, with nearly 25% of human diabetic outpatients having low serum magnesium.
- While one study showed no difference in presentation of ionized magnesium levels in dogs with diabetes when compared to controls, hypomagnesemia should still be considered in diabetic patients following aggressive insulin therapy for diabetic ketoacidosis.

RISK FACTORS

- Total parenteral nutrition
- Polyuric renal disease
- Diuretic administration
- Peritoneal dialysis
- Diabetes mellitus and diabetic ketoacidosis
- Lactation
- Gastrointestinal malabsorption syndromes



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Signs of hypomagnesemia are vague and multisystemic; therefore, other causes of neuromuscular abnormalities, especially other electrolyte abnormalities, must be investigated. • Consider cardiac abnormalities, intoxications, and renal diseases.

LABORATORY FINDINGS

Note: 12 mg of magnesium = 1 mEq of magnesium; to convert from mg/dL to mEq/L, divide by 1.2.

Drugs That May Alter Laboratory Results

- Serum is favored over plasma because the anticoagulant used for plasma samples can contain citrate or other ions that bind magnesium. • EDTA, sodium fluoride-oxalate, sodium citrate, and intravenous calcium gluconate can falsely decrease serum magnesium values.

Disorders That May Alter Laboratory Results

- Hemolysis can falsely elevate serum magnesium. • Hypercalcemia (> 16 mg/dL) and hyperproteinemia (> 10 g/dL) can also falsely elevate serum magnesium.
- Hyperbilirubinemia and lipemia can cause falsely decreased serum magnesium.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Low serum magnesium. • If patient is azotemic, consider renal causes. • Tubular casts in urinary sediment might indicate nephrotoxicity. • Hypokalemia,

(CONTINUED)

hyponatremia, and hypocalcemia are common findings with hypomagnesemia and should alert the clinician to the possibility of hypomagnesemia.

OTHER LABORATORY TESTS

- Diagnosis of magnesium depletion can be difficult since <1% of total body magnesium is located in serum; only 55% of the magnesium in plasma is in the active (ionized) form; 33% is bound to plasma proteins and 12% is chelated with divalent anions such as phosphate and sulfate; magnesium assays (spectrophotometry) measure all three fractions.
- Ionized magnesium can be measured with an ion-selective electrode or by ultrafiltration of plasma; alternative methods of evaluating magnesium status include measurement of mononuclear blood cell magnesium levels or quantifying retention from a loading dose.
- Urinary magnesium determination might help differentiate conditions associated with high urinary magnesium loss from conditions of low intake or absorption.
- Human studies suggest that retention of >40–50% of an administered magnesium load indicates magnesium depletion, while retention of <20% indicates adequate magnesium stores.

DIAGNOSTIC PROCEDURES

Electrodiagnostics (e.g., electromyography and electrocardiography) might reveal effects of hypomagnesemia but will not differentiate the cause.



TREATMENT

APPROPRIATE HEALTH CARE

- Treatment depends on the underlying cause and severity of hypomagnesemia.
- Management includes treatment of the underlying condition(s) and magnesium replacement.
- Mild hypomagnesemia might resolve with treatment of the underlying disorder; however, if hypomagnesemia is severe, intensive care and magnesium replacement are needed.

NURSING CARE

Hypomagnesemia is a common finding in critically ill, hospitalized veterinary patients. Nursing should focus on the underlying disorder(s).

ACTIVITY

Activity restrictions should be based on concurrent conditions.

DIET

There are no dietary recommendations for hypomagnesemia other than meeting the patient's caloric requirements with a balanced, appropriate diet that takes into account all concurrent problems.



MEDICATIONS

DRUG(S) OF CHOICE

- Magnesium sulfate can be diluted in 5% dextrose in water.
- Emergency loading is accomplished with 0.15–0.3 mEq/kg of magnesium sulfate or magnesium chloride over 5–60 minutes.
- Rapid replacement can be accomplished by administering 0.75–1 mEq/kg/day (0.03 mEq/kg/h) of magnesium sulfate or magnesium chloride as a constant-rate intravenous infusion; the solution of magnesium salts should be <20%; the magnesium infusion should use a separate intravenous line to minimize interactions with other minerals.
- Administer 0.3–0.5 mEq/kg/day (0.013–0.02 mEq/kg/h) of magnesium sulfate or magnesium chloride for slow replacement.

CONTRAINdications

- Do not use aminoglycosides; hypomagnesemia potentiates their nephrotoxicity.
- Do not use cisplatin chemotherapy.

PRECAUTIONS

- Discontinue digoxin if possible.
- Use diuretics with caution.
- Hypermagnesemia is possible with overzealous treatment of hypomagnesemia.
- Azotemic patients requiring magnesium therapy should receive a lower dose and more frequent monitoring than patients with normal kidney function to prevent iatrogenic hypermagnesemia.

POSSIBLE INTERACTIONS

- Magnesium sulfate is incompatible with sodium bicarbonate, hydrocortisone, and dobutamine HCl; avoid mixing other drugs with magnesium sulfate solution.
- Avoid calcium-containing compounds; they lower the serum magnesium concentration.
- Additive CNS depression can occur when parenteral magnesium sulfate is used with CNS depressant sedatives, neuromuscular blocking agents, and anesthetics.
- Combined use of parenteral magnesium sulfate and non-depolarizing neuromuscular blocking agents has resulted in excessive neuromuscular blockade.
- Use magnesium supplementation cautiously with digitalis compounds to avoid serious conduction disturbances.
- Calcium supplements might negate the effects of parenteral magnesium.



FOLLOW-UP

PATIENT MONITORING

- Measurement of serum magnesium and calcium concentrations daily
- Continuous

HYPOMAGNESEMIA

ECG monitoring, especially during magnesium infusion

POSSIBLE COMPLICATIONS

Severe hypomagnesemia can be fatal.

EXPECTED COURSE AND PROGNOSIS

Outcome is dependent on resolution of the underlying disease(s).



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Hyperthyroidism • Hypocalcemia
- Hypokalemia • Hyponatremia
- Hypoparathyroidism • Hypophosphatemia

PREGNANCY/FERTILITY/BREEDING

Effects on the fetus are identical to effects on the dam.

SEE ALSO

Hypocalcemia

ABBREVIATIONS

- ATP = adenosine triphosphate
- CNS = central nervous system
- Cl = chloride
- EDTA = ethylene diamine tetraacetic acid
- Mg = magnesium
- Na = sodium
- PTH = parathyroid hormone

INTERNET RESOURCES

<http://www.merck.com/mmpe/sec12/ch156/ch156i.html>

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H

HYPOMYELINATION



BASICS

OVERVIEW

- Also known as “shaking puppies.”
- Congenital deficit in myelin deposition caused by either delayed myelination or a permanent lack of myelin at birth.
- Axons > 1–2 mm in diameter have a myelin cover produced by oligodendrocytes in the central nervous system (CNS), and Schwann cells in the peripheral nervous system (PNS). Myelin insulates axons and facilitates propagation of action potentials.
- Affected axons with deficit in myelin deposition can alter impulse conduction or trigger spontaneous discharges and then generate tremors. The degree of tremor is usually correlated with the severity of the abnormal myelin deposition.

H

SIGNALMENT

CNS

- Clinical signs appear at birth or when the puppy starts to ambulate.
- Dog—Springer spaniel, Samoyed, Chow Chow, Weimaraner, Bernese mountain dog, Dalmatian, Catahoula, rat terrier, border terriers, and Lurchers.
- Cat—Siamese and presumed in domestic shorthair and Birman cats.
- Predominant sex (X-linked)—Springer spaniel and Samoyed male puppies clinically affected, whereas females remain largely asymptomatic carriers; no sex differences reported in other breeds.

PNS

- Dog • Golden retriever—reported in both sexes

SIGNS

CNS

- Action-related repetitive myoclonus—rapid contractions and relaxation of diffuse skeletal muscles manifested as generalized body tremors that worsen with exercise and subside during rest or sleep. Some affected dogs and cats appear “bouncing.”
- The tremors diminish with time in the majority of affected dogs and usually resolved by 12 months of age or earlier; however, some dogs can retain a persistent fine tremor of the pelvic limbs.
- Some dogs also present with head bobbing and nystagmus.
- In Rat terriers, associated with goiter and clinical signs of congenital hypothyroidism.
- Springer spaniels and Samoyeds are usually affected for life.

PNS

- Clinical signs appear at 5–7 weeks of age.
- Generalized weakness, pelvic limb ataxia and paresis, muscle wasting and hyporeflexia that improve with age.
- Tremors are not present.

CAUSES & RISK FACTORS

- Genetic—X-linked recessive condition for CNS disease in Springer spaniels and autosomal recessive gene in Rat terriers,

Weimaraners, and border terriers.

- Genetic basis speculative for other breeds.
- Mutation identified in Weimaraners and Rat terriers.
- The carrier frequency in Weimaraners has been estimated to be 4.3%.
- Viral or toxic—possible in some breeds.
- PNS—undetermined; possibly genetic.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

CNS

- Cerebellar hypoplasia or abiotrophy—tremors in neonates; but cerebellar ataxia (hypermetric gait) and intention tremors more prominent.
- Storage diseases—associated with tremors; neonates are normal.
- Generalized tremor syndrome in dogs (historically identified as “white shakers” but other hair coat colors can be affected)—affected dogs are usually > 8 months old.
- Metabolic diseases (hypocalcemia, hypernatremia, hyponatremia, hypoglycemia).
- Feline polioencephalomyelitis—young to middle-aged cats and other neurologic signs are present (pareisis, seizures, hyperesthesia).
- Toxic—organophosphates, permethrins, mycotoxins: history of exposure to a toxic product.

PNS

- Muscular dystrophy—serum creatine kinase highly elevated.
- Congenital myasthenia gravis.
- Other polyneuropathies or myopathies.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

N/A

IMAGING

MRI—may detect white matter changes on CNS form.

DIAGNOSTIC PROCEDURES

CNS

- Presumed diagnosis based on signalment, clinical signs, and evolution.
- Histopathology (necropsy).
- DNA test for causative genetic mutation (currently available for Weimaraners and Rat terriers).

PNS

- Electromyography—usually normal to mild diffuse spontaneous activity.
- Motor nerve conduction velocity—small or no evoked potentials and slowed conduction.
- Nerve biopsy—insufficient myelin surrounding peripheral axons.



TREATMENT

None effective for either form.



MEDICATIONS

DRUG(S)

N/A



FOLLOW-UP

PREVENTION/AVOIDANCE

Avoid breeding from affected animals in which a genetic cause is suspected.

EXPECTED COURSE AND PROGNOSIS

- CNS—Springer spaniels and Samoyeds affected for life; other breeds usually improve by 1 year of age.
- PNS—dogs have normal lifespan.



MISCELLANEOUS

ABBREVIATIONS

- CNS = central nervous system
- MRI = magnetic resonance imaging
- PNS = peripheral nervous system

INTERNET RESOURCES

Genetic tests available at

- <https://www.vgl.ucdavis.edu/services/Weimaraner.php>
- <http://www.centerforanimalgenetics.com/congenital-hypothyroidism.html>
- <http://www.laboklin.co.uk/laboklin/showGeneticTest.jsp?testID=8443>

Video online

- <http://www.neurovideos.vet.cornell.edu/Video.aspx?vid=20-39>

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BASICS

DEFINITION

Serum sodium concentration below the lower limit of the reference range.

PATHOPHYSIOLOGY

Sodium is the most abundant cation in the extracellular fluid. Hyponatremia usually, but not always, reflects hypo-osmolality and is typically associated with a decreased total body sodium content. Either solute loss or water retention can theoretically cause hyponatremia. Most solute loss occurs in iso-osmotic solutions (e.g., vomit and diarrhea) and, as a result, water retention in relation to solute is the underlying cause in almost all patients with hyponatremia. In general, hyponatremia occurs only when a defect in renal water excretion is present.

SYSTEMS AFFECTED

- Nervous—severe neurologic dysfunction is not usually seen until serum sodium concentration falls below 110–115 mEq/L. Clinical signs may be more related to the rate of decline in serum sodium concentration than the actual nadir. Dogs with chronic hyponatremia often have mild, if any, clinical signs.
- Overly rapid correction of hyponatremia can also cause neurologic damage.

SIGNALMENT

Species

Dog and cat

SIGNS

- Lethargy
- Weakness
- Confusion
- Nausea/vomiting
- Seizures
- Obtundation
- Coma
- Other findings depend on the underlying cause.

CAUSES

Normal Osmolar Hyponatremia

- Hyperlipidemia
- Hyperproteinemia

Hyperosmolar Hyponatremia

- Hyperglycemia
- Mannitol infusion

Hypoosmolar Hyponatremia

Normovolemic

- Primary polydipsia
- Hypothyroid myxedema coma
- Hypotonic fluid infusion
- SIADH

Hypervolemic

- Congestive heart failure
- Hepatic cirrhosis

- Nephrotic syndrome
- Severe renal failure

Hypovolemic

- Gastrointestinal losses
- Renal failure
- Third space losses
- Cutaneous losses
- Diuresis
- Hypoadrenocorticism



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hypoadrenocorticism
- Severe GI disease
- Metabolic or respiratory acidosis (DKA)
- Congestive heart failure
- Primary polydipsia

LABORATORY FINDINGS

Drugs That May Alter Lab Results

- Mannitol can cause pseudohyponatremia.
- Diuretic administration can cause hyponatremia.

Disorders That May Alter Lab Results

Hyperlipidemia, hyperglycemia, and hyperproteinemia can cause pseudohyponatremia.

Valid if Run in a Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Low serum sodium concentration.
- Other abnormalities may point to the underlying cause.

OTHER LABORATORY TESTS

- Plasma osmolality is usually low; if plasma osmolality is normal or high, exclude hyperlipidemia, hyperglycemia, hyperproteinemia, and mannitol administration.
- Urine osmolality < 100–150 mOsmol/kg indicates primary polydipsia or reset osmostat. Urine osmolality > 150–200 mOsmol/kg indicates impaired renal water excretion.
- Urine sodium concentration < 15–20 mEq/L indicates low effective circulating volume, pure cortisol deficiency, primary polydipsia with high urine output. Urine sodium concentration > 20–25 mEq/L indicates syndrome of inappropriate ADH secretion, adrenal insufficiency, renal failure, reset osmostat, diuretic administration, or vomiting with marked bicarbonate loss.



TREATMENT

Inpatient versus outpatient treatment depends on severity of hyponatremia, associated neurologic dysfunction, and the underlying disorder.



MEDICATIONS

DRUG(S) OF CHOICE

- Treatment consists of addressing the underlying cause and increasing the serum sodium concentration if necessary. Overly rapid normalization of the hyponatremia can have potentially severe neurologic sequela and may be more detrimental than the hyponatremia itself. Therefore, isotonic saline is the fluid of choice in the large majority of cases. More aggressive correction of the serum sodium concentration with hypertonic saline is rarely necessary.

- Hypervolemic (edematous) patients are typically managed with diuretics and salt restriction. Isotonic saline and furosemide may be useful in more affected patients.

- Hypovolemic patients are managed by replacing the volume deficit with isotonic saline.

- The use of hypertonic saline may be considered in selected patients with severe symptomatic hyponatremia. The sodium deficit is estimated by $0.5 \times \text{lean BW (kg)} \times (120 - \text{serum sodium concentration})$. The serum sodium concentration is corrected by 10–12 mEq/L/day (0.5 mEq/L/h) or less. Once the serum sodium concentration reaches 120–125 mEq/L discontinue hypertonic saline and continue to slowly normalize the serum sodium concentration using isotonic saline or water restriction as dictated by the underlying cause of the hyponatremia.

- Other therapeutic interventions are dictated by the underlying cause of the hyponatremia.

H

PRECAUTIONS

Overly rapid correction of hyponatremia can result in neurologic damage (demyelination); avoid increasing serum sodium concentration by more than 10–12 mEq/L/day (0.5 mEq/L/h).



FOLLOW-UP

PATIENT MONITORING

- Serial serum sodium determinations to avoid overly rapid correction of the serum sodium concentration and to assure appropriate response to NaCl and other indicated therapies.
- Monitor hydration status.
- Monitor other serum electrolyte concentrations as indicated by the patient's clinical condition and underlying disorder.

PREVENTION/AVOIDANCE

Depends on the underlying disorder

POSSIBLE COMPLICATIONS

Depends on the underlying disorder

HYPONATREMIA

(CONTINUED)

EXPECTED COURSE AND PROGNOSIS

Depends on the underlying disorder



MISCELLANEOUS

ASSOCIATED CONDITIONS

Other electrolyte and acid-base abnormalities are often associated with the clinical disorders that cause hyponatremia.

SEE ALSO

- Cirrhosis and Fibrosis of the Liver
- Congestive Heart Failure, Left-Sided
- Hyperglycemia
- Hyperlipemia
- Hypoadrenocorticism (Addison's Disease)
- Myxedema and Myxedema Coma
- Nephrotic Syndrome
- Polyuria and Polydipsia
- Renal Failure, Chronic

ABBREVIATIONS

- ADH = antidiuretic hormone
- DKA = diabetic ketoacidosis
- SIADH = syndrome of inappropriate ADH secretion

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HYPOPARTHYROIDISM



BASICS

DEFINITION

Absolute or relative deficiency of parathyroid hormone secretion leading to hypocalcemia.

PATHOPHYSIOLOGY

- Dogs—most commonly idiopathic immune-mediated parathyroiditis.
- Cats—most commonly iatrogenic secondary to damaged or removed parathyroid glands during thyroidectomy for hyperthyroidism; idiopathic atrophy and immune-mediated parathyroiditis also seen (uncommon).

SYSTEMS AFFECTED

- Cardiovascular—ECG changes and bradycardia caused by altered neuromuscular activity.
- Gastrointestinal—anorexia and vomiting of unknown cause, possibly changes in gastrointestinal muscular activity.
- Nervous/Neuromuscular—seizures, tetany, ataxia, and weakness caused by increased neuromuscular activity resulting from diminished neuronal membrane stability.
- Ophthalmic—posterior lenticular cataracts of unknown cause.
- Renal/Urologic—PU/PD of unknown cause.
- Respiratory—panting caused by neuromuscular weakness and anxiety associated with neurologic and neuromuscular changes.

GENETICS

Unknown

INCIDENCE/PREVALENCE

- Dog—uncommon; exact prevalence not reported.
- Cat—common in bilaterally thyroidectomized cats (10–82% of patients, depending on surgical technique and surgical skill); spontaneous occurrence rare (nine cases reported in literature, five additional cats discussed in *Canine and Feline Endocrinology and Reproduction* textbook—see “Suggested Reading”).

SIGNALMENT

Species

Dog and cat

Breed Predilections

Toy poodles, miniature schnauzers, German shepherds, Labrador retrievers, and terrier breeds; mixed-breed cats.

Mean Age and Range

Dogs—mean age, 4.8 years; range, 6 weeks–13 years.

Cats—secondary to thyroidectomy, mean age 12–13 years, range 4–22 years; cats—spontaneous, mean age 2.25 years, range 6 months–7 years.

Predominant Sex

Dogs—female (60%); cats—male (64%)

SIGNS

Historical Findings

Dogs

- Seizures (49–86%)
- Ataxia/stiff gait (43–62%)
- Facial rubbing (62%)
- Muscle trembling, twitching, and fasciculations (57%)
- Growling (57%)
- Panting (35%)
- Weakness
- PU/PD
- Vomiting
- Anorexia

Cats

- Lethargy, anorexia, and depression (100%)
- Seizures (50%)
- Muscle trembling, twitching, and fasciculations (83%)
- Panting (33%)
- Bradycardia (17%)

Physical Examination Findings

Dogs

- Tense, splinted abdomen (50–65%)
- Ataxia/stiff gait (43–62%)
- Fever (30–70%)
- Muscle trembling, twitching, and fasciculations (57%)
- Panting (35%)
- Posterior lenticular cataracts (15–32%)
- Weakness
- Up to 20% may have normal physical examination results

Cats

- Muscle trembling, twitching, and fasciculations (83%)
- Panting (33%)
- Posterior lenticular cataracts (33%)
- Bradycardia (17%)
- Fever (17%)
- Hypothermia (17%)

CAUSES

See “Pathophysiology”

RISK FACTORS

- Dogs—N/A
- Cats—bilateral thyroidectomy for hyperthyroidism



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

The main problems associated with hypoparathyroidism, which must be differentiated from other disease processes, are seizures, weakness, and muscle trembling, twitching, and fasciculations.

Seizures

- Cardiovascular—syncope
- Metabolic—hepatoencephalopathy and hypoglycemia

- Neurologic—epilepsy, neoplasia, toxin, and inflammatory disease

Weakness

- Cardiovascular—congenital anatomic defects, arrhythmias, heart failure, and pericardial effusion
- Metabolic—hypoadrenocorticism, hypoglycemia, anemia, hypokalemia (especially cats), and hypothyroidism
- Neurologic/neuromuscular—myasthenia gravis, polymyositis, polyradiculoneuropathy, and spinal cord disease
- Toxic—tick paralysis, botulism, chronic organophosphate exposure, and lead poisoning

Muscle Trembling, Twitching, and Fasciculations

- Metabolic—puerperal tetany (i.e., eclampsia) and other causes of hypocalcemia
- Toxic—tetanus, strychnine poisoning, Eastern coral snake envenomation

CBC/BIOCHEMISTRY/URINALYSIS

- Results of hemogram and urinalysis usually normal; these tests are performed to rule-out other differential diagnoses.
- Hypocalcemia (usually < 6.5 mg/dL) and normal or mild to moderate hyperphosphatemia.
- Evaluate serum albumin carefully in all patients with hypocalcemia; hypoalbuminemia is the most common cause of hypocalcemia.
- The only other intrinsic disease process that reduces serum calcium and raises serum phosphorus is renal failure, which is easily distinguished from hypoparathyroidism by the presence of azotemia. Highly concentrated phosphate enema solutions can also cause hyperphosphatemia and hypocalcemia.

OTHER LABORATORY TESTS

Serum PTH determination—demonstrates undetectable or very low concentration of PTH; patients with other processes causing hypocalcemia (e.g., renal failure) have a normal-to-high concentration of PTH.

IMAGING

Radiography and ultrasonography are normal.

DIAGNOSTIC PROCEDURES

- ECG changes seen in patients with hypocalcemia include prolongation of the ST and QT segments; sinus bradycardia and wide T waves; T wave alternans is occasionally seen.
- Cervical exploration reveals absence or atrophy of the parathyroid glands.

PATHOLOGIC FINDINGS

- Dogs—normal tissue with mature lymphocytes, plasma cells, and fibrous connective tissue along with chief cell degeneration.
- Cats—parathyroid gland atrophy is more common, although histopathologic findings similar to those in dogs are found in cats.

H

HYPOPARATHYROIDISM

(CONTINUED)

Table 1

Vitamin D preparations.			
Preparation	Dose	Maximal Effect	Size
1,25 Dihydroxycholecalciferol (active vitamin D ₃ , calcitriol)	0.03–0.06 µg/kg/day Initial: 0.02–0.03 mg/kg/day Maint: 0.01–0.02 mg/kg/24–48h	1–4 days 1–7 days	0.25 and 0.5 µg capsules, 1.0 µg/mL oral solution, and 1 and 2 µg/mL injectable Currently unavailable; formerly available as 0.125 mg, 0.2 mg, 0.4 mg tablets and 0.2 mg/mL syrup
Ergocalciferol (vitamin D ₂)	Initial: 4,000–6,000 U/kg/day Maint: 1,000–2,000 U/kg/day-week	5–21 days	25,000 and 50,000 U capsules and 8,000 U/mL syrup

H**TREATMENT****APPROPRIATE HEALTH CARE**

- Hospitalize for medical management of hypocalcemia until clinical signs of hypocalcemia are controlled and serum calcium concentration is > 7 mg/dL.
- See Hypocalcemia for emergency inpatient management and appropriate fluid therapy.

NURSING CARE

Usually not required; hydration and nutritional support if anorexic.

ACTIVITY

Normal

DIET

Avoid calcium-poor diets; for dogs, puppy diets generally higher in calcium than adult dog food.

CLIENT EDUCATION

- Naturally occurring primary hypoparathyroid will require lifelong therapy and monitoring.
- Most cases of iatrogenic hypoparathyroidism (e.g., bilateral thyroidectomy) will recover over days to months and only require transient management and monitoring.

SURGICAL CONSIDERATIONS

None

**MEDICATIONS****DRUG(S) OF CHOICE*****Emergency/Acute Therapy***

See Hypocalcemia

Short-Term Post-tetany Therapy

See Hypocalcemia

Long-Term Therapy

- Vitamin D administration is needed indefinitely for primary hypoparathyroidism and total parathyroidectomy. The dosage should be increased or tapered on the basis of serum calcium concentration.
- Shorter-acting preparations of vitamin D are preferred so that overdosage (hypercalcemia) can be quickly corrected (see Table 1).
- A more economical approach to treatment is to maximize oral administration of calcium and reduce oral administration of vitamin D; calcium is usually less expensive than vitamin D (see Table 2). Dosage is influenced by each product's available elemental calcium content.

CONTRAINDICATIONS

See Hypocalcemia

Table 2

Calcium preparations.			
Preparation	Dose of Elemental Calcium	Available Calcium	Size Available (Needs to Be Converted to Elemental Calcium)
Calcium carbonate	Canine: 1–4 g/day Feline: 0.5–1 g/day	40%	Tablets—500, 600, 650, 1,250, 1,500 mg Chewable tablets—400, 420, 500, 750, 850, 1,000, 1,250 mg Capsules—1,250 mg Oral suspension—250 mg/mL
Calcium gluconate	Canine: 1–4 g/day Feline: 0.5–1 g/day	10%	Tablets—500, 650, 975 mg Chewable tablets—500 mg Capsules—500, 700 mg Powder for suspension—70 mg/ml
Calcium lactate	Canine: 1–4 g/day Feline: 0.5–1 g/day	13%	Tablets—650, 770 mg Capsules—500 mg
Calcium acetate	Canine: 1–4 g/day Feline: 0.5–1 g/day	25%	Tablets, gelcaps, and capsules—667 mg
Calcium citrate	Canine: 1–4 g/day Feline: 0.5–1 g/day	21%	Tablets—950, 1,150 mg Effervescent tablets—2,380 mg Capsules—850, 1,070 mg Powder for oral suspension—725 mg/ml
Calcium glubionate	Canine: 1–4 g/day Feline: 0.5–1 g/day	30%	Syrup—360 mg/ml

(CONTINUED)

PRECAUTIONS

All calcium preparations given orally can cause gastrointestinal disturbances; calcium carbonate may be less irritating because of its high calcium availability and lower dosage requirement.

POSSIBLE INTERACTIONS

- Injectable calcium solutions are reportedly incompatible with tetracycline drugs, cephalothin, methylprednisolone sodium succinate, dobutamine, metoclopramide, and amphotericin B.
- Thiazide diuretics used in conjunction with large doses of calcium may cause hypercalcemia.
- Patients on digitalis are more likely to develop arrhythmias if calcium is administered intravenously.
- Calcium administration may antagonize effects of calcium channel blocking agents (e.g., diltiazem, verapamil, nifedipine, and amlodipine).

ALTERNATIVE DRUG(S)

None

**FOLLOW-UP****PATIENT MONITORING**

- Hypocalcemia and hypercalcemia are both concerns with long-term management.
- Once serum calcium is stable and normal, assess serum calcium concentration monthly for the first 6 months, then every 2–4 months; goal is to maintain serum calcium between 8 and 10 mg/dL.
- Inform clients about clinical signs of hypocalcemia and hypercalcemia.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Hypocalcemia
- Hypercalcemia, which can lead to nephrocalcinosis and kidney injury (see Hypercalcemia)

EXPECTED COURSE AND PROGNOSIS

- With close monitoring of serum calcium and client dedication, the prognosis for long-term survival is excellent.
- Adjustments in vitamin D and oral calcium administration can be expected during the course of management, especially during the initial 2–6 months.
- Cats with hypoparathyroidism secondary to thyroidectomy usually require only transient treatment because they typically regain normal parathyroid function within 4–6 months, often within 2–3 weeks.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Excess muscular activity can lead to hyperthermia, which may necessitate treatment.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Hypocalcemia can lead to weakness and dystocia.

SEE ALSO

- Hypercalcemia
- Hyperthyroidism
- Hypocalcemia

HYPOPARATHYROIDISM**ABBREVIATIONS**

- Ca = calcium
- ECG = electrocardiography
- PTH = parathyroid hormone
- PU/PD = polyuria and polydipsia

INTERNET RESOURCES

<http://www.vet.uga.edu/VPP/CLERK/mcfarland/index.php>.

Suggested Reading

Bruyette DS, Feldman EC. Primary hypoparathyroidism in the dog: Report of 15 cases and review of 13 previously reported cases. *J Vet Intern Med* 1988, 2:7–14.

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Client Education Handout
available online

H

HYPOPHOSPHATEMIA



BASICS

DEFINITION

Serum phosphorus concentration
 $< 2.5 \text{ mg/dL}$

PATOPHYSIOLOGY

- Control of phosphorus is influenced by the actions and interactions of PTH and vitamin D with the gastrointestinal tract, bone, kidneys, and parathyroid glands.
- Decreased serum phosphorus concentration can be caused by translocation of phosphorus from the extracellular fluid in cells, decreased renal reabsorption, or decreased intestinal absorption of phosphorus.
- Low serum phosphorus can lead to ATP depletion, which affects cells with high ATP-energy demands (skeletal muscle, cardiac muscle, nerve tissue, and RBCs).
- Many important enzyme systems dependent on adequate phosphorus levels including: glycolysis, ammonogenesis, 1-hydroxylation of 25(OH)-cholecalciferol, and 2,3-diphosphoglycerate, which are essential for energy production, acid excretion, calcium balance, and tissue oxygenation, respectively.
- Required for maintenance of cell membrane integrity by playing an essential role in the production of ATP, guanosine triphosphate, cyclic AMP, and phosphocreatinine.
- Diabetic (ketotic and non-ketotic) patients at increased risk due to depleted phosphorus stores, lost muscle mass, and urinary losses. Insulin administration yields ATP from glycolysis, causing translocation of phosphorus.

SYSTEMS AFFECTED

- Hemic/Lymphatic/Immune—hemolysis, impaired oxygen delivery to tissues, impaired leukocyte and platelet function.
- Neurologic—impaired glucose uptake leads to encephalopathy, seizures, and coma.
- Musculoskeletal—rhabdomyolysis, weakness, pain, ventilator failure, and gastrointestinal ileus.
- Cardiac—impaired contractility.

SIGNALMENT

- Older dog and cat
- Diabetic patient

SIGNS

Historical Findings

Usually consistent with the primary condition responsible for the hypophosphatemia; however, evidence of severe hypophosphatemia (e.g., hemolysis) is usually not observed unless serum concentrations decrease to 1.0 mg/dL or less.

Physical Examination Findings

- Hemolytic anemia causes pallor, tachypnea, dyspnea, and/or red discolored urine.
- Skeletal and respiratory muscle weakness.
- Mental dullness.

CAUSES

- Maldistribution (translocation)—treatment of diabetes ketoacidosis, insulin administration or carbohydrate load, total parenteral nutrition or nutritional recovery, hyperventilation or respiratory alkalosis.
- Reduced renal reabsorption (increased renal loss)—primary hyperparathyroidism, renal tubular disorders (e.g., Fanconi syndrome), proximal tubule diuretics (e.g., carbonic anhydrase inhibitors), eclampsia (hypocalcemic tetany), hyperadrenocorticism, sodium bicarbonate administration.
- Reduced intestinal absorption (decreased intake)—phosphorus-deficient diets, vitamin D deficiency, malabsorption disorders, phosphate binders.
- Laboratory error—hemolysis, icterus, osmotic diuretic (e.g., mannitol) administration.

RISK FACTORS

- Phosphorus-deficient diets or parenteral nutrition (refeeding syndrome)
- Diabetes mellitus
- Prolonged anorexia, malnutrition, or starvation
- Primary hyperparathyroidism



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Concurrent hyperglycemia, glucosuria, ketonuria, and high anion gap metabolic acidosis—rule out diabetic ketoacidosis.
- Concurrent glucosuria, normoglycemia, isosthenuria \pm azotemia—rule out renal tubular defects.
- Concurrent hypercalcemia and proteinuria—rule out primary hyperparathyroidism.
- Concurrent hypocalcemia—rule out hypocalcemic tetany.
- Concurrent high serum alkaline phosphatase—rule out hyperadrenocorticism.
- Concurrent panhypoproteinemia—rule out intestinal malabsorption.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

Osmotic diuretics (e.g., mannitol) may falsely lower serum phosphorus concentrations.

Disorders That May Alter Laboratory Results

Hemolysis and icterus may falsely lower serum phosphorus concentrations.

Valid If Run In Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Serum phosphorus $< 2.5 \text{ mg/dL}$.
- Hyperglycemia, glucosuria, ketonuria, and high anion gap metabolic acidosis with diabetic ketoacidosis.
- Glucosuria, normoglycemia, isosthenuria, or azotemia with renal tubular defect.

- Hypercalcemia with primary hyperparathyroidism.
- Hypocalcemia with hypocalcemic tetany.
- High serum alkaline phosphatase, proteinuria with hyperadrenocorticism.
- Panhypoproteinemia with intestinal malabsorption.

OTHER LABORATORY TESTS

- Serum fructosamine—to diagnose or rule out diabetes mellitus.
- Parathyroid hormone assay—to diagnose or rule out hyperparathyroidism.
- PTH-rp for hypercalcemia of malignancy.
- Vitamin D metabolite measurement—to diagnose or rule out vitamin D deficiency.

IMAGING

- Radiography may reveal urolithiasis in cases of primary hyperparathyroidism or poor bone quality/pathologic fractures with disorders of vitamin D metabolism.
- Ultrasonography (cervical) may reveal parathyroid mass.

OTHER DIAGNOSTIC PROCEDURES

Surgical exploration of the cervical area may reveal a parathyroid mass.
 Urine anion gap can reveal renal tubular secretory defect.



TREATMENT

- Prevention is preferred.
- Asymptomatic patients with low (1.5–2.5 mg/dL), but not depleted, phosphorus concentrations may not need phosphate treatment.
- If caused by insulin administration or hyperalimentation, administer supplemental phosphorus.
- Severe hypophosphatemia ($< 1.5 \text{ mg/dL}$): patients need hospitalization and monitoring for hemolysis or hemolytic crisis. Intravenously administer isotonic electrolyte solution without calcium, supplemented with potassium phosphate.
- Fresh whole blood transfusion for severe hemolytic crisis.



MEDICATIONS

DRUG(S) OF CHOICE

- Potassium phosphate (3 mMol phosphate/mL and 4.4 mEq potassium/mL) given intravenously.
- Sodium phosphate (3 mMol phosphate/mL and 4 mEq sodium/mL) intravenously.
- Dosage—0.01–0.12 mMol/kg/h CRI. Monitor serum phosphorus every 6–8 hours.
- Discontinue therapy when serum phosphorus concentration reaches 2 mg/dL in order to avoid iatrogenic hypocalcemia and hyperphosphatemia.

(CONTINUED)

CONTRAINDICATIONS

- Hyperphosphatemia
- Hypocalcemia
- Hypercalcemia
- Renal failure
- Hyperkalemia
- Concurrent D_{2,5} and D₅ in LRS and dobutamine administration

PRECAUTIONS

- Concurrent diuretic administration, especially carbonic anhydrase inhibitors
- Renal disease

POSSIBLE INTERACTIONS

- ACE inhibitor (e.g., enalapril) administration
- Cardiac glycoside (e.g., digoxin) administration
- Potassium-sparing diuretics (e.g., spironolactone)

ALTERNATIVE DRUG(S)

- Oral phosphate supplement (e.g., phospho-soda) if not vomiting
- Milk (skim or low-fat) may be supplemented

**FOLLOW-UP**

- Measure serum phosphorus levels every 6–8 hours until within normal range.
- Monitor patients for hyperphosphatemia and discontinue treatment immediately.
- Check serum potassium level daily until both stable.

POSSIBLE COMPLICATIONS

- Hemolysis
- Respiratory depression and failure
- Cardiac arrest

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Concurrent hypokalemia is common in patients with diabetic ketoacidosis.
- Concurrent hypercalcemia in Keeshond dogs.

AGE-RELATED FACTORS

Usually presents in older dogs.

PREGNANCY/FERTILITY/BREEDING

- Concurrent hypocalcemia in the periparturient animal is caused by PTH-promoted renal excretion of phosphorus causing hypophosphatemia.

SEE ALSO

- Diabetes Mellitus with Ketoacidosis
- Hyperparathyroidism

HYPOPHOSPHATEMIA**ABBREVIATIONS**

- ACE = angiotensin converting enzyme
- ATP = adenosine triphosphate
- LRS = lactated Ringer's solution
- PTH = parathyroid hormone
- RBC = red blood cells

Suggested Reading

DiBartola SP, Autran de Morais H. Disorders of phosphorus: Hypophosphatemia and hyperphosphatemia. In: DiBartola SP, ed., Fluid Therapy in Small Animal Practice, 4th ed. Philadelphia: Saunders, 2012, pp. 195–211.

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H

HYPOPITUITARISM



BASICS

OVERVIEW

- A condition resulting from destruction of the pituitary gland by a neoplastic, degenerative, or anomalous process.
- Associated with low production of pituitary hormones including TSH, ACTH, luteinizing hormone, follicle-stimulating hormone, and GH.

SIGNALMENT

- Dog
- Age: 2–6 months
- Breeds—German shepherd, Karelian bear dog, spitz, toy pinscher, and Weimaraner
- Simple autosomal recessive in German shepherd and Karelian bear dog; mutation of the *Lhx3* gene

SIGNS

Historical Findings

- Mental retardation manifested as difficulty in housebreaking
- Slow growth noticed in first 2–3 months of life
- Proportionate dwarfism

Physical Examination Findings

- Retained puppy hair coat
- Thin, hypotonic skin
- Shriek bark
- Truncal alopecia
- Cutaneous hyperpigmentation
- Infantile genitalia
- Delayed dental eruption

CAUSES & RISK FACTORS

Congenital

- Cystic Rathke's pouch
- Isolated GH deficiency

Acquired

- Pituitary tumor
- Trauma
- Radiotherapy



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hypothyroid dwarfism; breed predilection and disproportionate dwarfism observed in patients with hypothyroidism.

- Other causes of stunted growth—portosystemic shunt, diabetes mellitus, hyperadrenocorticism, malnutrition, parasitism.

CBC/BIOCHEMISTRY/URINALYSIS

- Eosinophilia
- Lymphocytosis
- Hypophosphatemia
- Hypoglycemia

OTHER LABORATORY TESTS

- Corticotropin and TSH response tests; subnormal response to TSH and ACTH.
- Growth hormone and insulin-like growth factor assays; growth hormone assay not currently available in the United States; recommend measurement of IGF-1, which is low.
- Ghrelin-stimulation test—monitors changes in GH levels in response to ghrelin; requires GH assay.
- DNA testing.

IMAGING

Radiography may reveal epiphyseal dysgenesis and abnormal retention of phyeal growth plates.



TREATMENT

Manage medically on an outpatient basis.



MEDICATIONS

DRUG(S)

- Growth hormone—human, porcine, or bovine, if available; 0.1 IU/kg SC three times weekly for 4–6 weeks; repeat if necessary.
- Medroxyprogesterone acetate (2.5–5 mg/kg IM q 3 weeks, then q6 weeks after normal stature is achieved).
- Treat hypothyroidism with levothyroxine (22 µg/kg PO q24h).
- Glucocorticoids (e.g., prednisone, 0.2 mg/kg PO q24h) if ACTH response test results are subnormal; higher dosage of steroids is needed during periods of stress.

CONTRAINDICATIONS/POSSIBLE

INTERACTIONS

Hypersensitivity reactions and carbohydrate intolerance may develop with growth hormone supplementation.



FOLLOW-UP

PATIENT MONITORING

- Blood and urinary glucose concentration.
- Stop growth hormone supplementation if glucosuria develops or blood glucose is > 150 mg/dL.

POSSIBLE COMPLICATIONS

Neurologic complications caused by expansion of Rathke's pouch.

EXPECTED COURSE AND PROGNOSIS

- Skin and hair coat improve within 6–8 weeks of initiating growth hormone and thyroid supplementation.
- Generally no increase in stature because growth plates have usually closed by the time of diagnosis.
- Dogs often die at a young age (3–4 years) because of neurologic complications.
- Poor long-term prognosis.



MISCELLANEOUS

SEE ALSO

- Hypoadrenocorticism (Addison's Disease)
- Hypothyroidism

ABBREVIATIONS

- ACTH = adrenocorticotropin
- GH = growth hormone
- IGF-1 = insulin-like growth factor I
- TSH = thyroid stimulating hormone

Suggested Reading

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HYPOPYON



BASICS

OVERVIEW

- Hypopyon—accumulation of white blood cells in the anterior chamber of the eye. Inflammatory breakdown of blood-aqueous barrier allows entry of blood cells into the anterior chamber; chemoattractants mediate influx. Cells often settle in the ventral anterior chamber because of gravity. • Lipid flare—resembles hypopyon but turbidity of the anterior chamber is caused by a high concentration of lipids in aqueous humor. Requires breakdown of the blood-aqueous barrier and concurrent hyperlipidemia to occur.

SIGNALMENT

Affects both dogs and cats; no age or sex predilection.

SIGNS

- Hypopyon—white to yellow opacity within anterior chamber; may be a ventral accumulation of cells or may completely fill the anterior chamber. Fibrin accumulation in anterior chamber may prevent discrete settling of white blood cells, resulting in cells suspended within fibrin matrix. Concurrent ophthalmic signs include blepharospasm, epiphora, diffuse corneal edema, aqueous flare, miosis, iridal swelling, and vision loss.
- Lipid flare—diffuse milky appearance to anterior chamber. Concurrent ophthalmic signs may include vision loss, mild blepharospasm, and mild to moderate diffuse corneal edema.

CAUSES & RISK FACTORS

Hypopyon

Any cause of uveitis can result in hypopyon. Most commonly, hypopyon is associated with severe uveitis. Hypopyon can also result from neoplastic cell accumulation in ocular lymphoma.

Lipid Flare

Lipid flare results from hyperlipidemia and concurrent uveitis. Hyperlipidemia may also destabilize the blood-aqueous barrier directly. Post-prandial lipemia may occasionally result in lipemic aqueous if uveitis is present.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Hypopyon

Fibrin in anterior chamber—generally forms an irregular clot, not a ventrally located horizontal line.

Lipid Flare

- Severe aqueous flare—does not appear as milky/white as lipid flare. Animals with severe aqueous flare generally exhibit much more

ocular pain than animals with lipid flare. • Diffuse corneal edema—severe corneal edema may be confused with anterior chamber opacity, but corneal stromal thickening, keratoconus, and corneal bullae are noted with the former.

CBC/BIOCHEMISTRY/URINALYSIS

Hypopyon

Often normal; abnormalities related to underlying cause of uveitis may be present.

Lipid Flare

Elevated serum triglycerides and cholesterol; other abnormalities may be present related to underlying metabolic disorder(s).

OTHER LABORATORY TESTS

Hypopyon

None if hypopyon is related to obvious corneal disease; if related to uveitis, look for underlying cause of uveitis (see Anterior Uveitis—Dogs; Anterior Uveitis—Cats).

Lipid Flare

See Hyperlipidemia.

DIAGNOSTIC PROCEDURES

Anterior chamber centesis indicated with suspicion of neoplastic hypopyon (e.g., lymphoma); unrewarding under other circumstances.



TREATMENT

- Hypopyon requires aggressive treatment for uveitis and underlying cause. Outpatient treatment is adequate. • Lipid flare requires treatment for uveitis and underlying metabolic disorder. Outpatient treatment is adequate.



MEDICATIONS

DRUG(S)

Hypopyon

Corticosteroids

Topical

- Prednisolone acetate 1%—apply 2–6 times daily, depending on severity of disease.
- Dexamethasone 0.1%—apply 2–6 times daily, depending on severity of disease.
- Taper medication frequency as condition resolves.

Subconjunctival

- Triamcinolone acetonide 4–6 mg (dog); 4 mg (cat) by subconjunctival injection.
- Methylprednisolone 3–10 mg (dog); 4 mg (cat) by subconjunctival injection. • Indicated as one-time injection followed by topical and/or systemic anti-inflammatories.

Systemic

- Prednisone 0.5–2.2 mg/kg/day (dog); 1–3 mg/kg/day (cat); taper dose after 7–10 days. • Only use if systemic infectious causes of uveitis have been ruled out.

Nonsteroidal Anti-inflammatory Drugs

Topical

- Flurbiprofen—apply 2–4 times daily, depending on severity of disease.
- Diclofenac—apply 2–4 times daily, depending on severity of disease. • Much less effective than corticosteroids.

Systemic

- Carprofen 2.2 mg/kg PO q12h or 4.4 mg/kg PO QD (dog). • Meloxicam 0.2 mg/kg PO QD (dog). • Robenacoxib 1 mg/kg PO q24h; limit duration of use to 3 days (cat). • Meloxicam 0.2 mg/kg IV, SC, PO once, then 0.05 mg/kg IV, SC, PO q24h for 2 days, then 0.025 mg/kg q24–48h; limit duration of use to 4 days (cat). • Do not use concurrently with systemic corticosteroids.

Topical Mydriatic/Cycloplegic

- Atropine sulfate 1%—apply 1–4 times daily, depending on severity of disease. Use ointment instead of solution in cats to minimize salivation.

Lipid Flare

Topical Corticosteroids

- Prednisolone acetate 1%—apply 2–4 times daily, depending on severity of disease.
- Dexamethasone 0.1%—apply 2–4 times daily, depending on severity of disease.
- Taper medication as condition resolves.

Topical Mydriatic/Cycloplegic

Atropine sulfate 1%—apply 1–2 times daily, if necessary for perceived ocular discomfort.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Avoid the use of topical miotic medications.
- Topical and subconjunctival corticosteroids contraindicated if ulcerative keratitis is present. • Out of concern for secondary glaucoma, topical atropine should be used judiciously and IOP should be monitored.



FOLLOW-UP

PATIENT MONITORING

Recheck in 2–3 days. Intraocular pressure should be monitored to detect secondary glaucoma. Frequency of subsequent rechecks dictated by response to treatment.

EXPECTED COURSE AND PROGNOSIS

- Hypopyon—prognosis guarded to good; depends on underlying disease and response to treatment. • Lipid flare—prognosis good; generally responds quickly (within 24–72 hours) to moderate anti-inflammatory therapy; recurrence possible.



MISCELLANEOUS

ABBRÉVIACTION

PIFM = pre-iridal fibrovascular membrane

Author Ian P. Herring

Consulting Editor Paul E. Miller

HYPOTHENURIA



BASICS

DEFINITION

Urinary specific gravity between 1.000 and 1.006

PATHOPHYSIOLOGY

The ability to concentrate urine normally (dogs, > 1.030; cats, > 1.035) depends on a complex interaction between ADH, the protein receptor for ADH on the renal tubule, and a hypertonic renal medullary interstitium; interference with the synthesis, release, or actions of ADH, damage to the renal tubule, and altered tonicity of the medullary interstitium (medullary wash-out) can cause hyposthenuria.

H

SYSTEMS AFFECTED

Depends on the underlying disorder

SIGNALMENT

Species

Dog and cat

Breed Predilections

None

Mean Age and Range

None

Predominant Sex

None

SIGNS

- Polyuria and polydipsia
- Urinary incontinence—occasional
- Other signs depend on the underlying disorder

CAUSES

Any disorder or drug that interferes with the release or action of ADH, damages the renal tubule, causes medullary wash-out, or causes a primary thirst disorder (see "Differential Diagnosis").



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pyometra
- Cushing's disease
- Central diabetes insipidus (little or no ADH produced)
- Nephrogenic diabetes insipidus (resistance to ADH)
- Pyelonephritis
- Hyperthyroidism
- Hypercalcemia
- Early renal failure
- Primary liver disease
- Hypokalemia
- Hypoadrenocorticism

- Primary polydipsia—compulsive water drinking

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

Cortisone, lithium, demeclocycline, methoxyflurane, thiazide diuretics, and intravenous administration of fluids can all lower urine specific gravity into the hyposthenuric range.

Valid if Run in a Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Low urinary specific gravity (1.000–1.006), other abnormalities may point to the underlying cause.
- High serum ALP activity suggests hyperadrenocorticism or primary liver disease.
- High cholesterol common in patients with hyperadrenocorticism.
- Leukocytosis with a left shift in some patients with pyometra or pyelonephritis.
- Hyperkalemia and hyponatremia suggest hypoadrenocorticism.
- Low serum potassium confirms hypokalemia.
- Inflammatory sediment or bacteriuria consistent with pyelonephritis.
- Proteinuria common in patients with pyelonephritis, pyometra, and hyperadrenocorticism.

OTHER LABORATORY TESTS

ACTH levels to determine the cause of hyperadrenocorticism (i.e., pituitary-dependent vs. adrenal tumor).

IMAGING

- Radiography to assess renal size and shape and to detect calcified adrenal tumor or large uterus.
- Intravenous pyelogram to help diagnose pyelonephritis.
- Ultrasonography to assess adrenal size, renal and hepatic size and architecture, and uterine size.
- MRI or CT scan to assess a pituitary or hypothalamic mass that may be the cause of central diabetes insipidus or hyperadrenocorticism.

DIAGNOSTIC PROCEDURES

- ACTH stimulation test to screen for hyperadrenocorticism and hypoadrenocorticism.
- Low-dose dexamethasone-suppression test and urine/cortisol creatinine test to screen for hyperadrenocorticism.
- Serum bile acids to evaluate liver function.
- Note: dogs with hyperadrenocorticism often have mildly high bile acids.
- Modified water deprivation test to differentiate diabetes insipidus from

psychogenic polydipsia; see Appendix II for test protocol.



TREATMENT

- Depends on the underlying disorder.
- Do not restrict patient's water intake unless appropriate to the definitive diagnosis.
- Depends on the underlying disorder.



MEDICATIONS

DRUG(S) OF CHOICE

Depends on the underlying disorder



FOLLOW-UP

PATIENT MONITORING

Urine specific gravity, hydration status, renal function, and electrolytes

POSSIBLE COMPLICATIONS

Dehydration



MISCELLANEOUS

ASSOCIATED CONDITIONS

See "Differential Diagnosis"

ZOONOTIC POTENTIAL

None

SEE ALSO

- Diabetes Insipidus
- Hyperadrenocorticism (Cushing's Syndrome)—Cats
- Hyperadrenocorticism (Cushing's Syndrome)—Dogs

ABBREVIATIONS

- ACTH = adrenocortotropic hormone
- ADH = antidiuretic hormone
- ALP = alkaline phosphatase
- CT = computed tomography
- MRI = magnetic resonance imaging

Suggested Reading

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Acknowledgment The author and editors acknowledge the prior contribution of Rhett Nichols.



BASICS

Due to limited clinical literature in veterinary science much of the information below has been extrapolated from the human medical literature and experimental studies in animals.

DEFINITION

- Core body temperature drops below that required for normal metabolism. In primary hypothermia, the healthy individual's compensatory responses to heat loss are overwhelmed by exposure, whereas secondary hypothermia complicates many systemic diseases.
- Stage I—90–95°F (32–35°C)
- Stage II—82–90°F (28–32°C)
- Stage III—75–82°F (24–28°C)
- Stage IV—any temperature <75°F (24°C).

PATHOPHYSIOLOGY

• Normal thermoregulation balances heat gained or lost to the environment with heat produced via central thermogenesis. It is controlled by the hypothalamus with input from thermoreceptors. Heat can be gained or lost to the environment via four mechanisms including evaporation, radiation, convection, and conduction. Central thermogenesis generates heat via basal metabolism, muscle activity, and uncoupling of brown fat (neonates). • Heat production can be augmented via shivering and increased basal metabolic rate. Activation of both the sympathetic nervous and endocrine systems results in increased circulating levels of thyroid-releasing hormone, catecholamines, growth hormone, and glucocorticoids, which all contribute to increased glucose utilization and basal metabolic rate. • Adaptations to minimize heat loss include cutaneous vasoconstriction, piloerection, and behavioral responses such as curling up, sharing body heat, and seeking shelter.

SYSTEMS AFFECTED

- Cardiovascular—in mild hypothermia, sympathetic stimulation induces tachycardia and peripheral vasoconstriction with normal or elevated cardiac output and blood pressure (BP). As the patient becomes colder, depolarization of cardiac pacemaker cells is slowed resulting in bradycardia resistant to treatment with atropine; the resultant fall in cardiac output is balanced by an increase in systemic vascular resistance. At lower temperatures, bradycardia becomes progressively extreme and systemic vascular resistance falls as catecholamine release and adrenergic receptor responsiveness is blunted. Classic ECG findings include the presence of Osborn or J-waves, atrial and ventricular dysrhythmias, and prolongation of the PR, QRS, and QT intervals. Progression from sinus bradycardia through atrial fibrillation to ventricular fibrillation and ultimately asystole.
- Endocrine—sympathetic activation and

release of counter-regulatory hormones trigger increased glycogenolysis, gluconeogenesis, and lipolysis as well as inhibit the release and uptake of insulin resulting in hyperglycemia. When hypothermia develops slowly or is long-lasting, glycogen stores become depleted and hypoglycemia develops.

- Gastrointestinal—increased gastric acid production and reduced duodenal bicarbonate secretion may predispose patients to gastrointestinal ulceration. Ileus is common.
- Hemic—plasma shifts to the extravascular space, and the consequent hemoconcentration may lead to hyper- and hypocoagulopathy. Depressed enzymatic activity of clotting factors and platelet hyporeactivity may exacerbate hypocoagulability.
- Hepatobiliary/Pancreatic—hypoxia leads to hepatocellular damage and pancreatitis.
- Musculoskeletal—increased viscosity of joint fluid and muscle stiffness.
- Nervous—as core temperature falls, CNS metabolism and level of consciousness decrease in a linear fashion, and nerve conduction velocity progressively slows. Mild incoordination is followed by lethargy, obtundation and coma.
- Renal—peripheral vasoconstriction increases renal blood flow and glomerular filtration rate resulting in increased urine production. As core body temperature falls, progressive tubular dysfunction and antidiuretic hormone resistance contribute further to cold-diuresis. Later, urine production decreases as a result of falling cardiac output. Acute kidney injury may ensue.
- Respiratory—initial tachypnea is replaced by decreased respiratory rate and tidal volume and increased production of airway secretions. As the temperature falls protective airway reflexes are reduced. At temperatures below 93.2°F (34°C) ventilatory drive is attenuated and increased pulmonary vascular resistance leads to ventilation-perfusion mismatch. Progressive hypoventilation, apnea, and (more rarely) pulmonary edema may develop. Hypothermia also causes the oxyhemoglobin dissociation curve to shift to the left. This effect may be masked by concurrent lactic and respiratory acidosis that may become so profound it results in an overall right-shift.
- Skin—edema develops secondary to increased vascular permeability.

GENETICS

Unknown

INCIDENCE/PREVALENCE

Varies with geographic location

GEOGRAPHIC DISTRIBUTION

Most common in cold climates

SIGNALMENT

Species

Dogs and cats

Breed Predilections

Smaller breeds with increased surface area

Mean Age and Range

More common in neonates and geriatrics

SIGNS

General Comments

A thorough search should be made to find precipitating, comorbid conditions.

Historical Findings

- Known prolonged exposure to cold ambient temperatures.
- Possibly, disappearance from home or a history of trauma.

Physical Examination Findings

- Stage I—90–95°F (32–35°C)
- Stage II—82–90°F (28–32°C)
- Stage III—75–82°F (24–28°C)
- Stage IV—any temperature <75°F (<24°C)

Stage I 90–95°F (32–35°C)

- General
 - Lethargy
 - Weakness
 - Vigorous shivering (variable)
 - Cardiovascular
- Variable heart rate, rhythm, and BP
- Light pink to pale mucous membranes
- Neurologic
 - Confusion, agitation, or obtundation
 - Respiratory
 - Variable respiratory rate

Stage II 82–90°F (28–32°C)

- General
 - Collapse
 - Reduced shivering (variable)
 - Cardiovascular
- Bradyarrhythmia with hypotension
- Pale mucous membranes
- Musculoskeletal
- Muscle and joint stiffness
- Neurologic
- Obtundation, stupor, or coma
- Ataxia and hyporeflexia
- Respiratory
 - Reduced depth and rate of respiration

Stage III 75–82°F (24–28°C)

- General
 - Moribund with cold, edematous skin
 - Loss of shivering (variable)
- Cardiovascular
 - Bradyarrhythmia with hypotension
 - Pale mucous membranes
- Musculoskeletal
 - Muscle and joint stiffness
- Neurologic
 - Coma with fixed, dilated pupils
 - Areflexia
 - Respiratory
 - Reduced depth and rate of respiration or respiratory arrest
 - Pulmonary edema

Stage IV <75°F (<24°C)

- General
 - No vital signs
 - Cardiac arrest

CAUSES

- Inadequate thermogenesis
 - Normal thermogenesis is overwhelmed
 - Serious illness
 - Extreme heat loss
 - Excessive evaporation, conduction, convection, and radiation
 - Inability to vasoconstrict blood vessels or piloerect hair
 - Loss of behavioral adaptations
 - Thermoregulatory center failure
 - Hypothalamic injury or disease

RISK FACTORS

- Extremes of age
- Low body fat and glycogen stores
- Burn injury
- Intracranial injury or disease
- Hypothyroidism
- Diabetic ketoacidosis
- Sepsis
- Trauma
- General anesthesia
- Use of medications including but not limited to beta-blockers, barbiturates, narcotics, phenothiazines

H

HYPOTHERMIA

(CONTINUED)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Primary CNS disease, hypoglycemia, anemia, hepatic encephalopathy, myxedema, electrolyte disturbances, sepsis, intoxication, neoplasia, and death
- Bradyarrhythmia—cardiac disease, medication side effects, and intoxication

CBC/BIOCHEMISTRY/URINALYSIS

- Results are variable depending on the degree of hypothermia and presence of comorbid conditions
- CBC—hemoconcentration and thrombocytopenia
- Biochemistry—azotemia, hyper- and hypoglycemia, elevated liver enzyme activity, hyperbilirubinemia
- Urinalysis—isosthenuria, glucosuria

OTHER LABORATORY TESTS

- Blood gas—variable but metabolic and respiratory acidosis is common.
- Coagulation—hyperfibrinogenemia, DIC. In vivo prolongation of blood clotting times may not be reflected by in vitro assays and should correct with rewarming.
- Thyroid hormone evaluation may confirm underlying hypothyroidism.

IMAGING

To investigate recovery complications or comorbid conditions

DIAGNOSTIC PROCEDURES

None

PATHOLOGIC FINDINGS

- Findings in patients who succumb to primary accidental hypothermia are variable and nonspecific. If body cooling and death occur rapidly, necropsy findings are minimal but may include reddish discoloration of skin, hemorrhagic gastric erosions, and lipid deposits in epithelial cells of renal proximal tubules and other organs.
- Patients who die from secondary hypothermia may have similar findings; however, they will also have evidence of a separate and significant disease process.



TREATMENT

APPROPRIATE HEALTH CARE

Emergency inpatient intensive care until normothermic and stable

NURSING CARE

- Active external rewarming using warm blankets, heating pads, radiant heat, warm baths, or forced warm air, and administration of warm parenteral fluids (stage II) is used in patients with stage I-II hypothermia. Complications include core temperature after-drop whereby the return of cold blood from the periphery to the central circulation causes further core cooling. Rewarming of the trunk should be performed before the

extremities to minimize this risk.

- Techniques to warm patients with stage III-IV hypothermia include administration of warm humidified oxygen, warmed intravenous fluids, and bladder or gastric lavage with warm saline. More invasive and technically demanding methods include closed thoracic and peritoneal lavage, hemodialysis, continuous arteriovenous or veno-venous rewarming, and cardiopulmonary bypass.
- Whole-body immersion in hot water is contraindicated, as it will cause massive vasodilatation and hypotension and is likely to provoke dysrhythmias and cardiovascular collapse.
- Fluid therapy—most patients are initially volume depleted but must be closely monitored during resuscitation for volume overload. Crystalloid fluids administered intravenously should be warmed to 104°F (40°C).
- Hypotension is treated with volume resuscitation. The use of inotropic drugs is considered only in cases unresponsive to volume resuscitation.
- Patients with respiratory failure must be mechanically ventilated.

ACTIVITY

Minimally affected patients should be encouraged to be active, as muscle activity will generate more endogenous body heat.

DIET

- Withhold oral intake until patient is alert.

CLIENT EDUCATION

Prevention of exposure to cold temperatures is imperative in preventing primary hypothermia. Clients with very young and very old patients as well as those with serious medical conditions or taking medications that inhibit thermoregulatory ability should be counseled to keep their pets indoors and to take protective measures if they are to be exposed to cold temperatures.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

Hypoglycemic patients warrant dextrose supplementation.

CONTRAINDICATIONS

There is no evidence to support the routine use of steroids or antibiotics.



FOLLOW-UP

PATIENT MONITORING

- Continuous core body temperature.
- Continuous ECG and frequent BP (q1h) during rewarming.
- Frequent assessment (q6–12h) of electrolytes (sodium, potassium,

chloride, ionized calcium, magnesium, and phosphorus), acid-base status, packed cell volume, total protein, and blood glucose.

- Daily monitoring of blood urea nitrogen, urine specific gravity, coagulation indices, and liver enzymes in severely affected patients.

PREVENTION/AVOIDANCE

- Avoid prolonged exposure to cold.
- Monitor and maintain body temperature in anesthetized animals.

POSSIBLE COMPLICATIONS

- Peripheral vasodilation during rewarming may further drop body temperature.
- Iatrogenic burns.
- Return of cool peripheral blood to the heart may precipitate cardiac arrhythmias.
- Cardiac arrest.

EXPECTED COURSE AND PROGNOSIS

Variable—affected by severity of hypothermia, underlying cause, and general patient health status.



MISCELLANEOUS

ASSOCIATED CONDITIONS

None

AGE-RELATED FACTORS

Sick or hypoglycemic neonates can become markedly hypothermic in normal environments.

SEE ALSO

Shock, Cardiogenic

ABBREVIATIONS

- BP = blood pressure
- CNS = central nervous system
- DIC = disseminated intravascular coagulation
- ECG = electrocardiogram

Suggested Reading

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Client Education Handout available online



BASICS

DEFINITION

Clinical manifestations that result from inadequate production of thyroxine (T_4) and 3,5,3'-triiodothyronine (T_3) by the thyroid gland. Characterized by a generalized decrease in cellular metabolic activity.

PATHOPHYSIOLOGY

Acquired Hypothyroidism

- In dogs acquired hypothyroidism can be primary, secondary, or tertiary.
- Primary hypothyroidism is associated with a defect localized to the thyroid gland. The thyroid tissue has been destroyed or replaced and thus becomes less responsive to TSH and T_3 and T_4 levels gradually decline, with a compensatory increase in TSH.
- There are two common forms of primary hypothyroidism. Lymphocytic thyroiditis is an immune-mediated process characterized by chronic and progressive lymphocytic infiltration and destruction of the thyroid gland. This process is gradual and accounts for the slow onset of clinical signs associated with hypothyroidism. The immune-mediated process is associated with production of auto-antibodies, predominantly against thyroglobulin; however, auto-antibodies against T_3 and T_4 have been reported.
- Idiopathic thyroid atrophy is a separate form of thyroid destruction that does not demonstrate an inflammatory component and is caused by the replacement of normal thyroid tissue with adipose tissue.
- Together, these processes account for 95% of the clinical cases of hypothyroidism in dogs, each account for 50% of reported cases. Rare causes of primary hypothyroidism include neoplastic destruction of thyroid tissue, iodine deficiency, infection, and iatrogenic destruction secondary to drugs, surgery, or radioiodine treatment.
- Secondary acquired hypothyroidism is rare. The defect is localized to the pituitary, where the ability to synthesize and secrete TSH is impaired. Secondary hypothyroidism may be caused by pituitary tumors, congenital malformation of the pituitary, infection, or TSH suppression. Drugs, hormones, or concurrent illness can cause TSH suppression.
- Tertiary hypothyroidism (not reported in the veterinary literature) is hypothalamic in origin, and production of TRH is either decreased or non-existent.

Congenital Hypothyroidism

- Congenital hypothyroidism is a rare disease that is categorized as goitrous or non-goitrous. Goiter (enlargement of the thyroid gland) develops when there is increased release of TSH, along with an intact thyroid TSH receptor.

- An autosomal recessive form of congenital hypothyroidism has been reported in toy fox terriers, giant schnauzers, and Abyssinian cats. Affected animals have a thyroid peroxidase deficiency.
- Congenital hypothyroidism is also noted as an element of panhypopituitarism.

SYSTEMS AFFECTED

- Behavioral
- Cardiovascular
- Endocrine/Metabolic
- Gastrointestinal
- Nervous
- Neuromuscular
- Ophthalmic
- Reproductive
- Skin/Exocrine

GENETICS

- No known genetic basis for heritability associated with primary hypothyroidism in dogs.
- An autosomal recessive form of congenital hypothyroidism has been reported in toy fox terriers, giant schnauzers, and Abyssinian cats.

INCIDENCE/PREVALENCE

- Primary hypothyroidism is the most common endocrinopathy in dogs. Prevalence appears to average about 1:250.
- Hypothyroidism is rare in cats.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog, rarely cat

Breed Predilections

Larger-breed dogs are more likely to develop hypothyroidism (golden retriever, Doberman pinscher, Great Dane, Irish setter), though several smaller-breed dogs do appear to also be predisposed (miniature schnauzer, cocker spaniel, poodle, dachshund).

Mean Age and Range

Most commonly seen in middle age dogs, with the average age of onset being 7 years.

Predominant Sex

None

SIGNS

General Comments

Clinical signs associated with hypothyroidism are vague and involve many different systems.

Historical Findings

- Lethargy, weight gain, and hair loss are the most common signs reported by owners (40–50% of all cases).
- Pyoderma (often recurrent), hyperpigmentation of the skin and a dry, brittle hair coat (10% of cases).
- Rarely (< 5% of cases) facial paralysis, weakness, or conjunctivitis.

Physical Examination Findings

- The most commonly findings include dermatologic abnormalities, weight gain,

lethargy, and weakness. Most changes appear to be secondary to decreased metabolism due to a lack of circulating thyroid hormones.

- Dermatologic changes are common but are not noted in every patient.

- A dry, lackluster hair coat may be seen. Bilateral symmetrical non-pruritic truncal alopecia is reported in 88% of hypothyroid dogs. Hair loss is noted in areas of increased wear and usually includes the ventral thorax and neck, ventral abdomen, elbows and tail. Loss of primary hair is most common, with retention of guard hairs, resulting in a short, fine hair coat.
- Seborrhea is common and may be localized or have a more generalized distribution pattern.

- Pyoderma is noted in 14% of hypothyroid dogs and may be recurrent in nature. A lack of thyroid hormone will decrease T-cell function and humoral immunity, causing the skin to become more susceptible to infection. Generalized demodicosis and *Malassezia* spp. infections are common. Though primary dermatologic conditions are non-pruritic, pruritis may accompany secondary parasitic, yeast, or bacterial infections. Chronic changes to the skin can result in thickening and hyperpigmentation.

- Otitis externa.
- Weight gain.
- Decreased activity level.
- Most neurologic signs are associated with polyneuropathy and include weakness, facial nerve paralysis, vestibular signs (usually peripheral), and hyporeflexia. No data support an association between megaesophagus or laryngeal paralysis and hypothyroidism.
- Central nervous system signs, including seizures, ataxia and coma (myxedema coma) are rare.
- In males, decreased fertility, testicular atrophy, poor semen motility, and decreased libido have been reported in hypothyroid dogs. In females, hypothyroidism has been suggested to be associated with prolonged interestrous periods, failure to cycle, decreased libido, and inappropriate mammary gland development. However, data are lacking to support an association between decreased thyroid hormone levels and reproductive failure in males or females.

- Cardiovascular abnormalities, are rare. Bradycardia, arrhythmias, decreased conduction, decreased contractility, and diastolic dysfunction have been reported.
- Ocular changes including corneal cholesterol deposits, KCS, and conjunctivitis are seen in less than 1% of hypothyroid dogs.

Congenital Hypothyroidism

- Lethargy and general inactivity
- Dwarfism
- Alopecia
- Constipation (more common in cats)

CAUSES

- Lymphocytic thyroiditis

HYPOTHYROIDISM

(CONTINUED)

- Idiopathic thyroid atrophy
- Neoplasia
- Pituitary disease
- Congenital abnormalities
- Iodine deficiency (dietary)
- Iatrogenic (secondary to surgery or radiation)

RISK FACTORS

Surgical removal (bilateral) of the thyroid gland



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Primary dermatologic disease
- Other endocrinopathies (hyperadrenocorticism, diabetes mellitus, growth hormone deficiency)
- Pancreatitis
- Nephrotic syndrome
- Hepatobiliary disease

CBC/BIOCHEMISTRY/URINALYSIS

- Useful to rule out non-thyroidal illness.
- Normochromic, normocytic, and nonregenerative anemia is a common finding. 28–32% of hypothyroid dogs demonstrate anemia. The hypothyroid state does not affect erythrocyte lifespan.
- Hyponatremia.
- Hypercholesterolemia is present in over 75% of hypothyroid dogs.
- Hypertriglyceridemia.
- Elevated levels of cholesterol and triglycerides have been associated with atherosclerosis in dogs, although this is rare.
- No specific changes are noted on urinalysis.

OTHER LABORATORY TESTS

- Diagnosing hypothyroidism is complex. The TSH stimulation test is a reliable single test used to diagnose hypothyroidism and is considered the gold standard. However, there is limited access to test reagents and the cost is often prohibitive.
- Several tests are available to assess thyroid function, thyroid hormone levels, and antithyroglobulin antibody levels. These tests include the total T₄, free T₄, endogenous TSH, antithyroglobulin antibodies, anti-T₃ antibodies, anti-T₄ antibodies, total T₃, reverse T₃, and free T₃.
- Combination testing will yield a highly reliable result.

Total T₄

- Initial screening (high sensitivity) test of thyroid function.
- This test measures both protein-bound and free T₄ levels.
- Test is a direct assessment of the ability of the thyroid gland to produce hormone.
- A decreased total T₄ level is a common finding in hypothyroid animals but is not diagnostic of hypothyroidism as concurrent

illness can cause an artificial decrease in total T₄ level.

- Total T₄ level can be measured by ELISA, chemiluminescence, or radioimmunoassay. There is indication that in-house ELISA is less reliable than radioimmunoassay.

Free T₄

- Most valuable as a screening test (high sensitivity).
- Measures metabolically active portion of the total T₄ level.
- Hypothyroid animals would be expected to have a low free T₄ level.
- Concurrent illness has less effect on the free T₄ level compared with the total T₄ level.
- Measurement by equilibrium dialysis (fT₄ED) has been demonstrated to be more reliable than radioimmunoassay because it mitigates the influence of antithyroglobulin antibodies.
- Newer methods of fT₄ analysis utilize chemiluminescent technology with comparable sensitivity and specificity to fT₄ED.

Endogenous TSH Level

- Measurement of endogenous TSH is available using a canine assay.
- Cross-reactivity allows this assay to be used in cats; however, it may be accurate only 50% of the time in cats.
- This test has high specificity and low sensitivity, best used as a confirmatory test and not as a screening test.
- TSH level is expected to be elevated in primary hypothyroid animals due to loss of negative feedback.
- Interpretation of the TSH level requires knowledge of the total or free T₄ level.
- Methods of assessing TSH levels are less sensitive at low levels and evaluation of endogenous TSH cannot be used to diagnose secondary hypothyroidism.

Antithyroglobulin Antibodies

- Antithyroglobulin antibodies include antithyroglobulin, anti-T₃, and anti-T₄ antibodies.
- A positive titer is predictive of immune-mediated thyroiditis, and suggestive of hypothyroidism.
- Anti-T₃ and -T₄ antibodies are similar to T₃ and T₄ and can cross-react to falsely elevate these assay levels. In animals who are slightly hypothyroid (as measured by total T₄), the presence of anti-T₄ antibodies will make it appear as if these animals are euthyroid, leading to a delay in the diagnosis and treatment of hypothyroidism.

TSH Stimulation Test

- Historically considered the gold standard for diagnosing hypothyroidism.
- Pharmaceutical-grade bovine TSH was used to conduct this test; however, production has been halted.
- Recombinant human TSH can be used safely in both dogs and cats to effectively

conduct the test, but is expensive. Therefore, this test is unlikely to become routine and replace the total and free T₄ tests and the TSH assay as the preferred diagnostics.

Total T₃, Reverse T₃, and Free T₃

- Total T₃ measurement is an unreliable indicator of thyroid function.
- The total T₃ level has been demonstrated to be normal in up to 90% of hypothyroid dogs.
- The reverse T₃ level has not been validated in companion animals.
- Evaluation of total T₃, reverse T₃, and free T₃ levels is not recommended to assess thyroid function.

Non-thyroid Factors That Alter Thyroid Function Tests

- In addition to sick euthyroid syndrome, other factors alter the results of thyroid function tests, which may result in a misdiagnosis.
- Most non-thyroid factors cause an artificial decrease in thyroid hormone levels.
- Some drugs can decrease thyroid hormone levels and may result in an animal developing clinical signs of hypothyroidism. Sulfonamides, glucocorticoids, phenobarbital, NSAIDs, and clomipramine can decrease circulating thyroid hormone levels.
- With sulfonamides this effect is noted to occur within weeks of initiation of therapy and disappears 2 weeks after therapy has been discontinued.
- Glucocorticoids inhibit the entire hypothalamic-pituitary-thyroid axis and have a direct effect against thyroid hormone.
- Phenobarbital causes a decrease in thyroid levels only in animals receiving long-term treatment. Phenobarbital should not be administered for 4 weeks prior to thyroid function testing.
- The influence of NSAIDs is variable and evaluation of thyroid function should be made with caution and preferably after stopping NSAIDs well in advance of testing.
- Well-conditioned and athletic dogs consistently have lower total and free T₄ levels. Certain breeds have normal ranges of thyroid hormones that are different from other breeds. Greyhound, Scottish deerhound, Saluki, and whippet have total T concentrations that are well below the mean concentrations. Alaskan sled dogs have serum T₄, T₃, and fT₄ concentrations below the normal reference range.
- Recent vaccination causes a transient increase in circulating auto-antibody levels, which may cause a truly hypothyroid animal to appear euthyroid. Thyroid function testing should not be conducted if a patient has been vaccinated within the previous 2 weeks.

IMAGING

Radiographic Findings

Developmental bone problems (delayed epiphyseal ossification or dysgenesis) are

(CONTINUED)

usually noted with congenital hypothyroidism.

Ultrasonographic Findings

- Significant differences in thyroid gland volume and echogenicity exist between hypothyroid and euthyroid patients.
- No significant difference is noted between euthyroid and sick euthyroid subjects.
- Ultrasonography can be an adjunctive diagnostic tool to assist in the diagnosis of canine hypothyroidism.

PATHOLOGIC FINDINGS

- Lymphocytic thyroiditis is characterized by chronic and progressive lymphocytic infiltration and destruction of the thyroid gland. Cytotoxic T cells initiate inflammation, leading to thyrocyte destruction and parenchymal fibrosis.
- Idiopathic thyroid atrophy is characterized by the replacement of normal thyroid parenchyma with adipose and connective tissue.
- Many cutaneous changes are nonspecific. However, certain findings, including dermal thickening, myxedema, and vacuolation of arrector pili muscles, are most characteristic.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient medical management

CLIENT EDUCATION

- Life-long therapy required.
- Easily managed with oral thyroid hormone supplementation.
- Dose adjustments are common in the early stages of treatment.
- Most clinical signs will resolve over time with appropriate thyroid hormone supplementation.



MEDICATIONS

DRUG(S) OF CHOICE

- Synthetic thyroid hormone supplementation easily treats hypothyroidism.
- Levothyroxine sodium is available as both human and veterinary products.
- Generic forms of the drug should be avoided as human studies have demonstrated wide variability in the bioavailability of generic forms. If a generic form is used, always prescribe the same formulation.
- Hormone supplementation is initiated at 0.02 mg/kg PO q12h. Supplementation levels can be increased to a maximum of 0.8 mg per dog per treatment.
- Supplementation can often eventually be decreased to once daily once proper control is achieved.

- Levothyroxine doses for dogs exceed those for humans and may confuse pharmacists or human endocrinologists.

PRECAUTIONS

Patients with concurrent metabolic conditions (hepatic disease, endocrinopathies, renal disease, cardiac disease) should have supplementation started slowly (about 25% of recommended dose) and slowly increased over time (3 months) to the recommended maintenance level.

POSSIBLE INTERACTIONS

- Glucocorticoids, NSAIDs, furosemide may increase metabolism of levothyroxine.
- GI protectants can decrease absorption and administration should be separated from thyroid hormone supplementation by 2 hours.

ALTERNATIVE DRUG(S)

- If T_4 levels do not normalize after attempting monitoring and treatment with several different brands of levothyroxine, treatment can be attempted with liothyronine (4–6 mg/kg PO q8–12h).
- Monitoring is based on T_3 levels. However, there is no reliable method by which to measure T_3 .



FOLLOW-UP

PATIENT MONITORING

- Thyroid function testing is recommended 6 weeks after therapy has begun and then every 6–8 weeks for the first 6–8 months and then once to twice yearly.
- The total T_4 level should be monitored and timed so that blood is taken 6 hours after pill administration.
- Once stable and well controlled, the total treatment dose may be given once daily with excellent clinical results.
- For animals receiving supplementation once daily, blood should be taken immediately before the medication is given and then again 6 hours later.
- When supplementation therapy is appropriate, the total post-dose T_4 level should be high normal to slightly above normal.
- If the total T_4 level is significantly increased above normal, the medication dose should be decreased or the frequency of administration reduced.
- If the total T_4 level is low, an increase in the dose may be necessary.
- Before increasing dose, assess client compliance, evaluate gastrointestinal status to ensure there is no impact on absorption, and confirm there has been no change in the levothyroxine formulation.

PREVENTION/AVOIDANCE

Adequate hormone supplementation with routine monitoring should avoid recurrence of this condition.

POSSIBLE COMPLICATIONS

- If untreated hypothyroid animals are at increased risk of developing myxedema, myxedema coma and atherosclerosis.
- Oversupplementation of thyroid hormone can result in iatrogenic hyperthyroidism.

EXPECTED COURSE AND PROGNOSIS

- Primary hypothyroidism can be easily and successfully controlled, the prognosis for affected animals, when appropriately treated, is excellent. Resolution of clinical signs is an important predictor of adequate supplementation therapy.
- Significant improvement in attitude, activity level, and alertness should occur within 1 week of starting therapy.
- Dermatologic abnormalities improve slowly, with complete resolution taking up to 3 months.
- Polyneuropathies usually begin improving quickly; complete resolution may take several months.
- Anemia and serum cholesterol levels gradually resolve in the first weeks of therapy.
- Life expectancy expected to be normal.
- Congenital hypothyroidism has a guarded-to-poor prognosis.

H



MISCELLANEOUS

ASSOCIATED CONDITIONS

May rarely be associated with other endocrinopathies.

PREGNANCY/FERTILITY/BREEDING

- No issues relating to pregnancy.
- No definitive evidence suggesting an association with altered fertility.

SEE ALSO

Myxedema and Myxedema Coma

ABBREVIATIONS

- ELISA = enzyme-linked immunosorbent assay
- GI = gastrointestinal
- KCS = keratoconjunctivitis sicca
- NSAID = nonsteroidal anti-inflammatory drug
- T_4 = thyroxine, tetraiodothyronine
- T_3 = liothyronine, 3,5,3'-triiodothyronine
- TRH = thyrotropin-releasing hormone
- TSH = thyroid stimulating hormone

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**Client Education Handout
available online**



BASICS

DEFINITION

- A decrease in PaO_2 , resulting in marked desaturation of hemoglobin.
- PaO_2 at sea level ranges from 80 to 100 mmHg in normal animals.

PATHOPHYSIOLOGY

Six physiologic causes

- (1) low PIO_2
- (2) hypoventilation (increase in PaCO_2)
- (3) mismatching of alveolar ventilation and perfusion so that areas of the lung that are not ventilated properly are still perfused adequately
- (4) alveolar–capillary membrane diffusion defect
- (5) right-to-left cardiac or pulmonary shunting

SYSTEMS AFFECTED

- All organs—oxygen essential for normal cellular function; individual tissue oxygen requirements vary by organ.
- Cardiovascular—can result in focal or global ischemia; if prolonged, can develop arrhythmias and cardiac failure.
- Nervous—brain and CNS most important; hypoxemia can result in irreversible brain damage because there are no large oxygen stores in brain tissue.

SIGNALMENT

Any breed, age, and sex of dogs and cats

SIGNS

Historical Findings

- Episodes of coughing
- Breathing problems—especially open-mouth breathing
- Trauma
- Gagging
- Exercise intolerance
- Cyanosis
- Collapse

Physical Examination Findings

- Tachypnea
- Dyspnea
- Orthopnea
- Pale mucous membranes
- Cyanosis
- Coughing
- Open-mouth breathing
- Tachycardia
- Poor peripheral pulse
- Abnormal thoracic auscultation

CAUSES

- Low PIO_2 —high altitude (the higher the elevation, the lower the barometric pressure, which results in a decrease in PIO_2 ; FIO_2 is fixed at 0.21); suffocation; enclosure in small areas with improper ventilation.
- Hypoventilation—result of inadequate alveolar ventilation; muscular paralysis; upper

airway obstruction; air or fluid in the pleural space; restriction of the thoracic cage, diaphragmatic hernia; CNS disease.

- Mismatching of alveolar ventilation and perfusion—most common cause of hypoxemia and occurs with virtually any lung disease: pulmonary thromboembolism; pulmonary parenchymal disease (infectious or neoplastic); lower airway disease; pneumonia; pulmonary contusions; pulmonary edema; also during anesthesia or prolonged recumbency when a large region of lung becomes atelectatic.
- Alveolar–capillary membrane diffusion impairment—rarely clinically important.
- Right-to-left cardiac or pulmonary shunting—tetralogy of Fallot; ventricular septal defect; reversed patent ductus arteriosus; intrapulmonary arteriovenous shunt.

RISK FACTORS

- Sudden move to higher elevation
- Trauma
- Bronchopneumonia
- Pleural disease
- Anesthesia
- Cardiac disease
- Bronchial disease—chronic bronchitis, feline asthma
- Geriatric pulmonary or cardiac changes
- Diseases associated with risk of embolization, e.g., immune mediated hemolytic anemia, hyperadrenocorticism, neoplasia, pancreatitis, sepsis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Signs of tachypnea and/or dyspnea
- Excitement or anxiety
- Hyperthermia
- Pyrexia
- Head trauma
- Pain

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

N/A

Disorders That May Alter Laboratory Results

- Air bubbles in the arterial blood sample—falsely high PaO_2 values.
- Improper packaging of the arterial blood sample—falsely high PaO_2 values after approximately 30 minutes at room temperature.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- PCV—can be high with chronic condition; can be low if inflammatory or neoplastic.
- Liver enzyme elevation common with organ hypoxia.

OTHER LABORATORY TESTS

Arterial Blood Gases

- Collect arterial blood sample in an anaerobic manner, as follows: Use enough heparin to coat the needle and the inside of the syringe. Collect sample from femoral or dorsal pedal artery. Place a rubber stopper on the needle or covering the hub of the syringe, to prevent room air from entering the sample. Analyze sample within 15 minutes if left at room temperature; place sample on ice to extend safe time for analysis to 2–4 hours.
- Bedside or portable blood gas analyzers—several models available; make analysis more convenient.

IMAGING

Thoracic radiographs and echocardiography—evaluate intrathoracic disease; differentiate pulmonary and cardiac disease.

DIAGNOSTIC PROCEDURES

Pulse Oximetry

- Indirectly determines SaO_2 ; relation between PaO_2 and SaO_2 based on the oxyhemoglobin dissociation curve: $\text{SaO}_2 > 90\%$ when $\text{PaO}_2 > 60 \text{ mmHg}$.
- $\text{SaO}_2 < 95\%$ —considered abnormal, indicates $\text{PaO}_2 < 80 \text{ mmHg}$.
- Best results when probe used on the tongue of animals; thus may be limited to anesthetized, heavily sedated, or seriously ill patients with a low level of consciousness; keep tongue moistened for most accurate readings.
- Other successful probe sites—lip, ear; vulva (female), and prepuce (male); skin between toes; thin skin in the flank area.
- Poor results—least accurate in low-flow states such as hypotension (global low flow) or hypothermia (low flow to skin); falsely low values (usually < 85%) during carboxyhemoglobinemia (smoke inhalation).
- Rectal probes—should become available; will allow readings in awake patients.

Endoscopy or Lung Biopsy

Airway sampling often required to determine primary abnormality resulting in hypoxemia.



TREATMENT

Must identify and correct the primary cause.

OXYGEN THERAPY

- Most common supportive treatment.
- Corrects low-inspired oxygen, hypoventilation, and alveolar–capillary membrane diffusion defects; may not fully correct mismatching of ventilation and perfusion; does not correct right-to-left cardiac or pulmonary shunts and low cardiac output.
- May not be completely beneficial until adequate blood volume is established.

HYPOXEMIA

(CONTINUED)

- Delivery—directly from an oxygen source from the anesthetic machine via a face mask placed securely around the muzzle or from an E-tank fitted with an oxygen regulator through a face mask, intranasal catheter, or oxygen cage.
- Increase in FIO_2 —determined by the oxygen flow rate and the amount of oxygen mixed with room air.
- PPV—may be needed for ARDS or severe hypoventilation.

FLUID THERAPY

- Low cardiac output—fluid administration and inotropic support (e.g., dobutamine or dopamine) important.
- Cardiac failure—requires aggressive medical treatment; diuretics; afterload and preload reduction; inotropic support; oxygen administration; fluids indicated after institution of primary treatment; use caution with type and rate of fluids after initial stabilization.
- Hypovolemic, hemorrhagic, traumatic, or septic shock—requires aggressive fluid administration; crystalloids (90 mL/kg as fast as possible), hypertonic solutions (7% NaCl, 4 mL/kg), colloids (hetastarch, 20 mL/kg), hemoglobin-based oxygen-carrying solutions, or combination.
- Severe pulmonary contusion—hypertonic fluids or colloids, or combination preferred.



MEDICATIONS

DRUG(S) OF CHOICE

For bronchospasm—bronchodilators; terbutaline (0.01 mg/kg SC, IM, or IV q8h).

CONTRAINDICATIONS

- Aggressive fluid administration—not indicated for cardiac failure and pulmonary edema.

- Diuretics—not indicated for shock, low PIO_2 , alveolar–capillary membrane diffusion defects, mismatching of alveolar ventilation and perfusion, and right-to-left shunts.

PRECAUTIONS

- Inotropic drugs—arrhythmias may develop.
- Oxygen toxicity—from prolonged (> 12 hour) exposure to high-concentration (> 70%) oxygen; pulmonary edema, seizures, and death.

POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Decrease in respiratory effort and a decrease in cyanosis (if initially noted)—check efficacy of treatment and support.
- Arterial blood gas—determine resolution.
- Pulse oximetry—alternative; interpret results cautiously with hypotension, hypothermia, smoke inhalation, and non-tongue probe site.

POSSIBLE COMPLICATIONS

- Brain damage—depends on severity and duration of hypoxemia; partial or complete loss of neuronal function; dementia; seizures; loss of consciousness.
- Arrhythmias—may develop secondary to myocardial hypoxia; may be very difficult to treat effectively.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

PREGNANCY/FERTILITY/BREEDING

May adversely affect fetuses, especially during the first trimester of pregnancy.

SEE ALSO

- Cyanosis
- Dyspnea and Respiratory Distress
- Panting and Tachypnea

ABBREVIATIONS

- ARDS = acute respiratory distress syndrome
- CNS = central nervous system
- FIO_2 = fraction of oxygen in inspired air
- PaCO_2 = partial pressure of carbon dioxide in arterial blood
- PaO_2 = partial pressure of arterial oxygen
- PCV = packed cell volume
- PIO_2 = partial pressure of inspired oxygen
- PPV = positive-pressure ventilation
- SaO_2 = saturation of arterial blood with oxygen

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BASICS

DEFINITION

Increased total bilirubin concentration causing yellow tissue discoloration

PATOPHYSIOLOGY

- Bilirubin—derived from degradation of heme-containing proteins; most (80%) from senescent erythrocytes; remainder from other heme-containing proteins (e.g., P450 cytochromes, myoglobin).
- Unconjugated bilirubin—transported in plasma bound to albumin; diglucuronide conjugated after hepatocellular uptake.
- Conjugated bilirubin—transported in bile and expelled into the intestines where most is converted to other products: e.g., urobilinogen can undergo enterohepatic circulation, stercobilin colors feces brown.
- Hyperbilirubinemia—caused by increased bilirubin production (increased RBC destruction; *hemolytic jaundice*); heme exceeding the hepatic capacity for uptake, conjugation, or biliary excretion (*hepatocellular jaundice*), or interrupted biliary elimination (*post-hepatocellular jaundice*).
- Non-hemolytic jaundice is caused by hepatobiliary disease or bile peritonitis.

SYSTEMS AFFECTED

- Skin/Exocrine—skin discoloration (jaundice) reflects serum bilirubin > 2.5 mg/dL.
- Hepatobiliary—retained bile acids and markedly increased bilirubin may contribute to hepatocellular injury.
- Renal/Urologic—extreme hyperbilirubinemia may cause renal tubular injury.
- Nervous—extreme unconjugated hyperbilirubinemia may cause degenerative brain lesions (rare, kernicterus).

SIGNALMENT

Species

Dog and cat

Mean Age and Range

- Most causes—diseases of adult animals
- Young, unvaccinated dogs—at risk for infectious canine hepatitis

Predominant Sex

Adult female pure-bred dogs—at risk for immune-mediated hemolytic anemia

SIGNS

Historical Findings

Increased Formation—Hemolysis

- Vague signs: lethargy, weakness
- Gastrointestinal signs: anorexia, constipation, vomiting, weight loss • Jaundice
- Recent blood transfusion • Severe trauma: bleeding into muscle, abdomen, or hematoma formation • Rhabdomyolysis (rare cause)

Decreased Elimination—Cholestasis

- Vague GI signs: anorexia, vomiting, diarrhea, change in fecal color: non-obstructive jaundice is green, orange; obstructed jaundice is acholic. • Jaundice.

- Change in urine color: orange.
- Abdominal enlargement: if ascites.
- Polyuria and polydipsia.
- Altered mentation: if HE.

Physical Examination Findings

Increased Formation—Hemolysis

- Pallor, tachycardia, tachypnea, weakness, bounding femoral pulses, anemic heart murmur • Jaundice • Hepatomegaly/ Splenomegaly: EMH, RE hyperplasia
- Lymphadenopathy • Bleeding tendencies if thrombocytopenic • Orange feces • Fever • “Gelatinous” feel to skin (vasculopathy)
- Rhabdomyolysis: weakness, pain

Decreased Elimination—Cholestasis

- Weight loss • Jaundice • Hepatomegaly/ Splenomegaly • Abdominal effusion/Mass/Pain • Melenic, Orange, Green, or Acholic feces • Fever

CAUSES

Prehepatic Jaundice

- Hemolytic disorders: immune-mediated hemolysis; certain drugs (propylene glycol carriers in cats, trimethoprim sulfate); SLE; infectious disorders; toxins (e.g. oxidative injury: zinc, onions; phenols); severe hypophosphatemia • Incompatible blood transfusion • Infections—FeLV; *Mycoplasma haemofelis*; heartworm; *Babesia*; *Ehrlichia*; *Cytauxzoon* • Large volume blood resorption—hematomas, body cavities (e.g. hemangiosarcoma, warfarin)

Hepatic Jaundice

- Chronic idiopathic or familial hepatitis
- Adverse drug reactions—e.g., anticonvulsants; acetaminophen; trimethoprim sulfate; carprofen; stanozolol (cats); benzodiazepines (cats) (see Hepatotoxins)
- Cholangitis/cholangiohepatitis • Infiltrative neoplasia—lymphoma
- Cirrhosis (dogs) • Hepatic lipidosis (cats) • Massive liver necrosis: e.g., aflatoxin, cycad, NSAIDs (carprofen), copper associated injury • Systemic illnesses with hepatic involvement—leptospirosis (dogs); histoplasmosis; FIP; hyperthyroidism (cats); toxoplasmosis (cats) • Bacterial sepsis—originating anywhere in the body; may elaborate bacterial products that impair hepatic bilirubin processing/elimination.

Posthepatic Jaundice

Transient or persistent mechanical bile duct obstruction: (1) pancreatitis (transient obstruction); (2) neoplasia—bile duct, pancreas, duodenum; (3) intraluminal duct occlusion—cholelithiasis, sludged bile, liver flukes (cats), immune-mediated duct destruction (sclerosing cholangitis in cats), GB mucocele (dogs); (4) ruptured biliary tree causing bile peritonitis.

RISK FACTORS

- Young unvaccinated dogs—infectious disease, canine infectious hepatitis.
- Breed predisposition for familial hepatic disease—Labrador retriever, Doberman pinscher, Bedlington terrier, Cocker spaniel, Dalmatian

- Middle-aged, obese dogs—pancreatitis
- Anorectic, obese cats—hepatitis
- Lipidosis • Hepatotoxic drugs • Blunt abdominal trauma, chronic biliary tract disease, gallbladder mucocele—bile peritonitis
- Hemolytic anemia



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Prehepatic jaundice—usually abrupt onset; mucous membrane pallor; mild to moderate jaundice; weakness; tachypnea; cardiac murmur with severe anemia.
- Hepatic jaundice—breed risk for familial hepatitis; variable jaundice; otherwise normal mucous membranes; alteration in liver size (large or small); abdominal effusion (pure or modified transudate); polyuria and polydipsia; behavioral abnormalities of HE; coagulopathy.
- Posthepatic jaundice—chronic and/or recurrent bouts of apparent GI signs or pancreatitis with cholelithiasis; moderate or marked jaundice; otherwise normal mucous membranes; diffuse or cranial abdominal pain; cranial abdominal mass; abdominal effusion (septic, nonseptic, or bile peritonitis); bleeding tendencies; acholic feces unless melena.

LABORATORY FINDINGS

Disorders That May Alter Laboratory Results

- Bilirubin assay—based on the diazo reaction; assesses direct-reacting and total serum bilirubin; most yield reasonable total bilirubin results; values for direct bilirubin vary.
- Higher readings in heparinized plasma.
- Sample management—important; total bilirubin may decrease by 50% per hour with direct exposure to sunlight or artificial lighting.
- Hemolysis—variable effects on total bilirubin measured by spectrophotometry.
- Lipemia—falsely increases total bilirubin values measured by endpoint assays.
- Fractionation into conjugated and unconjugated—*unable to define causes of jaundice*, contrary to dogma.

CBC/BIOCHEMISTRY/URINALYSIS

Prehepatic Jaundice

- CBC—severe anemia (usually regenerative); blood smear may reveal autoagglutination, spherocytes, Heinz bodies, or parasites; hemoglobinemia with intravascular hemolysis, normal to low platelets, and normal to high WBCs, with a left shift.
- Biochemistry—normal to high ALT and ALP activity and BUN concentration; normal to low albumin; normal to high globulin; normal glucose and cholesterol; high bilirubin.

Hepatic Jaundice

- CBC—mild nonregenerative anemia; low MCV with chronic liver disease and

ICTERUS

(CONTINUED)

portosystemic shunting; variable WBC count. • Biochemistry—mildly to markedly high ALT ± ALP; normal to low albumin, BUN, glucose, and cholesterol. • Urinalysis—normal to dilute urine; bilirubinuria precedes hyperbilirubinemia; bilirubinuria is important in cats.

Posthepatic Jaundice

- CBC—± mild nonregenerative anemia; variable WBC count. • Biochemistry—increased ALT and moderate to markedly increased ALP; usually normal albumin, BUN, and glucose concentrations; normal to high cholesterol.

OTHER LABORATORY TESTS

- In-Saline autoagglutination slide test—with suspected RBC agglutination; may have reported high MCV. • Direct Coombs' test—submit if no evidence of autoagglutination.
- Osmotic fragility test—detects likelihood of RBC hemolysis tonicity challenge. • Blood smears—hemoparasites, spherocytes, schistocytes, anisocytosis (regenerative).
- Plasma zinc—if hemolytic anemia.
- ANA—with hemolytic anemia. • Serum bile acids—redundant if nonhemolytic jaundice already suspected. • Serology—for infectious diseases (e.g., FeLV, leptospirosis, mycoses) with signs of multisystemic illness and hepatic jaundice. • Abdominal effusion—characterize cell and protein content.
- Coagulation tests—prolonged values, especially PIVKA and PT, with bile duct occlusion; vitamin K₁ responsive. • Microbial culture and sensitivity—blood ± other specimens if inflammatory leukon and suspected bacterial infection (e.g., urinary tract, biliary tract, liver).

IMAGING

- Abdominal radiography—obscured by effusion; may reveal hepatomegaly, mass effect, mineral or gas interface in liver (emphysematous cholecystitis, choleliths); splenomegaly (hemolytic anemia, portal hypertension, abdominal neoplasia); metallic foreign body with zinc-induced hemolysis.
- Thoracic radiography—may reveal metastatic disease; sternal lymphadenopathy (reflecting abdominal disease); general lymphadenopathy (lymphosarcoma, systemic infection [fungal]). • Abdominal ultrasonography—may distinguish parenchymal liver disease from extrahepatic biliary obstruction; characterizes hepatic parenchymal lesions; may disclose abdominal neoplasia; may determine cause of abdominal effusion; used to target lesions, fluid, or cystocentesis sampling (aspirates or needle biopsy).

OTHER DIAGNOSTIC PROCEDURES

- Fine-needle aspiration—cytology of mass, lymph node, hepatic parenchyma, bile.
- Liver biopsy—bacterial culture of liver, bile, and other specimens obtained via celiotomy, blind percutaneous, keyhole, laparoscopic, or

ultrasound-guided techniques. • Surgical intervention—required for diagnosis and treatment of posthepatic disorders.

**TREATMENT**

- Depends on underlying cause
- Inpatient—for initial medical care. • Cage rest—to facilitate liver regeneration or reduce oxygen requirements if severe anemia.
- Diet—important for hepatic and posthepatic jaundice; nutritionally balanced with maximum protein tolerated by patient; carbohydrate based (dogs) with restricted protein for hepatic encephalopathy; restrict sodium if ascites. • Vitamin supplementation—water-soluble vitamins in all patients; parenteral vitamin K₁ for bile duct obstruction or severe cholestasis.

**MEDICATIONS****DRUG(S)**

- Prehepatic jaundice—eliminate inciting cause; see Anemia, Immune-Mediated; whole blood transfusion for life-threatening anemia.
- Hepatic/Posthepatic jaundice—treat specific disorders based on imaging, biopsy, and culture.

CONTRAINDICATIONS

- Avoid known hepatotoxic drugs. • Avoid tetracyclines unless clearly indicated—suppress hepatic protein synthesis, promote hepatic lipidosis. • Avoid analgesics, anesthetics, barbiturates—with hepatic failure.

PRECAUTIONS

- Sedatives—may precipitate HE.
- Corticosteroids—for nonseptic inflammation; increases risk for infection; may aggravate ascites (water and sodium retention), promotes VH (dogs) and hepatic lipidosis (cats).

POSSIBLE INTERACTIONS

Consider influence of altered hepatic metabolism on drug therapy; hypoalbuminemia influences potency of protein-bound drugs, enhancing effects (may lead to toxicity).

**FOLLOW-UP****PATIENT MONITORING**

- Prehepatic jaundice—recheck PCV and blood smears as needed; may require repeat transfusions; taper immunosuppressive drugs.
- Hepatic and posthepatic jaundice—recheck serum biochemical profile as dictated by underlying disease; continue symptomatic

and specific treatments until remission, varies with disease process.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Patients with immune-mediated hemolysis treated with immunosuppressive doses of corticosteroids are predisposed to thromboembolism, gastrointestinal ulcers, and infection. • Patients in hepatic failure: are susceptible to infections, enteric bleeding, and ascites. • Patients with reconstructive biliary surgery have risk for recurrent bacterial cholangitis.

SYNONYM

Jaundice

SEE ALSO

- Anemia, Heinz Body • Anemia, Immune-Mediated • Anemia, Regenerative
- Babesiosis • Blood Transfusion Reactions
- Cholangitis/Cholangiohepatitis Syndrome
- Cholelithiasis • Chronic Hepatitis
- Cirrhosis and Fibrosis of the Liver • Copper Associated Hepatopathy • Gallbladder Mucocele • Haemobartonellosis • Hepatic Failure, Acute • Hepatic Lipidosis
- Hepatitis, Infectious (Viral) Canine
- Hepatitis, Suppurative and Hepatic Abscess
- Hepatotoxins • Liver Fluke Infestation
- Lupus Erythematosus, Systemic (SLE)
- Pancreatitis • Zinc Toxicosis

ABBREVIATIONS

- ALP = alkaline phosphatase • ALT = alanine aminotransferase • ANA = antinuclear antibodies • BUN = blood urea nitrogen • EMH = extramedullary hematopoiesis • FeLV = feline leukemia virus
- FIP = feline infectious peritonitis • HE = hepatic encephalopathy • MCV = mean corpuscular volume • PCV = packed cell volume • PIVKA = proteins invoked by vitamin K absence or antagonism • PT = prothrombin time • RBC = red blood cell
- RE = reticuloendothelial • SLE = systemic lupus erythematosus • VH = vacuolar hepatopathy • WBC = white blood cell

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Consulting Editor Sharon A. Center



Client Education Handout available online

IDIOVENTRICULAR RHYTHM



BASICS

DEFINITION

If conduction of sinus node pacemaker impulses to the ventricles is blocked or the impulses decrease in frequency, the lower regions of the heart automatically take over the role of pacemaker for the ventricles, which results in ventricular escape complexes (Figure 1) or an idioventricular rhythm (Figure 2).

ECG Features

- A series of ventricular escape beats with a heart rate < 65 bpm in dogs and < 100 bpm in cats; heart rates of 65–100 bpm in dogs and 100–160 bpm in cats are often termed accelerated idioventricular rhythms.
- P waves may be absent or may precede, be hidden within, or follow the ectopic QRS complex.
- P waves are unrelated to the QRS complexes.
- QRS configuration—wide and bizarre; similar to that of a ventricular premature complex.

PATOPHYSIOLOGY

- May be hemodynamically important with slow ventricular rates.
- Does not occur in healthy animals.
- Subsidiary pacemakers seem to discharge more rapidly in cats than in dogs.

SYSTEMS AFFECTED

Cardiovascular

GENETICS

N/A

INCIDENCE/PREVALENCE

Unknown

SIGNALMENT*Species*

Dog and cat

Breed Predilections

- Atrial standstill in English springer spaniels and Siamese cats
- Pugs, miniature schnauzers, and Dalmatians prone to conduction abnormalities

Mean Age and Range

N/A

Predominant Sex

N/A

SIGNS*Historical Findings*

- Some animals asymptomatic
- Weakness
- Lethargy
- Exercise intolerance
- Syncope
- Heart failure

Physical Examination Findings

- Irregular rhythm associated with pulse deficits
- Variation in heart sounds

- Possible intermittent “cannon” waves in the jugular venous pulses (with AV block)

CAUSES

- Not a primary disease—a secondary result of a primary disease
- The escape rhythm is a safety mechanism to maintain cardiac output

Causes of Sinus Bradycardia and Sinus Arrest

- Increased vagal tone (high intracranial pressure, high ocular pressure)
- Drugs—digoxin, tranquilizers, propranolol, quinidine, and anesthetics
- Addison’s disease
- Hypoglycemia
- Renal failure
- Hypothermia
- Hyperkalemia
- Hypothyroidism

Causes of AV Block

- Congenital
- Neoplasia
- Fibrosis
- Lyme disease

RISK FACTORS

N/A

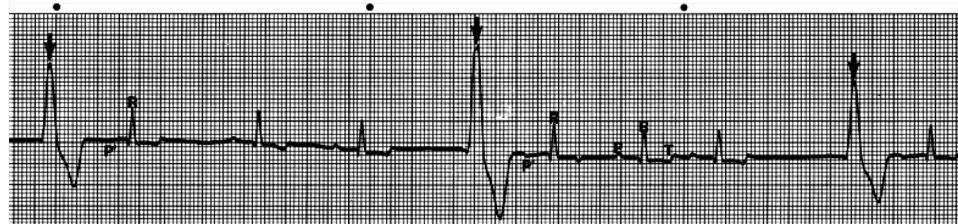


Figure 1.

Ventricular escape complexes (arrows) during various phases in the dominant sinus rhythm in a dog during anesthesia. The sinus rate increased (not shown) after anesthesia was stopped; 1/2 cm-1 mv. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

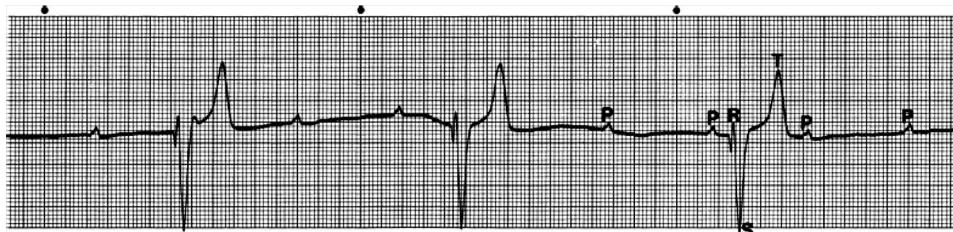


Figure 2.

Complete heart block. The P waves occur at a rate of 120, independent of the ventricular rate of 50. The QRS configuration is a right bundle branch block pattern. The regular rate and stable QRS indicate that the rescuing focus is probably near the AV junction. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

IDIOVENTRICULAR RHYTHM

(CONTINUED)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Ventricular tachycardia—dogs have a cardiac rate > 100 bpm; cats > 150 bpm.
- Slow heart rate in animals with right bundle branch block, left bundle branch block, or left anterior fascicular block; animals with these disturbances have the P waves associated with the QRS complexes.

CBC/BIOCHEMISTRY/URINALYSIS

- No specific findings
- Complete blood testing may suggest a metabolic abnormality

OTHER LABORATORY TESTS

- Drug toxicity
- Lyme's titer in animals with complete AV block

IMAGING

Echocardiogram may show structural heart disease.

DIAGNOSTIC PROCEDURES

Electrocardiography

PATHOLOGIC FINDINGS

Depend on underlying cause



TREATMENT

APPROPRIATE HEALTH CARE

- Rhythm is an escape or safety mechanism for maintaining cardiac output; do *not* direct treatment toward suppressing this escape rhythm, but toward the primary disease process that allows the escape rhythm to assume pacemaker control of the heart.
- Symptomatic treatment is directed toward increasing the heart rate.

NURSING CARE

May be required for underlying disease.

ACTIVITY

Symptomatic animals may require cage rest.

DIET

No modifications or restrictions unless required for management of the underlying condition.

CLIENT EDUCATION

Inform of the need to seek and specifically treat an underlying cause.

SURGICAL CONSIDERATIONS

Pacemaker implantation may be necessary.



MEDICATIONS

DRUG(S) OF CHOICE

- Atropine or glycopyrrolate usually indicated to block vagal tone or increase the heart rate.
- If those drugs are ineffective, isoproterenol, dopamine, dobutamine, or artificial pacing may be needed.

CONTRAINDICATIONS

Lidocaine, procainamide, quinidine, propranolol, diltiazem, or any other drug that slows the cardiac rate or reduces contractility.

PRECAUTIONS

Atropine is briefly vagotonic immediately post-injection and can temporarily exacerbate the condition.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Serial ECG may show clearing of the lesion or progression to complete heart block.
- Serial blood profiles may be needed to monitor progress of the primary disease process.
- Serial echocardiograms may show improvement or progressive changes in cardiac structure.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Prolonged bradycardia may cause secondary congestive heart failure or inadequate renal perfusion.

EXPECTED COURSE AND PROGNOSIS

- Arrhythmia may abate when the primary disorder is corrected.
- Guarded if condition is associated with cardiac or metabolic disorder; poor if the rate is not increased pharmacologically or if underlying cause cannot be identified and treated.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

SEE ALSO

- Atrial Standstill
- Atrioventricular Block, Complete, chapters

ABBREVIATIONS

- AV = atrioventricular
- ECG = electrocardiogram

INTERNET RESOURCES

www.vetgo.com/cardio

Suggested Reading

Kittleson MD. Electrocardiography. In: Kittleson MD, Kienle RD, eds., Small Animal Cardiovascular Medicine. St. Louis, MO: Mosby, 1998, pp. 72–94.

Tilley LP, Smith FW. Essentials of Electrocardiography: Interpretation and Treatment, 4th ed. Ames, IA: Wiley Blackwell, 2016 (in preparation).

Tilley LP, Smith FWK, Jr. Electrocardiography. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., Manual of Canine and Feline Cardiology, 5th ed. St. Louis, MO: Saunders Elsevier, 2015 (in press).

Author Larry P. Tilley

Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.



Client Education Handout
available online



BASICS

OVERVIEW

- Adynamic (paralytic, functional) ileus is defined as a transient and reversible intestinal obstruction resulting from inhibition of bowel motility.
- Lack of peristalsis of stomach, small bowel, or large bowel causes functional obstruction, as intestinal contents accumulate in the dependent areas of the gastrointestinal tract instead of being propelled in an aboral direction.
- Ileus is not a primary disease but a secondary complication of a number of disorders.
- Adynamic ileus is thought to occur secondary to electromechanical dissociation of the intestinal musculature due to increased sympathetic tone, release of humoral inhibitory factors (catecholamines, vasopressin, endogenous opiates), impaired release of prokinetic hormones (neurotensin, motilin), or hypokalemia.
- Secondary causes of intestinal pseudo-obstruction have been subclassified into developmental, infectious, inflammatory, auto-immune, metabolic, paraneoplastic, endocrine, and toxic etiologies.
- Lymphocytic leiomyositis represents a visceral myopathic form of chronic intestinal pseudo-obstruction that has been described in humans, dogs, horses, and cats. It is defined as lymphocytic infiltration of the muscularis propria and is thought to represent an auto-immune response to the myofibers of the muscularis propria layer of the bowel by T-lymphocytes.

SYSTEMS AFFECTED

- Gastrointestinal
- Autonomic nervous system

SIGNALMENT

Cat and dog

SIGNS

- Anorexia
- Vomiting
- Regurgitation
- Lethargy
- Diarrhea
- Weight loss
- Mild abdominal distention or discomfort secondary to accumulation of gas in the hypomotile bowel
- Failure to auscultate gut sounds after 2–3 minutes suggests ileus
- Gut sounds can be increased during the initial state (partial loss of motility).

CAUSES & RISK FACTORS

- Surgery (especially gastrointestinal surgery)
- Electrolyte imbalance (hypokalemia, hypomagnesemia, hypocalcemia)

- Acute inflammatory lesions of the bowel, peritoneal cavity, pancreas, or other abdominal organs
- Unrelieved mechanical obstruction
- Intestinal ischemia
- Gram-negative sepsis
- Endotoxemia
- Shock
- Retroperitoneal injury
- Uremia
- Autonomic neuropathies (dysautonomia, spinal cord injury)
- Visceral myopathies associated with auto-immune disease
- Use of anticholinergic drugs
- Intestinal overdistension (aerophagia)
- Lead poisoning
- Stress (cold and noise)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Adynamic ileus must be differentiated from mechanical obstruction caused by:
 - Intestinal foreign bodies
 - Inflammatory bowel disease
 - Intussusception
 - Intramural abscess
 - Incarcerated or strangulated hernia
 - Volvulus
 - Mesenteric infarction
 - Parasites
 - Adhesions
 - Postoperative stricture
 - Impaction
 - Congenital malformation
 - Inflammatory or traumatic lesions
 - Neoplasia

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram changes depend on primary cause of ileus.
- Serum chemistry profiles and urinalysis help assess electrolyte disturbances (especially hypokalemia) and presence of azotemia.

OTHER LABORATORY TESTS

- Measurement of pancreatic lipase concentration (Spec or SNAP cPL or fPL) to assess for pancreatitis.
- Fecal parvovirus ELISA test in puppies with ileus and diarrhea.

IMAGING

Abdominal Radiographic Findings

- Stomach and/or intestinal loops are distended with gas and fluid. Common radiographic patterns include:
 - Generalized gas ileus—consider aerophagia, smooth muscle paralyzing drugs, generalized peritonitis, or enteritis
 - Generalized fluid ileus—consider enteritis, diffuse intestinal neoplasia
 - Localized gas ileus—consider localized peritonitis (pancreatitis), early bowel

obstruction, disruption of the arterial supply

- Localized fluid ileus—consider foreign body, neoplastic obstruction, intussusception.

Ultrasonography

- Differentiate adynamic ileus from mechanical intestinal obstructions.
- Identify pancreatitis or peritonitis.
- Careful evaluation of the intestinal layers for loss of normal layering associated with infiltrative neoplasia, thickening of the muscularis propria layer and/or submucosal layer associated with inflammatory bowel disease or small cell lymphoma, and attenuation of the muscularis layer associated with fibrosis secondary to leiomyositis.

DIAGNOSTIC PROCEDURES

BIPS (Barium-Impregnated Polyethylene Spheres)

- Confirm adynamic ileus.
- Delayed gastrointestinal transit along with retention of BIPS in the stomach.
- Scattering of BIPS throughout the entire upper gastrointestinal tract.

Upper Gastrointestinal (GI) Series

Upper GI series can be performed to help assess for presence of partial intestinal obstructions or delayed gastric and intestinal motility. Gastric and intestinal transit times must be interpreted cautiously following administration of liquid barium in light of marked variation in emptying times from animal to animal, and the stress of hospitalization can delay gastric and intestinal transit times.

Other Procedures to Consider

- Non-invasive electrogastrography is used experimentally to assess gastric myoelectrical activity in dogs.
- Abdominocentesis with peritoneal effusion to confirm peritonitis.
- Gastrointestinal endoscopy or exploratory laparotomy to rule out mechanical obstruction.
- Full-thickness intestinal biopsies are necessary to diagnose intestinal leiomyositis because the disorder affects the muscularis propria layer of the bowel which is typically not accessible via endoscopic biopsy.
- Spinal radiographs, myelogram, spinal MRI, CT, CSF analysis to identify spinal cord injury.
- Ocular response test with 0.1% pilocarpine and 0.25% physostigmine for dysautonomia.



TREATMENT

- Identify and treat the primary underlying cause.
- Correct electrolyte abnormalities (especially hypokalemia) if present.

ILEUS

(CONTINUED)

- Use of prokinetic drugs such as cisapride, metoclopramide or erythromycin should be considered, depending on the underlying cause.
- Gastrointestinal decompression of the stomach via nasogastric tube is beneficial in select cases.



MEDICATIONS

DRUG(S)

- Metoclopramide is most effective when administered as a CRI (1–2 mg/kg/24h). Intravenous bolus injections (0.4 mg/kg IV q6h) are less effective in light of the relatively short half-life (90 min) in dogs.

Metoclopramide does not affect colonic motility and should be avoided in animals with colonic ileus or megacolon.

- Cisapride (0.3–0.5 mg/kg q12h) is a far more potent and effective prokinetic compared to metoclopramide and affects gastric, small intestinal, and colonic motility.
- Erythromycin (1–2 mg/kg PO q12h) has prokinetic activity on the stomach and small intestine.
- Cyclosporine (5 mg/kg q12–24h) can be administered for management of intestinal leiomyositis or other immune-mediated disorders affecting the intestinal tract.
- Prednisone (1 mg/kg q12h with progressive tapering over 10–12 weeks) can be administered for management of leiomyositis or inflammatory bowel disease.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Anticholinergic drugs (e.g., atropine, glycopyrrrolate)

- Opiates (e.g., morphine, hydromorphone, oxymorphone, butorphanol)
- Opiate antidiarrheals (e.g., paregoric, diphenoxylate hydrochloride/atropine sulfate, loperamide hydrochloride)



FOLLOW-UP

PATIENT MONITORING

- Monitor and correct electrolyte imbalance if present.
- Abdominal auscultation to evaluate gastrointestinal motility.
- Survey abdominal radiographs to evaluate gastric and intestinal distension.

PREVENTION/AVOIDANCE

Avoid anticholinergic drugs and opiates if not indicated.

POSSIBLE COMPLICATIONS

Animals with adynamic ileus are predisposed to the development of intestinal dysbiosis, bacterial translocation, and sepsis.

EXPECTED COURSE AND PROGNOSIS

Prognosis depends on successful resolution of primary disease process.



MISCELLANEOUS

ASSOCIATED CONDITIONS

See "Causes & Risk Factors"

PREGNANCY/FERTILITY/BREEDING

Ileus has been reported in a lactating bitch with hypomagnesemia and hypocalcemia.

SYNONYMS

- Adynamic ileus—functional ileus, paralytic ileus.
- Pseudo-obstruction—chronic, more segmental adynamic ileus.
- Mechanical ileus—generally addressed in current literature as mechanical obstruction.

ABBREVIATIONS

- CSF = cerebrospinal fluid
- CT = computed tomography
- ELISA = enzyme-linked immunosorbent assay
- MRI = magnetic resonance imaging

Suggested Reading

Guilford WG. Motility disorders of the bowel. In: Guilford WG, Center SA, Strombeck DR, Williams DA, Meyer DJ. Strombeck's Small Animal Gastroenterology, 3rd ed. Philadelphia: Saunders, 1996, pp. 335–336. Couraud L, Jermyn K, Yam PS, et al. Intestinal pseudo-obstruction, lymphocytic leiomyositis and atrophy of the muscularis externa in a dog. Vet Rec 2006, 159(3): 86–87.

Novellas R, Simpson KE, Gunn-Moore DA, Hammond GJ. Imaging findings in 11 cats with feline dysautonomia. J Feline Med Surg 2010, 12(8):584–591.

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Client Education Handout
available online

ILICIT/CLUB DRUG TOXICOSIS



BASICS

OVERVIEW

Intoxication with illicit and club drugs covers a wide range of pharmaceuticals. Included in this list are barbiturates, benzodiazepines (see Benzodiazepines and Other Sleep Aids Toxicosis), cocaine, GHB, LSD, marijuana, MDMA, methamphetamine and other designer amphetamines (see Amphetamines and ADD/ADHD Medication Toxicosis), opioids, and PCP.

PATHOPHYSIOLOGY

- Barbiturates: sedative hypnotics with anticonvulsant effects causing CNS depression.
- Cocaine: increases CNS norepinephrine, serotonin and dopamine levels, increases catecholamine release and is a myocardial stimulant causing CNS and cardiac stimulatory signs.
- GHB: synthetic GABA derivative causing CNS depression.
- LSD: CNS stimulation and hallucinations by increasing serotonin and glutamate in the CNS, binds dopamine and α -adrenergic receptors.
- Marijuana: binds to cannabinoid receptors in the CNS, and affects dopamine, GABA, histamine, 5-HTP, norepinephrine, and prostaglandin levels leading to sedation or agitation.
- MDMA: increases serotonin, catecholamine and dopamine in the CNS, leading to CNS stimulation and hallucinations.
- Opioids: bind to opioid receptors causing CNS depression.
- PCP: Inhibits glutamate and stimulates α -adrenergic receptors, which potentiates the effects of norepinephrine, epinephrine, and serotonin. It is a sympathomimetic and hallucinogen.

Systems Affected

- Cardiovascular: Cocaine, GHB, LSD, MDMA, methamphetamine, PCP—arrhythmias, hypertension; Barbiturates, marijuana, opioids—arrhythmias, hypotension.
- Musculoskeletal: Cocaine, PCP—tremors.
- Nervous: Cocaine, LSD, MDMA—stimulatory effect; Barbiturates, GHB—depressive effect; Marijuana, opioids, PCP—sedative to stimulatory effects, ataxia.
- Ophthalmic: Cocaine, LSD, MDMA—mydriasis; Opioids – miosis.
- Respiratory: Barbiturates, opioids—respiratory depression (rare).

SIGNS

- Barbiturates—sedation (rarely agitation), ataxia, bradycardia, hypotension, respiratory depression (rare), coma.
- Cocaine—agitation, mydriasis, tachycardia, hypertension, tremors, seizures.
- GHB, opioids—lethargy, weakness, coma, respiratory depression.
- LSD—mydriasis, disorientation, hallucinations, agitation (rarely sedation), tachycardia.
- Marijuana—sedation (sometimes agitation), ataxia,

hypotension, coma.

- MDMA—agitation, mydriasis, hyperthermia, tachycardia, tremors, hallucinations, seizures, death.
- PCP—depression to agitation, hypertension, tachycardia, tremors, seizures.

CAUSES & RISK FACTORS

Ingestion of club drugs may occur in animals that live with people who take these pharmaceuticals or police dogs.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Barbiturates, GHB, opioids—meningitis, meningoencephalitis, hepatic encephalopathy, ethanol, ethylene glycol, phenothiazines.
- Cocaine—caffeine, metaldehyde, MDMA.
- LSD, PCP—ketamine, MDMA, psilocybin.
- Marijuana—psilocybin, MDMA, amphetamines, benzodiazepines, barbiturates, serotonergic medications (SSRIs, TCAs, MAOIs).
- MDMA—meningitis, meningoencephalitis, hepatic encephalopathy, amphetamines, cocaine, metaldehyde, psilocybin, serotonergic medications (SSRIs, TCAs, MAOIs).

CBC/BIOCHEMISTRY/URINALYSIS

No direct abnormalities. May detect CK and K elevation (rhabdomyolysis) and myoglobinuria secondary to tremors.

OTHER LABORATORY TESTS

OTC illicit drug screens (urine) are available for barbiturates, benzodiazepines, cocaine, marijuana, MDMA, methamphetamine, opioids, and PCP. The OTC tests are not approved for use in animals but appear to be reliable except for the marijuana test (false negatives). All can be detected using GC/MS in a human hospital or diagnostic laboratory but turn-around time decreases the usefulness of these tests.



TREATMENT

- Inpatient care should be provided in a dark quiet place. Thermoregulation is important, along with fluid therapy to maintain body temperature and BP. Fluids will also help to protect the kidneys from myoglobinuria.
- Monitor for respiratory depression (barbiturates, opioids). Intubate and ventilate if needed.
- Emesis (if asymptomatic and recent ingestion) or gastric lavage (if large amount ingested).



MEDICATIONS

DRUG(S)

- Activated charcoal (1–2 g/kg PO) with cathartic (if severe signs are expected).

- Agitation: phenothiazines (acepromazine 0.025–0.05 mg/kg IV, titrate up as needed); cyproheptadine (dog, 1.1 mg/kg; cat, 2–4 mg PO q4–6h or can be given rectally if vomiting).
- Agitation, seizures: benzodiazepines (diazepam 0.5–2 mg/kg IV) (see "Contraindications").
- Tremors: methocarbamol (dog, cat 50–150 mg/kg IV).
- Tachycardia: propranolol (dog, cat 0.02 mg/kg IV).
- Naloxone: reversal agent for opioids (dog, cat 0.01–0.1 mg/kg IV).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Do not use diazepam when treating agitation secondary to MDMA (increases dysphoria and morbidity).



FOLLOW-UP

PATIENT MONITORING

Blood pressure, heart rate, urine color: q1h, then less frequently as the patient remains stable.

EXPECTED COURSE AND PROGNOSIS

Signs occur quickly (within minutes to hours). Most will have a good prognosis if treated and will recover in 24–36 hours. Marijuana ingestion signs could last up to 72 hours.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Barbiturates, LSD, cocaine, and MDMA have been associated with severe birth defects in humans and animals. Opioids and PCP cross the placenta and have been associated with fetal intoxications and low birth weight.

SEE ALSO

- Amphetamines and ADD/ADHD Medication Toxicosis
- Antidepressant Toxicosis—SSRIs and SNRIs
- Benzodiazepines and Other Sleep Aids Toxicosis

ABBREVIATIONS

- CK = creatine kinase
- GHB = gamma hydroxybutyric acid
- LSD = lysergic acid diethylamide
- MAOI = monoamine oxidase inhibitor
- MDMA = methylenedioxymethamphetamine, ecstasy
- PCP = phencyclidine
- SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant

Suggested Reading

Bischoff K. Toxicity of drugs of abuse. In: Gupta RC, ed., Veterinary Toxicology: Basic and Clinical Principles, 2nd ed. New York: Elsevier, 2012, pp. 469–489.

Author Tina Wismer

Consulting Editor Lynn R. Hovda

IMMUNODEFICIENCY DISORDERS, PRIMARY



BASICS

DEFINITION

Diminished ability to mount an effective immune response due to heritable defects in the immune system.

PATHOPHYSIOLOGY

- Defects in the cell-mediated, humoral, complement, and phagocytic systems have all been described in the veterinary literature.
- Defects involving the humoral immune response—associated with a high susceptibility to bacterial infection.
- Defects involving the cell-mediated immune response—associated with a high susceptibility to viral, fungal, and protozoal infections.
- Defects in the phagocytic or complement system—associated with disseminated infection.

SYSTEMS AFFECTED

- Hemic/Lymphatic/Immune—defect in a specific cell population in lymphoid tissue.
- Skin/Exocrine/Respiratory/Gastrointestinal—chronic or recurrent infections.
- Other organ systems—dissemination of infection, failure to thrive.

GENETICS

Typically breed-specific with variable modes of inheritance.

INCIDENCE/PREVALENCE

Rare

SIGNALMENT

Species

Dog and cat

Breed Predilections

- X-linked severe combined immunodeficiency—basset hounds, Cardigan Welsh corgis.
- Severe combined immunodeficiency disease—Jack Russell terriers.
- IgA deficiency—beagles, German shepherds, and Chinese Shar-Peis.
- IgM deficiency—Doberman pinschers.
- Thymic hypoplasia—dwarfed Weimaraners.
- Cyclic hematopoiesis—gray collies.
- Chediak-Higashi syndrome—Persian cats.
- Leukocyte adhesion deficiency—Irish setters.
- Complement deficiency—Brittany spaniels.
- Bactericidal defect—Doberman pinschers.
- Transient hypogammaglobulinemia—Samoyeds.

Mean Age and Range

Primary immunodeficiency diseases typically expressed in the first year of life.

Predominant Sex

X-linked recessive severe combined immunodeficiency disease of basset hounds—males affected and females are carriers.

SIGNS

General Comments

Depends on the level at which the immune response is defective; ranges from chronic respiratory and gastrointestinal signs and skin infections to life-threatening conditions.

Historical Findings

- High susceptibility to infection and failure to respond to appropriate, conventional antibiotic therapy.
- Lethargy.
- Anorexia.
- Skin infection.
- Failure to thrive.
- Signs often appear when maternal antibody concentrations decline.
- Vaccine-induced disease by modified live virus preparation.

Physical Examination Findings

- Hallmark—failure to thrive.
- Clinical signs attributable to infections.

CAUSES

Congenital



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Patients must be rigorously evaluated for underlying disease process that may cause secondary (acquired) immunodeficient state (e.g., hyperadrenocorticism, FeLV, and FIV).
- Patients are typically young with recurrent infection that fails to respond to conventional treatment.

CBC/BIOCHEMISTRY/URINALYSIS

CBC may indicate deficiencies in specifically affected cell lines or chronic inflammation.

OTHER LABORATORY TESTS

- Serum protein electrophoresis—demonstrate gross deficiency in immunoglobulin concentration.
- Serum immunoglobulin quantitation—evaluate humoral immune system, identify selective immunoglobulin deficiency, support diagnosis of agammaglobulinemia.
- The lymphocyte transformation test—evaluate the cell-mediated immune system and identify animals with T-lymphocyte deficiency.
- Bactericidal assays—evaluate neutrophil function.
- Serum concentration of complement components—diagnose complement deficiency.

- Enumeration of lymphocyte subsets by immunofluorescence with monoclonal antibodies—identify deficiency of specific cell lines.

- Other more specific tests to evaluate immune function in veterinary species are available, but obtaining reliable results generally requires access to research laboratories that perform these tests.

DIAGNOSTIC PROCEDURES

In some patients, bone marrow and lymph node biopsy aids in classifying the type of immune deficiency.

PATHOLOGIC FINDINGS

- Lesions vary; depend on the specific defect; most are the result of recurrent or opportunistic infection involving the skin, ear canal, and respiratory and gastrointestinal systems.
- Lesions of septicemia common in animals with severe defects.
- T-lymphocyte defects—hypoplastic or dysplastic lesions of the thymus and T-lymphocyte-dependent areas of secondary lymphoid tissues.
- B-lymphocyte defects—hypoplastic or dysplastic lesions of the bone marrow or B-lymphocyte-dependent areas of secondary lymphoid tissues.
- Lymphoid hypoplasia or hyperplasia may be seen, depending on the overall defect and the occurrence of infection.



TREATMENT

APPROPRIATE HEALTH CARE

- Hospitalization may be necessary to control life-threatening infection.
- Outpatient management possible for some patients.

NURSING CARE

Supportive care appropriate to the nature of the infection.

ACTIVITY

Determined largely by the severity of the defect and the occurrence of infection.

DIET

- Dietary management may be required to ensure that the patient is maintained at an adequate level of nutrition.
- Potential sources of infectious agents such as raw meat must be avoided.

CLIENT EDUCATION

- Inform client that the animal cannot be cured.
- Discuss why the patient has high susceptibility to infection.

(CONTINUED)

IMMUNODEFICIENCY DISORDERS, PRIMARY

- Discuss and advise as to the heritability of the disease.
- Discuss the possibility of littermates being affected.
- Avoid exposure to ill animals.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Antibiotics to control infections
- γ -Globulin or plasma preparations can be used in conjunction with antibiotics to control infection in patients with humoral defect.
- Symptomatic treatment for secondary disease states.

CONTRAINDICATIONS

γ -Globulin or plasma preparations should not be administered to patients with selective IgA deficiency because many affected patients have high concentrations of anti-IgA antibodies and may develop anaphylaxis.

PRECAUTIONS

Modified live virus vaccines should not be administered to patients with suspected T-lymphocyte deficiencies because they may induce disease in these patients.

**FOLLOW-UP****PATIENT MONITORING**

- For clinical signs of secondary infection.
- Routine physical examination to assess efficacy of antibiotic therapy.

PREVENTION/AVOIDANCE

- Do not breed affected animals.
- Pedigree analysis to determine the mode of inheritance and prevent propagating the defect.

POSSIBLE COMPLICATIONS

Infection

EXPECTED COURSE AND PROGNOSIS

- The severity of the defect determines the course and prognosis.
- Patients with minor defects can be successfully managed.

**MISCELLANEOUS***Suggested Reading*

Datz CA. Noninfectious causes of immunosuppression in dogs and cats. Vet Clin North Am Small Anim Pract 2010, 40(3):459–467.

Gershwin LJ. Autoimmune diseases in small animals. Vet Clin North Am Small Anim Pract 2010, 40(3):439–457.

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Consulting Editor Alan H. Rebar

I

IMMUNOPROLIFERATIVE ENTEROPATHY OF BASENJIS



BASICS

OVERVIEW

- An immunologically mediated disease characterized by progressive, chronic intermittent diarrhea, anorexia, and weight loss. These are associated with an intense lymphoplasmacytic, infiltrative gastroenteritis or enteritis and concurrent evidence of protein-losing enteropathy, malabsorption, and maldigestion.
- Hypergammaglobulinemia is present due to increased concentrations of serum IgA.
- Systems affected include gastrointestinal, immune, skin, renal, endocrine, and hepatobiliary.

I

SIGNALMENT

- Young to middle-aged Basenji—usually < 3 years of age
- Related dogs often affected

SIGNS

- Chronic intermittent diarrhea
- Severe progressive weight loss
- Anorexia often preceding diarrhea
- Bilaterally symmetric alopecia
- Decreased body condition score
- Attitude—usually bright and alert
- Vomiting is variable in severity but common

CAUSES & RISK FACTORS

- Pathogenesis is unclear but an interaction between abnormal immune responses, genotype and possibly a contribution by environmental factors is hypothesized.
- Mode of inheritance is not known.
- Episodic worsening of symptoms has been associated with stressful events—boarding, estrus, transport, vaccination, etc.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Lymphangiectasia, lymphoplasmacytic enteritis, eosinophilic enteritis, histoplasmosis, exocrine pancreatic insufficiency, intestinal lymphoma, intestinal microbial dysbiosis, giardiasis, metabolic disorders, intestinal parasitism.

CBC/BIOCHEMISTRY/URINALYSIS

- Hypoproteinemia
- Severe hypoalbuminemia
- Hyperglobulinemia
- Mature neutrophilia often present
- Poorly regenerative anemia associated with chronic inflammatory disease
- Moderately increased hepatic enzymes—seen with advanced disease

OTHER LABORATORY TESTS

- Hypergammaglobulinemia due to increased serum IgA.
- Depression of xylose absorption curve correlates with severity of clinical disease.
- May have hypergastrinemia and hyperchlorhydria.
- No one test or histologic finding is definitive or pathognomonic.

IMAGING

Abdominal ultrasound may demonstrate diffuse small bowel thickening (4–6 mm) or normal gastrointestinal wall layering, and lack of other visceral abnormalities.

OTHER DIAGNOSTIC PROCEDURES

- Endoscopic appearance of the small bowel usually appears abnormal but may be normal. Biopsies are always required for an accurate diagnosis.
- Genetic testing (DNA) is not available at this time.

PATHOLOGIC FINDINGS

- Consistent pathologic lesions include uniform thickening of the small bowel, generalized infiltration of the intestinal lamina propria with lymphocytes and plasma cells, and blunting and fusion of villous tips.
- May be gastric rugal fold hypertrophy, lymphocytic gastritis and/or gastric mucosal atrophy, blunting and widening of intestinal villi, and mild dilation of lacteals.
- Presence and severity of gastric lesions do not correlate with severity of intestinal lesions.
- Other associated lesions include thyroid parafollicular cell atrophy, ulceration of the pinna, gastric acinar atrophy, and glomerulonephritis.



TREATMENT

- Outpatient medical management unless dehydration or other severe complications exist.
- Advise clients not to breed affected dogs or their littermates.
- Minimize stressful episodes.
- Use dietary trials, often with reduced long chain triglycerides, to determine what diet is best tolerated.



MEDICATIONS

DRUG(S)

Immunosuppressive/Anti-inflammatory Drugs

- Variable success reported but considered the mainstay of treatment.

- Prednisone (1 mg/kg PO q12h for 2–4 weeks, then slowly taper over 3–4 months to achieve 0.5–1 mg/kg PO q48h).
- Chlorambucil (0.25 mg/kg PO q72h with monitoring for adverse effects) or other immunosuppressive medications can be tried.

Antibiotics

- Trials of antibiotics are variably helpful for affected individuals that may have intestinal microbial dysbiosis.
- Metronidazole (10–20 mg/kg PO q12–24h).
- Tylosin (5–10 mg/kg PO q24h).

Nutritional Supplements/Adjunctive Treatment

- Use of omega-3 fatty acid-rich diets or supplements is thought to potentially favor improved membrane stability and decreased inflammatory responses in the affected gut but there is little specific data available to support this hypothesis.
- Use of probiotics is commonly advised and may favor reduced risk of dysbiosis and a lowered state of inflammatory responses by the gut associated lymphoid tissues but no specific data are available to support this hypothesis.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Anticholinergics contraindicated



FOLLOW-UP

- Diarrhea and weight loss usually show initial improvement with treatment.
- Recurrence of signs is common.
- Long-term prognosis poor over the course of months to a few years.



MISCELLANEOUS

Suggested Reading

- Breitschwerdt EB. Immuno-proliferative enteropathy of Basenjis. Semin Vet Med Surg Small Anim 1992, 7:153–161.
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Author Mark E. Hitt

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Client Education Handout
available online



BASICS

DEFINITION

Inability to retain feces, resulting in involuntary passage of fecal material.

PATHOPHYSIOLOGY

- Reservoir fecal incontinence develops when disease processes reduce the capacity or compliance of the rectum.
- Sphincter incontinence develops when the external anal sphincter is anatomically disrupted (i.e., non-neurogenic sphincter incontinence) or denervated (i.e., neurogenic sphincter incontinence).
- Neurogenic sphincter incontinence can be caused by pudendal nerve damage, sacral spinal cord disease, autonomic dysfunction, and generalized peripheral neuropathy or myopathy.
- Damage to, or degeneration of, the levator ani and coccygeus muscles may also contribute.

SYSTEMS AFFECTED

- Gastrointestinal • Nervous

GENETICS

No known genetic basis for development of any types of incontinence—reservoir, sphincter or neurogenic.

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

- Dog and cat.
- Although any age animal may be affected, incidence increases in older patients.

SIGNS

Historical Findings

- Reservoir incontinence—promotes an urge to defecate; signs include frequent, conscious defecation without dribbling of feces; defecation may be associated with tenesmus, dyschezia, or hematochezia.
- Sphincter incontinence—associated with involuntary expulsion or dribbling of fecal material, especially during excitement or barking and coughing.
- Question clients about previous neurologic disease, anorectal surgery and/or trauma, house training, deworming, and whether the pet seems to defecate voluntarily or involuntarily; also obtain information regarding the pet's diet, current medications, and concurrent systemic clinical signs, especially neurologic signs.
- Concurrent urinary incontinence suggests neurogenic sphincter incontinence.

Physical Examination Findings

- Reservoir incontinence—may include anorectal sensitivity or pain on digital palpation, a rectal mass or thickening of the rectal mucosa; external anal sphincter

tone and non-neurogenic sphincter incontinence anal reflex are normal.

- Non-neurogenic sphincter incontinence—may include evidence of perineal trauma or perianal fistulas; the anal reflex is present, but the external anal sphincter may not completely close if the sphincter has been anatomically disrupted.
- Neurogenic sphincter incontinence—may include loss of tone to the external anal sphincter, but anal tone is a poor indicator of anal sphincter function; the anal reflex is absent or diminished.
- Do a complete neurologic examination on all animals with sphincter incontinence; additional findings suggesting lumbosacral spinal cord disease include loss of voluntary movement and tone to the tail, lumbosacral pain, flaccid posterior paresis or paralysis, and hyporeflexic myotatic reflexes to the pelvic limbs.
- Diffuse lower motor neuron signs suggest generalized peripheral neuropathy or myopathy; upper motor neuron signs to the pelvic limbs suggest CNS disease cranial to the lumbosacral plexus.

CAUSES

Reservoir Incontinence

- Colorectal disease—colitis, irritable bowel syndrome, and neoplasia.
- Diarrhea—large volumes of feces from any cause can overwhelm the absorptive and storage capacity of the colon.

Non-neurogenic Sphincter Incontinence

- Traumatic anal injuries—bite wounds, severely abscessed anal sacs, laceration, or gunshot.
- Iatrogenic—the external anal sphincter and levator ani muscles can be anatomically disrupted during anorectal surgery.
- Perianal fistulas.

Neurogenic Sphincter Incontinence

- CNS—degenerative myelopathy, spinal dysraphism, spina bifida, trauma, intervertebral disc extrusion, neoplasia, meningoileitis (various causes), fibrocartilaginous embolism, other vascular compromises.
- Cauda equina syndrome—L6–L7 or L7–S1 intervertebral disc extrusion, spondylosis deformans, congenital spinal canal stenosis, lumbosacral instability, discospondylitis, and neoplasia.
- Peripheral neuropathy—fungal, immune-mediated, drug-induced (e.g., vincristine sulfate), dysautonomia, and idiopathic.
- Myopathy/neuromuscular disorder.
- Degeneration (aging)—multiple factors are likely involved, including atrophy of the muscles involved in fecal continence, weakness, degenerative neuropathy, and senility.

RISK FACTORS

- Colonic disease
- Anorectal disease and surgery
- CNS disease and peripheral neuropathy



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Gastrointestinal disease from any cause can increase the urge to defecate without directly altering the reservoir capacity of the colon.
- Unlike sphincter incontinence, gastrointestinal disease is often associated with weight loss, vomiting, tenesmus, dyschezia, and hematochezia.
- Behavior disorders (e.g., separation anxiety), unlike fecal incontinence, are often associated with destructive activities or excessive vocalization.
- Inadequate house training usually occurs in young dogs or dogs recently introduced to an indoor environment or in cats with litter box aversion (not enough boxes, soiled box, poor location, new litter, etc.).

CBC/BIOCHEMISTRY/URINALYSIS

- Results usually unremarkable.
- Urinalysis may show evidence of lower urinary tract infection (e.g., pyuria, hematuria), especially with concurrent urinary incontinence.

OTHER LABORATORY TESTS

- Perform fecal flotation to help rule out parasitism as a cause of diarrhea.
- A rectal scraping is indicated in regions where histoplasmosis or pythiosis are endemic.

IMAGING

- Lateral and ventrodorsal survey radiography of the lumbosacral spine may show evidence of intervertebral disc extrusion, discospondylitis, vertebral neoplasia, spina bifida, lumbosacral trauma, or vertebral malformation.
- Myelography and epidurography are also useful in demonstrating compressive lesions within the spinal canal.
- CT and MRI may be necessary to demonstrate some compressive lesions and intraparenchymal spinal cord lesions.

OTHER DIAGNOSTIC PROCEDURES

- Electromyography to evaluate external anal sphincter, levator ani, and coccygeus muscles for evidence of denervation or myopathy.
- Evaluation of other muscles recommended to help localize the neurologic lesion—diffuse denervation vs. focal spinal cord lesion.
- Can evaluate the pudendal-anal reflex electrophysiologically.
- Muscle and nerve biopsy for myopathy and peripheral neuropathy.
- Analysis of cerebrospinal fluid collected by lumbar puncture may reveal evidence of a CNS infectious or inflammatory process, neoplasia, or trauma.
- Perform colonoscopy and colorectal mucosal biopsy if reservoir incontinence is suspected.



TREATMENT

- If possible, identify the underlying cause; fecal incontinence may resolve if the

INCONTINENCE, FECAL

(CONTINUED)

underlying cause is successfully treated (e.g., spinal cord decompression, colitis, etc.). • Dietary—fecal volume can be reduced by feeding low-residue commercial diets or foods such as cottage cheese and rice and/or tofu. Feed pet at established times to better control times needed to defecate. Increasing fecal volume with high insoluble fiber diets is contraindicated. • Frequent warm water enemas will diminish the volume of feces in the colon and thus decrease the incidence of inappropriate defecation. • Environmental changes (e.g., making the pet an outside pet) may increase client satisfaction and thus avoid euthanasia of an otherwise healthy animal. • Reflex defecation can sometimes be induced in animals with posterior paralysis (e.g., a mild pinch of the toe on a pelvic limb or tail); similarly, applying a warm washcloth to the anus or perineum may stimulate defecation. • Surgical reconstruction of anorectal lesions may markedly improve fecal continence in patients with non-neurogenic sphincter incontinence. • Fascial slings and silicone elastomer slings have met with variable success in treating neurogenic sphincter incontinence in dogs. • Prognosis is poor if the underlying cause cannot be identified and successfully corrected; discuss the prognosis with the client early in the evaluation to avoid unrealistic expectations.



MEDICATIONS

DRUG(S) OF CHOICE

- Opiate motility-modifying drugs (e.g., diphenoxylate hydrochloride and loperamide hydrochloride) increase segmental contraction of the bowel and slow passage of fecal material, thus increasing the amount of water absorbed from the feces.
- Anti-inflammatory agents, such as glucocorticoids and sulfasalazine, may benefit patients with suspected reservoir incontinence due to inflammatory bowel disease or colitis.
- Improvement in signs may be achieved if specific therapy for perianal fistula, IBD, or other reservoir or non-neurogenic causes of incontinence can be given, but there are no specific drugs effective in patients with neurogenic incontinence.

CONTRAINDICATIONS

- Do not use motility-modifying drugs in patients with diarrhea if an infectious or toxic cause is suspected.
- Do not use opiate motility modifiers in patients with respiratory disease; use cautiously in patients with liver disease.
- Use of opiates in cats is generally not recommended.
- Do not use diets containing high concentrations of insoluble fibers as this will produce a large, bulky stool that is difficult to pass or may cause obstipation (especially in cats).

PRECAUTIONS

- Motility-modifying drugs may cause constipation and bloat.
- Opiate motility-modifying drugs may cause sedation.

POSSIBLE INTERACTIONS

Increased sedation and respiratory depression are possible when opiates are used concurrently with other CNS depressants (e.g., barbiturates, general anesthetics, and tranquilizers).

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- If fecal incontinence is due to an underlying neurologic cause, use serial neurologic examinations to monitor patient progress.
- Radiographic procedures, EMG, CSF analysis, and electrodiagnostic studies can also be used to follow progress.
- Check fecal consistency and volume and make sure the pet does not become constipated.
- Adjust diet and motility-modifying drug dosages to find the appropriate therapy for each individual patient.

POSSIBLE COMPLICATIONS

- Neurogenic sphincter incontinence is often unresponsive despite appropriate dietary, medical, and surgical treatment.
- 50% of pets with fecal incontinence were euthanized in a recent study.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

- Exposure to animal feces increases the risk of exposure to zoonotic parasites.
- Advise clients about zoonotic diseases (e.g., cutaneous and visceral larval migrans and toxoplasmosis).

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Incontinence, Urinary
- Intervertebral Disc Disease, Thoracolumbar

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- EMG = electromyography
- IBD = inflammatory bowel disease
- MRI = magnetic resonance imaging

INTERNET RESOURCES

Veterinary Information Network:
<http://www.vin.com/VIN.plx>

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INCONTINENCE, URINARY



BASICS

DEFINITION

Loss of voluntary control of micturition, usually observed as involuntary urine leakage.

PATHOPHYSIOLOGY

Usually a disorder of the storage phase of micturition. Urine storage failure is caused by impaired urinary bladder accommodation, failure of urethral continence mechanisms, or anatomic bypass of urinary storage structures. Partial outlet obstruction and other causes of urinary bladder overdistension may cause paradoxical, or overflow, urinary incontinence.

SYSTEMS AFFECTED

- Renal/Urologic.
- Nervous.
- Skin/Exocrine—urine scald and perineal and ventral dermatitis, recessed vulva.

INCIDENCE/PREVALENCE

Urinary incontinence may affect ~ 20% of spayed female dogs, especially large-breed dogs.

SIGNALMENT

- Dog and (rarely) cat.
- Most common in middle-aged to old neutered female dogs; also observed in juvenile females and (rarely) neutered males.
- Medium- to large-breed dogs most often affected.

CAUSES*Neurologic*

- Disruption of local neuroreceptors, peripheral nerves, spinal pathways, or higher centers involved in the control of micturition can disrupt urine storage. Generalized peripheral lower motor neuron disorders or autonomic disorders also can cause urinary incontinence.
- Lesions of the sacral spinal cord, such as a congenital malformation, cauda equina compression, lumbosacral disc disease, or traumatic fractures or dislocation, can result in a flaccid, overdistended urinary bladder with weak outlet resistance. Urine retention and overflow incontinence develop.
- Lesions of the cerebellum or cerebral micturition center affect inhibition and voluntary control of voiding, usually resulting in frequent, involuntary urination or leakage of small volumes of urine.

Urinary Bladder Storage Dysfunction

- Poor accommodation of urine during storage or urinary bladder overactivity (detrusor instability) leads to frequent leakage of small amounts of urine.
- Urinary tract infections, chronic inflammatory disorders, infiltrative neoplastic lesions, external compression, and chronic partial outlet obstruction are potential causes.
- Congenital urinary bladder hypoplasia may accompany ectopic ureters or other developmental disorders of the urogenital tract.
- Idiopathic

detrusor instability has been associated with feline leukemia virus infection in cats and unknown causes in dogs.

Urethral Disorders

- If urethral closure provided by urethral smooth muscle, striated muscle, and connective tissue does not prevent leakage of urine during storage, intermittent urinary incontinence is observed.
- Examples—congenital urethral hypoplasia or incompetence, acquired urethral incompetence (i.e., reproductive hormone-responsive urinary incontinence), urinary tract infection or inflammation, prostatic disease or prostatic surgery.

Anatomic

- Developmental or acquired anatomic abnormalities that divert urine from normal storage mechanisms or interfere with urinary bladder or urethral function.
- Ectopic ureters can terminate in the distal urethra, uterus, or vagina.
- Patent urachal remnants divert urine outflow to the umbilicus.
- Vestibulovaginal anomalies, congenital urocystic hypoplasia, or urethral hypoplasia.
- Intrapelvic bladder neck location may contribute to urine leakage due to urethral incompetence.
- Vulvar and perivulvar conformation abnormalities may contribute to urine pooling and intermittent urine leakage.

Urine Retention

- Overflow observed when intravesicular pressure exceeds outlet resistance.

Mixed Urinary Incontinence

- Mixed or multiple causes may occur in dogs and cats, e.g., combinations of urethral and bladder storage dysfunction and combinations of anatomic and functional disorders.

RISK FACTORS

- Neutering increases the risk of development of urethral incompetence, especially in large dogs (> 20 kg).
- Early neutering (< 3 months) increases the risk of urinary incontinence in female dogs.
- Conformational characteristics such as bladder neck position, urethral length, and concurrent vaginal anomalies may increase the risk of urinary incontinence in female dogs.
- Obesity may increase the risk of urinary incontinence in neutered female dogs.
- Other possible risk factors for urethral incompetence include breed, large body size, polyuria, and early tail docking.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiating Similar Signs

- Voluntary but inappropriate urination (usually behavioral).
- Urethral discharges, often associated with prostatic disease in male dogs and vaginal disorders in female dogs.

- Urine spraying or inappropriate urination in cats can be confused with urinary incontinence.
- Polyuria—may precipitate or exacerbate urinary incontinence or lead to nocturia and inappropriate urination; a urine specific gravity may rule in or out clinically important polyuria.

Differentiating Causes

- Neurogenic causes of urinary incontinence—usually cause a large, distended urinary bladder and other neurologic deficits such as weak anal or tail tone, depressed perineal sensation, and proprioceptive deficits.
- Dogs with urethral incompetence typically exhibit intermittent occurrences of urinary incontinence, observed most often at night or while the animal is sleeping. Physical examination reveals a small urinary bladder and no other defects.
- Urine pooling—affected dogs may leak small amounts of urine after voiding.
- Historical and physical findings in patients with urinary bladder storage dysfunction resemble those observed in patients with urethral incompetence, although increased frequency of urination or apparent urgency may be additional clinical signs.
- Historical signs in male dogs with prostatic disease include tenesmus, hind limb weakness, dysuria, and pollakiuria. Physical findings include prostatomegaly, lumbosacral pain, pain on prostatic palpation, and hind limb trembling or weakness.
- Recessed or juvenile vulvar conformation may contribute to urine pooling.

CBC/BIOCHEMISTRY/URINALYSIS

- Hematologic and biochemical analyses may be indicated in patients with polyuria disorders (see Polyuria and Polydipsia).
- Urinalysis may reveal evidence of urinary tract infection (e.g., pyuria, hematuria, and bacteria) or polyuria (e.g., low urine specific gravity).

OTHER LABORATORY TESTS

- Test cats for feline leukemia virus infection
- Urine culture in dogs with urethral incompetence

IMAGING*Radiographic Findings*

- Contrast radiography is indicated in juvenile animals and animals exhibiting urinary incontinence shortly after surgical procedures or traumatic incidents.
- Excretory urography, contrast tomography, or magnetic resonance nephrography allows visualization of the kidneys, ureteral terminations, and urinary bladder.
- Retrograde vaginourethrography allows visualization of the vaginal vault, urethra, and urinary bladder. Ectopic ureters usually fill with contrast media in these retrograde studies.
- Double-contrast cystography may be required for full visualization of bladder structure and identification of urinary bladder lesions.

INCONTINENCE, URINARY

(CONTINUED)

Ultrasonographic Findings

- Can use for evaluation of the kidneys, ureters, and urinary bladder to identify uroliths, masses, hydronephrosis or hydroureter, or evidence of pyelonephritis.

DIAGNOSTIC PROCEDURES

- Neurologic examination—examination of anal tone, tail tone, perineal sensation, and bulbospongiosus reflexes.
- Urethral catheterization—may be required to assess patency of the urethra if urine retention is observed.
- Cystoscopy—may visualize bladder, urethra, and ectopic ureteral terminations.



TREATMENT

I

APPROPRIATE HEALTH CARE

- Usually as outpatient.
- Address partial obstructive disorders and primary neurologic disorders specifically if possible.
- Identify urinary tract infection and treat appropriately.
- Ectopic ureters and congenital urethral hypoplasia can often be surgically corrected; endoscopic-guided laser ablation has been utilized for intramural ectopic ureters. Functional abnormalities of urethral competence or urinary bladder storage may accompany the anatomic disorder and require ancillary medical treatment.
- Teflon or collagen bulking agents can be injected into urethral submucosa to control incontinence.
- Surgical procedures such as colposuspension, cystourethropexy, and prosthetic sphincter implantation have been described for the treatment of refractory incontinence.



MEDICATIONS

DRUG(S) OF CHOICE

Urethral Incompetence

- Manage with α -adrenergic agonists (e.g., phenylpropanolamine 1–1.5 mg/kg PO q8–12h or 1.5 mg/kg PO q24h, ephedrine 1–4 mg/kg PO q8–12h) or reproductive hormones (e.g., conjugated short-acting estrogens, estradiol 1–2 mg/dog PO q24h for 7 days, then 0.5–1 mg/dog q24–48h if required, and testosterone or diethylstilbestrol 0.1–1 mg/dog PO q24h for 5–7 days then 0.1–1 mg/dog PO q4–7 days PRN).
- α -adrenergics and reproductive hormones can be co-administered for a synergistic therapeutic effect.
- Depot deslorelin, a gonadotropin-releasing hormone analogue (5–10 mg/dog, or dogs \leq 30 kg use a 4.7 mg implant, for dogs $>$ 30 kg use a 9.4 mg implant) or depot leuprorelin (1 mg/kg or

11–25 mg/dog) have also been used in refractory cases.

- Imipramine (5–15 mg/dog PO q12h), a tricyclic antidepressant with anticholinergic and α -agonist actions, provides an alternative method of treatment especially if there may be inappropriate voiding with a suspected behavioral origin.

Detrusor Instability

- Manage with anticholinergic or antispasmodic agents (e.g., oxybutynin, approximately 0.2 mg/kg PO q8–12h, up to 5 mg total dose q8–12h).

Prostatic Disease

- See Prostatomegaly; Prostatitis and Prostatic Abscess.

CONTRAINDICATIONS

- Estrogen in immature bitches with congenital USMI (urethral sphincter mechanism incompetence), intact bitches, or male dogs.
- Adrenergic agonists in patients with cardiac disease, renal disease, and hypertensive disorders.
- Anticholinergic agents in patients with glaucoma or cardiac disease.

PRECAUTIONS

- Long-acting estrogen compounds rarely cause signs of estrus and bone marrow suppression, and exacerbate immune-mediated disease. However, bone marrow suppression due to estrogen therapy is usually fatal. Therefore, use the minimum effective dose for the minimum amount of time.
- Testosterone administration can cause signs of aggression or libido, exacerbate prostatic disease, and contribute to the development of perineal hernia or perianal adenoma.
- Adrenergic agonists can cause restlessness, tachycardia, and hypertension.
- Anticholinergic agents can cause nausea, vomiting, and constipation.

POSSIBLE INTERACTIONS

- Do not administer tricyclic antidepressants concurrently with monoamine oxidase inhibitors (e.g., selegiline). • The risk of hypertension increases if α -adrenergic agonists are administered concurrently with tricyclic antidepressants.



FOLLOW-UP

PATIENT MONITORING

- Patients receiving α -adrenergic agents—observe during the initial treatment period for adverse effects.
- Patients receiving long-term estrogen—initial, 1 month, and periodic hemograms.
- Periodic urinalysis and urine culture.
- Expect excellent response to medical treatment in 60–90% of treated patients.
- Once a therapeutic effect is achieved, slowly reduce the dose and

frequency of drugs to the minimum required.

- Consider combination treatment (α -adrenergic agonist with reproductive hormones or anticholinergic agents), deslorelin or surgical options if poor response to single-agent medication.

POSSIBLE COMPLICATIONS

- Recurrent and ascending urinary tract infection
- Urine scald and perineal and ventral dermatitis
- Refractory and unmanageable incontinence.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Urinary tract infection
- Vaginitis

PREGNANCY/FERTILITY/BREEDING

Although urinary incontinence is rare in pregnant animals, the use of estrogens or anticholinergic agents is not advised.

SYNONYMS

Enuresis

SEE ALSO

- Polyuria and Polydipsia
- Prostatitis and Prostatic Abscess
- Urinary Retention, Functional
- Urinary Tract Obstruction

Suggested Reading

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**Client Education Handout
available online**



BASICS

DEFINITION

Complaint that occurs in bitches historically showing abnormal cycling, copulation failure, conception failure, or pregnancy loss.

PATHOPHYSIOLOGY

- Normal fertility—requires normal estrous cyclicity with ovulation of normal ova into a patent, healthy reproductive tract; fertilization by normal spermatozoa; implantation of the conceptus into the endometrium; formation of the normal zonary placenta; and maintenance of pregnancy in the presence of high progesterone concentration throughout the approximately 2-month gestation.
- Breakdown in any of these processes causes infertility.

SYSTEMS AFFECTED

Reproductive

SIGNALMENT

- Animals of all ages; more common in old animals.
- Dogs > 6 years old—more likely to have underlying cystic endometrial hyperplasia; may be predisposed to uterine infection and failure of conception or implantation.
- Dog breeds predisposed to hypothyroidism—may have a higher prevalence; include golden retrievers, Doberman pinschers, dachshunds, Irish setters, miniature schnauzers, Great Danes, poodles, and boxers.

SIGNS

Historical Findings

- Failure to cycle.
- Failure to cycle normally—shortened interestrous interval (interestrous interval 4 months or less).
- Failure to copulate, poor semen quality or lack of functional spermatozoa.
- Failure to become pregnant and/or maintain pregnancy after normal copulation. Persistent estrus (> 3 weeks).

Physical Examination Findings

- Negative pregnancy exam after mating
- Positive pregnancy with no subsequent parturition

CAUSES

Animals acquired when already mature—possibility of previous ovariohysterectomy.

Dogs

- Insemination at the improper time in the estrous cycle—most common
- Subclinical uterine infection
- Cystic endometrial hyperplasia
- Male infertility factors
- Hypothyroidism
- Hypercortisolism
- Anatomic abnormality
- Chromosomal abnormality
- Abnormal ovarian function
- Brucella canis*
- Silent estrus

Cats

- Similar causes to those of dogs
- Lack of sufficient copulatory stimulus to induce

ovulation

- Systemic viral or protozoal infection

RISK FACTORS

- B. canis* (dogs)
- Hypothyroidism (dogs)
- Hypercortisolism (dogs and cats)—endogenous or exogenous
- Systemic viral infection (dogs and cats)—canine herpesvirus; FeLV; FIV
- Systemic protozoal infection (dogs and cats)—e.g., toxoplasmosis
- Any chronic, debilitating disease condition (dogs and cats)
- Congenital vaginal anomaly (dogs and cats)
- Old age



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Historical Information

- Extremely useful in distinguishing causes.
- Is the patient cycling? Primary anestrus = no overt estrous cycle by 2 years of age; secondary anestrus = no overt estrous cycle within 1 year of a normal cycle.
- Has the patient conceived or given birth in the past? If so, how recently? Litter size? Percentage of stillbirths? Percentage of litter weaned?
- Is the patient free of systemic viral or protozoal infection?
- Is the patient capable of normal copulation?
- Was the patient bred to a male of proven fertility (i.e., litter whelped within previous 6 months) at the proper time of the estrous cycle?
- Did the patient ovulate during the estrous cycle and maintain progesterone concentration consistent with pregnancy during the entire gestation?
- Is the bitch euthyroid?

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

*Serologic Test for *B. canis* (Dogs)*

- Rapid slide agglutination test—used as a screen; sensitive but not specific.
- If positive results—recommend recheck by an agar gel immunodiffusion test (Cornell University Diagnostic Laboratory, 607-253-3900) or bacterial culture or PCR of whole blood or lymph node aspirate.

Serum Progesterone Measurement

- Should remain high throughout gestation.
- May measure at the time of examination.
- If concentration < 2 ng/mL in mid-gestation and pregnancy loss occurs, insufficient luteal function indicated (hypoluteodism) [see Abortion, Spontaneous (Early Pregnancy Loss)—Dogs, and Premature Labor].
- Concentration > 2 ng/mL—may indicate diestrus; silent heat—estrus with no overt behavioral or physical changes; or pathologic production of progesterone from a luteal ovarian structure, functional ovarian neoplasm, or the adrenal gland.
- Quantitative (chemiluminescence,

fluorescence, enzyme immunoassay) progesterone assay is important to detect levels < 2.0 ng/mL. Rapid in-hospital assays are least accurate between 2 and 5 ng/mL.

Dogs

- Progesterone may be measured during proestrus and estrus to predict ovulation time and optimize breeding management.
- Concentration and ovulation—
1–1.9 ng/mL, probable ovulation in 3 days (recheck); 2–2.9 ng/mL, ovulation in 2 days; 3–3.9 ng/mL, ovulation in 1 day;
4–10 ng/mL, ovulation that day.
- Optimal breeding day for single breeding to produce maximum litter size—2 days after ovulation.
- Day of ovulation from onset of proestrus or estrus extremely variable; not well correlated with standing behavior (see Breeding, Timing).

Cats

- Progesterone may be measured after breeding to assess induction of ovulation.
- Concentration > 2 ng/mL—indicates functional luteal tissue.

Other Tests

- Bacterial culture for uterine organisms (dogs and cats)—vaginal discharge originating in the uterus during proestrus or estrus is collected directly by hysterotomy or transcervical catheterization, or indirectly from the anterior vagina using a guarded swab.
- Thyroid hormone testing (dogs)—may measure resting serum concentration of T₃ or T₄ and cTSH.
- Serologic testing—canine herpesvirus and toxoplasmosis [see Abortion, Spontaneous (Early Pregnancy Loss)—Dogs]; FeLV, FIV, and toxoplasmosis [see Abortion, Spontaneous (Early Pregnancy Loss)—Cats].
- Karyotype (dogs and cats)—performed on heparinized blood samples of patients with primary or persistent anestrus; look for chromosomal abnormalities that can cause abnormal sexual differentiation (testing done by Molecular Cytogenetics Laboratory, Texas A&M University, (979)-862-2879/458-0520; Veterinary Genetics Laboratory, Univ. Calif. Davis, (530) 752-2211) (see Sexual Development Disorders).
- Serum cortisol assay (dogs and cats)—if the resting serum concentration is high, investigate the underlying cause.
- Semen evaluation (dogs and cats)—direct evaluation to rule out oligospermia or azoospermia recommended; alternatively, may test-breed the male to another female to prove fertility; rule out azoospermia in tomcat by finding spermatozoa in a vaginal flush or swab specimens from the queen or in urine collected by cystocentesis from the tom. (See Infertility, Male—Dogs.)
- Serum AMH/progesterone, LH/estrogen for determination of ovarian presence.

INFERTILITY, FEMALE—DOGS

(CONTINUED)

IMAGING

- Radiography and ultrasonography—normal ovaries and a non-gravid uterus usually not visible with radiography; normal ovaries and non-gravid uterus visible with newer high-resolution equipment and frequency near-field imaging; large ovaries may indicate cystic ovarian disease or neoplasia; visible uterus may indicate cystic endometrial hyperplasia.
- Positive-contrast procedures—vaginography in dogs; hysteroscopy in dogs and cats; performed prepubertally or when the patient is in estrus; may reveal anatomic abnormality (e.g., abnormal structure and impatency) (see Vaginal Malformations and Acquired Lesions).
- Ultrasound—may diagnose pregnancy as early as 20–24 days after ovulation; useful for documenting pregnancy loss; useful for detecting suspected cystic ovarian or neoplastic ovarian disease, cystic endometrial hyperplasia, and intraluminal fluid.

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DIAGNOSTIC PROCEDURES

- Laparotomy (dogs and cats)—assess anatomy of the tubular tract and gonads.
- Hysterotomy—to obtain a direct uterine culture specimen; biopsy of the uterus or ovaries.



TREATMENT

- Cats—seasonal breeders; depend on photoperiod; cycle when exposed to long day length, normally from late January to mid-October; induce year-round cycling by a daily light exposure of ≥ 12 hours; for a non-cycling cat during the physiologic breeding season, ask client about the queen's housing and exposure to light.
- Heritable cause (e.g., thyroid insufficiency)—counsel owner regarding the advisability of retaining the patient in the breeding program.
- Surgical resection of vaginal anomalies (dogs)—may ease natural service and vaginal delivery of pups.
- Surgical repair of impotent tubular tract (dogs and cats)—difficult procedure; prognosis for future fertility guarded.
- Surgical drainage of ovarian cysts (dogs and cats)—efficacy unknown.
- Unilateral ovariectomy of neoplastic ovary (dogs and cats)—future fertility depends on resumption of normal function of the remaining ovary and lack of metastasis.
- Estrus suppression for one to two estrous cycles may benefit bitches with short interestrous interval (4 months or less).
- Prognosis for future fertility—initially good, because the most common cause is improper breeding management; worsens with other causes.



MEDICATIONS

DRUG(S) OF CHOICE

- Antibiotics (dogs and cats)—for uterine infection; choice depends on bacterial culture and sensitivity test of the uterus or of vaginal discharge during proestrus or estrus.
- L-Thyroxine—for thyroid insufficiency; dogs: 0.01–0.02 mg/kg PO q12h; prognosis for future fertility with return to euthyroid state guarded.

Gonadotropin Therapy

- For induction of ovulation.
- GnRH, which causes release of endogenous LH from the pituitary, or hCG, which has LH-like activity.
- Cats not adequately stimulated to ovulate at the time of copulation—GnRH (25 µg/cat IM or hCG 250 IU/cat IM) at time of breeding.
- Ovarian cystic disease—cats: GnRH (25 µg/cat IM) or hCG (250 IU/cat IM); dogs: GnRH (50 µg/dog IM) or hCG (1,000 IU/dog half IV, half IM); causes ovulation or luteinization of cystic ovarian tissue.
- Estrus induction (dogs)—diethylstilbestrol (5 mg q24h PO for 9 days or until signs of proestrus induced); bromocriptine (20 µg/kg q12h PO for 21 days); cabergoline (5 µg/kg q24h PO for up to 30 days or until signs of proestrus induced); deslorelin (2.1 mg implant, Ovuplant; placed in vestibule; must have progesterone < 0.5 mg/mL at start; implant removed after ovulation confirmed: progesterone > 10 ng/mL).
- Estrus suppression (dogs)—megestrol acetate (2 mg/kg PO daily for 8 days if begun within first 3 days of proestrus or 0.5 mg/kg PO daily for 32 days if begun in anestrus) or mibolerone (dose dependent on body weight; 30 µg PO daily for dogs weighing 0.5–12 kg, 60 µg daily for 12–23 kg, 120 µg daily for 23–45 kg, 180 µg daily for greater than 45 kg and for German shepherd dogs and their crosses).

CONTRAINDICATIONS

- Treatment with progestins, including megestrol acetate, contraindicated in bitches with cystic endometrial hyperplasia or history of progesterone-dependent disease.
- Treatment with mibolerone contraindicated in Bedlington terriers and other breeds with familial liver disease.
- All hormonal therapies contraindicated in potentially pregnant bitches.



FOLLOW-UP

PATIENT MONITORING

- L-Thyroxine (dogs)—blood concentrations of T₃ and T₄ rechecked after 1 month of

supplementation to ensure adequate absorption of medication and resumption of a euthyroid state.

- Ultrasonography (dogs and cats)—to definitively diagnose pregnancy; monitor gestation.
- Progesterone assay (dogs and cats).



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Infertility caused by endocrinopathy—signs of dermatologic abnormality (e.g., alopecia with thyroid insufficiency or hypercortisolism); systemic signs of disease (e.g., polydipsia and polyuria with hypercortisolism).
- Bitches with a vaginal anatomic abnormality—persistent or recurrent urinary tract disease or vaginitis.

ZOONOTIC POTENTIAL

B. canis infection—organism is less readily shed if affected animals are gonadectomized; stress good hygiene.

SEE ALSO

See "Causes"

ABBREVIATIONS

- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- GnRH = gonadotropin-releasing hormone
- hCG = human chorionic gonadotropin
- LH = luteinizing hormone
- T₃ = triiodothyronine
- T₄ = thyroxine
- TSH = thyroid stimulating hormone

Suggested Reading

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Client Education Handout
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BASICS

DEFINITION

- Diminished or absent fertility; does not imply sterility.
- Results from a wide range of problems that prevent the delivery of sufficient numbers of spermatozoa to fertilize ovulated, mature oocytes in the bitch or excessive numbers of biochemically/structurally compromised spermatozoa.

PATHOPHYSIOLOGY

- Spermatogenesis—encompasses the formation and development of spermatozoa from spermatogonia to mature spermatozoa; a coordinated, hormonally controlled, cyclic process; approximately 70 days required for a complete phase: the testicular phase is 61.9 days; the epididymal phase is 10–14 days. Testicular problems require at least 70 days for recovery; epididymal problems require up to 10–14 days.
- Azoospermia—no spermatozoa in the ejaculate.
- Oligozoospermia—low numbers of spermatozoa.
- Teratospermia—high numbers of abnormally shaped spermatozoa.
- Asthenospermia—reduced motility.
- Primary causes—impaired or arrested spermatogenesis; blockage of the excurrent ducts; genitourinary inflammation; testicular neoplasia; environmental stress; congenital abnormality; endocrine abnormality.

SYSTEMS AFFECTED

- Reproductive
- Endocrine/Metabolic
- Musculoskeletal
- Nervous

GENETICS

- The incidence of verifiable heritable causes of infertility in the stud dog is increasing.
- Cryptorchidism—likely a heritable, sex-limited polygenic autosomal recessive trait in dogs; associated with increased frequency of inguinal/umbilical hernias, patellar luxation, preputial and penile problems.
- Alpha-L-fucosidase deficiency is a storage disorder causing acrosomal dysgenesis.
- Primary ciliary dyskinesia (PCD)—congenital abnormality of ciliary ultrastructure; absent, irregular, or asynchronous motility patterns of all ciliated cells; diagnosed by electron microscopy of spermatozoa.
- Hypothyroidism—effect on male fertility is probably minimal.

INCIDENCE/PREVALENCE

True incidence unknown; is probably increasing with continued in-breeding. The percentage is probably higher than expected as the full degree of genetic effects has not yet been realized.

SIGNALMENT

Species

Dog

Breed Predilections

Relatively higher prevalence of specific problems seen in breeds with a small genetic pool or with intensive in-breeding.

Mean Age and Range

Prevalence increases with age.

SIGNS

General Comments

General complaint—no puppies produced; whelping rate < 75% when bred with correct timing to fertile bitches; owner suspects male dog infertility.

Historical Findings

- Age of testicular descent
- Age at first attempted mating
- Dog's temperament (high-strung)
- Libido and breeding behavior
- Frequency and number of matings
- Method used to time breedings
- Type of semen used for breeding (fresh, fresh-extended, chilled-extended, or frozen)
- Ability for the dog's sperm cells to survive chilling or freezing
- Handling of semen and route of insemination
- Litter size(s)
- Familial history of infertility
- Degree of in-breeding
- Fertility status of bitches bred
- *Brucella canis* status of all breeding animals
- Current and previous drug and dietary therapies, especially corticosteroids and steroid hormones
- Previous medical or surgical illnesses

Physical Examination Findings

- Sheath and penis—palpate to identify masses or adhesions.
- Non-erect penis—exteriorize to identify clinically important lesions of the superficial mucosa and any damage to the os penis.
- Testes and epididymides—palpate and examine, note the size and symmetry of the epididymides relative to the testes.
- Internal urethra and prostate—digital rectal palpation to determine location, size, and symmetry.

CAUSES

Incorrect timing of breeding—most common cause

Congenital

- Chromosomal abnormalities: XYY syndrome and XX disorder of sexual development (see Sexual Development Disorders).
- Germinal cell aplasia—biopsy reveals “Sertoli cell only” syndrome.
- Segmental aplasia of the epididymis or vas deferens—causes either oligospermia (unilateral) or azoospermia (bilateral).

Acquired

- Incomplete ejaculation—unfamiliar surroundings; slippery flooring; no estrous bitch; dominant owner or bitch present.
- Obstruction of the efferent ducts, epididymides, or ductus deferens—leads to azoospermia if bilateral; sperm granuloma, spermatocele, acute inflammation, chronic inflammatory stenosis, segmental aplasia, neoplasia, previous vasectomy, and attempts to pack testes into a scrotal location.

- Hyperthermia/heat stroke. Inflammation or infection of the testes—especially *Escherichia coli*; requires prompt and aggressive treatment to prevent infertility.
- Hypothyroidism—role unclear and extremely rare; evaluate thyroid function with poor semen quality; may be associated with decreased libido.
- Hyperprolactinemia—role unclear; evaluate prolactin levels with azoospermia.
- Hyperadrenocorticism—causes testicular atrophy and oligospermia; probably reversible.
- Drugs—parasiticides, corticosteroids, anabolic steroids, estrogens, androgens, progestagens, GnRH agonists/antagonists, ketoconazole, amphotericin B, some antifungal agents, may interfere with or interrupt spermatogenesis; assess all topical and systemic therapies.
- Environmental toxins—endocrine-disrupting contaminants can affect the hypothalamic-pituitary-gonadal axis and gonadal steroidogenesis; effects in the dog unknown but suspected.
- Trauma, environmental damage, testicular neoplasia, systemic disease, ischemia, and heat stress—may cause transient infertility or sterility.
- Prostatic disease—can markedly reduce semen quality and libido.
- In-breeding—reduces fertility; reduced-fertility lines might only be salvaged by concerted breeding program and out-crosses with highly fertile animals.
- Lymphocytic orchitis—familial in some breeds (e.g., beagles and borzois); affected animals may be fertile when young; accelerated rate of fertility loss with age.
- Retrograde ejaculation—some retrograde flow into the bladder normal.

RISK FACTORS

- Congenital disorders affecting reproductive function—not uncommon; tend to occur in selected breeds.
- Teaser bitches and stud dogs not tested for infectious diseases (e.g., *B. canis* and bacterial culture of genital tract) before clinical use.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Before extensive diagnostic work on the male, determine that the bitches are fertile (previous litters) and that the breedings were optimally timed (see Infertility, Female—Dogs, and Breeding, Timing).

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal.
- Brucellosis or prostatitis—variable changes in the leukogram (normal or leukocytosis) and urinalysis (high numbers of leukocytes); depends on the time-course of the infection; false negative Brucellosis test possible, antibiotic therapy may cause false negative.
- Systemic illness—may impair reproductive function, but infertility is usually not the primary complaint on examination.

INFERTILITY, MALE—DOGS

(CONTINUED)

OTHER LABORATORY TESTS

Endocrine Profile

- Resting testosterone—normal, intact dogs, 0.4–10 ng/mL (1–4 ng/mL common range).
- Androgenic tissue (detect bilaterally cryptorchid)—serum testosterone concentration increases 100% over the resting value 2–3 hours after injection with either 1–2 µg/kg GnRH or 40 IU/kg hCG; resting serum AMH.
- Primary testicular failure—low testosterone and high FSH and LH.
- Germinal compartment failure—normal testosterone and high FSH; FSH high due to the loss of inhibin secretion from viable Sertoli cells.
- Hypogonadism—low testosterone, FSH and LH.
- Thyroid function—evaluated by baseline T₃ and T₄, TSH values, and stimulation testing (see Hypothyroidism).
- *B. canis*—screen with 2 mercaptoethanol rapid slide agglutination test (ME-RSAT); confirm with agar gel immunodiffusion test (AGID).

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IMAGING

Ultrasonography—identify lesions that alter the testicular and epididymal architecture (e.g., neoplasia, spermatocele, orchitis, epididymitis); evaluate the prostate gland for hyperplasia, chronic prostatitis, cyst, abscess, or neoplasia (see Prostate Disease in the Breeding Male Dog).

DIAGNOSTIC PROCEDURES

Breeding Soundness Examination

- Pivotal to ensure that all appropriate information is collected and must always consist of two semen collections.
- Sperm-rich and prostatic portions of the ejaculate—collect as separate fractions by use of a sterile artificial vagina and sterile, graduated, non-toxic plastic tubes in the presence of an estrous bitch.
- Sperm-rich fraction—volume; concentration, motility, and morphologic characteristics of sperm cells; cytologic examination; qualitative and quantitative cultures.
- Prostatic fraction and urine—cytologic examination; qualitative and quantitative cultures.
- Culture results—must be correlated with clinical and cytologic evidence of an active infection; evidence of inflammation if greater than 3–5 WBC/hpf observed (especially sperm-rich fraction).
- Prostatic fraction that indicates a clinically important infection—reevaluate by other sampling techniques that avoid contamination from the penile mucosa and prepuce; negative cytology possible with chronic prostatitis.
- Azoospermic or oligospermic ejaculate—recollect 1 hour later and again on several occasions before confirming infertility.

Epididymal Markers

ALP concentration in seminal fluid—normal 8,000–40,000 U/mL; epididymal in origin; may indicate obstruction if <5,000 U/mL

and a complete ejaculate was obtained; pathologic effects of obstruction are more easily seen from ALP concentration if ALP is performed on two ejaculates collected 1 hour apart.

PATHOLOGIC FINDINGS

- Testicular biopsy—determines the degree of spermatogenesis and the integrity of the blood-testis barrier; differentiates obstruction of efferent ducts from testicular hypoplasia and degeneration; allows an informed prognosis.
- Incisional biopsy—diagnostically superior to aspiration or needle biopsy; Bouin's fixative recommended for processing.



TREATMENT

ACTIVITY

- Restrict if activity or use is thought to be producing hyperthermia (see Heat Stroke and Hyperthermia).
- No restriction for other causes of infertility.

DIET

Ensure adequate diet and mineral supplementation; avoid supplementation of products containing excessive or undefined amounts of steroid hormones, e.g., extracts of testes, ovaries, and adrenals.

CLIENT EDUCATION

- Inform client that return to function may require at least 70 days from correction of identified cause(s).
- Stress patience and check patient regularly to ensure that the condition is not worsening.

SURGICAL CONSIDERATIONS

Reanastomosis of blocked excurrent epididymal ducts (vasectomies) has been successful for re-establishment of sperm production.



MEDICATIONS

DRUG(S) OF CHOICE

- Specific medications must be administered at a dosage and time-course that ensures tissue penetration. Antibiotics (for penetration and spectrum)—chloramphenicol, trimethoprim-sulfas, erythromycin, and enrofloxacin; recommended for a minimum of 3–4 weeks to allow adequate and sustained levels within the reproductive tract.
- Retrograde ejaculation—pseudoephedrine used with limited success in men, 4–5 mg/kg PO q8h, or 1 and 3 hours before collection; phenylpropanolamine, 4–8 mg/kg PO q24h, starting 5 days prior to collection.

CONTRAINDICATIONS

- Trimethoprim-sulfas—contraindicated if predisposed to keratitis sicca.

- Chloramphenicol and trimethoprim-sulfas—reportedly induce blood dyscrasias.
- Chloramphenicol—associated with anorexia and vomiting, but still may have the best tissue penetration.



FOLLOW-UP

PATIENT MONITORING

Recheck at intervals that take into account the length of the spermatogenic cycle (70 days) but are frequent enough to allow detection of deteriorating condition.

PREVENTION/AVOIDANCE

Avoid exposure to environmental temperature extremes (heat or cold).

POSSIBLE COMPLICATIONS

50–60% return to fertility after diagnosis and appropriate treatment.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Brucellosis infection—discospondylitis, polyarthritis, posterior paresis, fever, and uveitis.
- Prostatic disease—obstipation, locomotor difficulties, fever, hematuria, pollakiuria, and dysuria.
- Lymphocytic orchitis—lymphocytic thyroiditis.

AGE-RELATED FACTORS

- Daily sperm output and morphologically normal sperm cells decline with age.
- Difficult to assess the effect of age alone on fertility.
- Most old, infertile dogs have concurrent diseases (e.g., systemic or prostatic disease, testicular neoplasia, osteoarthritis) that have documented effects on fertility or libido.

ABBREVIATIONS

- ALP = alkaline phosphatase
- AMH = anti-müllerian hormone
- FSH = follicle-stimulating hormone
- GnRH = gonadotropin-releasing hormone
- hCG = human chorionic gonadotropin
- hpf = high power field
- LH = luteinizing hormone
- TSH = thyroid stimulating hormone
- WBC = white blood cell

Suggested Reading

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Client Education Handout
available online

INFLAMMATORY BOWEL DISEASE



BASICS

DEFINITION

A group of chronic enteropathies characterized by persistent or intermittent gastrointestinal (GI) signs with histopathologic evidence of intestinal inflammation. The form of IBD is generally categorized by the predominant mucosal cellular infiltrate, such as lymphocytic-plasmacytic enteritis, eosinophilic enteritis, or granulomatous enteritis.

PATHOPHYSIOLOGY

- Poorly understood but likely due to complex interplay between mucosal immunity and environmental factors (i.e., dietary and bacterial antigens) in genetically-susceptible dogs. Aberrant host immune responses are likely triggered by antigens derived from members of the commensal microbiota.
- Damage results from the elaboration of cytokines, release of proteolytic and lysosomal enzymes, complement activation secondary to immune complex deposition, and generation of oxygen free radicals which damage the intestinal epithelial barrier.
- Host genetic susceptibility involving defects in innate immunity is suspected in dogs, and possibly cats.

SYSTEMS AFFECTED

- Gastrointestinal
- Hepatobiliary
- Hemic/Lymphatic/Immune—rarely
- Musculoskeletal—rarely
- Ophthalmic—rarely
- Respiratory—rarely
- Skin/Exocrine—rarely

GENETICS

Defects in some host susceptibility genes have been identified in German shepherd dog, boxer, and soft-coated Wheaten terrier.

INCIDENCE/PREVALENCE

IBD is the most common histopathologic diagnosis in dogs and cats with chronic GI signs.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Some canine breeds are predisposed (e.g., immunoproliferative enteropathy of basenjis and Lundehunds, histiocytic colitis of French bulldogs and boxers, and gluten-sensitive enteropathy in Irish setters); an increased incidence is also seen in German shepherds.
- Siamese cats may be predisposed.
- Common in mongrel dogs and cats.

Mean Age and Range

Most common in middle-aged animals, although younger animals (< 2 years old) may be affected.

Predominant Sex

N/A

SIGNS

Historical Findings

- Dogs—chronic intermittent vomiting, large and/or small bowel diarrhea, and weight loss are common.
- Cats—anorexia is most common, followed by weight loss, vomiting, and diarrhea.
- Borborygmus, flatulence, hematochezia, abdominal pain, and mucoid stools are less commonly reported.

Physical Examination Findings

- Varies from an apparently healthy animal to a thin, lethargic animal.
- Poor hair coat is frequently noted.
- Abdominal palpation may reveal pain, thickened bowel loops, and mesenteric lymphadenopathy (especially in cats). Ascites may occur in dogs with protein-losing enteropathy. Abdominal palpation can also be unremarkable.

CAUSES

- Pathogenesis is unknown but most likely multifactorial.
- Etiology likely involves complex interactions between host genetics, mucosal immunity, and environmental (diet, intestinal bacteria) factors.

Infectious Agents

- Attaching and invasive *E. coli* has been associated with granulomatous mucosal lesions in dogs with granulomatous colitis.
- Giardia*, *Salmonella*, *Campylobacter*, and normal resident microbiota have been implicated.

Dietary Agents

- Meat proteins, food additives, artificial coloring, preservatives, milk proteins, and gluten (wheat) are all proposed causative agents.
- Dietary factors appear important in the pathogenesis of chronic intestinal inflammation in canine and feline IBD.

Genetic Factors

- Certain forms of IBD are more common in some breeds of dogs and cats.
- Defects in innate immunity (e.g., mutations in *TLR2*, *TLR5*, and *nod2* as seen in German shepherd dogs) that perturb mucosal homeostasis may predispose an individual susceptible to the development of IBD.
- Affected boxers have mutations in host gene *NCF2* which is required for clearance of intracellular bacteria.

RISK FACTORS

Current hypotheses suggest that IBD is a multifactorial disorder conditioned by genetic, immunologic, and environmental factors.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cats—hyperthyroidism, intestinal neoplasia (especially small cell lymphoma), adverse food reactions, granulomatous FIP and other viral

infections (e.g., FeLV and FIV), renal and hepatic insufficiency, exocrine pancreatic insufficiency, intestinal parasitism, and antibiotic responsive enteropathy (ARD) are primary differentials.

- Dogs—intestinal neoplasia, motility disorders, adverse food reactions, lymphangiectasia, exocrine pancreatic insufficiency, intestinal parasitism, and ARD are primary differentials.

CBC/BIOCHEMISTRY/URINALYSIS

- Results may be unremarkable; these tests more often serve to eliminate other differential diagnoses.
- Mild, nonregenerative anemia of chronic disease. Mild leukocytosis ± a left shift is sometimes seen with mucosal disruption (e.g., erosions).
- Mild peripheral eosinophilia may be seen in dogs and cats with eosinophilic enteritis, food allergy, and intestinal parasites amongst other causes.
- Cats with IBD may show alterations in serum total protein (i.e., hyperproteinemia) and albumin concentrations and with increased liver enzyme (e.g., ALT and/or ALP) activities.
- Hypoproteinemia is more common in dogs with IBD than in cats.
- Cobalamin deficiency reported in both dogs and cats with involvement of the ileum.

OTHER LABORATORY TESTS

- Useful to eliminate other differentials.
- Dogs—tests include evaluation of exocrine pancreatic function (cTLI), serology for pancreatitis (Spec cPL), and serum cobalamin and folate assays to localize small intestinal disease.
- Cats—T₄ and FeLV/FIV serology are recommended; fasting serum TLI (if exocrine pancreatic insufficiency is suspected); serology for pancreatitis (Spec fPL), and serum cobalamin and folate assays to localize small intestinal disease.

IMAGING

- Survey abdominal radiographs—usually unremarkable. Radiographic imaging is most useful in documenting abnormalities in organs outside of the alimentary tract.
- Barium contrast studies—may reveal mucosal abnormalities and thickened bowel loops. Normal findings do not eliminate the possibility of IBD.
- Ultrasonography—may indicate increased intestinal wall thickness (particularly the muscularis propria and submucosal layers) and mesenteric lymphadenopathy. However, these abnormalities, even if present, are not specific for IBD.

DIAGNOSTIC PROCEDURES

- Perform an elimination dietary trial to eliminate adverse food reactions. If GI signs resolve within 2 weeks, then a diagnosis of adverse food reaction is made and no further diagnostic work-up is required.
- Always perform fecal floatations for nematode and protozoal parasites.
- Definitive diagnosis of IBD requires intestinal biopsy and histopathology, usually obtained via endoscopy.
- Exploratory laparotomy may be

INFLAMMATORY BOWEL DISEASE

(CONTINUED)

indicated if endoscopy is unavailable or to collect full-thickness mucosal specimens.

- Use clinical scoring indices such as the canine inflammatory bowel disease activity index (CIBDAI) to define initial IBD disease burden and to assess response to therapy. Concurrent evaluation of C-reactive protein serves as a useful biomarker of active inflammation in dogs.

PATHOLOGIC FINDINGS

Morphologic evidence of mucosal inflammation including epithelial changes, architectural distortion (e.g., erosion/ulceration, crypt hyperplasia, fibrosis, loss of colonic goblet cells), and increased lamina propria cellularity. New histopathologic guidelines for defining the severity of gastrointestinal inflammation have been recently described.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient, unless the patient is debilitated from dehydration, hypoproteinemia, or cachexia.

NURSING CARE

- If the patient is dehydrated or must have food restricted because of intractable vomiting, any balanced fluid such as lactated Ringer's solution is adequate (for a patient without other concurrent disease); otherwise, select fluids on the basis of secondary diseases.
- If there is severe hypoalbuminemia from protein-losing enteropathy, consider use of colloids, such as hetastarch, to control effusions.

ACTIVITY

No restrictions

DIET

- Feed an intact protein or hydrolysate elimination diet to help reduce intestinal inflammation.
- Correct hypocobalaminemia by means of weekly parenteral cobalamin injections for the first 6 weeks and thereafter every 2–3 weeks or as needed based on repeat testing of cobalamin concentrations.
- Fiber supplementation (e.g., fermentable fiber such as pumpkin, Metamucil) is suggested in dogs and cats with colitis.
- Fish oil (n-3 fatty acids) as a free radical scavenger to reduce intestinal inflammation.
- Probiotics may be of benefit in some animals but are clinically unproven at this time. These supplements must be given continuously over several weeks for potential benefit to be realized.

CLIENT EDUCATION

- Emphasize to the client that IBD is not cured but is controllable in most instances.
- Relapses are common; clients should be patient during the various food and

medication trials that are often necessary to get the disease under control.

SURGICAL CONSIDERATIONS

No surgical procedures are available for relief of IBD in veterinary patients.



MEDICATIONS

DRUG(S) OF CHOICE

- See discussion under specific diseases.
- Affected animals with an immune cellular infiltrate should be treated with immunosuppressive drug regimens. Dogs with granulomatous colitis associated with AIEC are treated with fluoroquinolone antibiotics (see chapter, Colitis, Histiocytic Ulcerative, for details).

CONTRAINDICATIONS

If secondary problems are present, avoid therapeutic agents that might be contraindicated for those conditions.

PRECAUTIONS

See discussion under specific diseases

POSSIBLE INTERACTIONS

See discussion under specific diseases

ALTERNATIVE DRUG(S)

See discussion under specific diseases



FOLLOW-UP

PATIENT MONITORING

- Periodic (q2–4 weeks) physical and laboratory evaluations may be necessary until the patient's condition stabilizes. Serum albumin provides important prognostic information in dogs; serum cobalamin deficiency will delay complete clinical recovery in both dogs and cats.
- Monitor serum cobalamin concentrations in hypocobalaminemic dogs and cats.
- No other follow-up may be required except yearly physical examinations and assessment during relapse.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Dehydration, malnutrition, adverse drug reactions, hypoproteinemia, hypocobalaminemia, anemia, and diseases secondary to therapy or resulting from the above-mentioned problems.

EXPECTED COURSE AND PROGNOSIS

- Generally a good-to-excellent short-term prognosis.
- Poor long-term prognosis in dogs with IBD has been associated with severe clinical disease, marked endoscopic (duodenal) abnormalities, ascites, and hypoalbuminemia.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- See discussion under specific diseases.
- Cats may demonstrate concurrent inflammatory lesions in the liver and/or pancreas (so called "triaditis").

AGE-RELATED FACTORS

- See discussion under specific diseases.
- The workup and differentials are essentially the same, regardless of age.
- Some differentials are more likely in younger individuals (i.e., intestinal parasitism vs. neoplasia).
- Counsel clients about breeding and monitoring for the appearance of other diseases.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

See discussion under specific diseases

SEE ALSO

- Colitis, Histiocytic Ulcerative
- Gastroenteritis, Eosinophilic
- Gastroenteritis, Lymphocytic-Plasmacytic

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- ARD = antibiotic responsive diarrhea
- CIBDAI = canine IBD activity index
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- GI = gastrointestinal
- IBD = inflammatory bowel disease
- Spec cPL or fPL = canine or feline pancreatic lipase activity
- T₄ = thyroxine
- TLI = trypsin-like immunoreactivity

INTERNET RESOURCES

Veterinary Information Network:
<http://www.vin.com/VIN.plx>

Suggested Reading

Allenspach K, Wieland B, Grone A, et al.
Chronic enteropathies in dogs: Evaluation of risk factors for negative outcome. J Vet Intern Med 2007; 21:700–708.

Day MJ, Bilzer T, Mansell J, et al.

International standards for the histopathological diagnosis of gastrointestinal inflammation in the dog and cat: A report from the World Small Animal Veterinary Association Gastrointestinal Standardization Group. J Comp Pathol 2008, Suppl 1:S1–S43.

Simpson KW, Jergens AE. Pitfalls and progress in the diagnosis and management of canine inflammatory bowel disease. Vet Clin North Am Small Anim Pract 2011, 41(2):381–398.

Author Albert E. Jergens

Consulting Editor Stanley L. Marks



**Client Education Handout
available online**

INSOLUBLE OXALATE PLANT TOXICOSIS



BASICS

OVERVIEW

- Over 200 species of plants contain insoluble oxalate crystals.
- Most houseplants are in the Araceae family; many are found in homes and offices.
- Common names vary; scientific names must be used for accurate identification.
- Insoluble oxalate crystals are not absorbed systemically and signs are often self-limiting.
- Signs are generally limited to irritation of oral mucosa; other signs occur more rarely.
- *Dieffenbachia* spp. (dumbcane) ingestion by dogs and cats is associated with more serious outcomes including death.
- Cats ingesting *Philodendron* spp. may exhibit more severe clinical signs.
- Common plants include:
 - *Aglaonema commutatum* (Chinese evergreen)
 - *Anthurium* spp. (flamingo flower)
 - *Arisaema amurense* (Jack-in-the-pulpit)
 - *Dieffenbachia* spp. (dumbcane)
 - *Epipremnum* spp. (pothos, devil's ivy, variegated philodendron)
 - *Philodendron* spp. (sweetheart vine, fiddle leaf)
 - *Schefflera actinophylla* (umbrella plant)
 - *Spathiphyllum* spp. (peace lily)
 - *Syngonium* spp. (arrowhead vine)
 - *Zantedeschia* spp. (calla lily).

SIGNALMENT

- Indoor cats and dogs primarily, although pets may be exposed by houseplants moved outside during summer months.
- Dogs tend to chew and destroy the entire plant; cats nibble on leaves.
- May occur more often in younger pets that are bored or inquisitive.

SIGNS

- Rapid onset, often within minutes of exposure.
- *Oral*: vocalization, pawing at muzzle, head shaking, hypersalivation, edema of lips, tongue or pharynx; rarely gagging, choking, and vomiting.
- *Ocular*: pawing at eyes, photophobia, conjunctival swelling.
- *Respiratory*: RARELY, dyspnea from pharyngeal swelling and inflammation.

CAUSES & RISK FACTORS

- Plants in environment.
- Insoluble oxalate crystals are arranged in bundles called raphides which are contained in idioblasts within plant stems and leaves.
- Chewing or biting on plant material releases the crystals from stems and leaves until the idioblast is emptied.
- Crystals act as miniature pins or mechanical irritants to mucous membranes but are not absorbed systemically.
- Potential for chemical irritation with release of prostaglandins, histamine, proteolytic enzymes.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Caustic agents (alkalis and acids in household products; drain cleaners).
- Other agents causing oral irritation (capsaicin, detergents, topical spot-on flea and tick products).
- Quaternary ammonium compounds (> 2% in cats).
- Stinging nettle (*Urtica dioica*) ingestion.
- Systemic disease causing oral lesions.

CBC/BIOCHEMISTRY/URINALYSIS

- Rarely performed unless prolonged vomiting.
- CBC, electrolytes, serum chemistry.

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Exam of oral cavity including visualization of pharynx.
- Fluorescein ophthalmic stain if ocular signs are present.

PATHOLOGIC FINDINGS

- Death rarely occurs.
- Few cases with severe erosive, ulcerative glossitis; oropharyngeal edema.



TREATMENT

- Generally limited to supportive care.
- IV fluids if dehydrated from excessive salivation or vomiting.
- *Oral*: irrigation of oral cavity with copious amounts of cool fluids; small amounts of calcium containing product (milk, yogurt, etc.) to bind oxalate crystals.
- *Ocular*: lavage for 15 minutes with tepid water.
- *Respiratory*: Endotracheal tube or temporary tracheostomy if dyspnea severe.



MEDICATIONS

No specific antidote available.

DRUGS

- Antiemetics as needed:
 - Maropitant 1 mg/kg SQ q24h.
 - Ondansetron 0.1–0.2 mg/kg IV q8–12h.
- GI protectants as needed:
 - H2 blockers (famotidine, ranitidine).
 - Omeprazole 0.5–1 mg/kg PO daily.
 - Sucralfate 0.25–1 g PO q8h.
- Pain

medication as needed:

- Butorphanol 0.1–0.5 mg/kg IV, IM, SQ.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Corticosteroids – the use is controversial, but dexamethasone phosphate 0.125–0.5 mg/kg IV, IM, SQ may be useful in severe inflammatory conditions.



FOLLOW-UP

PATIENT MONITORING

Monitor for signs of dyspnea and respiratory difficulty.

Prevention/Avoidance

Identify plants in household and keep away from pets.

POSSIBLE COMPLICATIONS

- Corneal abrasion or ulcer from pawing at eyes.
- Erosive ulcers in the mouth and gastrointestinal tract.
- Pharyngeal edema and death (rare).

EXPECTED COURSE AND PROGNOSIS

- Most signs are mild to moderate and of short duration generally lasting 2–4 hours; less often signs last 12–24 hours.
- Excellent prognosis as signs are generally self-limiting.



MISCELLANEOUS

AGE-RELATED FACTORS

Young pets are more frequently represented; likely due to boredom and inquisitive nature.

INTERNET RESOURCES

- <http://plants.usda.gov/java/>
- <http://www.petpoisonhelpline.com/poisons>
- <http://www.aspca.org/pet-care/animal-poison-control/toxic-and-non-toxic-plants>

Suggested Reading

Peterson K, Beymer J, Rudloff E, et al. Airway obstruction in a dog after *Dieffenbachia* ingestion. *J Vet Emerg Crit Care* 2009, 19(6):635–639.

Author Lynn R. Hovda

Consulting Editor Lynn R. Hovda

Acknowledgment Erica Cargill



**Client Education Handout
available online**

INSULINOMA



BASICS

DEFINITION

Functional pancreatic islet β -cell tumor that secretes an excess quantity of insulin independent of glucose concentration.

PATHOPHYSIOLOGY

Excessive insulin secretion leads to excessive glucose uptake and use by insulin-sensitive tissues and reduced hepatic production of glucose; this causes hypoglycemia and its associated clinical signs.

SYSTEMS AFFECTED

- Nervous—seizures, disorientation, abnormal behavior, collapse, polyneuropathy/ peripheral neuropathy, posterior paresis, and ataxia.
- Musculoskeletal—weakness and muscle fasciculations.
- Gastrointestinal—polyphagia and weight gain.

INCIDENCE/PREVALENCE

- Dogs—uncommon
- Cats—rare

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Dogs—Labrador retrievers, standard poodles, boxers, fox terriers, Irish setters, German shepherds, golden retrievers, and collies.
- Cats—none; possibly Siamese.

Mean Age and Range

- Dogs—middle-aged to old; mean = 10 years; range = 3–14 years.
- Cats—mean = 15 years; range = 12–17 years.

SIGNS

General Comments

- Often episodic.
- May or may not be related to fasting, excitement, exercise, and/or eating.
- Dogs generally demonstrate more than one clinical sign with progression over time.

Historical Findings

- Dogs—generalized and/or focal seizures are most common. Additional findings may include weakness, posterior paresis, collapse, muscle fasciculations, bizarre behavior, lethargy and depression, ataxia, polyphagia, weight gain, polyuria and polydipsia and exercise intolerance.
- Cats—seizures, ataxia, muscle fasciculations, weakness, lethargy and depression, anorexia, weight loss, and polydipsia.

Physical Examination Findings

- Usually within normal limits unless in a hypoglycemic crisis with the aforementioned signs.
- Obesity is common.
- Polyneuropathy can be seen rarely in dogs (paresis to paralysis, muscle atrophy, and/or hyporeflexia).

CAUSES

Most dogs and cats have single insulin-producing B-islet cell carcinoma or

adenocarcinoma of the pancreas. Approximately 50% or greater of dogs and cats with insulinomas will develop or present with metastasis.

RISK FACTORS

For hypoglycemic episodes—fasting, excitement, exercise and eating.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Extrapancreatic tumor hypoglycemia—paraneoplastic hypoglycemia has been documented in dogs with numerous tumors including hepatocellular carcinoma, metastatic mammary carcinoma, primary pulmonary carcinoma, and others; these tumors generally secrete insulin or insulin-like factors.
- Perform a complete hypoglycemic workup and rule out causes such as iatrogenic insulin, neonatal/toy breed hypoglycemia, ingestion of oral hypoglycemic agents, hepatic failure, sepsis, hypoadrenocorticism, hunting dog hypoglycemia and glycogen storage diseases.
- Seizures and collapse—consider a variety of differentials including cardiovascular (e.g., syncope), metabolic (e.g., anemia, hepatoencephalopathy, hypocalemia, and hypoadrenocorticism) and neurologic (e.g., epilepsy, neoplasia, toxin, and inflammatory disease).

CBC/BIOCHEMISTRY/URINALYSIS

- Results often within normal limits except for hypoglycemia (<65–70 mg/dL in majority of patients).
- Normoglycemia does not rule out the presence of an insulinoma. A small percentage of patients may be intermittently normoglycemic, which is thought to be due to counter-regulatory hormone production (e.g., epinephrine, glucocorticoids, glucagon).

OTHER LABORATORY TESTS

Simultaneous Fasting Glucose and Insulin Determinations

- Upon initiating fasting (patients should always be hospitalized and monitored closely during this time due to the high risk for extreme hypoglycemia episodes), collect baseline blood samples and then hourly or bihourly for serum glucose determination and serum storage. When the serum glucose drops below 60 mg/dL, submit that serum sample for simultaneous glucose and serum insulin determination. When the insulin is elevated in the face of hypoglycemia an insulinoma is highly likely, whereas if the insulin is within normal limits in the face of hypoglycemia then insulinoma is possible. If the insulin value is below normal limits during the hypoglycemia then an insulinoma is unlikely, but multiple sampling may be necessary.

- Formulas utilizing simultaneous hypoglycemic glucose and insulin values such

as the insulin:glucose ratio and the amended insulin:glucose ratio are falling out of favor due to poor specificity.

IMAGING

- Thoracic and abdominal radiography—helpful for evaluation of metastatic disease and/or extrapancreatic tumor-induced causes of hypoglycemia as well as some other differential diagnoses.
- Ultrasonography—fewer than 50% of pancreatic masses are clearly identified through ultrasonography.
- CT—superior technique for detection of primary insulinomas in dogs; however, false-positive lymph node metastases are common and problematic; should primarily be used for preoperative delineation/ confirmation of a primary pancreatic mass.
- Scintigraphy and SPECT—intermittently successful in detecting insulinomas.
- Intraoperative ultrasound—widely used for grossly occult tumor detection in human insulinomas; rarely reported in veterinary medicine.

DIAGNOSTIC PROCEDURES

Exploratory laparotomy—indicated when insulinoma is suspected based on the aforementioned physical, biochemical and/or imaging results.

PATHOLOGIC FINDINGS

Histopathologically, primary pancreatic insulinomas in dogs are generally either B-islet cell carcinomas or adenocarcinomas and occasionally are adenomas, though dogs with adenomas may subsequently develop metastasis, suggesting limitations with delineation of malignancy potential with light microscopy of insulinomas. In cats, most have been malignant with metastasis commonly noted.



TREATMENT

APPROPRIATE HEALTH CARE

- Hospitalize for workup and surgery since life-threatening hypoglycemia is a very real possibility.
- Outpatient if the owner declines surgery and the patient is not clinically hypoglycemic.

NURSING CARE

For emergency hypoglycemic episodes, administer 50% dextrose (1 mL/kg IV slowly over 1–3 minutes) to control seizures/severe hypoglycemic signs. Once the emergency hypoglycemia clinical signs abate, follow with fluid therapy with 2.5% dextrose (increase to 5% if needed to control clinical signs). Alternatively, if the patient can eat, frequent feedings of an appropriate diet (see below) may replace dextrose-containing fluids in many patients.

ACTIVITY

Restricted

(CONTINUED)

INSULINOMA**DIET**

- Feed four to six small meals a day. • Food should be high in protein, fat, and complex carbohydrates and low in simple sugars.
- Avoid semimoist foods that dilute the aforementioned fat, protein, and carbohydrate levels.

CLIENT EDUCATION

Client should be educated about the signs of hypoglycemia and seek immediate attention if they occur.

SURGICAL CONSIDERATIONS

• Surgical management improves prognosis over medical therapy alone. • Medical management to prevent severe hypoglycemia is important before an exploratory laparotomy. Most patients respond well to frequent small feedings and corticosteroids. In rare refractory cases, the use of IV fluids containing 2.5% to 5% dextrose and/or glucagon may be necessary. • Objectives include confirmation of the diagnosis, elucidation of the presence/absence of any extra-pancreatic metastases and/or other disease and removal of as much cancerous tissue as possible. • At surgery, most insulinomas can be visualized and/or palpated. If a pancreatic mass can't be found, intraoperative ultrasound may be beneficial. In rare cases, IV 1% methylene blue (3 mg/kg added to 250 mL 0.9% NaCl, given IV slowly over 30–45 minutes) may be used to delineate an occult pancreatic insulinoma; however, hemolytic anemia, pseudocyanosis, and hemoglobinuric nephrotoxicity are possible side effects; therefore, routine use is not recommended. • Approximately 15% of dogs have multiple primary insulinomas, so always examine the entire pancreas. • Biopsy regional lymph nodes and carefully evaluate the liver (and other abdominal contents) with biopsy of any abnormalities. Approximately 40–50% of dogs will have metastasis. In one study, of 14 dogs suspected to have extra-pancreatic metastasis from a primary pancreatic insulinoma, only 8 (57%) had histologic evidence of metastasis. Therefore, the presence of what appears to be metastasis should be biopsied and not automatically lead to intraoperative euthanasia.

**MEDICATIONS****DRUG(S) OF CHOICE*****Emergency/Acute Therapy***

See "Nursing Care" above

Long-Term Therapy

- If dietary therapy is ineffective, glucocorticoids such as prednisone may be given at an initial dosage of 0.25 mg/kg PO q12h and be increased as needed to 2–3 mg/kg PO q12h. • Diazoxide (Proglycem) stimulates hepatic

gluconeogenesis/glycogenolysis and inhibits insulin secretion. Diazoxide may be given at 5–60 mg/kg PO q12h (start low and increase as needed) in addition to dietary modifications and/or glucocorticoids when they are becoming less effective. Diazoxide can be difficult to locate and be prohibitively expensive for some clients though less expensive compounded sources are becoming more readily available. • Streptozocin is a nitrosourea that semi-selectively targets pancreatic B cells. Streptozotocin may be given at 500 mg/m² slowly IV over 2 hours after a 3-hour 0.9% NaCl diuresis and followed with a 2-hour diuresis. This protocol may be repeated every 3 weeks until normoglycemia is achieved. Streptozotocin is emetogenic and can be hepatotoxic and/or nephrotoxic. • Glucagon is gluconeogenic and may be used at 5 ng/kg/minute CRI (to effect) to treat acute severe refractory hypoglycemia. • The synthetic somatostatin analogues ocreotide (10–20 µg SC q8–12h) or lanreotide (no determined dose in veterinary species) may be utilized to prevent hypoglycemia in dogs refractory to conventional treatments.

CONTRAINdications

Insulin

PRECAUTIONS

- Dextrose boluses, when given alone, may precipitate further hypoglycemic crises.
- Glucocorticoids used at high dosages for prolonged periods can cause iatrogenic hyperadrenocorticism. • Diazoxide may cause bone marrow suppression, gastrointestinal irritation, aplastic anemia, cataracts, thrombocytopenia and tachycardia in humans. • Streptozocin can cause emesis, hepatic failure, renal failure, diabetes mellitus, and pancreatitis.

POSSIBLE INTERACTIONS

Hydrochlorothiazide can potentiate diazoxide.

**FOLLOW-UP****PATIENT MONITORING**

- Teach client to monitor for return and/or progression of signs of hypoglycemia.
- In-hospital serum glucose determinations are important for monitoring for return and/or progression of insulinoma-associated hypoglycemia.

POSSIBLE COMPLICATIONS

Recurrent or progressive episodes of hypoglycemia

EXPECTED COURSE AND PROGNOSIS

- Dogs that undergo exploratory laparotomy are more likely to become and remain euglycemic longer and have longer survivals than dogs managed by medical means. Even in the presence of local metastatic disease, any

reduction of tumor burden is likely to improve glycemic control with medical therapies. The median length of euglycemia control after surgery is inversely correlated with the stage of disease and varies from 14 months for those dogs without evidence of metastasis to only 2–3 months for those dogs with nodal and/or distant metastasis. The median survival time is also inversely correlated with the stage of disease and varies from about 16–19 months (range, 2–60 months) for dogs without evidence of metastasis to 7–9 months in dogs with evidence of nodal and/or distant metastasis. More recent studies have documented even longer median survival times of 17–18 months for all dogs with insulinoma and 25–42 months for those dogs undergoing surgical and medical therapies. • Cats—mean survival time, about 6.5 months; range, 0–18 months.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Obesity due to hyperinsulinemia

AGE-RELATED FACTORS

Younger dogs have shorter survival times.

SYNONYMS

- B-cell tumor • Hyperinsulinism
- Insulin-producing pancreatic tumor
- Insulin-secreting tumor • Islet cell adenocarcinoma • Islet cell tumor

SEE ALSO

Hypoglycemia

ABBREVIATION

- SPECT = single proton emission computed tomography

Suggested Reading

- Moore AS, Nelson RW, Henry CJ, et al. Streptozocin for treatment of pancreatic islet cell tumors in dogs: 17 cases (1989–1999). J Am Vet Med Assoc 2002, 221(6):811–818.
Polton GA, White RN, Brearley MJ, Eastwood JM. Improved survival in a retrospective cohort of 28 dogs with insulinoma. J Small Anim Pract 2007, 48(3):151–156.
Robben JH, Pollak YW, Kirpensteijn J, et al. Comparison of ultrasonography, computed tomography, and single-photon emission computed tomography for the detection and localization of canine insulinoma. J Vet Intern Med 2005, 19(1):15–22.
Author Virginia Gill
Consulting Editor Deborah S. Greco
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**Client Education Handout
available online**

INTERSTITIAL CELL TUMOR, TESTICLE



BASICS

OVERVIEW

Benign tumor of the testicle that arises from interstitial (Leydig) cells.

SIGNALMENT

- 33–50% of all testicular tumor in dogs but rare in cats.
- Median age, 10 years.
- Boxer, German shepherd, Afghan hound, Weimaraner, Shetland sheepdog, Collie, and Maltese may be at increased risk.

SIGNS

- Usually incidental finding.
- Fertility issues in breeding dogs.
- May be associated with testosterone secretion and perianal gland hyperplasia or adenomas.
- 4–20% of dogs will have more than 1 type of testicular tumor. Up to 50% of dogs will have bilateral tumors, only 12% of contralateral tumors will be palpable.

CAUSES & RISK FACTORS

- Generally unknown
- Cryptorchidism—may predispose



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Sertoli cell tumor
- Seminoma
- Hyperadrenocorticism—with feminization
- Hypothyroidism—with feminization

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal, unless estrogen excess causes bone marrow hypoplasia (rare).
- Various cytopenias—with estrogen excess (rare).

OTHER LABORATORY TESTS

- High serum estradiol concentration.
- Low serum testosterone concentration.

IMAGING

- Testicular sonography may aid in differential diagnoses.
- Abdominal ultrasonography for retained testicles and to evaluate for concurrent malignancies.

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Bilateral orchiectomy and scrotal ablation is the treatment of choice. Exploratory laparotomy for retained testicles.
- Histopathologic examination of appropriate tissue.
- Immunohistochemistry may be necessary to identify cell of origin in some cases.



MEDICATIONS

DRUG(S)

- None, unless bone marrow hypoplasia induces a dangerous cytopenia.
- Recombinant hematopoietic colony-stimulating factors—may be useful in treating bone marrow hypoplasia.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

None required, unless bone marrow hypoplasia

POSSIBLE COMPLICATIONS

Cytopenias caused by estrogen excess

EXPECTED COURSE AND PROGNOSIS

Bilateral orchiectomy and scrotal ablation are often curative.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Prostate disease—with testicular tumor
- Perianal gland hyperplasia/adenomas

SEE ALSO

- Sertoli Cell Tumor
- Seminoma

Suggested Reading

Lawrence JA, Saba C. Tumors of the Male Reproductive System. In: Withrow SJ, ed., Small Animal Clinical Oncology. St Louis, MO: Elsevier Saunders, 2013, pp. 557–571.

Morrison WB. Cancers of the reproductive tract. In: Morrison WB, ed., Cancer in Dogs and Cats: Medical and Surgical Management. Jackson, WY: Teton NewMedia, 2002, pp. 555–564.

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Client Education Handout
available online

INTERVERTEBRAL DISC DISEASE—CATS



BASICS

OVERVIEW

- Disc extrusion or protrusion causing myelopathy is more common in dogs; both Hansen's type I and type II disc disease, and acute, non-compressive nucleus pulposus extrusion are reported in cats.
- Type I disc disease is secondary to chondroid metaplasia and mineralization of the nucleus pulposus.
- Type II disc disease is secondary to fibroid degeneration and protrusion of the annulus fibrosus.
- With acute, non-compressive nucleus pulposus extrusion, normal nucleus pulposus is extruded through a tear in the dorsal annulus, resulting in a concussive or contusive injury, with minimal to no ongoing compression of the spinal cord.

SIGNALMENT

- For all reported cats with myelopathy secondary to disc disease—mean age 8.4 years, range 1.5–17 years.
- Cats with mineralized type I disc disease—mean age 7.3 years, range 2–13 years.
- Predominantly domestic breeds, several purebred (Oriental) breeds reported. Rare exotic large cat (tiger) reported.
- No sex predisposition.

SIGNS

- Majority of cats have thoracolumbar or lumbosacral disc disease; clinical signs are confined to pelvic limbs. Cervical disc disease is also described, in which case all four limbs may be affected.
- Signs are frequently acute but may be chronic.
- Paresis/paralysis.
- Ataxia.
- Gait abnormality, lameness, reluctance to jump.
- Spinal/back pain.
- Urinary/fecal incontinence.
- Abnormalities of tail carriage or tone.
- Loss of pain perception (if severe lesion).
- Hypoventilation (if severe cervical lesion).

CAUSES & RISK FACTORS

- Majority of cats reported had type I disc degeneration, with extrusion of mineralized nucleus pulposus into the vertebral canal resulting in spinal cord trauma and compression.
- Unlike dogs, where chondrodystrophic breeds (e.g., dachshunds) are predisposed to type I disc disease and subsequent extrusion, no obvious risk factors are apparent in cats.
- Most cats reported had clinically significant

disc protrusions or extrusions between T11 and S1. Similar to dogs, the presence of the intercapital ligament from T1–T10 may make disc protrusions in that region less likely.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Trauma • Vascular—ischemic neuromyopathy ("saddle thrombus")
- Neoplasia, especially lymphoma
- Vascular—ischemia to spinal cord
- Infectious—FIP, *Cryptococcus*, etc.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

N/A

IMAGING

- Vertebral column radiographs—narrowed disc space(s), mineralized discs in situ, mineralized disc material within the vertebral canal or overlying intervertebral foraminae.
- Myelography—extradural compressive lesion at the affected disc. • CT—extradural compression; mineralization of compressive material may be apparent. • MRI—T2 hyperintensity within injured cord; mineralized disc material appears hypointense on all imaging sequences; extradural compression may be apparent.

DIAGNOSTIC PROCEDURES

- Cerebrospinal fluid—unremarkable or contaminated with blood in most cats; neutrophilic pleocytosis noted in three cats.
- Histopathology of material removed at surgery—consistent with degenerative disc material (type I or II).



TREATMENT

- Surgical spinal cord decompression likely the most effective treatment for compressive disc disease. • Risks of spinal surgery should be discussed with the owner—hemorrhage, iatrogenic injury to the spinal cord, instability.
- Hemilaminectomy, ventral slot, lateral corpectomy, and lumbosacral dorsal laminectomy surgeries are described in the cat. • Postoperative care—good recumbent patient care, pain management, bladder management if incontinent cat (indwelling urinary catheter or manual expression), and appropriate physical therapy. • Fenestration of adjacent mineralized discs should be considered to avoid recurrence. • Medical management (cage rest, pain management) may be considered in ambulatory cats, but

more aggressive diagnostics and treatment should be considered in non-ambulatory cats and those with progressive neurologic signs.



MEDICATIONS

DRUG(S)

- Pain management, preferably opiates, if the cat tolerates them. • Efficacy of corticosteroids in feline disc disease has not been evaluated.



FOLLOW-UP

- Repeat neurologic examinations (at least 1–2 times/day) during hospitalization to monitor postoperative and medically managed patients for improvement or decline in neurologic status. • Strict cage rest for medically managed and postoperative patients for 4–6 weeks, then gradual increase in activity and physical therapy, as needed. • It is unknown whether long-term activity restriction is beneficial. • Because disc disease is uncommon in cats, possible recurrence rate is unknown, but in one cat that recovered well after hemilaminectomy, an additional mineralized disc extrusion caused paraplegia and necessitated a second surgery (unpublished data). • A few cats had persistent urinary retention in spite of good recovery of ambulation, requiring routine bladder expression by the client. • Majority of cats managed surgically (even two without pain perception) had a good-to-excellent outcome. • Very few cats were medically managed long-term, so prognosis with medical management is unknown.



MISCELLANEOUS

ABBREVIATIONS

- CT = computed tomography • FIP = feline infectious peritonitis • MRI = magnetic resonance imaging

Suggested Reading

Rayward RM. Feline intervertebral disc disease: A review of the literature. Vet Comp Orthop Traumatol 2002, 15:137–144.

Author Marguerite F. Knipe

Consulting Editor Joane M. Parent



Client Education Handout available online

INTERVERTEBRAL DISC DISEASE, CERVICAL



BASICS

DEFINITION

A degeneration of the cervical intervertebral discs that causes protrusion or extrusion of disc material into the spinal canal. The protruded or extruded disc material causes spinal cord compression (myelopathy) and/or nerve root compression (radiculopathy).

PATHOPHYSIOLOGY

- Classified as acute disc herniation (Hansen type I disc) or chronic disc protrusion (Hansen type II disc).
- Hansen type I disc degeneration is characterized by chondroid degeneration of the nucleus pulposus and acute rupture of the annulus fibrosus with extrusion of the nucleus pulposus into the spinal canal.
- Hansen type II disc degeneration is characterized by fibrinoid degeneration of the nucleus pulposus. This causes bulging and protrusion of the dorsal annulus fibrosus into the vertebral canal.
- Disc extrusion or protrusion into the spinal canal causes focal compression of the spinal cord (myelopathy) and/or focal compression of a nerve root (radiculopathy).
- Consequences of spinal cord compression are ischemia and demyelination.
- Dorsal disc extrusion or protrusion is more common than lateral disc extrusion or protrusion.
- Disc extrusion may be secondary to trauma but this rarely occurs.
- Surgical fusion of cervical vertebrae may alter the biomechanics of adjacent vertebral bodies and therefore predispose discs to protrusion or extrusion and this is termed the domino effect.

SYSTEM AFFECTED

Nervous system—either focal myelopathy or focal radiculopathy

GENETICS

- Not known.
- Chondrodystrophoid breeds (e.g., dachshund, beagle, Cocker spaniel) are most commonly affected with Hansen type I disc extrusion.
- Large-breed dogs (e.g., Doberman pinscher) are most commonly affected with Hansen type II disc extrusion.

INCIDENCE/PREVALENCE

- Cervical disc disease accounts for roughly 15% of all canine intervertebral disc disease.
- Eighty percent of disc extrusion occurs in dachshunds, beagles, and poodles.
- The incidence of degenerative disc disease in the overall canine population is about 2%, while the incidence in the dachshund population is about 25%.
- C3–C4 is reported to be the most common site of disc extrusion.

SIGNALMENT

Species

Dogs

Breed Predisposition

- Hansen type I—dachshund, poodle, beagle, Cocker spaniel
- Hansen type II—Doberman pinscher

Mean Age and Range

- Hansen type I—3–6 years of age
- Hansen type II—8–10 years of age

Predominant Sex

None recognized

SIGNS

Severity of clinical signs and spinal cord injury is dependent on several factors, including the rate and volume of disc protrusion or extrusion, spinal cord diameter relative to vertebral canal diameter, and the velocity of disc material that was extruded.

Historical Findings

- Neck pain—most common owner complaint.
- Stiff, stilted gait, reluctance to move the head and neck.
- Lowered head stance and muscle spasms of the head, neck, and shoulder.
- It has been reported that 10% of affected patients are tetraparetic.
- Muscle atrophy over the scapula.
- Patients may have neck pain and front leg lameness secondary to dorsolateral disc extrusion, also termed root signature or more appropriately a radiculopathy.

Physical Examination Findings

- Neck pain—elicited upon flexion and extension of the neck or by turning the neck from side to side. Pain can also be elicited by deep palpation of the cervical muscles.
- Wheelbarrow postural reflex may cause the patient to hit their nose on the ground due to neck pain.
- Herniation in the cervical region is often associated with minimal neurologic signs because the spinal canal area is greater and can accommodate more disc material before spinal cord compression.
- Occasionally patients have neck pain and apparent forelimb lameness (e.g., a thoracic limb that knuckles, appears lame, or is held in partial flexion) as a result of dorsolateral disc herniation (root signature/radiculopathy). This helps localize the lesion to C4–C7.
- Paresis with postural reaction deficits involving both thoracic and pelvic limbs may be present. The deficits can also be ipsilateral in nature.
- Pelvic limb paresis may be more severe than thoracic limb paresis.
- Pelvic limb spinal reflexes may be normal to exaggerated.
- Thoracic limb spinal reflexes may be normal to exaggerated when lesions are located in the C1–C6 spinal cord segment and may be

normal to decreased when the C6–T2 spinal cord segment is affected.

- There is no correlation between severity of clinical signs and the degree of compression.
- Bladder function may be upper motor neuron in nature or normal.

CAUSES

- Hansen type I—early chondroid degeneration of the cervical intervertebral disc and subsequent disc mineralization.
- Hansen type II—gradual fibroid degeneration of the cervical intervertebral disc.

RISK FACTORS

Obesity and repeated traumatic events in those breeds predisposed to intervertebral disc disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hansen type I disc disease
- Hansen type II disc disease
- Neoplasia
- Atlantoaxial instability
- Spinal fracture/luxation
- Discospondylitis
- Meningitis
- Fibrocartilaginous embolism
- Cervical vertebral instability
- Endocrine—hypothyroidism
- Spondylomyopathy
- Osteoarthritis
- Glycogen storage diseases

CBC/BIOCHEMISTRY/URINALYSIS

Should be performed in older animals in anticipation of general anesthesia and surgery.

OTHER LABORATORY TESTS

- CSF analysis—performed under general anesthesia prior to myelography. CSF should be collected through a cisternal tap since this site is closer to the lesion than a lumbar tap.
- CSF analysis reveals mild to moderate elevation in protein levels and mild to moderate pleocytosis.
- Hansen type I disc herniation is usually associated with more pronounced CSF changes than Hansen type II disc disease.
- EMG may be useful if the underlying cause is associated with denervation.

IMAGING

Cervical Spinal Radiography

- Well-positioned lateral and ventrodorsal survey radiographs of the cervical spine are always indicated.
- Animals should be anesthetized for this procedure.
- Classic findings include narrowed intervertebral disc space or disc space wedging, collapse of the articular facets, calcified disc material present in the intervertebral foramen or in the spinal canal.

(CONTINUED)

- Hansen type II disc disease may be associated with spondylosis deformans.
- May reveal evidence of discospondylitis, fracture/luxation, atlantoaxial instability, or lytic vertebrae suggestive of a bone tumor.

Myelography

- Survey cervical radiographs may be misleading; therefore, myelography is indicated in 90–95% of cervical disc patients.
- Either a cisternal or lumbar injection between L5 and L6 or L4 and L5 can be used but a lumbar injection is preferred.
- Lateral radiographs—reveal dorsal deviation of the ventral contrast column over the intervertebral disc space consistent with extradural compression.
- An intraforaminal or dorsolateral disc herniation is best seen on an oblique cervical radiograph, with the entire cervical spine positioned at a 45–60° angle to the table.
- Acute cases with spinal cord swelling can cause blockage of contrast material and prevent it from flowing past the obstruction, limiting the diagnostic capabilities of the image.

Enhanced Diagnostic Imaging

- MRI and CT have also been used for diagnosis of cervical intervertebral disc disease.
- MRI or CT is useful for diagnosing foraminal or lateral disc extrusions when routine radiology is normal.
- MRI is the best available method for early recognition of disc degeneration in dogs.
- MRI signs of cervical radicular compression are obliteration of epidural fat in the neural foramen, displacement of the nerve roots, facet joint degeneration, uncovertebral joint hypertrophy, and disc material within the neural foramen.
- CT may provide a diagnostic image when there is an obstruction of the contrast medium flow.

DIAGNOSTIC PROCEDURES

Cerebral spinal fluid analysis

PATHOLOGIC FINDINGS**Gross Findings**

- Hansen type I disc—white extruded disc material that has a granular consistency and is usually easily removed from the spinal canal.
- Hansen type II disc—firm protrusion of the dorsal annulus fibrosus that is adherent to the floor of the spinal canal and to the dura of the spinal cord. Type II discs are much more difficult to remove from the spinal canal.
- Spinal cord—in acute disc extrusion the spinal cord may appear bruised and swollen; in chronic disc protrusion the spinal cord may appear to be atrophied but is often normal in appearance.

Histopathologic Findings

- Hansen type I disc—shifting concentration of glycosaminoglycans, loss of water and

INTERVERTEBRAL DISC DISEASE, CERVICAL

proteoglycan content, and increased collagen content. The disc becomes more cartilaginous and undergoes dystrophic calcification.

- Hansen type II disc—a gradual fibroid metaplasia leaves the disc with increased glycosaminoglycan levels and lower collagen content. The nucleus does not undergo cartilaginous metaplasia.
- Spinal cord—dependent on the severity of the disease and type of disc disease. Hansen type II—demyelination and gliosis are seen. Hansen type I—hemorrhage and edema can be seen; with severe disease myelomalacia can be observed.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Conservative management—dependent on patient's history and presenting neurologic status. In general, conservative management is indicated with a gradual onset of clinical signs or clinical signs that are limited to hyperesthesia or mild ataxia.
- Surgical management—patients with repeated episodes of neck pain, patients presented with severe neck pain and neurologic deficits, or patients that have not responded to conservative management.

NURSING CARE

- Handling—minimal manipulation of the cervical spine and avoidance of jugular venipuncture if at all possible.
- Urination—monitor patients for complete emptying of the bladder; patients may need to have bladder manually expressed or intermittent bladder catheterization. In some cases, indwelling urinary catheter may need to be placed. Urinalysis, including culture and sensitivity, should be performed after removal of an indwelling catheter to make sure the patient did not obtain a nosocomial bacterial cystitis. Newer studies suggest performing a culture and sensitivity on the urine of all dogs undergoing spinal decompression surgery.
- Defecation—patients may need enemas and can be switched to low-residue diet to decrease the volume of feces.
- Recumbent patients—should be kept on a well-padded mat and turned every 4 hours. Patients should be checked for pressure sores over bony prominences.
- Physical therapy—hydrotherapy and passive range of motion of all joints should be performed as often as possible to prevent severe muscle atrophy.

ACTIVITY

- Minimal, no running or jumping. When patients are being walked, a harness should be used instead of a collar.
- With conservative management patients

should be strictly confined to cage rest for 3–4 weeks.

- Following surgery patients should have minimal activity and be leash-walked only for 4–6 weeks, then slowly reintroduced to full activity.

DIET

For obese patients, a reducing diet should be instituted.

CLIENT EDUCATION

- For conservative management, strict cage confinement should be emphasized.
- Weight loss if the animal is obese.
- Common clinical signs of animals with cervical disc disease.

SURGICAL CONSIDERATIONS

- When indicated the goal of surgery is to remove disc material from the spinal canal and therefore decompress the spinal cord and/or nerve root.
- Surgery usually provides immediate pain relief and eventual normal motor function.
- A ventral cervical slot is the most common surgical approach for the removal of disc material from the spinal canal.
- Disc material that has extruded dorsolaterally into the intervertebral foramen is removed via a lateral approach to the cervical spine or through a dorsal laminectomy.
- Fenestration alone for dogs with neck pain usually does not resolve clinical signs and is no longer recommended.

**MEDICATIONS****DRUG(S)**

- Low-dose glucocorticoid therapy may be beneficial in order to decrease the pain in animals that are being treated conservatively.
- Glucocorticoids given to animals without simultaneous strict cage confinement could exacerbate disc extrusion by encouraging exercise.
- NSAIDs can be used only if the animal is not currently or recently being given glucocorticoids.
- Muscle relaxants can be used, but are generally unsuccessful when used alone.

CONTRAINdications

Never use glucocorticoids with NSAIDs—this can cause severe gastrointestinal irritation and possibly intestinal perforation.

PRECAUTIONS

When using high-dose corticosteroids for cervical disc disease, patients should be placed on gastro-protectants to prevent gastrointestinal side effects associated with corticosteroids. Use of high-dose glucocorticoids is not well-supported by the literature and is generally not recommended.

INTERVERTEBRAL DISC DISEASE, CERVICAL

(CONTINUED)

POSSIBLE INTERACTIONS

NSAIDs in combination with glucocorticoids can cause gastrointestinal perforation or severe gastrointestinal bleeding, both situations leading to death.



FOLLOW-UP

PATIENT MONITORING

- Weekly evaluations should be performed until the resolution of clinical signs.
- All patients should be fitted with a harness, and neck collars should be avoided.

PREVENTION/AVOIDANCE

- Inherent in particular breeds.
- Keeping patients at an ideal weight may help.

I

POSSIBLE COMPLICATIONS

- Complications are uncommon.
- Continued neck pain,
- Deteriorating motor status,
- Subluxation/Luxation of vertebral bodies.

EXPECTED COURSE AND PROGNOSIS

- Prognosis for patients treated surgically or conservatively depends on neurologic signs at the time of presentation.
- Prognosis is generally favorable for most patients.
- Most patients treated conservatively have recurrence of disease and may require surgical intervention.
- A recovery rate of 56% has been found for patients with the loss of deep pain who underwent surgical decompression within 12 h of the onset of clinical signs. This rate falls to less than 5% if the surgical intervention is delayed for 48 h or more.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Animals predisposed to cervical disc disease are also the same breeds that are predisposed to thoracolumbar disc disease.

SEE ALSO

Intervertebral Disc Disease, Thoracolumbar

ABBREVIATIONS

- CSF = cerebrospinal fluid
- CT = computed tomography
- EMG = electromyogram
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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Author Otto I. Lanz

Consulting Editor Walter C. Renberg



Client Education Handout
available online

INTERVERTEBRAL DISC DISEASE, THORACOLUMBAR



BASICS

DEFINITION

Intervertebral discs degenerate by loss of water, cellular necrosis, and dystrophic calcification. Biomechanical properties of the disc deteriorate, and subsequently protrusion (Hansen type II) or extrusion (Hansen type I) of disc material occurs.

PATHOPHYSIOLOGY

- Intervertebral disc degeneration is initiated by one or more factors including trauma, chronic overload, decreased spinal mobility, age-related deterioration in collagen and cartilage, and hypermobility.
- Hansen type I refers to acute extrusion of nucleus pulposus through the annulus fibrosis into the vertebral canal. Hansen type I lesions typically occur in chondrodystrophic dogs, but may occur in larger non-chondrodystrophic dogs as well. Onset of neurologic signs is usually acute and often severe.
- Hansen type II lesions involve gradual protrusion (bulging) of the dorsal annular fibers into the vertebral canal associated with fibroid degeneration of the disc. Hansen type II lesions typically occur in nonchondrodystrophic dogs. The most common case presentation is of gradual onset of neurologic dysfunction and slow progression.
- Some sources describe a Hansen type III injury where the nucleus pulposus herniates with such force as to enter the spinal cord. Hansen type III injuries are rare, but carry a poor prognosis because they are commonly associated with myelomalacia and loss of deep pain response.
- Acute disc extrusion results in extruded material causing direct trauma to the spinal cord and residual disc mass leading to extradural spinal cord compression. Trauma and spinal cord compression results in ischemia and spinal cord changes that vary from mild demyelination to necrosis of both gray and white matter; events at the cellular level include release of vasoactive substances, increased intracellular calcium, and increased free radical formation and lipid peroxides.
- Pain due to dural irritation, nerve root impingement, or possibly discogenic (annular pain receptors) in origin.
- Disc herniation is rare between T3 and T10 owing to the barrier of the intercapital ligament between the dorsal annulus and spinal cord.

GENETICS

Early studies suggest a polygenic model with no dominance or sex linkage.

INCIDENCE/PREVALENCE

- Most common neurologic dysfunction in small animals; affects 2% of the canine population.

- Occurs less commonly in cats, but the exact incidence is unknown, and the disease is likely underdiagnosed or reported due to lack of suspicion as a differential diagnosis.

- In specific breeds, such as dachshunds, affected prevalence as high as 20% has been reported.
- Thoracolumbar disc disease comprises 85% of all disc herniations; 70% occur from T11 to L3.

SIGNALMENT

Species

Dog and occasionally cat

Breed Predilections

- Type I—dachshund; shih tzu, Lhaso apso; Pekingese, Cocker spaniel, Welsh corgis; toy and miniature poodles.
- Type II—large breeds but may occur in any breed.

Mean Age and Range

- Type I, 3–6 years of age
- Type II, 8–10 years of age; cats: mean age of 10 years

SIGNS

General Comments

Clinical signs depend on the type of herniation, velocity of disc contact with the spinal cord, amount and duration of cord compression, location (UMN or LMN), and regional spinal canal/spinal cord diameter ratio (cervical vs. thoracolumbar).

Historical Findings

- Onset may be peracute or acute in chondrodystrophoid dogs (type I disease) and may occur during vigorous activity.
- Larger dogs or smaller dogs with type II disease have a more insidious onset and tend to worsen with time.

Physical Examination Findings

- Thoracolumbar pain common in dogs; reluctant to ambulate and hunched posture; careful palpation of spinous processes and epaxial musculature produces distinct localized pain; often some degree of paraparesis with decreased or absent proprioception or decreased motor ability in the rear limbs.
- Spinal reflexes in the rear limbs are usually exaggerated (hyper) when lesion is between T3 and L3; reflexes are decreased (hypo) when lesion is caudal to L3.
- Superficial and deep pain perception may be decreased or absent in the rear limbs; presence of deep pain sensation is the single most reliable prognostic factor for return to acceptable function; pain perception should be conscious in nature and not confused with a withdrawal reflex (local spinal reflex). In animals with diminished deep pain, mydriasis or tachycardia may be useful in confirming the presence of deep pain.
- Forelimb function is normal with thoracolumbar disc rupture; occasionally Schiff-Sherrington phenomena may cause

increased muscle tone in the forelimbs, but this clinical sign is location related only and does not indicate a poor prognosis.

- Urinary incontinence or retention is common when the lesion affects motor function.
- Pain is less obvious in cats; the site of herniation is often lumbar.

CAUSES

- Chondroid or fibroid degeneration of the thoracolumbar intervertebral discs.
- 15% of animals with spinal fractures have been reported to have disc extrusions in addition to the fracture/luxation.

RISK FACTORS

Type I disease most often affects chondrodystrophic breeds.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Type I—trauma causing fracture/luxation, neoplasia, discospondylitis, fibrocartilaginous embolism; differentiated by history, survey radiography, and myelography.
- Type II—degenerative myelopathy, spinal neoplasia, discospondylitis, orthopedic disease; differentiated by history, radiography, and careful orthopedic and neurologic examination.

CBC/BIOCHEMISTRY/URINALYSIS

- Elevation of liver enzymes common if patient has received corticosteroids for pain or neurologic disease.
- Urine retention/incontinence increases risk of urinary tract infection characterized by leukocytes, protein, and bacteruria on urinalysis.

OTHER LABORATORY TESTS

CSF analysis performed routinely in conjunction with myelography if there is high suspicion of another disease process; may be normal but more typically shows mild to moderate increase in protein with or without pleocytosis.

IMAGING

- Thoracolumbar spinal radiography with the patient anesthetized. Unanesthetized radiographs can be used to rule out neoplasia and other processes, but can be misleading for thoracolumbar disc disease.
- Survey radiographs rule out some other disease processes.
- Diagnostic radiographs taken under general anesthesia may reveal a narrowed or wedged disc space, collapsed articular facet space, and small intervertebral foramen with increased or mineralized density within the spinal canal.
- Accuracy and sensitivity of survey radiographs for determining a specific site of disc herniation is low.

INTERVERTEBRAL DISC DISEASE, THORACOLUMBAR

(CONTINUED)

DIAGNOSTIC PROCEDURES

- MRI is now considered the diagnostic mode of choice when available due to the noninvasive nature and increased information about disease process and localization obtained. Presence of a hyperintense spinal cord lesion as long as the body of L2 on a T2-weighted image in deep-pain-negative dogs is associated with a poorer prognosis.
- CT with or without contrast is often diagnostic in chondrodystrophic dogs; dystrophic calcification of extruded material is easily visualized and lateralization can be easily determined. Contrast enhancement can differentiate disc disease from neoplastic or granulomatous processes.
- Myelography performed with iohexol was previously the method of choice and is still indicated when CT or MRI is not available. The contrast agent is usually introduced at L5–L6. Positive diagnosis is an extradural mass lesion causing spinal cord compression adjacent to the affected disc; spinal cord swelling may be evidenced by thinning of contrast columns over several intervertebral spaces.
- Lateralization is more consistent when determined from both oblique and dorsoventral myelogram views..
- CSF analysis is an important addition when alternative causes of neuropathy are likely differential diagnoses or when imaging findings are equivocal or nondiagnostic.

PATHOLOGIC FINDINGS

Gross

- Extruded disc material (type I disease)—white to yellow and “toothpaste” consistency; if chronic, may be hardened and adhered to surrounding structures.
- Protruded disc material (type II disease)—usually firm, grayish-white, and may be adherent to surrounding structures.
- Spinal cord may appear normal or be swollen and discolored in acute severe disease.

Histopathologic

- Degenerated discs have decreased amounts of proteoglycans, glycosaminoglycans, and water; discs may become mineralized or cartilaginous.
- Spinal cord lesion depends upon type and severity of disc extrusion or protrusion; acute, severe disease may cause hemorrhage, edema, tissue necrosis; chronic disease demyelination of white and in some cases gray matter.



TREATMENT

APPROPRIATE HEALTH CARE

- Guidelines for therapy based on classification of clinical condition.
- Class 1—back pain only, first episode.
- Class 2—recurrent back pain, ataxia, mild paraparesis, motor ability good.

- Class 3—severe paraparesis, proprioceptive deficits, motor ability affected but still present.
- Class 4A—complete paralysis (no motor ability) with deep pain perception present.
- Class 4B—complete paralysis, no deep pain perception present.
- Class 1 patients treated medically unless pain persists.
- Class 2 patients treated medically initially with serial neurologic exam, surgery if patient remains static or condition declines.
- Classes 3 and 4A—immediate surgical therapy; prognosis good.
- Class 4B—surgical therapy and fair prognosis if within the first 12–48 hours of occurrence. Poor prognosis if deep pain perception has been absent for > 48 hours.
- Serial neurologic examination important for all affected animals.

NURSING CARE

- Absolute restricted confinement for 2–4 weeks or until ambulatory.
- Minimize spinal manipulation and support spine when handling patient.
- Ensure ability to urinate or consider bladder expression, intermittent catheterization, or indwelling urinary catheter for patients in classes 3–4B.
- Recumbent patients should be kept clean on padded bedding placed on elevated cage racks and turned frequently to prevent formation of decubital ulcers.
- Manual evacuation of the bowel or enemas may be necessary to promote defecation.
- Physical therapy with passive manipulation of rear limbs begun early followed by more intense therapy (hydrotherapy) for animals with neurologic deficits.
- Carts useful in many patients in promoting return to function; patient tolerance is limiting factor.

ACTIVITY

- Restricted movement most important part of medical management.
- Cage rest in hospital or enforced cage rest as an outpatient for 2–4 weeks for class 1 patients or postoperative animals.

DIET

Weight reduction if patient is obese.

CLIENT EDUCATION

- Some degree of restricted activity may be important for the remainder of the animal's life since it has disc disease.
- Most animals in classes 1–4A have a good to excellent prognosis for return to function, i.e., ambulation with bowel and bladder continence; patients in class 4B have a poorer but not hopeless prognosis; percentages vary but up to approximately 50% may regain deep pain and some function.

SURGICAL CONSIDERATIONS

- Strongly indicated for animals in classes 3 and 4, also within the first 12–48 hours for

class 4B dogs; also indicated for static or worsening class 1 and 2 dogs.

- Primary surgical goal is to relieve spinal cord compression by disc mass removal via hemilaminectomy, dorsal laminectomy, or pediculectomy; disc fenestration alone rarely indicated but is highly recommended as an adjunct to decompression at the primary site.
- Hemilaminectomy is the surgical procedure of choice for most thoracolumbar discs. Studies indicate improved return to function, minimized spinal destabilization, and decreased formation of compressive laminectomy scars in the long-term postoperative period.
- Foramenotomy and pediculectomy are similar to hemilaminectomy and may allow a more limited approach and decreased cord manipulation.
- Dorsal laminectomy is the procedure of choice for disc herniation in the region of the lumbosacral plexus or where extensive examination of the spinal cord is necessary.
- Recurrence of clinical signs in animals in the immediate postoperative period may be due to further extrusion of disc from the original site if unfenestrated. Later recurrence of clinical signs after recovery usually due to protrusion/extrusion at adjacent sites. Several studies indicate 8% long-term recurrence of clinical signs in dogs after initial hemilaminectomy and active site fenestration due to protrusion/extrusion at other sites.
- Surgical controversies remain over the issues of multiple site prophylactic disc fenestrations performed during the decompressive surgery and the timing and prognosis for return to function after surgery in patients showing no deep pain.



MEDICATIONS

DRUG(S) OF CHOICE

- NSAIDs or narcotics may be used as an analgesic in class 1 cases.
- Narcotic analgesics may be necessary postoperatively; hydromorphone (0.05–0.2 mg/kg IV or IM, SC q4h). Transdermal lidocaine or fentanyl may be useful modes of analgesic administration in some animals.
- Gabapentin (Neurotin), an NMDA receptor antagonist, may be useful at 5–10 mg/kg PO q12h in dogs with chronic pain sensitization.
- Methocarbamol (25–45 mg/kg q8h) may be useful in cases where muscle spasm is contributing to pain; more applicable with cervical disease.
- Bethanechol (5–15 mg/dog PO) and phenoxybenzamine (0.25 mg/kg PO q8–12h) or prazosin 1 mg/15 kg PO q8–12h variably helpful in managing bladder dysfunction associated with spinal cord lesion.

(CONTINUED)

INTERVERTEBRAL DISC DISEASE, THORACOLUMBAR

- Previous indications for methylprednisolone sodium succinate for treatment of acute pain are now controversial for efficacy. The high potential for side effects may outweigh the small gains from the drug.

PRECAUTIONS

- Glucocorticoid use is discouraged in cases of IVDD where drug side effects such as gastrointestinal hemorrhage and intestinal perforation often far outweigh benefits. Potent glucocorticoids such as dexamethasone should never be used.
- Glucocorticoids are contraindicated within 48 hours of using an NSAID in dogs.
- Use of glucocorticoids without cage confinement may decrease pain, thereby encouraging excessive activity and leading to further disc herniation and deterioration of clinical condition.

ALTERNATIVE DRUG(S) AND THERAPIES

- Acupuncture use has been described, but efficacy has yet to be determined.
- Chiropractic therapy has no proven benefits for IVDD and may potentially be harmful to the animal.
- Percutaneous therapeutic lasers do not reach the site of inflammation and are likely not efficacious.
- Discolysis by enzymatic injection or laser ablation described but not proven therapy in dogs.

**FOLLOW-UP****PATIENT MONITORING**

- Patients treated medically should be reevaluated two to three times daily for worsening neurologic signs for the first 48 hours after onset.

- If stable, reevaluate daily, then weekly, until clinical signs have resolved.
- Patients treated surgically are evaluated twice daily until improvement is noted; urinary bladder function or awaiting development of an autonomic bladder are the limiting factors for hospitalization.

POSSIBLE COMPLICATIONS

- Recurrence of signs associated with disc herniation at original or at new site.
- Deterioration of clinical signs with or without surgery; continued inflammatory processes initiated by the initial extrusion may result in myelomalacia or diminished function.
- Rarely, development of ascending or descending myelomalacia; occurs in class 4A or 4B dogs 3–5 days following injury and is characterized by variable and changing neurologic findings, possible fever, possible dyspnea; extreme pain, and progressive neurologic signs with the forward movement of the inflammation. Such animals are often euthanized when diagnosed.

EXPECTED COURSE AND PROGNOSIS

- Overall prognosis for dogs in classes 1–4A good to excellent (85–95%); those treated conservatively may experience recurrence of clinical signs.
- Recurrence rates of dogs without fenestration at the time of laminectomy range from 5–30%.
- Dogs in class 4B have a variable (10–75%) chance of recovery; overall a guarded but seemingly favorable prognosis if surgery is performed within 48 hours and the animal is allowed sufficient time to recover.

**MISCELLANEOUS****ABBREVIATIONS**

- CSF = cerebrospinal fluid
- CT = computed tomography
- IVDD = intervertebral disc disease
- LMN = lower motor neuron
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug
- UMN = upper motor neuron

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Author James K. Roush

Consulting Editor Walter C. Renberg

**Client Education Handout available online**

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INTUSSUSCEPTION



BASICS

DEFINITION

- Invagination of one intestinal segment into the lumen of the adjacent segment.
- Intussusceptions are classified according to their localization within the gastrointestinal tract. • Ileocolic and jejunolejunal intussusceptions are the types most commonly encountered in small animals. Others that have been described include gastroesophageal, duodenolejunal, and cecocolic. • The segment entrapped within the lumen of the intussusception is called the intussusceptum. The engulfing segment is called the intussuscipiens. • Most commonly, the orad segment is found to be engulfed within the aborad segment.

PATOPHYSIOLOGY

- The exact mechanism of intussusception generation is not known. • Many affected animals are young (<1 year of age), and have a history of recent enteritis. • Gastrointestinal irritation may cause the orad segment to undergo a hyperperistaltic state, and invaginate into the more flaccid aborad segment. • The occurrence of an intussusception leads to a mechanical obstruction of the gastrointestinal tract. This obstruction can be either partial or complete.
- Vascular compromise commonly occurs in the intussusceptum and can occasionally occur in the intussuscipiens. Compromise of venous drainage in the face of an intact arterial blood supply leads to marked edema and intramural hemorrhage that may eventually progress to extravasation of blood into the intestinal lumen. • Persistence of the intussusception can lead to eventual decreased oxygen delivery to the mucosal layer. This can lead to the eventual failure of the mucosal barrier and loss of an effective barrier to bacteria and endotoxin entering the bloodstream from the bowel lumen. • With time, vascular compromise can lead to intestinal necrosis and eventual leakage of contents into the peritoneal cavity. This leads to the development of septic peritonitis.

SYSTEMS AFFECTED

- Gastrointestinal—mechanical obstruction, ileus. • Cardiovascular—fluid loss (vomiting and diarrhea) can lead to hypovolemia.

SIGNALMENT

Species

Intussusceptions have been reported in dogs and cats but are more common in dogs.

Breed Predilections

- German shepherd dogs appear to be predisposed to gastroesophageal intussusceptions, accounting for approximately 60% of the reported cases of

this condition. This breed also appears to be overrepresented in the other types of intussusceptions. • Siamese cats may be predisposed.

Mean Age and Range

- Due to the risk factors for development of an intussusception (i.e., parasitism, viral enteritis, dietary indiscretion, foreign body ingestion), animals affected with this disease are often younger.
- Older animals with an intussusception should be carefully screened for diseases that can cause an alteration of peristalsis such as intestinal neoplasia or other mural diseases.

Predominant Sex

- It was originally felt that males outnumber females with gastroesophageal intussusception. Recent reports have called this into question.
- There is no documented sex predilection for other types of intussusceptions in small animals.

SIGNS

General Comments

- Clinical signs associated with the intussusception depend on the anatomic region of the intussusception.
- In general, intussusceptions occurring in more orad segments have more severe clinical signs and disease progression.
- Gastroesophageal intussusceptions typically cause more severe clinical signs than intussusceptions located in a more aborad location.
- The severity of clinical signs also depends upon the completeness of the obstruction.

Historical Findings

- Vomiting.
- Diarrhea (which may or may not have fresh blood or melena present).
- Abdominal pain.
- Abdominal distention.
- Anorexia.
- Weight loss.
- These signs most commonly are acute in onset but may have been occurring for weeks or months.

Physical Examination Findings

- May display overt abdominal pain/discomfort.
- Depending on the severity of the intussusception as well as the length of time that it has been present, some patients may show signs of cardiovascular compromise.
- A sausage-shaped mass may be palpable in the abdomen. The ability to palpate the intussusception is variable.
- Ileocolic intussusceptions may present with protrusion of the intussusceptum from the rectum. This can be differentiated from a rectal prolapse via probing along the side of the protruding tissue. The presence of a blind-ending fornix indicates the existence of a rectal prolapse rather than an intussusception.

CAUSES

- Any disease that alters gastrointestinal motility may lead to an intussusception. Known causes include: enteritis, recent abdominal surgery, intestinal mural disease, and intestinal parasitism.
- Intussusceptions

occur in 8–33% of dogs that undergo renal allograft transplantation and 5% of dogs that undergo hematopoietic cell grafts. The reason for this is unclear, but may be related to immunosuppressive drugs.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Any disease that can cause vomiting and diarrhea.
- Some intussusceptions can be chronic in nature; therefore, a chronic history of vomiting and/or diarrhea does not rule out an intussusception. This list includes but is not limited to intestinal parasites, viral enteritis (e.g., parvoviral infections), bacterial enteritis, foreign bodies, inflammatory bowel disease, mesenteric volvulus, and intestinal neoplasia.

CBC/BIOCHEMISTRY/URINALYSIS

- Leukogram—can range from normal to leukopenia (especially with sepsis or parvoviral infection) to leukocytosis (either stress response or in some septic patients).
- Hematocrit can be elevated (dehydration or underlying hemorrhagic gastroenteritis) or decreased (cases of intraluminal hemorrhage).
- Biochemical analysis—can show derangements of electrolytes due to loss through vomiting or diarrhea. These can include hyponatremia, hypochloridemia, hypokalemia. May be azotemic (prerenal) if significantly dehydrated. May also be hypoalbuminemic due to effusive loss into intestinal lumen. This can occur in the event of intestinal permeation changes subsequent to eventual intestinal mucosal necrosis.
- Urinalysis—may reveal elevated specific gravity in response to dehydration.

OTHER LABORATORY TESTS

- May see elevated lactate levels due to vascular compromise to intestinal segment.
- Blood gas evaluation may reveal a metabolic acidosis secondary to dehydration and hypoperfusion. Alternately, if the obstruction results in primarily gastric vomiting (pyloric obstruction), a hypochloremic, hypokalemic, metabolic alkalosis may be present.

IMAGING

- Plain radiographs may reveal an obstructive intestinal pattern. The degree of intestinal distention may be related to the degree of obstruction.
- Plain radiographs may or may not reveal evidence of a soft tissue mass consistent with the intussusception.
- With gastroesophageal intussusception, a soft tissue mass may be seen within the lumen of the esophagus near the esophageal hiatus of the diaphragm. These findings can be confused with a hiatal hernia, but the severity of the clinical signs typically associated with a hiatal hernia are much more mild compared to a

(CONTINUED)

gastroesophageal intussusception.

- Abdominal ultrasound is very helpful in the diagnosis of abdominal intussusceptions. The intussusception appears as a target patterned mass on transverse sections, and as a multitude of parallel lines on longitudinal sections.
- Upper GI contrast studies or barium enemas can be helpful in supporting the diagnosis of an intussusception.

PATHOLOGIC FINDINGS

- Examination of the intussusception reveals a telescoping of a segment of bowel into the adjacent segment.
- Histopathologic examination reveals variable degrees of venous congestion, vascular compromise, bowel wall necrosis, and peritonitis.



TREATMENT

APPROPRIATE HEALTH CARE

Initial efforts should be focused on patient stabilization as well as correction of dehydration and existing electrolyte abnormalities.

NURSING CARE

- Intravenous fluid administration to correct dehydration as well as replace anticipated ongoing losses through vomiting and diarrhea.
- Typically, isotonic crystalloids are used. Specific choice of fluid type is dictated by electrolyte derangements.

ACTIVITY

Recommend controlled activity for 10–14 days postoperatively.

DIET

- If patient is vomiting intractably—NPO. If this occurs postoperatively, ileus may be an underlying cause.
- Most patients can readily be fed within 24 hours of surgical correction.

CLIENT EDUCATION

- Immediate surgical intervention is the recommended treatment for intussusceptions.
- Stress the importance of the identification and treatment of an underlying cause.
- Complications may include: perioperative mortality, septic peritonitis, protracted hospital stay to stabilize, and recurrence. Recurrence rates have been reported to be 6–27%.

SURGICAL CONSIDERATIONS

- Surgical correction should be performed as soon as the patient is stable enough to withstand anesthesia and surgery. This is a surgical emergency.
- A full abdominal exploratory should be performed to assist in the identification of any potential underlying causes. Also, multiple intussusceptions may be present in one patient.
- Some intussusceptions can be manually reduced by gently milking the intussusceptum from

within the intussusciens. Upon reduction, the bowel may or may not be viable.

- In the event that manual reduction is not possible, or the bowel has questionable viability, an intestinal resection and anastomosis is necessary.
- Enteroplication has been proposed as a procedure for preventing recurrence. A recent article identified some dogs that necessitated a second surgical procedure to correct problems sustained from the enteroplication procedure. It is important to exercise care when performing this procedure. Briefly, the loops created in the bowel should be gentle, and sharp turns in the bowel loops are to be avoided. The submucosal layer of the adjacent loops of bowel should be included in the sutures, but the lumen should not be entered.



MEDICATIONS

DRUG(S) OF CHOICE

- The prophylactic use of antibiotics is recommended. The choice of antibiotics should be dictated by the bacteria that are encountered.
- Manual reduction of an intussusception is considered a clean surgical procedure, while an intestinal resection and anastomosis is considered a clean-contaminated procedure.
- Long-term antibiotic administration is not recommended except in cases in which septic peritonitis is present either preoperatively or postoperatively.

CONTRAINdications

Some surgeons feel that medications that stimulate peristalsis (e.g., metoclopramide) are contraindicated due to the potential for facilitating an environment for the recurrence of an intussusception.



FOLLOW-UP

PATIENT MONITORING

- Postoperatively, patients should be maintained on intravenous fluids and pain medications.
- Most recurrences occur within the first few days of surgery, but recurrences have been reported up to 3 weeks after surgery.
- Intestinal dehiscence typically occurs 3–5 days postoperatively. The signs, diagnosis, and treatment of septic peritonitis are covered elsewhere in this book.

PREVENTION/AVOIDANCE

Prevention of many of the underlying causes can be achieved through such actions as vaccination against parvovirus, intestinal parasite control, limiting situations in which patients can be exposed to dietary indiscretion or foreign body ingestion.

INTUSSUSCEPTION

POSSIBLE COMPLICATIONS

- Recurrence—6–27% of patients.
- Septic peritonitis—may result from postoperative intestinal dehiscence or intraoperative contamination.
- Short bowel syndrome is a rare complication that can occur with massive resections (generally > 70% in dogs) of the small intestine.

EXPECTED COURSE AND PROGNOSIS

- Highly dependent upon underlying cause, location of intussusception, and condition at presentation.
- Generally, as the intussusception moves more aborad, the prognosis improves as these patients are less severely affected.
- Gastroesophageal intussusceptions have a grave prognosis with mortality rates approaching 95%, while intestinal intussusceptions hold a good prognosis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Can be associated with intestinal parasites, viral enteritis, intestinal mural diseases.
- Gastroesophageal intussusceptions are typically associated with an underlying esophageal disorder.

AGE-RELATED FACTORS

Younger patients are typically affected with underlying enteritis (viral or bacterial) or intestinal parasitism. Older patients are more commonly affected with intestinal neoplasia.

SEE ALSO

- Gastrointestinal Obstruction • Peritonitis

ABBREVIATIONS

- GI = gastrointestinal

Suggested Reading

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Diagnosis and treatment of intussusceptions in dogs. Compend Contin Educ Pract Vet 2002, 24:110–127.

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IRIS ATROPHY



BASICS

OVERVIEW

- Degeneration of iris tissues; both the iris stroma and posterior iris epithelium can be affected, resulting in loss of iris sphincter and dilator muscle function, atrophy of iris vessels, and loss of iris pigment.
- Both the pupillary margin and more peripheral portions of the iris can be affected, resulting in an iris that is thin or has areas of full-thickness tissue loss.
- Senile or secondary change.
- Secondary iris atrophy is usually a result of chronic inflammation (uveitis).
- Iris sphincter muscle frequently affected by atrophy, resulting in incomplete pupillary constriction and possibly an abnormal pupil shape (dyscoria).
- Irregular scalloped, moth-eaten pupil margin a common manifestation.
- Pupil margin may remain unaffected; peripheral loss of iris tissue can cause large holes in the iris that resemble multiple pupillary openings.
- Vision largely unaffected.
- May cause discomfort in bright-light settings.

SIGNALMENT

- Dog—common aging change; all breeds, but affects small breeds (e.g., miniature and toy poodles, miniature schnauzers, and Chihuahuas) more commonly.
- Cat—uncommon; most common with blue irides.
- Secondary—any breed of dog or cat.

SIGNS

Historical Findings

- Large or dyscoric pupil in one or both eyes.
- Photophobia.
- Previous episodes of uveitis.

Physical Examination Findings

- Incomplete or absent pupillary light reflex accompanied by a normal menace response and dazzle reflex.
- Anisocoria may be present with unilateral or asymmetric presentation.
- Irregular, scalloped edge to the pupillary margin; dyscoria.
- Tapetal reflex visible through thin or absent areas of the iris on transillumination: translucent patches or holes within the iris stroma—may resemble additional pupils.

- Strands of iris occasionally remain, spanning across portions of the pupil.
- Secondary—may be accompanied by any sign associated with chronic uveitis.

CAUSES & RISK FACTORS

- Normal aging
- Uveitis
- Glaucoma



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Must differentiate from congenital iris anomalies.
 - Iris aplasia—rare in dog and cats.
 - Iris hypoplasia—differentiate based on age at first presentation of signs.
 - Iris coloboma—a complete, full-thickness area of lack of development of all layers of the iris; frequently associated with the merle condition; may also see associated lack of lens zonules and an indentation of the lens posterior to the colobomatous iris area; differentiate based on age and presence of associated abnormalities.
 - Polycoria—more than one pupil, each with the ability to constrict due to the presence of an iris sphincter.
 - Persistent pupillary membranes—arise from the collarette (midportion) of the iris, not from the free pupillary margin.
- Pupil dilation due to glaucoma—elevated IOP, corneal edema, conjunctival ± episcleral vascular injection, enlargement of the globe may also be present; may also be blind.
- Adhesions of the iris to the lens or cornea (posterior or anterior synechia) as a result of uveitis or trauma—differentiate based on associated abnormalities consistent with uveitis or perforating trauma (e.g., full-thickness corneal scar).

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Tonometry—low IOP possible if secondary to uveitis; high IOP if secondary to glaucoma or if the uveitis has also caused a secondary glaucoma; normal IOP if primary senile iris atrophy.



TREATMENT

- Irreversible.
- Secondary—successful treatment aimed at controlling the underlying disease may halt progression of the condition.
- Patient may exhibit photophobia because of inability to constrict the pupil; provide adequate shade.



MEDICATIONS

DRUG(S)

- Senile—none
- Secondary—depending on underlying disease

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Topical atropine—exacerbates pupillary dilation and photophobia.



FOLLOW-UP

- Senile—may continue to progress with age.
- Secondary—usually does not progress once the primary disease is controlled.



MISCELLANEOUS

SEE ALSO

- Anterior Uveitis—Cats
- Anterior Uveitis—Dogs
- Glaucoma

ABBREVIATION

- IOP = intraocular pressure

Suggested Reading

Hendrix DVH. Diseases and surgery of the canine anterior uvea. In: Gelatt KN, Gilger BC, Kern TJ, eds., Veterinary Ophthalmology, 5th ed. Ames, IA: Wiley-Blackwell, 2013, pp. 1146–1198.

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IRON TOXICOSIS



BASICS

OVERVIEW

- Iron—essential element for living organisms; may be lethal when ingested in large quantities.
- Sources of large concentrations of readily ionizable iron—multivitamins; dietary mineral supplements; human pregnancy supplements; some slug and snail baits; some types of hand warmers; some iron-fortified fertilizers; some oxygen absorber sachets (used for spoilage prevention).
- Overdose—loss of normal mucosal limitations of iron absorption; corrosive to GI mucosa.
- Circulating iron in excess of the TIBC—very reactive; causes oxidative damage to any cell type.
- Damage to mitochondria—loss of oxidative metabolism.
- Primary systems affected—gastrointestinal; hepatic; cardiovascular; nervous.

SIGNALMENT

- Dogs; possible in other species.
- All ages are susceptible.

SIGNS

General Comments

- History—generally indicates ingestion of pills or other iron-containing materials.
- Patients that remain asymptomatic for the first 6–8 hours are unlikely to develop any later signs.
- Onset occurs in four stages.

Stage I (0–6 hours)

- Vomiting • Diarrhea • Depression • GI hemorrhage • Abdominal pain

Stage II (6–24 hours)

Apparent recovery (latent period)

Stage III (12–96 hours)

- Vomiting • Diarrhea • Depression • GI hemorrhage • Shock • Tremors • Abdominal pain • Metabolic acidosis

Stage IV (2–6 weeks)

GI stricture formation

CAUSES & RISK FACTORS

- Ingestion of iron-fortified pills or other soluble iron-containing materials.
- Dogs—likely to ingest a large number of pills or other materials, owing to indiscriminate eating behavior.
- Toxic dose (dogs)— $> 20 \text{ mg/kg}$ of elemental/absorbable iron.
- Metallic iron and iron oxide (rust)—not readily ionizable/absorbable; not associated with toxicoses.
- Take care when calculating iron ingestion; iron salts vary in elemental iron content (between 12% and 63%).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other causes of severe gastroenteritis and shock, gastric torsion, snake bite,

caustic/corrosive ingestion, viral/bacterial enteritis, garbage ingestion, heat prostration.

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis • Hyperglycemia • Normal to high AST, ALT, ALP, and serum bilirubin

OTHER LABORATORY TESTS

Metabolic acidosis

Serum Analysis for Total Serum Iron and TIBC

- Indicates poisoning and need for treatment:
- Serum iron $> 350\text{--}500 \mu\text{g/dL}$ serum or
- Serum iron concentration $>$ TIBC.
- Monitor at 2–3 hours and 5–6 hours post-ingestion in asymptomatic patients; absorption rates vary with tablet dissolution and serum iron concentrations can change rapidly.
- Use only clear, non-hemolyzed serum as hemolysis increases iron content.

IMAGING

Radiography—intact iron-containing pills may be radio-dense; pill bezoars or pills adhered to mucosa may be visible.

DIAGNOSTIC PROCEDURES

- Post-mortem analysis for iron in tissues—often ineffective due to the reactive nature of free iron and the systemic distribution of reactive binding.
- Analysis of GI or stomach contents—may aid in documenting high iron exposures.

PATHOLOGIC FINDINGS

- Primary gross lesions—hemorrhage in the GI tract and liver; hepatomegaly.
- Histopathologic lesions—GI necrosis with potential of hepatocellular and vascular endothelial necrosis



TREATMENT

- Correct hypovolemic shock—intravenous fluids.
- Correct acidosis—intravenous sodium bicarbonate if severe.

Decontamination

- Prevent further GI and systemic damage—removal of unabsorbed iron from the stomach; lessens duration and severity of signs.
- Oral milk of magnesia or aluminum hydroxide (precipitates iron in GI tract) in asymptomatic patient.
- Emesis—induced for asymptomatic patient: 3% hydrogen peroxide 1–2 mL/kg PO or apomorphine 0.04 mg/kg IV or IM.
- Gastric lavage—performed when emesis is contraindicated or when pill bezoars are identified.
- Emergency gastrotomy—indicated if lavage fails to remove adherent pills or bezoars.

Chelation

- Chelate when serum iron $> 350\text{--}500 \mu\text{g/dL}$ or serum iron $>$ TIBC.
- Deferoxamine mesylate—iron chelator of choice.
- Calcium disodium EDTA has been used but may not reduce mortality.
- Duration of therapy—until signs have resolved AND serum iron is

consistently below 300 $\mu\text{g/dL}$ or TIBC is greater than serum iron.



MEDICATIONS

DRUG(S)

- Deferoxamine mesylate (iron chelator)—15 mg/kg/h SLOW IV infusion or 40 mg/kg IM q4–6h or 40 mg/kg SLOW IV q4–6h.
- Antiemetic—maropitant 1 mg/kg SQ q24h, ondansetron 0.1–0.2 mg/kg SQ, IV q8–12h.
- GI protectant—sucralfate 0.5–1 g PO q8–12h; oral antacids.
- H2 antagonist (cimetidine, ranitidine, famotidine) or proton pump inhibitor (omeprazole 0.5–1 mg/kg PO q24h).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Activated charcoal—does not bind iron.
- Gastric lavage—contraindicated in presence of hematemesis; increased risk of perforation.
- Intravenous deferoxamine—must be given slowly or may precipitate cardiac arrhythmias.
- Deferoxamine—teratogenic; use in patients only if benefits outweigh risks.



FOLLOW-UP

- Liver enzymes—monitored up to 24 hours after excess circulating iron is controlled.
- Watch for evidence of GI obstruction for 4–6 weeks after poisoning.



MISCELLANEOUS

SEE ALSO

Poisoning (Intoxication) Therapy

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- GI = gastrointestinal
- TIBC = total iron binding capacity

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IRRITABLE BOWEL SYNDROME



BASICS

DEFINITION

A condition characterized by chronic intermittent signs of gastrointestinal (often colonic) dysfunction and/or dysmotility in the absence of structural GI pathology or alternative diagnosis.

PATOPHYSIOLOGY

- A psychosomatic relationship is hypothesized to exist between the behavior of the patient and responses of the autonomic nervous system and the enteric nervous system.
- Potential interactive causes may include abnormal colonic motility, dietary fiber deficiency, dietary intolerances, stress/anxiety, and concurrent gastrointestinal pathology.

INCIDENCE/PREVALENCE

The incidence of IBS in dogs as a primary disorder is unknown but is thought by the author to be < 5%.

SIGNALMENT

Species

Dog (uncommon); cat (rare)

Breed Predilections

Any breed; suspected to be more common in active working dogs or individual dogs with anxious temperaments.

SIGNS

Historical Findings

- Chronic, intermittent signs of large bowel disease are most common: frequent passage of small amounts of feces with increased mucus and hematochezia and dyschezia. Constipation may occur with clinical signs alternating between diarrhea and constipation.
- Abdominal pain, segmental ileus (bloating), vomiting, and nausea may also occur.

RISK FACTORS

- Stress (e.g., changes in the household, change of diet, separation anxiety) may or may not be associated with episodes in some patients.



DIAGNOSIS

- Based on the exclusion of all other potential causes of large bowel signs.
- Reserve for patients that have undergone a comprehensive workup including gastrointestinal biopsies, and therapeutic deworming (particularly inclusive for whipworms), increased fiber-rich (soluble and/or insoluble) and elimination diets without resolution of signs.

DIFFERENTIAL DIAGNOSIS

Causes of Large Bowel Disease

- Whipworms • IBD • *Clostridium perfringens* or *C. difficile*—associated diarrhea

- Invasive adherent *Escherichia coli*—associated granulomatous colitis
- Fiber-responsive large bowel diarrhea
- Dietary indiscretion (foreign body–induced coloproctitis) or intolerance
- Pancreatitis can cause inflammation of the transverse colon with signs of colitis
- Histoplasmosis • Pythiosis • Colorectal neoplasia • Cecal inversion • Gluten enteropathy • Anal sacculitis • Megacolon (colorectal pseudo-obstruction)

Diseases with Similar Signs

- Dysuria/stranguria—exclude with observation, urinalysis, and imaging.
- Prostatic disease—exclude with rectal examination and imaging.
- Peritoneal adhesions.
- Disorders or injury affecting innervation of GI tract via intestinal intrinsic nervous system, vagal nerve, and pelvic nerve plexuses.

CBC/BIOCHEMISTRY/URINALYSIS

Usually unremarkable

OTHER LABORATORY TESTS

Fecal flotation and rectal scraping cytology typically unremarkable.

IMAGING

- Survey and contrast radiographic studies of the abdomen—unremarkable or may show segmental luminal gas distention.
- Abdominal ultrasonography—unremarkable.

DIAGNOSTIC PROCEDURES

Endoscopy or exploratory surgery with biopsy generally unremarkable.

PATHOLOGIC FINDINGS

- Usually unremarkable.
- Concurrent chronic intestinal disease (e.g., IBD) may be present and needs to be successfully managed prior to pursuing diagnosis and treatment for IBS.



TREATMENT

DIET

A highly digestible diet with added blend of soluble and insoluble fiber often helps (e.g., psyllium, wheat dextrin); if increased soluble fiber is not helpful, then try an increase of insoluble (methylcellulose) fiber; either may result in variable improvement in any given case.



MEDICATIONS

DRUG(S) OF CHOICE

- Drug therapy may range from several short-term (days) to life-long.
- Most cases of canine IBS can involve both gastrointestinal hypermotility (spasmodic) and potential sensory changes thought to result in forms of dysmotility via interference with GI intrinsic nervous system activity.
- Librax (an antispasmodic with anxiolytic) or gabapentin (5–10 mg/kg q12h) for possible neuropathic pain (if pelvic plexus stimulation is suspected).
- Start at lower end of dosage range.

antispasmodic with anxiolytic) or gabapentin (5–10 mg/kg q12h) for possible neuropathic pain (if pelvic plexus stimulation is suspected).

- Start at lower end of dosage range.

Motility Modifiers

- Opiate antidiarrheals improve signs by increasing rhythmic segmentation.
- Loperamide 0.1–0.2 mg/kg PO q8–12h.
- Diphenoxylate 0.05–0.2 mg/kg PO q8–12h.
- Gabapentin (1–10 mg/kg q12h) for possible neuropathic pain.
- Cisapride (prokinetic) 0.5 mg/kg to maximum of 10 mg PO q8–12h if clinical signs of constipation predominates.

Antispasmodic-Tranquilizer-Anxiolytic Combinations

- Used to relieve anxiety, abdominal cramping, bloating, and distress.
- Librax—chlor diazepoxide (anxiolytic) and clidinium bromide (anticholinergic), 0.1–0.25 mg of clidinium/kg PO q8–24h.
- Darbazine—isopropamide (anticholinergic) and prochlorperazine (tranquilizer), 0.14–0.22 mg/kg SC q12h; oral.
- Aminopentamide 0.01–0.02 mg/kg PO, IM, SC.

Parenteral Antiemetics

- If nausea and vomiting preclude the use of oral medication, administer antiemetics parenterally for 1–2 days.
- Maropitant 1 mg/kg SC dogs q24h SC in dogs.
- Prochlorperazine 0.1–0.5 mg/kg q6–24h SC or IM.

Serotonin-like Antagonists

Ramosetron is a potent and selective serotonin (5-HT3) receptor antagonist that has been helpful in humans with diarrhea-predominant IBS; no reports have been found beyond experimental testing in normal dogs.

CONTRAINDICATIONS

- Opiates—respiratory dysfunction, hepatic encephalopathy, constipation and/or severe debilitation.
- Anticholinergics—cardiac disease, renal disease, hypertension, constipation and/or hyperthyroidism.



FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS

- Improved stools, decreased mucus, and relief of dyschezia and abdominal distress within 1–2 days of starting medication.
- In some dogs, signs completely resolve following therapy; others have long-term episodic signs.

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IVERMECTIN AND OTHER MACROCYCLIC LACTONES TOXICOSES



BASICS

OVERVIEW

- Includes ivermectin, milbemycin, moxidectin, selamectin, and others.
- Toxicity—dogs given large extra-label dosages (> 10–15 times recommended dosage).
- Ivermectin—binds to glutamate-gated chloride ion channels in invertebrate nerve and muscle cells causing subsequent paralysis and death of the parasite. Also interacts with other ligand-gated chloride channels including those gated by gamma-aminobutyric acid.
- Sensitivity—collies and certain other breeds are more sensitive to high doses of ivermectin. This sensitivity has been associated with an inherited deletion of the ABCB1 gene that encodes a transmembrane protein pump called P-glycoprotein. P-glycoprotein is believed to transport ivermectin out of brain tissue and into circulation.

SIGNALMENT

- Dogs.
- Collies—most commonly affected.
- Dogs homozygous for the ABCB1 gene deletion also affected; heterozygous dogs can react at higher doses. The ABCB1 gene mutation has been found in Shetland sheepdogs, Australian shepherds, Old English sheepdogs, German shepherds, English shepherds, longhaired whippets, silken windhounds, and a variety of mixed-breed dogs.
- No age or sex predilections.

SIGNS

- Mydriasis
- Depression
- Drooling/salivation
- Vomiting
- Ataxia
- Tremors
- Disorientation
- Weakness, recumbency
- Non-responsiveness
- Blindness
- Bradycardia
- Hypoventilation
- Coma
- Death

CAUSES & RISK FACTORS

- Extra-label use at high dosage
- Breed sensitivity—see above



DIAGNOSIS

- Based on history and clinical signs
- No specific tests useful in confirming the diagnosis

DIFFERENTIAL DIAGNOSIS

- Overdoses of other insecticides such as pyrethrins, pyrethroids, organophosphorous and carbamate compounds
- Other toxicants or diseases affecting the CNS

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

Arterial blood gases—may reveal high PaCO₂ and low PaO₂ caused by respiratory depression and hypoventilation.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Physostigmine 1 mg IV; temporary (30–40 minutes) return to consciousness or resumed alertness and muscle activity after the administration supports but does not confirm diagnosis; does not speed recovery; not indicated for treatment; glycopyrrolate administered first may prevent severe bradycardia.



TREATMENT

- Primarily supportive and symptomatic care.
- If patient is alert, activated charcoal repeated every 4–6 hours.
- Important goals—proper fluid therapy, maintenance of electrolyte balance, nutritional support, and prevention of secondary complications.
- Nutritional support— institute early, preferably within 2–3 days of exposure; severe CNS depression or coma may last for weeks.
- Frequent turning of patient, appropriate bedding, physical therapy, attentive nursing care, and other standard treatment measures for a recumbent patient important.
- Apply ocular lubricants.
- Mechanical ventilation—may be required with respiratory depression.
- Use of an intravenous lipid emulsion (ILE) has been successful in ameliorating clinical signs in some cases. May not be effective in dogs with ABCB1 homozygous mutations.



MEDICATIONS

DRUG(S)

- No known reversal agent.
- Atropine or glycopyrrolate—may be administered as needed to treat bradycardia.
- 20% intravenous lipid emulsions: bolus dose 1.5 mL/kg over 2–3 min; continuous rate infusion of 0.25 mL/kg/min for 30–60 min. Check serum q2h and if not lipemic; repeat as needed; if no clinical improvement after 3 doses, discontinue.

CONTRAINdications/POSSIBLE INTERACTIONS

- Other drugs known to cause toxicity in dogs with the ABCB1 mutation: loperamide, doxorubicin, vincristine, vinblastine, acepromazine, butorphanol, emopside, and erythromycin.
- Do not use ivermectin concurrently with ketoconazole.
- Concomitant extra-label use of ivermectin and spinosad may produce clinical signs.



FOLLOW-UP

- Prognosis and eventual outcome—depends on individual and breed sensitivity, amount of drug ingested or injected, how rapidly clinical signs develop, response to supportive treatment, and overall health of patient.
- Convalescence may be prolonged (several weeks); good supportive care in many seemingly hopeless cases has resulted in complete recovery.



MISCELLANEOUS

SEE ALSO

- Heartworm Disease—Dogs
- Poisoning (Intoxication) Therapy

ABBREVIATIONS

- CNS = central nervous system
- GABA = gamma-aminobutyric acid

Suggested Reading

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available online

JOINT LUXATIONS



BASICS

DEFINITION

Luxation is the complete disruption of the contiguous articular surfaces of a joint when the supporting structures around the joint are damaged or missing. Subluxation is a partial disruption.

PATHOPHYSIOLOGY

• All synovial joints have a joint capsule that joins the articulating bones together. The fibrous layer of this capsule is a primary stabilizer of the joint. Most joints have additional ligaments that reinforce the joint capsule to improve the resistance to movement outside of the normal range of motion of that joint. All motion joints also have a system of muscles and tendons that exert forces on the joint to control movement. The co-contraction forces around a joint are very influential on the stability of that joint. Instability occurs when the stabilizing system is damaged or disrupted or does not develop normally.

• If the laxity is clinically apparent, then the situation is generally described as luxation or subluxation of that joint.

• Luxation may occur as a result of traumatic forces causing the joint to move beyond the elastic limits of the supporting tissues.

• Secondary changes are set in motion by the damage to the tissues that create early, and then later, more chronic joint damage.

SYSTEMS AFFECTED

• Musculoskeletal—primarily the intra-articular environment and the support structures around the joint including joint capsule, collateral ligaments, and support muscle/tendon units.

• Neurologic—neurologic feedback and supply to the support system may also be affected.

GENETICS

• Hyper laxity syndrome is an inherited factor in humans. Puppies may show temporary hyper laxity when confined.

• Hip dysplasia is a form of inherited laxity of the hip joint.

• Shoulder luxation is an inherited predisposition in small breeds such as miniature poodles.

• Femoropatellar instability leading to medial patellar luxation is a common inherited disease in small-breed dogs.

• Ehlers-Danlos syndrome is a congenital collagen disorder that leads to joint laxity.

INCIDENCE/PREVALENCE

Some forms of laxity/luxation (hip dysplasia and medial patella luxation) are very common.

GEOGRAPHIC DISTRIBUTION

None observed

SIGNALMENT

Breed Predilections

- Varies with the joint affected.
- Hip—large breeds show clinical signs of hip dysplasia more frequently than smaller breeds, but breeds of all sizes can have radiographic signs.
- Traumatic luxations are not breed-specific in any joint.
- Congenital shoulder luxation occurs most commonly in miniature breeds (poodle).
- Stifle luxation most commonly involves rupture of both cruciate ligaments and one of the collateral ligaments.
- Medial patella luxation is more common in small-breed dogs.
- Spinal luxations occur as a result of trauma, with associated injury to the spinal cord.

Mean Age and Range

- Traumatic—any age.
- Congenital laxity/luxation is typically seen in the juvenile dog, with secondary degenerative joint disease showing later in life.

Predominant Sex

None

SIGNS

- Abnormal anatomic position of one bone in relation to the adjoining bone.
- Hip luxation is commonly cranio-dorsal (the displacement of the femoral head in relation to the acetabulum).
- Shoulder luxation is commonly medial.
- Elbow luxation is commonly proximo-lateral.
- Carpal and tarsal luxations commonly result in varus, valgus, or hyperextension when stressed.
- Acute swelling, pain, and non-use of the limb are usually seen with acute luxation. Partial weight-bearing may occur with subluxation or chronic luxation.

CAUSES

- Traumatic displacement of normal tissues beyond their elastic limit.
- Minimal stress on abnormally unstable joints of congenital etiology.

RISK FACTORS

- Abnormal conformation, causing elevated joint stresses
- Fatigue, causing muscle weakness and incoordination
- Neurologic abnormalities
- Access to moving vehicles



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Fractures
- Joint disease—immune-mediated, septic, or degenerative

CBC/BIOCHEMISTRY/URINALYSIS

- No abnormalities expected that are directly related to the luxation.
- Trauma-induced abnormalities in traumatic situations.

OTHER LABORATORY TESTS

Arthrocentesis may eliminate non-traumatic joint disease.

IMAGING

- Radiographs confirm the diagnosis by documenting the anatomic malalignment.
- Stress views may be needed in some situations.

DIAGNOSTIC PROCEDURES

- Palpation of the laxity/luxation (Ortolani, cranial drawer, medial patella luxation, stress-induced laxity/instability).
- Palpation of the position of the displaced bone.

PATHOLOGIC FINDINGS

- Trauma-induced hemorrhage, edema, and disruption of ligaments and joint capsule.
- Secondary changes related to degenerative joint disease.



TREATMENT

APPROPRIATE HEALTH CARE

Rest, reduce mobility, reduce swelling, control pain, and stabilize the joint or salvage the limb by removing the source of pain.

NURSING CARE

- Immobilize the joint with a bandage/splint if the affected joint is distal to the inguinal or axial areas.
- Cold compresses for 5–10 minutes four or five times a day initially to reduce inflammation.

ACTIVITY

Cage rest until joint stabilization, then slow return to function to encourage healing and strengthening of soft tissue support of the limb.

DIET

Normal

CLIENT EDUCATION

Activity and weight gain increase the likelihood of degenerative changes in the long term.

SURGICAL CONSIDERATIONS

- Closed reduction under anesthesia may be successful if the support structures are intact and no anatomic aberrations are present. This method is generally not recommended for the hock, carpus or stifle.
- Failing closed reduction, an open surgical approach may be used. After reduction, some form of surgical stabilization (e.g., toggle pin for hip luxation) should be applied to reduce the possibility of reluxation. After surgical closure, an external support sling is often used

(CONTINUED)

JOINT LUXATIONS

to limit movement until the tissues around the joint have healed (e.g., Ehmer sling after cranio-dorsal hip luxation reduction, spica splint after elbow luxation reduction).

- The incidence of reluxation is high, especially in the case of congenital luxations.
- Salvage procedures include prosthetic joint replacement, surgical removal of bone-to-bone contact points (femoral head and neck osteotomy), arthrodesis, and amputation.

**MEDICATIONS****DRUG(S) OF CHOICE**

- NSAIDs decrease prostaglandin synthesis by inhibiting cyclooxygenase enzymes:
 - Carprofen (2.2 mg/kg PO or SC q12h, or 4.4 mg/kg PO or SC q24h).
 - Deracoxib (1–2 mg/kg PO q24h).
 - Firocoxib (5 mg/kg PO q24h).
 - Meloxicam (0.1 mg/kg PO or SC q24h).
- Tramadol (1–4 mg/kg PO q8–12h)
- Serotonin reuptake inhibitor, in combination with NSAID.

CONTRAINDICATIONS

- Gastrointestinal sensitivity
- Liver or renal pathology

PRECAUTIONS

Stop medications if diarrhea or vomiting is seen.

POSSIBLE INTERACTIONS

- Other NSAIDs
- Steroids

ALTERNATIVE DRUG(S)

Analgesics

**FOLLOW-UP****PATIENT MONITORING**

- Always take a radiograph after reduction.
- Take follow-up radiographs when the splint/sling is removed (typically 2–4 weeks post-reduction).

PREVENTION/AVOIDANCE

- Fenced-in yards
- Keep the sling in place until healing has occurred

POSSIBLE COMPLICATIONS

- Reluxation
- Infection after surgery
- Implant failure of joint prosthetic

EXPECTED COURSE AND PROGNOSIS

- Return of function is expected unless a complication occurs.
- The high incidence of reluxation makes the prognosis guarded.
- Progressive degenerative joint disease.

**MISCELLANEOUS****SYNONYMS**

Dislocation

SEE ALSO

- Arthritis (Osteoarthritis)
- Hip Dysplasia

ABBREVIATION

- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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**Client Education Handout
available online**

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KERATITIS, EOSINOPHILIC—CATS



BASICS

OVERVIEW

- Feline eosinophilic keratitis is a presumed immune-mediated inflammation of the cornea characterized by perilimbal corneal vascularization, white-pink corneal infiltrate, and corneal edema.
- Synonym—proliferative keratitis.

SIGNALMENT

Young adult to middle-aged cats most commonly affected.

SIGNS

- Unilateral or bilateral.
- Usually little to no ocular pain.
- Serous to mucoid ocular discharge.
- Limbal superficial corneal vascularization 90–360° (temporal or inferior nasal quadrants usually are first affected).
- White to pink flat or raised granular corneal infiltrate.
- Multifocal small white gritty corneal deposits.
- Corneal edema.
- With or without corneal ulceration.
- Conjunctival and third eyelid hyperemia, chemosis and thickening with or without a cobblestone texture to the surface.

CAUSES & RISK FACTORS

- Feline herpesvirus-1 may be associated with FEK but the exact role is unclear: 76% of FEK specimens were PCR positive for FHV-1 in one study but 0% were positive in another.
- The exact etiopathogenesis is unknown but proposed theories are: (1) Type I hypersensitivity with IgE mediated mast cell and eosinophil degranulation, (2) Type IV reaction where sensitized T-lymphocytes via IL-5 stimulate local eosinophil-mediated corneal damage.
- Culture, histopathology, and electron microscopy have ruled out bacterial and fungal infection as consistent etiologic causes, although secondary bacterial keratitis may occur.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Chronic corneal ulceration with secondary corneal vascularization (granulation tissue).
- FHV-1 stromal keratitis—appears similar to FEK but lacks the proliferative component, and more severe ocular pain and corneal ulceration are usually present.
- Corneal neoplasia: (1) lymphoma—concurrent conjunctival and/or uveal infiltration is common, (2) squamous cell carcinoma—rarely involves cornea in cats.
- Chlamydia psittaci* or *Mycoplasma felis*—usually conjunctival diseases without corneal involvement.

CBC/BIOCHEMISTRY/URINALYSIS

Peripheral eosinophilia may be present.

OTHER LABORATORY TESTS

- Corneal cytology provides definitive diagnosis and should be done first. See numerous eosinophils, free eosinophil granules and/or mast cells, neutrophils, lymphocytes, plasma cells and epithelial cells.
- Cytology helps rule out chlamydia and mycoplasma.
- FHV-1 nested PCR—limited diagnostic value since normal healthy cats may carry FHV-1 and have positive PCR results.
- IFA testing for *Chlamydia psittaci*.
- Fluorescein staining to evaluate for corneal ulceration.

DIAGNOSTIC PROCEDURES

- Keratectomy and histopathology may confirm a diagnosis in chronic or nonresponsive cases.
- Specimens show epithelial cell layer hypertrophy and hyperplasia, corneal vascularization, excrescences with nuclear debris and amorphous eosinophilic material, numerous eosinophils, free eosinophil granules, deeper layers of thickened basement membrane and eosinophilic material and stromal thickening with eosinophils, mixed inflammatory cells and granulation tissue.



TREATMENT

Usually medical on outpatient basis.



MEDICATIONS

DRUG(S)

- Topical cyclosporine A q8–12h, then tapered to the lowest effective frequency of application and/or discontinued. Can use in cats in which megestrol and topical corticosteroids are contraindicated (diabetes, FHV-1, etc). May be irritating or cause blepharitis.
- Topical corticosteroids—1% prednisolone acetate or 0.1% dexamethasone sodium phosphate (initially q6–12h for 5–7 days, then gradually taper to the lowest effective frequency of application, q2–7 days). May eventually be discontinued in many cats.
- Adjunctive topical and/or systemic anti-viral therapy may be warranted in cases with history or clinical signs compatible with FHV-1 infection.
- Subconjunctival corticosteroids—triamcinolone acetonide (0.1–0.2 mL q3–7 days); use only in cats that are difficult to treat with topical medications.
- Megestrol acetate—2.5 mg PO q24h × 3–5 days, then 2.5 mg PO q48h × 3–5 days, then gradually decrease frequency after every 3–5 treatments to the lowest effective

frequency (e.g., 2.5 mg PO q7 days) or eventually discontinue.

- Systemic prednisolone—start with 2.2 mg/kg PO q12h and taper. Use only if a cat will not tolerate topical corticosteroid or cyclosporine A therapy or megestrol acetate.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Topical corticosteroid administration may be associated with recrudescence of FHV-1 keratoconjunctivitis and therefore should be used judiciously and monitored carefully. The client should be advised to immediately report any adverse change in the condition of the eye (blepharospasm, corneal edema, increased ocular discharge, etc.).
- Megestrol acetate causes adrenal cortical suppression and may result in diabetes mellitus, polyphagia, temperament change, mammary gland hyperplasia, or neoplasia and pyometra. It should not be used in cats with hepatic disease or other illness.



FOLLOW-UP

- Response to therapy is usually rapid.
- Complete resolution may take several days to months. Many cats require long-term therapy to control the disease.
- Corneal vascularization and infiltrate may resolve completely with minimal corneal scarring.
- Recurrences in both the short and long term are common following discontinuation of therapy.



MISCELLANEOUS

FEK is not typically associated with the dermatologic eosinophilic granuloma complex.

ABBREVIATIONS

- FEK = feline eosinophilic keratitis/keratoconjunctivitis
- FHV-1 = feline herpesvirus-1
- IFA = immunofluorescent antibody test
- PCR = polymerase chain reaction

Suggested Reading

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KERATITIS, NONULCERATIVE



BASICS

DEFINITION

An inflammatory disorder of the cornea that does not retain fluorescein stain.

PATHOPHYSIOLOGY

A pathologic response resulting in reduced corneal clarity secondary to edema, inflammatory cell infiltration, vascularization, pigmentation, lipid or calcium deposition, or scarring.

SYSTEMS AFFECTED

Ophthalmic

GENETICS

- No proven genetic basis in dogs or cats.
- Chronic superficial keratitis (pannus)—inherited predisposition considered in the German shepherd.

INCIDENCE/PREVALENCE

Common cause of eye disease in dogs and cats.

GEOGRAPHIC DISTRIBUTION

Chronic superficial keratitis is more common in regions of high UV light exposure.

SIGNALMENT

Species

- Dog—chronic superficial keratitis (pannus); pigmentary keratitis; pigmentary keratopathy of pugs; nodular granulomatous episclerokeratitis (see Episcleritis); KCS (see Keratoconjunctivitis Sicca).
- Cat—eosinophilic keratitis (see Keratitis, Eosinophilic—Cats), herpesvirus (stromal form); corneal sequestration; KCS uncommon and usually secondary to chronic herpesvirus infection.

Breed Predilections

Dogs

- Chronic superficial keratitis (pannus)—highest prevalence in German shepherds and sighthounds.
- Pigmentary keratitis—notably brachycephalic breeds with exposure keratopathy from lagophthalmia, tear film deficiencies, and trichiasis.
- Pigmentary keratopathy of pugs—suspect genetic condition that results in progressive corneal pigmentation, cause currently unknown.
- NGE—prevalent in cocker spaniels, collies, and Shetland sheepdogs.
- KCS—brachycephalic breeds, cocker spaniels, English bulldogs, West Highland white terriers, Cavalier King Charles spaniels.

Cats

- Eosinophilic keratitis—most prevalent in domestic shorthair.
- Corneal sequestration—most prevalent in brachycephalic breeds.

Mean Age and Range

- Dogs: chronic superficial keratitis—may occur at any age; higher risk between 3 and 6 years (younger in greyhounds); pigmentary keratitis—may occur at any age; pigmentary keratopathy of pugs—may occur at any age;

NGE—may occur at any age; in collies—young to middle-aged (mean 3.8 years); KCS—usually middle-aged to older.

- Cats: herpesvirus—all ages; eosinophilic keratitis and corneal sequestrum—all ages except neonates.

Predominant Sex

- Dogs: female predisposition reported for pannus and KCS.
- Cats: castrated male predisposition reported for eosinophilic keratitis.

SIGNS

Historical Findings

May cause variable corneal discoloration and ocular discomfort.

Physical Examination Findings

Dogs

- Chronic superficial keratitis—usually bilateral, cornea vascularization ranging from superficial vessels to dense granulation tissue with variable pigmentation; lateral or ventrolateral cornea with entire cornea affected in advanced cases; thickened and depigmented third eyelids; white deposits (corneal degeneration) may be present at the leading edge of corneal lesion; may lead to blindness.
- Pigmentary keratitis—appears as focal to diffuse, brown discoloration of the cornea; often associated with corneal vascularization or scarring.
- Pigmentary keratopathy of pugs—brown corneal pigmentation originating from medial cornea and progressing towards central cornea.
- NGE—bilateral or unilateral, raised, fleshy masses affecting the lateral limbus and cornea; corneal deposits, edema and vascularization may also occur in adjacent corneal stroma; slow to rapidly progressive; third eyelids may appear thickened.
- KCS—may be unilateral or bilateral; mucoid ocular discharge, conjunctival hyperemia, corneal vascularization, pigmentation, and scarring; corneal ulceration may occur.

Cats

- Herpesvirus (stromal form)—unilateral or bilateral; stromal edema, infiltrates, deep vascularization and scarring; often occurs with ulceration; may threaten vision if severe scarring.
- Eosinophilic keratitis—usually unilateral; raised vascularized lesion with pink-white infiltrates that form gritty plaques; may retain fluorescein stain at the periphery of the lesion.
- Corneal sequestrum—usually unilateral but can be bilateral; appears as amber, brown, or black plaques of the central or paracentral cornea; can vary in size and depth of the affected cornea; edges may appear raised; corneal vascularization is variable; may retain fluorescein at periphery of lesion.

CAUSES

Dogs

- Chronic superficial keratitis—presumed to be immune-mediated; high altitude and subsequent increase in UV radiation exposure increase the prevalence and severity of disease.

- Pigmentary keratitis—secondary to chronic corneal irritation; evaluate for primary underlying ocular conditions; frequently associated with exposure keratopathy and KCS.
- Pigmentary keratopathy of pugs—unknown, thought to have genetic basis.
- NGE—presumed to be immune mediated.
- KCS—bilateral—usually immune mediated or drug-induced; unilateral—congenital, iatrogenic, neurogenic.

Cats

- Herpesvirus (stromal form)—immune-mediated T-cell lymphocyte reaction to herpesvirus antigen rather than a cytopathic effect of the virus.
- Eosinophilic keratitis—possible hypersensitivity reaction; high incidence of animals PCR positive for FHV-1; fewer positive for Chlamydia-like agents.
- Corneal sequestrum—unknown; likely due to chronic corneal irritation or ulceration; suggested relationship with herpesvirus.

RISK FACTORS

Dogs—chronic superficial keratitis more likely to occur at high altitudes secondary to increased UV exposure.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Dogs

- Infectious keratitis is usually ulcerative and painful; cytology of the cornea reveals white blood cells, organisms present.
- Neoplasia—rare involvement of sclera or cornea; distinguish based on color, age of animal, breed predilection; usually unilateral; response to topical anti-inflammatory therapy.

Cats

- Infectious keratitis—usually ulcerative and painful; cytologic examination of cornea reveals white blood cells, organisms present.
- Stromal herpesvirus may be associated with ulcerative keratitis and secondary bacterial infection.
- Neoplasia—very rare.

DIAGNOSTIC PROCEDURES

Dogs

Chronic superficial keratitis: cytologic examination of corneal or conjunctival scrapings reveals lymphocytes, plasma cells, and mast cells; biopsy can be considered; clinical examination usually considered diagnostic.

NGE: biopsy of episcleral nodular mass or cornea (superficial keratectomy); Schirmer tear test for pigmentary keratitis, KCS, or any corneal disease of undetermined cause; normal values are ≥ 15 mm/min; values < 15 mm/min suggest KCS but should be interpreted with consideration of the breed and ocular findings.

Cats

Herpes: conjunctival or corneal scrapings for PCR are most successful for diagnosis; IFA or

KERATITIS, NONULCERATIVE

(CONTINUED)

viral culture are of limited value; interpretation can be difficult; eosinophilic keratitis: cytology of cornea positive for eosinophils; biopsy of the cornea (superficial keratectomy) can be considered for eosinophilic keratitis or sequestrum but is usually unnecessary.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—generally sufficient.
- Inpatient—cases that warrant surgery due to inadequate response to medical therapy.

CLIENT EDUCATION

Dogs

Typically require life-long treatment; disease is controlled rather than cured.

Cats

• Herpesvirus—ocular discomfort and keratitis often recurrent. • Eosinophilic keratitis—disease controlled rather than cured. • Corneal sequestrum—may slough spontaneously, however cornea may rupture; clinical course often protracted without surgery; removal of sequestrum by superficial keratectomy may be curative, although recurrence is possible.

SURGICAL CONSIDERATIONS

Dogs

• Chronic superficial keratitis—superficial keratectomy for severe disease in which vision is impaired due to corneal pigmentation; patients still require indefinite medical treatment to prevent recurrence; β -irradiation with a strontium-90 probe is noninvasive and may be performed in severe cases. • Pigmentary keratitis—superficial keratectomy may be performed only after initial underlying cause is corrected; only in severe cases that threaten vision. • Pigmentary keratopathy of pugs—high likelihood of recurrence after superficial keratectomy. • NGE—superficial keratectomy is diagnostic; medical treatment is still required. • KCS—parotid duct transposition or permanent partial tarsorrhaphy to reduce exposure.

Cats

• Eosinophilic keratitis—superficial keratectomy is diagnostic but not curative; medical treatment is preferred. • Corneal sequestrum—superficial keratectomy may be curative; recurrence is possible.



MEDICATIONS

DRUG(S) OF CHOICE

Dogs

- Chronic superficial keratitis—topical corticosteroids (1% prednisolone or 0.1%

dexamethasone q6–12h); topical 0.2–2% cyclosporine, 1% pimecrolimus, or 0.03% tacrolimus q8–12h; agents can be used alone or in combination for more severe cases; subconjunctival corticosteroid injection can be used as an adjunct to topical therapy in severe cases (triamcinolone acetonide 2–8 mg). • Pigmentary keratitis—treatment directed at underlying cause; topical corticosteroids if primary cause is inflammatory; lubricants and cyclosporine or tacrolimus if primary condition is KCS; cyclosporine or tacrolimus may reduce pigmentation in all cases. • Pigmentary keratopathy of pugs—topical cyclosporine 0.2–2% or tacrolimus 0.02–0.03% may arrest progression of corneal pigmentation; topical corticosteroids may help temporarily reduce density of corneal pigment. • NGE—topical corticosteroids and/or cyclosporine as described above; systemic azathioprine (2 mg/kg/day initially, then gradually reduce) may be effective when used alone or in combination with topical medications. • KCS—topical 0.2–2% cyclosporine, or 0.02–0.03% tacrolimus q8–12h (see Keratoconjunctivitis Sicca).

Cats

• Herpesvirus—topical antiviral agents recommended: cidofovir 0.5% q12h or ; trifluridine (Viroptic) q4–6h for 2 days, then taper. Systemic antiviral agents include: famciclovir 40 mg/kg PO q8h. For inflammation, topical nonsteriodals or cyclosporine q12h may be used; oral lysine (250 mg q12h to 500 mg q12–24h) may also be of benefit. • Eosinophilic keratitis—topical corticosteroids (1% prednisolone or 0.1% dexamethasone) q6–12h; patient monitored for ulceration or worsening of clinical signs; topical antivirals can be used in combination with corticosteroids if concurrent herpesvirus; use of topical cyclosporine also reported (0.2–1.5%) with variable results; megestrol acetate (Ovaban, 5 mg PO q24h for 5 days, then 5 mg q48h for 1 week, then 5 mg weekly for maintenance) is highly effective, but rarely associated with transient diabetes mellitus. • Corneal sequestrum—topical triple antibiotic q8–12h for associated corneal ulceration; artificial tear lubrication may relieve discomfort; topical antivirals can be used if herpesvirus infection is suspected; topical 1% atropine ointment q12–24h for pain associated with concurrent uveitis if present.

CONTRAINDICATIONS

Topical corticosteroids are contraindicated with corneal ulcers; topical atropine is contraindicated with KCS, glaucoma, or lens luxation.

PRECAUTIONS

• Azathioprine may cause gastrointestinal signs, pancreatitis, hepatotoxicity, and myelosuppression. • Megestrol acetate—not

FDA approved for use in cats; possible side effects include polyphagia, diabetes mellitus, mammary hyperplasia, mammary neoplasia, and pyometra. • Famciclovir—monitoring of CBC, chemistry profile recommended; anorexia, polydipsia reported.



FOLLOW-UP

PATIENT MONITORING

Periodic ocular examination recommended to evaluate efficacy of topical and systemic medications; examine at 1- to 2-week intervals, gradually lengthening the interval with remission or resolution of clinical signs; evaluate response to therapy and taper medications based on resolution of clinical signs; complete resolution of pigmentation may not occur. UV light protection (tinted goggles) is recommended for pannus.

POSSIBLE COMPLICATIONS

All of the above may lead to continued ocular discomfort, visual defects, or blindness in severe cases.



MISCELLANEOUS

SEE ALSO

- Corneal Sequestrum—Cats
- Episcleritis—Cats
- Keratitis, Eosinophilic—Cats
- Keratitis, Ulcerative
- Keratoconjunctivitis Sicca

ABBREVIATIONS

- FHV-1 = feline herpesvirus type 1
- IFA = immunofluorescent assay
- KCS = keratoconjunctivitis sicca
- NGE = nodular granulomatous episclerokeratitis
- PCR = polymerase chain reaction

Suggested Reading

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Client Education Handout
available online

KERATITIS, ULCERATIVE



BASICS

DEFINITION

Inflammation of the cornea associated with loss of the corneal epithelium (corneal erosion) or loss of variable amounts of the underlying corneal stroma (corneal ulcer).

PATHOPHYSIOLOGY

- May be caused by any condition (traumatic or non-traumatic) that disrupts the corneal epithelium or stroma.
- Ulcers—classified as superficial or deep, uncomplicated or complicated.
- Superficial—involves the epithelium and possibly the superficial stroma.
- Deep—involves a greater thickness of stroma and may extend to Descemet's membrane (descemetocele), possibly leading to rupture of the globe.
- Complicated—persistence of underlying/inciting cause, microbial infection, or production of degradative enzymes.
- Epithelial wound healing—adjacent corneal epithelial cells loosen and begin migration over the defect within a few hours; mitosis occurs within a few days to restore normal epithelial thickness; healing process complete in 5–7 days in uncomplicated, superficial ulcers.
- Stromal wound healing—slower, more complex; can be in an avascular or vascular manner; in shallow wounds, epithelial migration may be sufficient to fill the defect; epithelium may cover some deeper ulcers even when epithelium and stromal regeneration are insufficient to restore normal corneal thickness (non-ulcerated divot defect is called a facet); stroma usually heals by fibrovascular infiltration, which may take several weeks and often results in loss of or decrease in corneal clarity.
- Stromal ulcers—often complicated by microbial infection or enzymatic destruction initiated by microbial organisms, host inflammatory cells, or corneal epithelial or stromal cells; enzymatic destruction may result in gelatinous appearance of the corneal stroma, called a melting or malacic ulcer.

SYSTEMS AFFECTED

Ophthalmic

GENETICS

- No proven basis, although breed predilections are seen.
- May be secondary to other corneal diseases that have breed predispositions and presumably a genetic basis, such as corneal epithelial dystrophy in Shetland sheepdogs and corneal endothelial dystrophy in Boston terriers.

INCIDENCE/PREVALENCE

Common

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Dogs—brachycephalic breeds predisposed.
- SCCED/indolent erosion—occurs in any breed.
- Cats—Persian, Himalayans, Siamese, and Burmese predisposed to feline corneal sequestrums (see Corneal Sequestration—Cats).

Mean Age and Range

- Age of onset—variable; determined by cause.
- SCCED—middle-aged and older dogs.

SIGNS

Historical Findings

- May be acute or chronic (SCCED).
- Tearing, squinting, rubbing at eyes.
- Owners may report the appearance of a film over the eye (often corneal edema); prolapsed third eyelid.
- Herpetic ulcers (cats)—may have history of respiratory disease.

Physical Examination Findings

- Nonspecific—serous to mucopurulent ocular discharge, blepharospasm, nictitans prolapse, conjunctival hyperemia.
- Superficial—may note one or more circumscribed, linear, or geographic defects in the cornea.
- Deep stromal ulcer or descemetocele—may appear as a crater-like defect.
- Depending on cause and duration—may see neovascularization, pigmentation, scarring, inflammatory cell infiltrate (yellow to cream-colored opacity with indistinct margins, often surrounded by corneal edema), collagenolytic activity (melting) of the corneal stroma.
- SCCED—loose or redundant epithelial edges; may demonstrate fluorescein stain extending into areas with seemingly intact epithelium (ring of less intense staining).
- Reflex anterior uveitis—mild or severe, secondary to ulceration; severe may result in hypopyon; severe suggests concurrent bacterial infection.

CAUSES

- Trauma—blunt; penetrating; perforating.
- Adnexal disease—ectopic cilia, entropion, ectropion, eyelid mass, distichiasis.
- Lagophthalmos (inability to close eyelids completely)—results in exposure keratitis; may be breed related in brachycephalic dogs and cats; may be caused by exophthalmos, buphthalmos, or may be neuroparalytic from facial nerve paralysis.
- Tear-film abnormality—quantitative tear deficiency (KCS); qualitative tear film deficiency caused by mucin deficiency or some other unidentified tear abnormality.
- Infection—usually secondary in dogs; can be primary infection of herpesvirus in cats.
- Primary corneal disease—endothelial dystrophy; other endothelial disease.
- Miscellaneous—foreign body (corneal or conjunctival); chemical burns; neurotrophic keratitis (loss of trigeminal sensation); immune-mediated disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Fluorescein dye retention—diagnostic.
- Other causes of a red and painful eye—conjunctivitis, uveitis, KCS, glaucoma (see Red Eye).
- May develop concurrently with other causes of a red eye (e.g., secondary to KCS).

OTHER LABORATORY TESTS

- Corneal culture and sensitivity—aerobic bacteria; particularly for complicated, deep, or rapidly progressive corneal ulcers.
- Herpesvirus (cats)—PCR or IFA for herpesvirus available; negative test does not rule out herpesvirus infection.

DIAGNOSTIC PROCEDURES

Fluorescein Staining

- Homogeneous stain uptake—superficial or stromal ulcer; may be circular to geographic, linear, or combination; location and shape may help determine cause (e.g., linear may indicate foreign body or rubbing of ectopic cilia); interpretation of depth subjective.
- SCCED—may have leakage of stain under surrounding loose epithelium.
- Crater-like defect that retains stain at the periphery but is clear at center—Descemetocele—may also see Descemet's membrane bulging forward if defect is large.
- Crater-like defect with pooling of stain transiently but can be easily rinsed—previous stromal ulcer that has epithelialized (facet); must be distinguished from a descemetocele.

Other

- Cytologic evaluation of cornea and gram, Giemsa, or Wright staining may reveal microbial or fungal organisms and may help direct initial antimicrobial therapy.
- Rose Bengal corneal stain (cats) may delineate superficial, linear, epithelial ulcers (dendritic ulcers), which are considered pathognomonic for herpesvirus infection.
- Schirmer tear test may identify ulceration associated with KCS; it is contraindicated in very deep ulcers or descemetoceles.

PATHOLOGIC FINDINGS

- Ulcers—typically suppurative inflammation, possibly neovascularization, loss of epithelium and basement membrane; possibly organisms.
- SCCEDs—superficial hyalinized zone in stroma; epithelial lipping around erosions; varying degrees and types of leukocytic infiltrate and fibrosis.



TREATMENT

APPROPRIATE HEALTH CARE

Hospitalize deep or rapidly progressive ulcers; these may require surgery and/or frequent medical treatments.

KERATITIS, ULCERATIVE

(CONTINUED)

NURSING CARE

Keep facial hair out of eyes and clean.

ACTIVITY

- Restrict with deep stromal ulcer or descemetocle to prevent rupture.
- Prevent self-trauma with Elizabethan collar.

CLIENT EDUCATION

- Instruct client to wait at least 5 minutes between medications if more than one ophthalmic drop is prescribed; wait longer between ointments.
- Advise client to contact veterinarian if patient appears more painful or the eye markedly changes in appearance.
- SCCED—discuss protracted course with client; usually achieve healing within 2–6 weeks but may require weekly rechecks and multiple procedures.

SURGICAL CONSIDERATIONS

- Superficial ulcers do not usually require surgery if the inciting cause has been eliminated.
- Ulcer that extends one-half or greater corneal thickness and particularly to Descemet's membrane may benefit from surgery.
- Descemetocle or full-thickness corneal laceration—considered a surgical emergency for possible referral.

Procedures

- SCCED—debridement of loose epithelium with a dry, sterile, cotton-tipped swab after application of topical anesthesia (50% success rate); punctate or grid keratotomy easily performed after epithelial debridement with topical anesthesia (80% success rate); superficial keratectomy is more invasive and may cause more scarring but has 100% success rate; application of a contact lens or nictitans flap after any of these procedures may improve comfort and aid healing.
- Diamond burr keratotomy for SCCED/indolent erosion only; use gently over surface of erosion; may be associated with increased risk of infection post-procedure.
- Rotational pedicle conjunctival flap, corneoscleral transposition, corneal transplant—surgical procedures for ulcers > 50% thickness of the stroma and descemetocles.
- Cyanoacrylate repair (corneal glue)—can be used for deep ulcers; promotes corneal vascularization and stabilizes cornea, but has somewhat lower success rate compared to other corneal surgeries.



MEDICATIONS

DRUG(S) OF CHOICE

Antibiotics

- Topical agents—indicated for all patients.
- Frequency of application—determined by severity and the preparation used; ointments have a relatively long contact time and are

applied q6–12h; solutions are applied more frequently (4, 6, 8, or even 12 times daily) in the initial treatment of complicated ulcers; solutions probably more appropriate in deep ulcers.

- Commonly used agents—erythromycin (cats); triple antibiotic, gentamicin, and tobramycin.

- Uncomplicated ulcers or superficial erosions—combination of neomycin, polymyxin B, and bacitracin an excellent first choice; broad spectrum of antimicrobial activity; often used 2–3 times/day for prophylactic therapy.
- Complicated ulcers—often use combination therapy of cefazolin (use IV solution to make 33–50 mg solution in saline or artificial tears for topical use) with either an aminoglycoside (tobramycin, gentamicin) or fluoroquinolone (ciprofloxacin, ofloxacin); particularly in rapidly progressive, deep, or melting ulcers; frequency depends on severity but usually a minimum of q3–4h.

Atropine

- 1% ointment or solution.
- Indicated for reflex anterior uveitis; frequency—usually q8–24h to effect (mydriasis).

Antiviral Agents

- Indicated for herpetic ulcers in cats.
- Trifluridine (Viroptic) solution—q4–6h until clinical response is observed; then reduce for 1–2 weeks after clinical signs have subsided.

Nonsteroidal Anti-inflammatory Drugs

- May be indicated for anti-inflammatory and analgesic properties.
- Aspirin: dogs, 10–15 mg/kg PO q12h.

CONTRAINDICATIONS

- Topical corticosteroids—contraindicated with any corneal erosion or ulcer.
- Topical NSAIDs—contraindicated with herpetic ulcers, melting ulcers.
- Topical atropine—contraindicated with glaucoma, KCS.

PRECAUTIONS

- Topical NSAIDs (flurbiprofen, diclofenac)—may delay corneal healing, may potentiate corneal melting.
- Trifluridine, neomycin—may be irritating.
- Topical cyclosporine can be used safely in uncomplicated ulcer in KCS patients.

POSSIBLE INTERACTIONS

Combining antibiotics in solution may inactivate some antibiotics.

ALTERNATIVE DRUG(S)

- Acetylcysteine—anticollagenolytic agent used for treatment of melting ulcers; efficacy is controversial; dilute 20% stock solution to 5–10% with artificial tears; apply q2–4h.
- Autologous serum—anticollagenolytic agent; keep refrigerated; avoid contamination; discard after 48 hours.



FOLLOW-UP

PATIENT MONITORING

- Superficial ulcers—repeat fluorescein stain in 3–6 days; if it persists 7 days or longer, either inciting cause has not been eliminated or the patient has an SCCED.
- Deep stromal or rapidly progressive ulcers—assess every 24 hours initially if outpatient until improvement is seen; many of these patients are hospitalized or undergo surgery; decrease frequency of antibiotic therapy as condition improves.

PREVENTION/AVOIDANCE

- Brachycephalic dogs—lubricant ointment administration, permanent partial tarsorrhaphy surgery, or both may help prevent recurrent ulceration.
- KCS-related ulcers—lifelong treatment of KCS (cyclosporine) or parotid duct transposition surgery to prevent continued ulceration.
- Herpesvirus (cats)—may try oral lysine 250 mg PO q12h to prevent viral replication; may decrease severity and/or frequency of outbreaks.

POSSIBLE COMPLICATIONS

Progressive corneal ulceration—rupture of globe; endophthalmitis; secondary glaucoma; phthisis bulbi; blindness; blind and painful eye (may require enucleation).

EXPECTED COURSE AND PROGNOSIS

- Uncomplicated superficial ulcer—usually heals in 5–7 days.
- SCCED—may persist for weeks to months; may require multiple procedures.
- Deep corneal ulcer treated medically—may require several weeks for fibrovascular repair of defect; does not always granulate satisfactorily; continued deterioration of ulcer and globe rupture are possible.
- Deep ulcer treated with conjunctival flap—frequently results in more comfort within a few days after surgery; blood supply to flap can be cut in 4–6 weeks if healed well to decrease scarring.



MISCELLANEOUS

ABBREVIATIONS

- IFA = immunofluorescent antibody test
- KCS = keratoconjunctivitis sicca
- NSAID = nonsteroidal anti-inflammatory drug
- PCR = polymerase chain reaction
- SCCED = spontaneous chronic corneal epithelial defects

Author Ellison Bentley

Consulting Editor Paul E. Miller



Client Education Handout
available online

KERATOCONJUNCTIVITIS SICCA



BASICS

OVERVIEW

- Deficiency of the aqueous layer of the precorneal tear film.
- Causes corneal/conjunctival drying and resultant surface inflammation.

SIGNALMENT

- Common in dog; rare in cat.
- Predisposed dog breeds—many brachycephalic and spaniel breeds, miniature schnauzers, poodles, bloodhounds, Samoyeds, West Highland white terriers, and Yorkshire terriers.
- Inheritance—undefined.
- Age of onset—variable and depends on the inciting cause.

SIGNS

- Conjunctival hyperemia.
- Mucoid to mucopurulent ocular discharge—intermittent to persistent depending on severity.
- Blepharospasm.
- Corneal changes—dryness, superficial vascularization, pigmentation, fibrosis, ulceration.
- Blepharitis due to ocular exudates.
- Severe disease—impaired vision or blindness.
- Cats are less symptomatic than dogs.

CAUSES & RISK FACTORS

- Immune-mediated/idiopathic—most common and possibly associated with other immune-mediated diseases (e.g., atopy).
- Infectious—canine distemper virus; chronic blepharoconjunctivitis (e.g., chronic herpes in cats).
- Iatrogenic—removal of the third eyelid gland (especially in at-risk breeds); radiation therapy.
- Congenital—Yorkshire terriers overrepresented.
- Neurologic—loss of parasympathetic innervation to lacrimal gland, trigeminal nerve deficit, or dysautonomia; neurogenic parasympathetic loss may have ipsilateral dry nose.
- Traumatic—after ocular proptosis or orbit inflammation.
- Systemic disease—diabetes mellitus, Cushing's disease, hypothyroidism or any debilitating disease.
- Drug-induced—systemic sulfonamides (e.g., trimethoprim-sulfadiazine) or etodolac.
- Transient KCS—general anesthesia and atropine.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Often confused with allergic or bacterial conjunctivitis.
- Dogs with KCS may have concurrent secondary bacterial overgrowth.
- Differentiate with Schirmer tear test.

DIAGNOSTIC PROCEDURES

- Schirmer tear test—decreased results diagnostic; normal value (dogs): at least 15 mm/min of wetting; symptomatic patients: usually < 10 mm/min of wetting; difficult to interpret in cats.
- Fluorescein staining—corneal ulcers.
- Conjunctival cytology—may indicate the nature and degree of bacterial overgrowth.
- Aerobic bacterial culture and sensitivity if initial treatment is unsuccessful.



TREATMENT

- Outpatient—unless secondary severe corneal ulceration.
- Inform client that medical therapy is generally life-long.
- When solutions and ointments are prescribed, instruct client to use the solution(s) before the ointment(s) and wait at least 5 minutes between treatments.
- Advise client to call at once if ocular pain increases because patients are predisposed to corneal ulceration.
- Parotid duct transposition—surgical procedure that reroutes the parotid duct to deliver saliva to the ocular surface if KCS is refractory to lacrimogenic therapy; more common with congenital KCS; saliva can be irritating to the cornea and result in mineral deposits; some patients require ongoing topical medical therapy.



MEDICATIONS

DRUG(S)

- Lacrimostimulants: Cyclosporine 0.2% ointment or 1–2% compounded solution; tacrolimus 0.02–0.03% compounded solution or ointment—Therapy q12h recommended (q8h if severe or refractory).
- For neurogenic KCS—pilocarpine 0.2% topically q8h or very careful oral pilocarpine dosing regimen given narrow therapeutic window (see "Suggested Reading").

- For feline KCS—antiviral therapy (see Conjunctivitis—Cats).
- Lacrimomimetics: artificial tears—help moisten the ocular surface to improve comfort and reduce signs; use viscous solutions or gels q2–12h depending on severity and ointment before bedtime; can reduce frequency once patient responds to lacrimostimulant therapy.
- Broad-spectrum antibiotics—topical ointment q6–8h for 3–4 weeks; indicated for secondary bacterial overgrowth.
- Ocular cleansing: use eye wash to remove discharge and debris prior to medications; if mucoid discharge is very tenacious 5% N-acetylcysteine can be used q6–12h as a mucinolytic agent prior to eye rinsing.
- Corticosteroids—topical; minimize inflammation; helpful in reducing corneal vascularization and pigmentation once aqueous tears improve; not commonly used due to corneal ulcer risk.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Topical cyclosporine or tacrolimus—rarely irritating.
- Pilocarpine—initially irritating topically; systemic side effect risk.
- Topical corticosteroids—avoid with ulcerative keratitis or if severe KCS given ulcer predilection.



FOLLOW-UP

- Recheck at regular intervals—monitor response and progress.
- Schirmer tear test—performed 4–6 weeks after initiating cyclosporine or tacrolimus (patient should receive the drug the day of the visit).
- Usually requires life-long treatment
- Good prognosis but refractory cases may require more aggressive therapy or surgery.



MISCELLANEOUS

ABBREVIATION

KCS = keratoconjunctivitis sicca

Suggested Reading

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Author Rachel A. Allbaugh

Consulting Editor Paul E. Miller

LAUTIC ACIDOSIS (HYPERLACTATEMIA)



BASICS

DEFINITION

- Hyperlactatemia is defined as a serum lactate concentration > 1.5 mmol/L in dogs and puppies > 70 days of age and > 1.8 mmol/L in cats.
- Lactic acidosis is hyperlactatemia with an arterial pH below the normal range.

PATOPHYSIOLOGY

- Lactic acid is the end product of aerobic and anaerobic glucose metabolism; at physiologic pH, lactic acid immediately dissociates to lactate and hydrogen ions. Small amounts of lactate are formed daily in healthy individuals, but clinically significant lactate accumulation can be due to anaerobic glycolysis. Lactic acid is produced during normal physiologic processes (e.g., exercise) and during pathologic processes (e.g., shock, seizures).
- Normally, liver and kidney lactate metabolism maintains a balance between lactate production and clearance, while providing a consistent source of glucose to the brain and red blood cells, which preferentially use glucose; the hydrogen ion produced during lactic acid dissociation is used in gluconeogenesis, which is important in maintaining acid-base balance.
- In most critically ill or injured patients, hyperlactatemia and lactic acidosis are due to conditions that cause tissue hypoxia, with a shift to anaerobic glycolysis.
- Inadequate perfusion, severe hypoxemia, increased oxygen demand, decreased hemoglobin concentration, or combinations of these factors can cause tissue hypoxia.
- Depending on the duration and severity of hypoxia, hyperlactatemia and possibly lactic acidosis might develop.
- Hyperlactatemia generally develops when tissue perfusion is adequate and acid-base buffering systems are intact.
- Clinically evident tissue hypoperfusion does not usually occur in patients with hyperlactatemia alone, but "occult" hypoperfusion might be present that is not detectable by routine monitoring and might represent a precursor phase to overt hypoperfusion.
- Lactic acidosis can occur with abnormal metabolic regulation secondary to marked tissue hypoxia and hypoperfusion, certain drugs or toxins, or congenital defects in carbohydrate metabolism; buffering systems usually cannot cope with the developing acidosis.
- The severity of hyperlactatemia and acidosis in critically ill or injured patients reflects the severity of tissue hypoxia; evaluation of lactate levels helps assess the degree of tissue hypoperfusion and hypoxia.
- Studies in human trauma and shock patients demonstrate that lactate predicts

outcome and that mortality is correlated with the severity of the lactic acidosis: the higher the lactate level, the greater the mortality.

- Lactate measurement allows reliable assessment of the response of critically ill or injured people to initial and continuing resuscitative therapy.
- Lactate concentrations are increased in critically ill and injured dogs; an apparent association exists between severity of lactate increase and outcome, and differences in lactate concentrations between varying diseases/injuries (seizures, ethylene glycol and aspirin intoxication, and major trauma).
- Numerous clinical and experimental studies in critically ill humans and critically ill/injured dogs clearly show blood lactate measurement to be a useful tool for assessing the severity of tissue hypoxia, response to therapy, and prognosis.

SYSTEMS AFFECTED

- Persistent lactic acidosis can cause severe cardiovascular complications including impaired cardiac contractility, impaired pressor response to catecholamines, increased sensitivity of the myocardium to ventricular arrhythmias, and reduced cardiac output. These changes increase the likelihood of organ hypoperfusion leading to further tissue hypoxia.
- Persistent lactic acidosis can impair normal coagulation leading to hemorrhagic complications in trauma and postoperative patients.
- As acidosis and tissue hypoxia become more severe, failure of multiple organ systems and even death can occur.

SIGNALMENT

Dog and cat

SIGNS

General Comments

Usually relate more to the underlying disorder than to direct effects of acidosis. As tissue hypoperfusion, hypoxia, and acidosis worsen, signs of dysfunction can occur in any organ system.

Historical Findings

Disorders causing lactic acidosis are common; historical facts should prompt suspicion of an underlying acidosis.

Physical Examination Findings

- Tachypnea is usually present due to attempted respiratory compensation.
- Most patients with acidosis are hypovolemic and demonstrate poor tissue perfusion or dehydration—dark mucous membranes, prolonged capillary refill time, and increased skin turgor.
- Severely acidotic patients might have cardiac dysrhythmias and poor contractility.

CAUSES

- Two types, A and B, based on the clinical presence or absence of hypoperfusion or tissue hypoxia.

- Type A lactic acidosis—more common; due to decreased or inadequate oxygen delivery and oxygen consumption (i.e., poor tissue perfusion and tissue hypoxia).

- Causes of type A include shock, regional hypoperfusion, arterial obstruction, severe hypoxemia, severe anemia, carbon monoxide poisoning, severe asthma, and severe motor seizures.

- Type B lactic acidosis—includes all other causes of lactic acidosis; subdivided into 3 subsets (B₁, B₂, B₃); characterized by the absence of hypoxemia or poor tissue perfusion. Many causes of type B lactic acidosis might be "occult" hypoperfusion not detectable by routine monitoring parameters or possibly combinations of types A and B lactic acidosis.

- The most common causes of type B lactic acidosis in veterinary medicine include neoplasia, alklosis, sepsis, renal failure, liver disease, catecholamine use (norepinephrine, epinephrine), and intoxications (strychnine, cyanide, ethylene glycol, salicylates, acetaminophen, propylene glycol).

- Elevated blood lactate has been observed in patients with lymphoma and meningioma. Though the type and cause of the high lactate in these animals is not clearly understood, the presence of a high lactate should alert the clinician to evaluate other markers of perfusion (heart rate, mucous membrane color, pulse quality, capillary refill, serum creatinine) before attempting aggressive fluid resuscitation.

RISK FACTORS

- Risk factors for development of hyperlactatemia and lactic acidosis relate directly to risk factors for the specific disorders causing the underlying tissue hypoxia.
- In general, young animals are more at risk for traumatic shock and intoxications.
- Older animals are more likely to develop neoplasia, renal failure, heart failure, liver disease, severe anemia, and vascular disorders; consult the risk factors for these specific disorders.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Differential diagnoses for hyperlactatemia and lactic acidosis include those disorders described under "Causes."
- Any severely ill or injured animal is suspect for an underlying acidosis and evaluating the lactate concentration can aid in diagnosis.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

- Activated charcoal use, catecholamines, salicylates, acetaminophen, terbutaline, nitroprusside, halothane, bicarbonate, and propylene glycol all can cause

(CONTINUED)

mild-to-moderate increase in lactate concentration in the absence of true tissue hypoperfusion and hypoxia.

- Lower lactate concentrations are found in samples with sodium citrate anticoagulant than in those with heparin and EDTA.
- Even small amounts of lactate-containing intravenous fluids (e.g., lactated Ringer's solution) can cause false increases in circulating lactate concentration in a blood sample if not properly cleared from the catheter or tubing through which the intravenous fluid was being given.

Disorders That May Alter Laboratory Results

- Stress, trembling, resisting restraint, excitement, and venous stasis can increase lactate to 2.5–5.0 mmol/L, but in these instances lactate usually normalizes in ≤ 2 hours.
- Seizures or extreme muscular exertion can increase lactate to 4–10 mmol/L, but lactate usually normalizes in ≤ 2 hours.
- Several types of neoplasia increase lactate concentrations because tumor cells preferentially use anaerobic glucose metabolism as part of the cancer cachexia syndrome.
- Alkalosis, sepsis, liver disease, and renal failure also can increase lactate concentrations by mechanisms other than poor tissue perfusion and hypoxia.
- Failure to detect elevated lactate concentration does not ensure adequate perfusion to all organs; significant organ hypoperfusion can still exist that might ultimately lead to multiple organ failure.
- Regional hypoperfusion, especially splanchnic, occurs in the absence of, or before, increases in systemic lactate and metabolic acidosis and often despite therapy that successfully maintains blood pressure, cardiac output, heart rate, DO_2 , VO_2 , and respiratory parameters.

Valid if Run in Human Laboratory?

- Yes; semiautomated and automated techniques are available for rapid measurement of lactate concentration in microliter samples of whole blood, serum, and plasma.
- Lactate concentration is ideally measured on an arterial sample; however, clinically, there is no significant difference between sampling sites; maintain consistency with sites for serial measurement.

CBC/BIOCHEMISTRY/URINALYSIS

- Few specific CBC findings would suggest causes for hyperlactatemia and lactic acidosis.
- Biochemical and urinalysis findings help determine the underlying cause; examples include renal azotemia and markedly increased serum osmolality seen with ethylene glycol intoxication; renal azotemia, hyperkalemia, and tubular casts seen with acute renal failure; and increased lactate

concentration, increased total protein, and increased hematocrit with dehydration and poor tissue perfusion in a shock patient.

OTHER LABORATORY TESTS

- Arterial blood gas analysis might help define the extent of a concurrent respiratory disorder or a mixed acid-base disorder.
- Additional tests (e.g., ethylene glycol, serum and urine glucose, serum and urine ketones) might be helpful, depending on the suspected cause.



TREATMENT

- Hyperlactatemia alone is seldom significant enough to prompt specific therapy and is more important as a marker of possible severe or developing systemic problems. Aggressive treatment is not recommended for elevated blood lactate in the absence of other signs of circulatory shock. Fluid resuscitation is not indicated if acidosis does not accompany the high blood lactate.
- Detection of hyperlactatemia, with or without acidosis, should drive the clinician to seek causes of hypoperfusion and should dictate early therapeutic interventions to improve tissue oxygen delivery to halt organ ischemia and avert progression to circulatory shock.
- Lactic acidosis is often severe, and aggressive therapy to correct the underlying cause(s) and specifically treat the acidosis is usually indicated.



MEDICATIONS

DRUG(S) OF CHOICE

- Specific drug and fluid use depends on the underlying cause.
- Many causes of hyperlactatemia and lactic acidosis are characterized by fluid volume deficits; thus, aggressive fluid therapy is traditionally the first step in treatment.
- The use of alkalinizing and pH-neutral isotonic crystalloid fluids might be preferred in cases of hypovolemic lactic acidosis to more rapidly normalize blood pH.
- Though controversial, sodium bicarbonate therapy to correct blood $\text{pH} < 7.2$ might be indicated when the pH fails to increase in response to aggressive fluid resuscitation.

PRECAUTIONS

- Sodium bicarbonate is reserved for patients with a $\text{pH} < 7.2$ to avoid the cardiovascular effects of severe acidosis. It should only be used to correct the pH to 7.2. This can be accomplished by calculating the bicarbonate deficit or giving small empirical doses of 1–2 mEq/kg and rechecking blood pH.
- Sodium bicarbonate is likely to be more effective in patients with a normal anion gap

metabolic acidosis (normal lactate) than patients with high anion gap metabolic acidosis, as the latter develops metabolic alkalosis when organic anions (lactate or ketoacids) are converted to bicarbonate during hemodynamic recovery.

- With 10–15% of the bicarbonate immediately converted to CO_2 , it is important that the patient ventilation increases to prevent a further drop in pH.
- Possible complications of sodium bicarbonate therapy include volume overload from excess sodium, paradoxical CNS acidosis, hypocalcemic tetany and a left-shift of the oxygen-hemoglobin dissociation curve from iatrogenic alkalosis.



FOLLOW-UP

PATIENT MONITORING

- Serial lactate determinations are more valuable than single (admission, peak) lactate levels; monitor lactate over time in critical patients.
- The ability of a patient to clear lactate predicts response to therapy and survival.
- Continue checking other parameters that help gauge the response to therapy for the underlying cause.

PREVENTION/AVOIDANCE

Owners should understand the early warning signs of the condition(s) that led to lactic acidosis in their pet with instructions to seek prompt medical attention should they recur.

POSSIBLE COMPLICATIONS

- People with lactic acidosis are at greater risk of developing multiple organ failure and have a higher mortality rate than patients without lactic acidosis.
- Dogs and horses with elevated lactate concentrations and lactic acidosis have poorer outcomes as well.
- Lactate > 6 – 6.5 mmol/L suggests tissue hypoperfusion (e.g., shock) or local ischemia (e.g., gastric necrosis in GDV patients).

EXPECTED COURSE AND PROGNOSIS

- Lactic acidosis that quickly corrects with supportive therapy indicates resolution of the primary disorder. Lactic acidosis that fails to respond is a grave prognostic indicator.
- Serial blood lactate and pH concentrations will be more prognostic than single measurements as clinicians gauge response to therapy.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Lactic acidosis can be found along with any condition causing tissue hypoxia.

LACTIC ACIDOSIS (HYPERLACTATEMIA)

(CONTINUED)

- Elevated blood lactate has been noted in patients with lymphoma and menigioma. These patients could have concurrent acidosis. In these patients, other parameters should be used to assess tissue perfusion as blood lactate can remain elevated despite adequate resuscitation.

SEE ALSO

Acidosis, Metabolic

ABBREVIATIONS

- EDTA = ethylene diamine tetra-acetate
- GDV = gastric dilatation and volvulus

Suggested Reading

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**Client Education Handout
available online**



BASICS

DEFINITION

A disturbance in gait and locomotion in response to pain, anatomic disruption, or injury.

Pathophysiology

- Severe, sharp pain—limited limb movement during all phases of locomotion, little to no load bearing in motion or at rest.
- Milder, dull, or aching pain—reduced loading and ground contact time during all phases of locomotion.
- Pain produced only during certain phases of movement—patient adjusts its motion and gait to minimize discomfort.
- Anatomic dysfunction resulting in certain normal motions being altered or impossible.

SYSTEMS AFFECTED

- Musculoskeletal • Nervous

SIGNALMENT

- Any age or breed of dog.
- Age, breed, and sex predilection—depend on specific disease.

SIGNS

General Comments

- Unilateral forelimb—head and neck moves upward when the affected limb is placed on the ground and drops when the sound limb loads.
- Unilateral hindlimb—pelvis drops when affected leg loads, rises when it unloads.
- Bilateral hindlimb—forequarters carried lower to shift weight forward.
- Always assess the patient's neurologic status, especially with a suspected proximal lesion.

Historical Findings

- Complete history—identify known trauma; alterations with weather, exercise tolerance, response to rest, effect of previous treatments.
- Determine speed of onset of lameness.
- Determine progression—static; slow; rapid.
- Determine consistency—intermittent, constant, associations.
- How does the patient show pain?

Physical Examination Findings

- Perform a complete routine examination.
- Observe posture—standing, getting up or lying down, sitting.
- Observe gait—walking; trotting; climbing stairs; doing figure eights.
- Palpate—asymmetry of muscle mass (measure and compare); bony prominences.
- Manipulate bones and joints, beginning distally and working proximally.
- Assess—instability; incongruency; pain; range of motion (measure); abnormal sounds.
- Examine suspected area of involvement last—by starting with normal limbs, patient may relax, allowing comparison of normal to abnormal reactions.

CAUSES

Forelimb

Growing Dog (< 12 Months of Age)

- Osteochondrosis of the shoulder • Shoulder luxation or subluxation—congenital

- Osteochondrosis of the elbow • Ununited anconeal process • Fragmented medial coronoid process • Elbow incongruity
- Avulsion or calcification of the flexor muscles—elbow • Asymmetric growth of the radius and ulna • Panosteitis • Hypertrophic osteodystrophy • Trauma—soft tissue; bone; joint • Infection—local; systemic
- Nutritional imbalances • Congenital anomalies

Mature Dog (> 12 Months of Age)

- Degenerative joint disease • Bicipital tenosynovitis • Calcification or mineralization of supraspinatus or infraspinatus tendon
- Contracture of supraspinatus or infraspinatus muscle • Soft tissue or bone neoplasia—primary; metastatic • Trauma—soft tissue; bone; joint • Panosteitis
- Polyarthropathies • Polymyositis
- Polyneuritis

Hindlimb

Growing Dog (< 12 Months of Age)

- Hip dysplasia • Avascular necrosis of femoral head—Legg-Calvé-Perthes disease
- Osteochondritis of stifle • Patella luxation—medial or lateral • Osteochondritis of hock
- Panosteitis • Hypertrophic osteodystrophy
- Trauma—soft tissue; bone; joint
- Infection—local; systemic • Nutritional imbalances • Congenital anomalies

Mature Dog (> 12 Months of Age)

- Degenerative joint disease (hip dysplasia)
- Cruciate ligament disease • Avulsion of long digital extensor tendon • Soft tissue or bone neoplasia—primary; metastatic • Trauma—soft tissue; bone; joint • Panosteitis
- Polyarthropathies • Polymyositis
- Polyneuritis

RISK FACTORS

Breed (size), overweight, strenuous activity



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Must differentiate musculoskeletal from neurogenic and metabolic causes.

CBC/BIOCHEMISTRY/URINALYSIS

Muscle injury elevates creatine phosphokinase levels.

OTHER LABORATORY TESTS

Depends on suspected cause

IMAGING

- Radiographs—recommend two views of region of interest.
- CT, MRI, ultrasound, and nuclear scintigraphy where appropriate.

DIAGNOSTIC PROCEDURES

- Cytologic examination of joint fluid—identify and differentiate intra-articular disease.
- EMG—differentiate chronic neuromuscular from musculoskeletal disease.
- Muscle and/or nerve biopsy—reveal and identify neuromuscular disease.



TREATMENT

Depends on underlying cause



MEDICATIONS

DRUG(S) OF CHOICE

- Analgesics and NSAIDs—minimize pain; decrease inflammation; meloxicam (load 0.2 mg/kg PO, then 0.1 mg/kg daily PO—liquid), carprofen (2.2 mg/kg PO q12h), deracoxib (3–4 mg/kg PO q24h—chewable) for 7 days for postoperative pain.

PRECAUTIONS

NSAIDs—gastrointestinal irritation or renal/hepatic toxicity may preclude use in some patients.

ALTERNATIVE DRUG(S)

Chondroprotective drugs (e.g., polysulfated glycosaminoglycans, glucosamine, and chondroitin sulfate)—may be of benefit in limiting cartilage damage and improving regeneration.

L



FOLLOW-UP

PATIENT MONITORING

Depends on underlying cause



MISCELLANEOUS

SEE ALSO

Chapters covering musculoskeletal and neuromuscular disorders

ABBREVIATIONS

- CT = computed tomography
- EMG = electromyogram
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug

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Client Education Handout
available online

LARYNGEAL DISEASES



BASICS

DEFINITION

- The larynx is made of cartilage structures surrounding the rima glottis. The functions of the larynx are to control airflow during respiration, protect the lower airways from aspiration during swallowing, and control phonation.
- Laryngeal diseases in dogs and cats include laryngeal paralysis, acute laryngitis, obstructive laryngitis, laryngeal collapse in brachycephalic airway syndrome (BAS), foreign body obstruction, neoplasia, and trauma.

PATOPHYSIOLOGY

- Decreased diameter of the laryngeal opening increases resistance to airflow and results in stridor on inspiration. The decrease in airflow will lead to hypoxemia, cyanosis, or respiratory distress and a decrease in heat exchange (heat intolerance, hyperthermia).
- Inflammation or lesions of the vocal cords can lead to aphonia or change in bark/meow.

SYSTEMS AFFECTED

- Respiratory—aspiration pneumonia and hypoventilation with cyanosis can occur when laryngeal function is impaired.
- Cardiovascular—hypoxemia may lead to tachycardia.
- Gastrointestinal—retching, regurgitation, vomiting, and/or dysphagia can when polyneuropathy causes laryngeal paralysis and esophageal dysfunction; esophagitis is frequently associated with BAS.
- Nervous—depression, stupor, or coma may occur if severe laryngeal obstruction leads to severe hyperthermia.

GENETICS

- Juvenile laryngeal paralysis in the Bouvier des Flandres is transmitted as a dominant trait.
- In laryngeal paralysis associated with polyneuropathy in the Leonberger dog, X-linked inheritance is suggested.
- No other laryngeal disorder has been proven to be genetic in the dog or cat, but familial conditions and breed predispositions have been reported.

INCIDENCE/PREVALENCE

- More common in dogs than in cats.
- Currently, congenital laryngeal paralysis is only sporadic in the Bouvier des Flandres.
- Idiopathic laryngeal paralysis is a common disease of older large-breed dogs; exact prevalence unknown.
- BAS is a common syndrome in French and English bulldogs.
- Laryngeal trauma and neoplasia are rare.

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Familial laryngeal paralysis/polyneuropathy complex occurs in the Dalmatian, rottweiler, Leonberger, and Pyrenean mountain dog

(Great Pyrenees).

- Congenital laryngeal paralysis is found in Bouvier des Flandres, huskies, husky-crosses, white German shepherds, and probably bull terriers.

- Idiopathic acquired laryngeal paralysis is most often found in large-breed dogs (especially Labrador and golden retrievers).
- BAS is found in brachycephalic breeds of dogs.
- Golden retrievers are prone to laryngeal rhabdomyoma.
- Upper airway obstruction due to laryngeal collapse or narrowed laryngeal opening occurs in Norwich terriers.

Mean Age and Range

- Congenital and familial laryngeal paralysis—onset of signs usually in the first months of life (2 and 8 months). Later in the Leonberger, 1–9 years, and white German shepherd, 2 years.
- Acquired laryngeal paralysis—possible at any age but more frequent in older dogs.
- Neoplasia—middle-aged to old dogs.

SIGNS

Historical Findings

- Panting.
- Exercise and heat intolerance.
- Noisy respiration.
- Change of voice.
- Occasional cough.
- Severe cases—inspiratory respiratory distress, collapse, syncope, or even sudden death.
- Polyneuropathy, polymyopathy, or myasthenia gravis—regurgitation, weakness, abnormal gait (pattern of abnormalities varies).
- Absence of signs is possible in Norwich terriers with upper airway obstruction.

Physical Examination Findings

- Panting, polypnea, and inspiratory stridor in canine cases.
- Respiration is less noisy in cats with laryngeal disease.
- Cyanosis.
- Hyperthermia frequent.
- Aspiration pneumonia—fever, crackles on respiratory auscultation.
- Polyneuropathy, polymyopathy, or myasthenia gravis—paraparesis or tetraparesis with decreased spinal reflexes.
- Leonberger with familial polyneuropathy—high-stepping pelvic-limb gait with depressed spinal and cranial nerve reflexes.
- Rottweilers with laryngeal paralysis/polyneuropathy complex—cataracts frequently observed.
- Normal physical examination in some Norwich terriers with upper airway obstruction.

CAUSES

- Laryngeal paralysis:
 - Congenital—(1) neuronal degeneration of the nucleus ambiguus (Bouvier des Flandres and husky); (2) idiopathic.
 - Acquired—(1) polyneuropathy—idiopathic; familial (laryngeal paralysis-polyneuropathy complex); immune-mediated; (2) myasthenia gravis; (3) polymyopathy—idiopathic; immune-mediated; infectious (toxoplasmosis, neosporosis); (4) ventral cervical or cranial thoracic lesion—neoplasia or trauma affecting one or both recurrent nerves; examples

include lymphoma of the vagus nerve in the cat and traumatic neuropathy secondary to thyroidectomy.

- Acute laryngitis:
 - Cause often not found.
 - Virus—canine parainfluenza virus, feline herpes virus 1.

Bacteria—*Bordetella bronchiseptica*.

- Gastroesophageal reflux.
- Idiopathic chronic obstructive laryngitis (lymphoplasmacytic, granulomatous)

Laryngeal neoplasia:

- Dog—rhabdomyoma, rhabdomyosarcoma, adenocarcinoma, squamous cell carcinoma, lipoma, extramedullary plasmacytoma.

Cat—lymphoma, squamous cell carcinoma.

Trauma: injuries caused by foreign bodies.

- Neck trauma, bite wounds.
- Laryngeal collapse secondary to BAS.
- Idiopathic laryngeal malformation, collapse in Norwich terriers.

RISK FACTORS

Breed associations. Risk factors for developing severe or fatal clinical signs include obesity, hot or humid temperature (especially in a closed environment), and concurrent lower airway or pulmonary disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pharyngeal diseases—also cause gagging, stridor, and cough. Dysphagia is not seen with laryngeal disease but may be present in the case of pharyngeal lesion.
- Tracheal diseases may be confused with laryngeal disease in some cases. Cough is more frequent in tracheal disease than in laryngeal disease while inspiratory stridor is more frequent in laryngeal disease.

CBC/BIOCHEMISTRY/URINALYSIS

- No specific abnormalities.
- Leukocytosis may be present in aspiration pneumonia.
- Mild-to-moderate increase in liver enzymes if chronic hypoxemia.
- Hypercholesterolemia may be present if concurrent hypothyroidism is present.

OTHER LABORATORY TESTS

- If laryngeal paralysis secondary to polyneuropathy/polymyopathy:
 - Thyroid panel in the dog.
 - Antibody titers against *Toxoplasma gondii* (dog and cat) and *Neospora caninum* (dog).
 - Anticholinesterase receptor antibody titer.

IMAGING

- Thoracic radiographs—to rule-out aspiration pneumonia as a complication, other lower airway conditions, and a mediastinal mass as a cause of laryngeal paralysis.
- If vomiting/regurgitation present—barium swallow with fluoroscopy (to identify esophageal dysfunction, reflux esophagitis/hiatal hernia coexisting in some cases of brachycephalic airway syndrome).

(CONTINUED)

- Pharynx/larynx radiographs or ultrasonography—to identify potential mass.

DIAGNOSTIC PROCEDURES

Laryngoscopy

- Method of choice to identify laryngeal paralysis, collapse, mass, trauma, foreign body, or laryngitis. • General anesthesia or deep sedation is required. • Laryngeal paralysis:
 - Diagnosis confirmed by loss of abduction of arytenoid cartilages during deep inspiration.
 - Usually bilateral but unilateral paralysis is possible in the early course of the disease.
 - Unilateral paralysis has been described in cats. ◦ False-positive result possible because of the influence of general anesthesia on laryngeal function. Intravenous doxapram HCl (1–2 mg/kg) to increase respiratory effort is advised if the diagnosis is in doubt.

Esophagoscopy

When vomiting/regurgitation is observed to rule out reflux esophagitis or hiatal hernia.

Retrograde Rhinoscopy

When pharyngeal disease is suspected or in the case of BAS.

PATHOLOGIC FINDINGS

- Laryngeal paralysis:
 - Gross findings—redness, swelling, and thickening of the arytenoid cartilages and the vocal folds.
 - Histopathology—nonspecific edema and inflammation of laryngeal mucosa and submucosa; denervation atrophy of laryngeal muscles in the case of neuropathy of recurrent laryngeal nerve(s).
 - Idiopathic chronic obstructive laryngitis:
 - Histopathology—lymphoplasmacytic, granulomatous, or pyogranulomatous inflammation of the laryngeal submucosa.



TREATMENT

APPROPRIATE HEALTH CARE

Paralysis:

- Outpatient medical management—for stable patients awaiting surgery. • Emergency:
 - Sedation/anesthesia. ◦ Prednisolone succinate (30 mg/kg IV, then 15 mg/kg IV after 6 hours, prednisolone 0.5 mg/kg PO q12h till surgery). ◦ Cooling therapy with IV fluids, a blowing fan, and cold water on the neck or alcohol on paws.

NURSING CARE

Paralysis:

- Avoid warm, poorly ventilated environments, stress, and intense excitation as these further compromise normal cooling mechanisms and proper air exchange. • Avoid cervical collars. • Avoid weight gain.

ACTIVITY

Exercise should be severely restricted in animals suffering from laryngeal paralysis, especially in warm temperatures.

DIET

Loss of weight is advocated in overweight patients with laryngeal paralysis.

CLIENT EDUCATION

- Paralysis:
 - Discuss the importance of surgery and the risk of not performing surgery (chronic hypoxemia, heat stroke, risk of suffocation, and death).
 - Discuss potential complications of surgery.
 - Discuss the guarded prognosis with surgery in cases with polyneuropathy.
 - Discuss the potential heritability of this condition in certain breeds.
- Neoplasia:
 - Discuss surgical/chemotherapeutic options.

SURGICAL CONSIDERATIONS

- Paralysis—surgery (unilateral arytenoid lateralization) is the treatment of choice in both dogs and cats; bilateral surgical correction is not advised because it increases the risk of aspiration pneumonia; oral prednisolone therapy (anti-inflammatory doses) should be given for a few days before surgery to decrease laryngeal edema.
- Neoplasia—surgery can be curative in some cases, for rhabdomyoma, rhabdomyosarcoma, lipoma or squamous cell carcinoma; tracheostomy may improve quality of life if surgical excision is not possible.



MEDICATIONS

DRUG(S) OF CHOICE

- Paralysis—if surgery is declined, oral prednisolone therapy (0.5 mg/kg q12h for 1 week then progressive tapering of dosage to 0.5 mg/kg q48h).
- Lymphoma (mainly in cats)—chemotherapy (see Lymphoma—Cats).

PRECAUTIONS

Usual safety precautions if chemotherapy is administered.



FOLLOW-UP

PATIENT MONITORING

- Immediate post-surgical period—check rectal temperature (should remain normal).
- Monitor for aspiration pneumonia (short and long term).
- If surgery is successful, exercise, stridor, and heat intolerance should decrease.

POSSIBLE COMPLICATIONS

- Paralysis—recurrence of clinical signs are uncommon if surgery is correctly performed; aspiration pneumonia is possible as the larynx is placed in a fixed open position; risk of aspiration pneumonia increased if bilateral arytenoid lateralization is performed or if dysphagia due to pharyngeal and/or esophageal dysfunction coexists.
- Tumor—recurrence of clinical signs if complete

resection is not possible, increased risk of aspiration pneumonia in the postoperative period.

EXPECTED COURSE AND PROGNOSIS

- Idiopathic paralysis—good with surgery; guarded to poor if surgery is declined.
- Paralysis associated with esophageal dysfunction—poor.
- Tumor—guarded to good in the case of successful resection of a benign tumor; poor in the case of carcinoma, even with radiation therapy; variable in the case of feline lymphoma.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Laryngeal paralysis is sometimes associated with a mass in the anterior mediastinum or the ventral cervical region.
- Coexistence of megaesophagus, weakness, or abnormal gait with laryngeal paralysis suggests polyneuropathy, polymyopathy, or myasthenia gravis.

AGE-RELATED FACTORS

Congenital and familial laryngeal paralysis—onset of clinical signs in the first year of life.

PREGNANCY/FERTILITY/BREEDING

Dogs affected with congenital laryngeal paralysis or laryngeal paralysis/polyneuropathy complex should not be bred.

SEE ALSO

- Brachycephalic Airway Syndrome
- Cyanosis • Myasthenia Gravis

ABBREVIATIONS

- BAS = brachycephalic airway syndrome

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LEAD TOXICOSIS



BASICS

DEFINITION

Intoxication (blood lead > 0.4 ppm, although somewhat variable) owing to acute or chronic exposure to some form of lead.

PATHOPHYSIOLOGY

- Cell damage is due to the ability of lead to substitute for other polyvalent cations (especially divalent cations such as Ca and Zn) important for cell homeostasis.
- Diverse biologic processes are affected, including metal transport, energy metabolism, apoptosis, ion conduction, cell adhesion, inter- and intracellular signaling, enzymatic processes, protein maturation, and genetic regulation.

SYSTEMS AFFECTED

- Gastrointestinal—unknown mechanism, likely damage to peripheral nerves.
- Nervous—capillary damage; alteration of membrane ionic channels and signaling molecules.
- Renal/urologic—damage to proximal tubule cells due to enzyme disruption and oxidative damage.
- Hemic/Lymph/Immune—interference with hemoglobin synthesis, increased fragility and decreased survival of RBCs, release of reticulocytes and nucleated RBCs from bone marrow, inhibition of 5'-pyrimidine nucleotidase causing retention of RNA degradation products, aggregation of ribosomes resulting in basophilic stippling.

GENETICS

N/A

INCIDENCE/PREVALENCE

- True incidence unknown.
- Decreasing prevalence in dogs—owing to elimination of sources.
- Steady to increasing prevalence in cats—increased awareness and diagnosis.
- Higher prevalence during warmer months.
- Higher prevalence in young animals—greater bioavailability of lead and more permeable blood-brain barrier.

GEOGRAPHIC DISTRIBUTION

- Low socioeconomic status of pet-owning family associated with high blood lead concentration in pets.
- Areas with older homes/buildings.

SIGNALMENT

Species

Dog and cat: dogs more commonly than cats

Breed Predilections

N/A

Mean Age and Range

Mainly dogs < 1 year of age

Predominant Sex

N/A

SIGNS

General Comments

- Primarily gastrointestinal and neurologic.
- Gastrointestinal—often precede CNS signs; predominant with chronic, low-level exposure.
- CNS—occur more often with acute exposure, more common in younger animals.

Historical Findings

History of renovation of older house or building or ingestion of lead objects.

Physical Examination Findings

- Vomiting
- Diarrhea
- Anorexia
- Abdominal pain
- Regurgitation due to megaesophagus
- Lethargy
- Hysteria
- Seizures
- Blindness
- Cats—central vestibular abnormalities such as vertical nystagmus and ataxia reported

CAUSES

- Ingestion of some form of lead—paint and paint residues or dust from sanding; car batteries; linoleum; solder; plumbing materials and supplies; lubricating compounds; putty; tar paper; lead foil; golf balls; lead object (e.g., shot, fishing sinkers, drapery weights), leaded glass.
- Use of improperly glazed ceramic food or water bowl.
- Lead paint or lead-contaminated dust or soil are common sources for exposure; cats ingest lead as a result of self-grooming.

RISK FACTORS

- Age < 1 year.
- Living in economically depressed areas.
- Living in old house or building that is being renovated.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Dogs

- Canine distemper
- Infectious encephalitides
- Epilepsy
- Bromethalin, methylxanthine, or tremorgenic mycotoxin toxicosis
- NSAID toxicosis
- Heat stroke
- Intestinal parasitism
- Intussusception
- Foreign body
- Pancreatitis
- Infectious canine hepatitis

Cats

- Degenerative or storage diseases
- Hepatic encephalopathy
- Infectious encephalitides

- Organophosphate, bromethalin, or methylxanthine toxicosis

CBC/BIOCHEMISTRY/URINALYSIS

- Between 5 and 40 nucleated RBCs/100 WBCs without anemia.
- Absence of nucleated RBC does not rule out the diagnosis.
- Anisocytosis, polychromasia, poikilocytosis, target cells, hypochromasia.
- Basophilic stippling of RBCs; often difficult to detect.
- Neutrophilic leukocytosis.
- Cats—elevated AST and ALP reported.
- Urinalysis—mild nonspecific renal damage; glucosuria; hemoglobinuria.

OTHER LABORATORY TESTS

Lead Concentration

- Toxic—antemortem whole blood: > 0.4 ppm (40 µg/dL); post-mortem liver and/or kidney: > 5 ppm (wet weight).
- Blood lead concentrations fluctuate and do not necessarily correlate with total body burden.
- Lower values—must be interpreted in conjunction with history and clinical signs.
- No normal “background” blood lead concentrations; typically less than 0.05 ppm.
- Blood concentrations—do not correlate with occurrence or severity of clinical signs.
- CaNa₂EDTA mobilization test—collect one 24-hour urine sample; administer CaNa₂EDTA (75 mg/kg IM); collect a second 24-hour urine sample; with toxicosis, urine lead increases 10–60-fold post-EDTA (succimer could conceivably be substituted for CaNa₂EDTA but this has not been evaluated).

IMAGING

May note radiopaque material in gastrointestinal tract; not diagnostic.

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

- Gross—may note paint chips or lead objects in gastrointestinal tract.
- Intranuclear inclusion bodies—may note in hepatocytes or renal tubular epithelial cells; intracellular storage form of lead; considered pathognomonic.
- Cerebrocortical lesions—spongiosis, vascular hypertrophy, gliosis, neuronal necrosis, demyelination.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—first course of chelation, depending on severity of clinical signs.
- Outpatient—orally administered chelators.

NURSING CARE

- Balanced electrolyte fluids—Ringer's solution; replacement of hydration deficit.

(CONTINUED)

- Gastric lavage or whole bowel irrigation—may be indicated.

ACTIVITY

N/A

DIET

N/A

CLIENT EDUCATION

- Inform client of the potential of adverse human health effects of lead.
- Notify public health officials.
- Determine the source of the lead.

SURGICAL CONSIDERATIONS

Removal of lead objects from the gastrointestinal tract.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Evacuation of gastrointestinal tract—saline cathartics; sodium or magnesium sulfate (dogs, 2–25 g; cats 2–5 g PO as 20% solution or less).
- Control of seizures—diazepam (given to effect; dogs and cats, 0.5 mg/kg IV) or phenobarbital sodium (administer in increments of 10–20 mg/kg IV to effect).
- Alleviation of cerebral edema—mannitol (0.25–2 g/kg of 15% to 25% IV, slow infusion over 30–60 minutes) and dexamethasone (2.2–4.4 mg/kg IV).
- Some evidence that antioxidants or thiol-containing drugs may be useful—vitamins C and E, α -lipoic acid, N-acetylcysteine; optimal doses not determined.
- B vitamins, especially thiamin, may also be useful; optimal doses not determined.
- Reduction of lead body burden: chelation therapy
 - CaNa₂EDTA (dogs and cats, 25 mg/kg SC, IM, IV q6h for 2–5 days); dilute to a 1% solution with D₅W before administration; may need multiple treatment courses if blood lead concentration is high; allow 5-day rest period between treatment courses.
 - Succimer—alternative to CaNa₂ EDTA; orally administered chelating agent; 10 mg/kg PO q8h for 5 days followed by 10 mg PO q12h for 2 weeks; allow 2-week rest period between treatments; may administer per rectum if clinical signs such as emesis preclude oral administration; cats successfully treated with 10 mg/kg PO q8h for 17 days; advantages over other chelators: can be given PO allowing for outpatient

treatment; does not increase lead absorption from the gastrointestinal tract; not reported to be nephrotoxic; chelation of essential elements such as zinc and copper is not clinically significant.

CONTRAINDICATIONS

CaNa₂EDTA—do not administer to patients with renal impairment or anuria; establish urine flow before administration; do not administer orally.

PRECAUTIONS

- CaNa₂EDTA—safety in pregnancy not established; teratogenic at therapeutic doses although in human medicine is recommended over succimer for pregnant patients.
- Succimer—safety in pregnancy not established; fetotoxic at doses much higher (100 to 1,000 mg/kg) than recommended therapeutic dose.

POSSIBLE INTERACTIONS

CaNa₂EDTA—depletion of zinc, iron and manganese with long-term therapy.

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

Blood lead—should be < 0.1 ppm; assess 10–14 days after cessation of chelation therapy.

PREVENTION/AVOIDANCE

- Test paint, dust, soil prior to animal access if likelihood of lead contamination.
- Determine source of lead and remove it from the patient's environment.

POSSIBLE COMPLICATIONS

Occasionally, permanent neurologic signs (e.g., blindness).

EXPECTED COURSE AND PROGNOSIS

- Signs should dramatically improve within 24–48 hours after initiating chelation therapy.
- Prognosis—favorable with treatment.
- Uncontrolled seizures—guarded prognosis.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

Dogs < 1 year of age—more likely to be affected.

LEAD TOXICOSIS**ZOONOTIC POTENTIAL**

None; however, humans in the same environment may be at risk for exposure.

PREGNANCY/FERTILITY/BREEDING

- Transplacental passage—may cause neonatal poisoning.
- Lactation—lead mobilized from bones unlikely to poison nursing animals.

SYNOMYMS

Plumbism

ABBREVIATIONS

- ALP = alkaline phosphatase
- AST = aspartate aminotransferase
- Ca = calcium
- CNS = central nervous system
- NSAID = nonsteroidal anti-inflammatory drug
- RBC = red blood cells
- WBC = white blood cells
- Zn = zinc

INTERNET RESOURCES

None

Suggested Reading

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LEFT ANTERIOR FASCICULAR BLOCK



BASICS

DEFINITION

- Conduction delay or block in the anterior fascicle of the left bundle branch (Figures 1 and 2).
- Left ventricle activation then altered or delayed toward the blocked fascicle and corresponding papillary muscle.

ECG Features

- QRS complex—normal duration.
- Left axis deviation—dogs, $< +40^\circ$; cats, $< 0^\circ$

- Small q waves and tall R waves in leads I and aVL—small q not essential.
- Deep S waves (exceeding the R waves) in leads II, III, and aVF.

PATHOPHYSIOLOGY

- Anatomic basis still speculative—anterior fascicle vulnerable because it has a single blood supply, is long and thin, and is located in the turbulent outflow tract of the left ventricle.
- No hemodynamic compromise.

SYSTEMS AFFECTED

Cardiovascular

GENETICS

N/A

INCIDENCE/PREVALENCE

- Most commonly described form of bundle branch block in cats.
- Uncommon in dogs.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat

Breed Predilections

N/A

Mean Age and Range

N/A

Predominant Sex

N/A

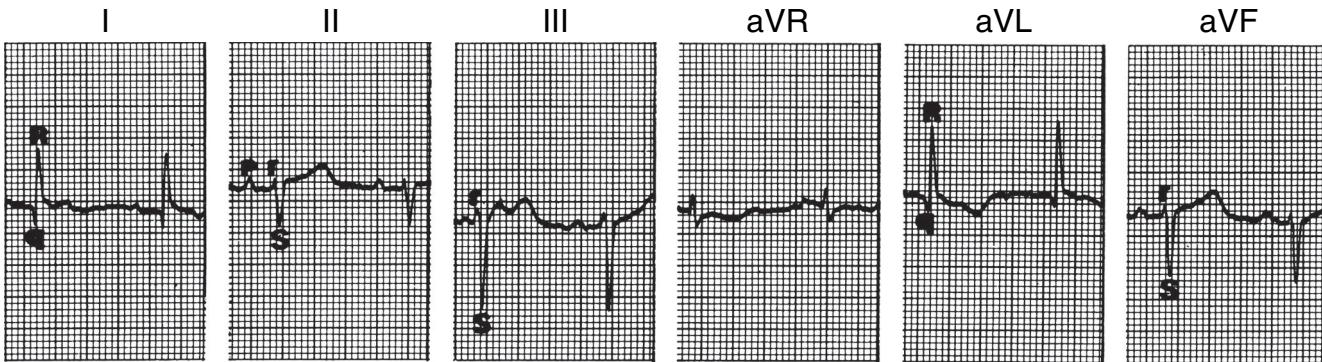


Figure 1.

Left anterior fascicular block in a cat with hypertrophic cardiomyopathy. Severe left axis deviation (-60°) with a qR pattern in leads I and aVL and an rS pattern in leads II, III, and aVF. The QRS complexes are of normal duration. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

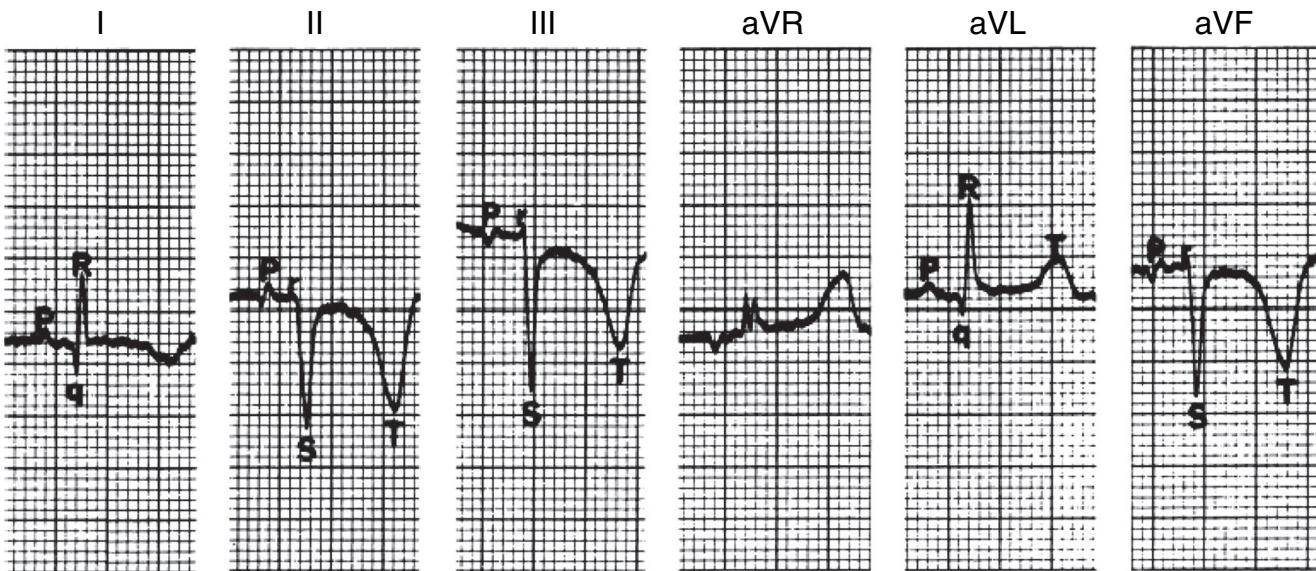


Figure 2.

Left anterior fascicular block in a dog with hyperkalemia (serum potassium, 5.3 mEq/L). There is abnormal left axis deviation (-60°) with a qR pattern in leads I and aVL and an rS pattern in leads II, III, and aVF. The large T waves are compatible with hyperkalemia. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

(CONTINUED)

LEFT ANTERIOR FASCICULAR BLOCK

SIGNS**Historical Findings**

- Signs usually associated with the underlying cause
- Usually an incidental ECG finding

Physical Examination Findings

No associated signs or hemodynamic compromise

CAUSES

- Hypertrophic cardiomyopathy (cats).
- Left ventricular hypertrophy (e.g., mitral insufficiency, aortic stenosis, aortic body tumor, hypertension, and hyperthyroidism).
- Hyperkalemia (e.g., urethral obstruction, acute renal insufficiency, and Addison's disease).
- Ischemic cardiomyopathy (e.g., arteriosclerosis of the coronary arteries, myocardial infarction, and myocardial hypertrophy that obstructs coronary arteries).
- Surgical repair of a cardiac defect (e.g., ventricular septal defect or aortic valvular disease).
- Restrictive cardiomyopathy (cats).
- Fibrosis.

RISK FACTORS

N/A

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- Left ventricular enlargement—absence of left ventricular enlargement on thoracic radiograph or cardiac ultrasound supports a diagnosis of left anterior fascicular block.
- Right bundle branch block—deep, wide S waves in leads I, II, III, and aVF causing a right axis deviation; in patients with left anterior fascicular block, leads I and aVL are positive and leads II, III, and aVF have deep S waves resulting in a left axis deviation.
- Altered position of the heart within the thorax—thoracic radiographs help identify mass or foreign body that may be displacing the heart.
- Suspect hyperkalemia if signs of urethral obstruction, renal insufficiency, or hypoadrenocorticism (Addison's disease); determine serum potassium concentration.

CBC/BIOCHEMISTRY/URINALYSIS

Hyperkalemia possible

OTHER LABORATORY TESTS

N/A

IMAGING

- Echocardiogram may show structural heart disease.

- Thoracic and abdominal radiographs may show mass, pulmonary metastatic lesion, foreign body, or abnormal cardiac position.

DIAGNOSTIC PROCEDURES

- Electrocardiography.
- Long-term ambulatory monitoring (Holter) may reveal intermittent bundle branch block.

PATHOLOGIC FINDINGS

Possible lesions or scarring on endocardial surface in the path of the bundle branches; applying Lugol's iodine to the endocardial surface within 2 hours post-mortem enables clear visualization of the conduction system.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Treatment unnecessary
- Treat underlying cause

NURSING CARE

Unnecessary

ACTIVITY

Unrestricted unless indicated by underlying condition

DIET

No modifications unless indicated by underlying condition

CLIENT EDUCATION

Fascicular block per se does not cause hemodynamic compromise; combined with right bundle branch block it may develop into second- or third-degree AV block, making treatment essential; need to treat underlying cause.

SURGICAL CONSIDERATIONS

N/A

**MEDICATIONS****DRUG(S) OF CHOICE**

Treatment directed toward the underlying primary disease (e.g., drugs to lower the serum potassium in hyperkalemia).

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

**FOLLOW-UP****PATIENT MONITORING**

ECG regularly

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Causative lesion could progress and lead to a more serious arrhythmia or complete heart block.

EXPECTED COURSE AND PROGNOSIS

No hemodynamic compromise

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Atrioventricular Block, Complete (Third Degree)
- Atrioventricular Block, First Degree
- Atrioventricular Block, Second Degree chapters
- Left Bundle Branch Block
- Right Bundle Branch Block

ABBREVIATIONS

- AV = atrioventricular
- ECG = electrocardiogram

INTERNET RESOURCES

www.vetgo.com/cardio.

Suggested Reading

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Author Larry P. Tilley

Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

L

LEFT BUNDLE BRANCH BLOCK



BASICS

DEFINITION

Conduction delay or block in both the left posterior and left anterior fascicles of the left bundle (Figures 1 and 2); a supraventricular impulse activates the right ventricle first through the right bundle branch; the left ventricle is activated late, causing the QRS to become wide and bizarre.

ECG Features

- QRS prolonged—dogs, > 0.08 second; cats, > 0.06 second
- QRS wide and positive in leads I, II, III, and aVF
- Block can be intermittent or constant

PATHOPHYSIOLOGY

- Because the left bundle branch is thick and extensive, the lesion causing the block must be large.
- Usually an incidental ECG finding—does not cause hemodynamic abnormalities.

SYSTEMS AFFECTED

Cardiovascular

GENETICS

N/A

INCIDENCE/PREVALENCE

Uncommon in cats and dogs. In cats with hypertrophic cardiomyopathy, left bundle branch block is not as commonly seen as left anterior fascicular block.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Cat and dog

Breed Predilections

N/A

Mean Age and Range

N/A

Predominant Sex

N/A

SIGNS

Historical Findings

- Usually an incidental ECG finding—does not cause hemodynamic abnormalities.
- Signs usually associated with the underlying condition.

Physical Examination Findings

Does not cause signs or hemodynamic compromise.

CAUSES

- Cardiomyopathy.
- Direct or indirect cardiac trauma (e.g., hit by car and cardiac needle puncture).
- Neoplasia.
- Subvalvular aortic stenosis.
- Fibrosis.
- Ischemic cardiomyopathy (e.g., arteriosclerosis of the coronary arteries, myocardial infarction, and myocardial hypertrophy that obstructs coronary arteries).

RISK FACTORS

N/A

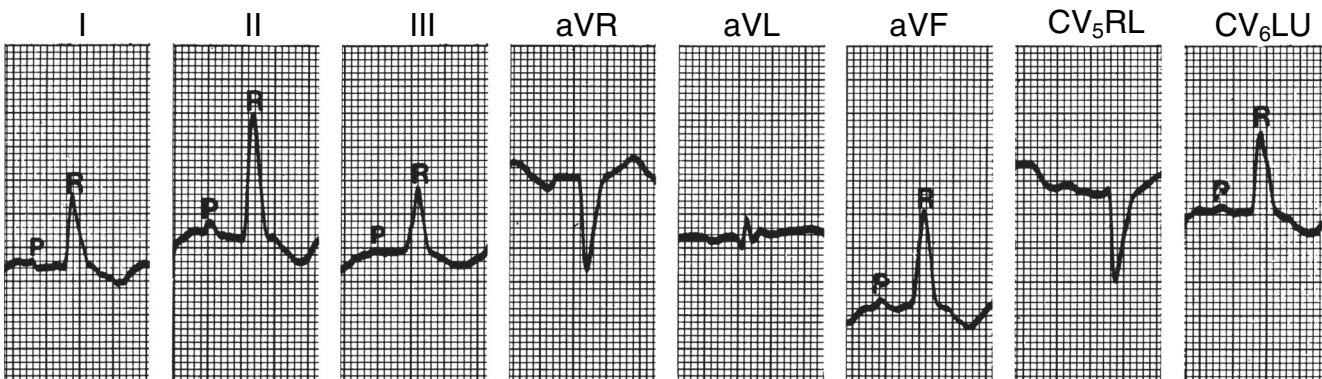


Figure 1.

Left bundle branch block in a cat with hypertrophic cardiomyopathy. The QRS complex is of 0.07-second duration and is positive in leads I, II, III, aVF. Neither a Q wave nor an S wave occurs in these leads. The QRS complex is inverted in lead aVR. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)



Figure 2.

Intermittent left bundle branch block in a Chihuahua. QRS complexes are wider (0.07–0.08 second) in the second, third, and fourth complexes and in the last three complexes. Consistent PR interval confirms a sinus origin for the abnormal-appearance QRS complexes (lead II, 50 mm/second, 1 cm = 1 mV). (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

(CONTINUED)

LEFT BUNDLE BRANCH BLOCK**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- Left ventricular enlargement.
- No left ventricular enlargement on thoracic radiograph or cardiac ultrasound studies supports diagnosis of isolated left bundle branch block.
- Can also be confused with ventricular ectopic beats, but the PR interval is usually constant and left bundle branch block has no pulse deficits.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

- Echocardiography may reveal structural heart disease; absence of left heart enlargement supports a diagnosis of left bundle branch block.
- Thoracic and abdominal radiographs may show masses or pulmonary metastatic lesions; traumatic injuries could result in localized or diffuse pulmonary densities.

DIAGNOSTIC PROCEDURES

- Electrocardiography.
- Long-term ambulatory monitoring (Holter) may reveal intermittent left bundle branch block.

PATHOLOGIC FINDINGS

Possible lesions or scarring on endocardial surface in the path of the bundle branches; applying Lugol's iodine to the endocardial surface within 2 hours post-mortem enables clear visualization of the conduction system.

**TREATMENT****APPROPRIATE HEALTH CARE**

Directed toward the underlying cause

NURSING CARE

Generally not necessary

ACTIVITY

Unrestricted unless required for management of underlying condition

DIET

No modifications unless required for management of underlying condition

CLIENT EDUCATION

- Left bundle branch block per se does not cause hemodynamic abnormalities.
- Lesion causing the block could progress, leading to more serious arrhythmias or complete heart block.

SURGICAL CONSIDERATIONS

N/A

**MEDICATIONS****DRUG(S) OF CHOICE**

N/A (unless required for management of underlying condition)

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

Serial ECG may show clearing or progression to complete heart block

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Causative lesion could progress, leading to a more serious arrhythmia or complete heart block.
- First- or second-degree AV block may indicate involvement of the right bundle branch.

EXPECTED COURSE AND PROGNOSIS

No hemodynamic compromise

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Atrioventricular Block, Complete (Third Degree)
- Atrioventricular Block, First Degree
- Atrioventricular Block, Second Degree—Mobitz I
- Atrioventricular Block, Second Degree—Mobitz II
- Left Anterior Fascicular Block
- Right Bundle Branch Block

ABBREVIATIONS

- AV = atrioventricular
- ECG = electrocardiogram

INTERNET RESOURCES

www.vetgo.com/cardio.

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Suggested Reading

Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992.

Tilley LP, Smith FW. Essentials of Electrocardiography: Interpretation and Treatment, 4th ed. Ames, IA: Wiley Blackwell Publishing, 2016 (in preparation).

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Author Larry P. Tilley

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LEGG-CALVÉ-PERTHES DISEASE



BASICS

DEFINITION

A spontaneous degeneration of the femoral head and neck leading to collapse of the coxofemoral joint and osteoarthritis.

PATHOPHYSIOLOGY

- Precise cause unknown; a specific vascular lesion not identified.
- Histologic evidence—points to infarction of vessels serving the proximal femur.
- Necrosis of subchondral bone—leading to collapse and deformation of the femoral head during normal loading.
- Articular cartilage—becomes thickened; cleft development; fraying of superficial layers.
- Simultaneous osseous degeneration and repair—characteristic of ischemia and revascularization of bone.
- No evidence of hypercoagulability or other blood-clotting abnormalities.

SYSTEMS AFFECTED

Musculoskeletal—causes a hind leg lameness; insidious in onset.

GENETICS

- Manchester terriers—multifactorial inheritance pattern with a high degree of heritability. Miniature poodles and West Highland white terriers—simple autosomal recessive trait.
- Hereditary predisposition likely.

INCIDENCE/PREVALENCE

- Common among miniature, toy, and small-dog breeds
- No accurate estimates available

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog

Breed Predilections

- Toy breeds and terriers—most susceptible.
- Manchester terrier, miniature pinscher, toy poodle, Lakeland terrier, West Highland white terrier, and cairn terrier—higher than expected incidence.

Mean Age and Range

- Most patients are 5–8 months of age
- Range 3–13 months

Predominant Sex

None

SIGNS

General Comments

Usually unilateral; only 12–16% of cases are bilateral

Historical Findings

Lameness—usually gradual onset over 2–3 months; weight-bearing; occasionally leg is carried.

Physical Examination Findings

- Pain on manipulation of the hip—most common
- Crepitation of the joint—inconsistent
- Atrophy of the thigh muscles—nearly always noted
- Patient otherwise normal

CAUSES

- Unknown.
- Tamponade of the epiphyseal intracapsular subsynovial vessels serving the femoral head—suggested cause of ischemia leading to the pathologic changes.

RISK FACTORS

- Small, toy, and miniature breeds—increased risk
- Trauma to the hip region



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Medial patellar luxation—may occur independently; primary differential in young toy breed dogs.
- Rupture of the cranial cruciate ligament—primary differential in older dogs.
- Hip dysplasia—radiographic signs similar.
- Fracture of the femoral head/neck due to trauma.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

- Early radiographic changes—widening of the joint space; decreased bone density of the epiphysis; sclerosis and thickening of the femoral neck.
- Later radiographic changes—lucent areas within the femoral head.
- End-stage radiographic changes—flattening and extreme deformation of the femoral head; severe osteoarthritis—femoral neck fracture.

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

- Femoral head—removed during FHNE or total hip replacement; usually deformed with a thickened irregular articular surface.
- Early disease—histologically characterized by loss of lacunar osteocytes and necrosis of marrow elements; trabeculae surrounded by granulation tissue.
- Later disease—thickened metaphyseal trabeculae; mixture of necrosis and repair tissue typical of revascularization of bone.
- Advanced disease—osteoclastic activity; new bone formation.



TREATMENT

APPROPRIATE HEALTH CARE

- Rest and analgesics—reportedly successful in alleviating lameness in a minority of patients.
- Ehmer sling—successful in one patient; maintained for 10 weeks; increased risk of ankylosis. Not widely recommended.
- Insidious onset often prevents early recognition and possibility of successful conservative treatment.
- FHNE with early and vigorous exercise after surgery—treatment of choice.
- Micro THR has been reported to successfully restore normal ground reaction forces.

NURSING CARE

Post-Surgery

- Physical therapy—extremely important for rehabilitating the affected limb.
- Analgesics, anti-inflammatory drugs, and cold packing—3–5 days; important.
- Range-of-motion exercises—extension and flexion; initiated immediately.
- Small lead weights—attached as ankle bracelets above the hock joint; encourage early use of the treated limb.

ACTIVITY

- Post-surgery—early activity encouraged to improve leg use.
- Conservative therapy—restricted activity recommended.

DIET

Avoid obesity

CLIENT EDUCATION

- Warn owners of Manchester terriers, miniature poodles, and West Highland white terriers of the genetic basis of the disease; discourage breeding affected dogs.
- Warn client that recovery after FHNE may take 3–6 months.

SURGICAL CONSIDERATIONS

FHNE or micro THR—treatment of choice



MEDICATIONS

DRUG(S) OF CHOICE

NSAIDs—preoperative or postoperative; minimize joint pain; reduce synovitis; carprofen (2.2 mg/kg PO q12h), etodolac (10–15 mg/kg PO q24h), meloxicam (0.2 mg/kg PO, IV, or SC first day—then 0.1 mg/kg q24h), deracoxib (1–2 mg/kg PO q24h for OA, 3–4 mg/kg for postoperative pain PO q24h; do not exceed 7 days), firocoxib (5 mg/kg PO q24h), buffered or enteric-coated aspirin (10–25 mg/kg PO q8–12h).

(CONTINUED)

CONTRAINDICATIONS

NSAIDs—gastrointestinal upset may preclude use in some patients.

PRECAUTIONS

NSAIDs—inhibition of platelet activity may increase hemorrhage at surgery; discontinue aspirin for at least 1 week before surgery, if possible; usually cause some degree of gastric ulceration.

POSSIBLE INTERACTIONS

NSAIDs—do not use in conjunction with glucocorticoids; risk of gastrointestinal tract ulceration; consider appropriate wash-out times when switching from one NSAID to another.

ALTERNATIVE DRUG(S)

Chondroprotective drugs (e.g., polysulfated glycosaminoglycans, glucosamine, and chondroitin sulfate)—little help in advanced disease; no evidence to suggest that these drugs prevent or reverse the disease process.

**FOLLOW-UP****PATIENT MONITORING**

- Post-surgical progress checks—2-week intervals; necessary to ensure compliance with exercise recommendations.
- Conservative therapy—reevaluate (physical examination, radiographs) to determine if surgery is needed.

PREVENTION/AVOIDANCE

- Discourage breeding of affected animals.
- Do not repeat dam-sire breeding that resulted in affected offspring.

POSSIBLE COMPLICATIONS

Limiting postoperative exercise may result in less than optimal limb function.

EXPECTED COURSE AND PROGNOSIS

- FHNE—good to excellent prognosis for full recovery (84–100% success rate).

- Micro THR—excellent prognosis for full recovery.
- Conservative therapy—reported to alleviate lameness after 2–3 months in about 25% of patients.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

Usually affects juvenile small-breed dogs, but mature dogs may be affected by chronic disease.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Aseptic necrosis of the femoral head
- Avascular necrosis of the femoral head
- Coxa magna
- Coxa plana
- Osteochondritis juvenilis
- Perthes disease

SEE ALSO

- Cruciate Ligament Disease, Cranial
- Hip Dysplasia
- Patellar Luxation

ABBREVIATIONS

- FHNE = femoral head and neck excision
- NSAID = nonsteroidal anti-inflammatory drug
- OA = osteoarthritis
- THR = total hip replacement

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Author Larry Carpenter

Consulting Editor Walter C. Renberg



**Client Education Handout
available online**

L

LEIOMYOMA, STOMACH, SMALL AND LARGE INTESTINE



BASICS

OVERVIEW

Uncommon benign tumor arising from the smooth muscle of the stomach and intestinal tract; with immunohistochemistry these tumors may be reclassified as a gastrointestinal stromal tumor (GIST) or GIST-like.

SIGNALMENT

- Dog more commonly affected than cat
- Middle-aged to older (> 6 years) dogs and cats
- No breed predisposition

SIGNS

Historical Findings

- Relate to location in the gastrointestinal tract
- Stomach—vomiting
- Small intestine—vomiting; weight loss; borborygmus; flatulence
- Large intestine and rectum—tenesmus; hematochezia; sometimes rectal prolapse

Physical Examination Findings

- Stomach—no specific abnormalities.
- Small intestine—often no abnormal findings; may feel mid-abdominal mass; occasionally distended, painful loops of small bowel.
- Large intestine and rectum—may feel palpable mass per rectum.

CAUSES & RISK FACTORS

Unknown

L



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Foreign body
- Inflammatory bowel disease
- Parasites
- Adenocarcinoma
- Leiomyosarcoma
- GIST
- GIST-like
- Lymphoma
- Pancreatitis

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal.
- Hypoglycemia—occasionally associated with paraneoplastic syndrome.

• Stomach and small intestine—may see microcytic hypochromic anemia (iron-deficiency anemia).

OTHER LABORATORY TESTS

N/A

IMAGING

- Abdominal ultrasonography*—may reveal a thickened wall of stomach or bowel; gastric leiomyoma most common at esophageal—gastric junction.
- Contrast radiography* (stomach and small intestine)—may reveal a space-occupying mass.
- Double-contrast radiography* (large intestine and rectum)—reveals a space-occupying mass.

DIAGNOSTIC PROCEDURES

Fine-Needle Aspirates

If mass or thickening seen with ultrasound, FNA with cytology may be performed to rule out other differentials; for leiomyomas cytology is generally low yield.

Upper Gastrointestinal Tract

Perform upper gastrointestinal tract endoscopy and mucosal biopsy; however, frequently non-diagnostic because tumors are deep to the mucosal surface or distal to scope length. Therefore surgical biopsy often required to confirm the diagnosis.

Large Intestine and Rectum

Colonoscopy may reveal a mass; mucosal biopsy may be non-diagnostic because of normal mucosal covering of the tumor; surgical biopsy often required. If mass can be palpated per rectum, transrectal biopsies may be obtained.



TREATMENT

- Surgical resection—treatment of choice; curative if tumor is respectable.
- Even large leiomyomas often can be removed successfully with narrow margins.



MEDICATIONS

DRUG(S)

If reclassified as a GIST (c-KIT positive), may consider a tyrosine kinase inhibitor (toceranib phosphate) as follow-up therapy.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- Complete resection—normal postoperative care; no additional follow-up necessary.
- Monitor blood glucose postoperatively if hypoglycemic prior to surgery.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Hypoglycemia—recognized as an associated paraneoplastic syndrome.

ABBREVIATIONS

- FNA = fine-needle aspirate
- GIST = gastrointestinal stromal tumor

Suggested Reading

Gillespie V, Baer K, Farrelly J, Craft D, Luong R. Canine gastrointestinal stromal tumors: immunohistochemical expression of CD34 and examination of prognostic indicators including proliferation markers Ki67 and AgNOR. *Vet Pathol* 2011; 48:283–291.

Frost D, Lasota J, Miettinen M.

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Author Laura D. Garrett

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LEIOMYOSARCOMA, STOMACH, SMALL AND LARGE INTESTINE



BASICS

OVERVIEW

- Uncommon malignant tumor arising from the smooth muscle of the stomach and intestinal tract.
- Tends to be locally invasive; metastatic rate up to 50%, usually intra-abdominal sites particularly the abdominal lymph nodes and liver.
- Prognosis fair to guarded.
- In the large intestine the cecum is often affected.
- Analyses reclassified many leiomyosarcomas to gastrointestinal stromal tumors (GIST) or GIST-like tumors; need immunohistochemistry to differentiate.
- True leiomyosarcomas occur rarely; however, this chapter will refer to these tumors as LMS as that is how they were characterized in the referenced papers.

SIGNALMENT

- Dog more commonly affected than cat
- Mostly middle-aged to older (> 6 years) dogs and cats
- No breed predisposition

SIGNS

Historical Findings

- Related to gastrointestinal tract.
- Stomach—vomiting; weight loss.
- Small intestine—vomiting; weight loss; diarrhea; borborygmus; flatulence.
- Large intestine and rectum—tenesmus, may lead to rectal prolapse; hematochezia.

Physical Examination Findings

- Stomach—nonspecific.
- Small intestine—may feel mid-abdominal mass; sometimes distended, painful loops of small bowel on abdominal palpation.
- Large intestine and rectum—may feel palpable mass per rectum.

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Foreign body
- Inflammatory bowel disease
- Parasites
- Adenocarcinoma
- Leiomyoma
- GIST
- GIST-like
- Lymphoma
- Pancreatitis

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal
- Anemia—may be hypochromic, microcytic (iron-deficiency anemia)
- Leukocytosis
- Hypoglycemia—reported as a paraneoplastic syndrome

IMAGING

- *Abdominal ultrasonography*—may reveal a thickened wall of the stomach or bowel.
- *Positive contrast radiography* (stomach and small intestine)—reveals a space-occupying mass.
- *Double-contrast radiography* (large intestine and rectum)—reveals a space-occupying mass.

DIAGNOSTIC PROCEDURES

Fine-Needle Aspirates

- If mass or thickening seen with ultrasound, FNA with cytology may show mesenchymal cells with features of malignancy supportive of a sarcoma.
- Any enlarged lymph node noted with ultrasound can have FNA and cytology to look for metastasis.

Upper Gastrointestinal Tract

- Endoscopy and mucosal biopsy—can perform, but results are frequently non-diagnostic because in some tumors deep to the mucosal surface, mass may be beyond reach of endoscope.
- Surgical biopsy—often required to confirm diagnosis.

Large Intestine and Rectum

- Colonoscopy—may allow a mass to be seen; mucosal biopsy may be non-diagnostic because of the normal mucosal covering of the tumor.
- Deep biopsy—perform if possible.



TREATMENT

- Surgical resection—treatment of choice.
- Cecal leiomyosarcoma least likely to have metastases.
- Surgery can provide prolonged survival for small intestinal masses.
- Carefully evaluate for metastasis before extensive surgery (e.g., mesenteric lymph nodes, liver, and lungs).



MEDICATIONS

DRUG(S)

If reclassified as a GIST (c-KIT positive), may consider a tyrosine kinase inhibitor (toceranib phosphate) as follow-up therapy.



FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS

- Leiomyosarcomas often metastasize to the liver and regional abdominal lymph nodes.
- An older case series showed:
 - Small intestinal cases had median survival of 12 months.
 - Cecal cases had median survival of 7.5 months, but most died of other diseases.
 - Gastric cases most rare, but the few reported had high rate of metastasis and short survival times.
 - Even dogs with metastasis can have prolonged survivals, with a median of 21.7 months reported in one study of dogs with metastatic LMS of the GI tract.
 - A recent report found similar survival times between dogs with leiomyoma, LMS, GIST, and GIST-like tumors:
 - 42 dogs with small intestinal tumors treated surgically had 1- and 2-year survivals of 62.6% and 52.3%.
 - 19 dogs with cecal tumors treated surgically

had 1- and 2-year survivals of 84.2% and 66%. • Complete resection—routine physical examination, thoracic radiography, and abdominal ultrasonography at 1, 3, 6, 9, and 12 months after surgery.

• Incomplete resection—symptomatic support to relieve clinical signs.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Hypoglycemia—reported as a paraneoplastic syndrome

ABBREVIATIONS

- FNA = fine-needle aspirate
- GI = gastrointestinal
- GIST = gastrointestinal stromal tumor
- LMS = leiomyosarcomas

Suggested Reading

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LEISHMANIASIS



BASICS

OVERVIEW

- Protozoan—genus *Leishmania*; causes two types of disease: cutaneous; and visceral.
- Affected dogs in the United States invariably acquired infection in another country unless part of the endemic foxhound population.
- *L. donovani infantum*—Mediterranean basin, Portugal, and Spain; sporadic cases in Switzerland, northern France, and the Netherlands.
- *L. donovani* complex or *L. brasiliensis*—endemic areas of South and Central America and southern Mexico.
- Considered endemic in foxhounds in the United States.
- Sandfly vectors—transmit flagellated parasites into the skin of a host. Vector unknown in United States.
- Cats—often localizes in skin.
- Dogs—invariably develop visceral disease; renal failure is the most common cause of death.
- Incubation period—1 month to several years.

SIGNALMENT

- Dogs—virtually all develop visceral (systemic) disease; 90% also have cutaneous involvement; no sex or breed predilection.
- Cats—cutaneous disease (rare); no sex or breed predilection.

SIGNS

Visceral

- Exercise intolerance; weight loss, anorexia, diarrhea, vomiting, epistaxis, and melena; lymphadenopathy and cutaneous lesions (90% of cases); emaciation; signs of renal failure (polyuria, polydipsia, vomiting) possible; neuralgia, polyarthritis, polymyositis, osteolytic lesions, and proliferative periostitis rare; fever and splenomegaly (30%); death is usually due to chronic proteinuric nephritis progressing to end-stage kidney disease, nephrotic syndrome, and/or systemic hypertension.

Cutaneous

- Dogs—hyperkeratosis is the most prominent finding; excessive epidermal scale with thickening, depigmentation, and chapping of the muzzle and footpads; hair coat dry, brittle, hair loss, intradermal nodules and ulcers; abnormally long or brittle nails in some patients.
- Cats—cutaneous nodules (especially on the ears) usually develop.

CAUSES & RISK FACTORS

- Travel to endemic regions (usually the Mediterranean), where dogs are exposed to infected sandflies.
- Transmission by blood transfusion, *in utero*, and direct contact can occur.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Visceral—blastomycosis; histoplasmosis; systemic lupus erythematosus; metastatic neoplasia; distemper; vasculitis.
- Cutaneous—other causes of hyperkeratosis.
- Skin biopsy—hyperkeratotic and nodular lesions; existence of organisms confirms diagnosis.
- Hyperglobulinemia—differentiate from chronic ehrlichiosis and multiple myeloma.

CBC/BIOCHEMISTRY/URINALYSIS

- Hyperproteinemia with hyperglobulinemia—nearly 100% of cases.
- Hypoalbuminemia—95% of cases.
- Proteinuria—85% of cases.
- High liver enzyme activity—55% of cases.
- Thrombocytopenia—50% of cases.
- Azotemia—up to 45% of cases.
- Leukopenia with lymphopenia—20% of cases.

OTHER LABORATORY TESTS

- Serologic diagnosis by IFA or ELISA available—most tests give cross-reaction to *Trypanosoma cruzi*; differentiate based on clinical signs, history, and likelihood of exposure. Rapid in-house immunochromatographic tests are also available.
- PCR—particularly sensitive on bone marrow, lymph nodes, spleen and skin, but also used to assess blood, bodily fluids, conjunctival scrapings, and histopathologic specimens.

DIAGNOSTIC PROCEDURES

- Cultures—skin, spleen, bone marrow, or lymph node biopsies or aspirates; by the Centers for Disease Control and Prevention.
- Cytology and histopathology with immunohistopathology—identify intracellular organisms in biopsies or aspirate specimens (listed above).

PATHOLOGIC FINDINGS

- Cell infiltration (mainly histiocytes and macrophages) and characteristic intracellular amastigote forms especially in skin, lymph nodes, liver, spleen, and kidney.
- Mucosal ulcerations—stomach, intestine, and colon occasionally found.



TREATMENT

- Outpatient.
- Emaciated, chronically infected animals—consider euthanasia; prognosis very poor.
- Diet—high-quality protein; special for renal insufficiency if necessary.
- Cats—single dermal nodule lesions are best surgically removed.
- Advise client of potential zoonotic transmission of organisms in lesions to humans.
- Inform client that organisms will never be eliminated,

and relapse, requiring treatment, is inevitable.

- A canine vaccine is available in Europe and some areas of South America.



MEDICATIONS

DRUG(S) OF CHOICE

- Sodium stibogluconate and meglumine antimonite may only be available from the CDC.
- Allopurinol—produces clinical cures but relapses occur. Best when used in combination with other drugs (meglumine or amphotericin B) as maintenance. Dose: 7 mg/kg PO q8h for 3 months, or 10 mg/kg/day PO for 2–24 months.
- Amphotericin B—0.5–0.8 mg/kg diluted in 50 mL dextrose 5% in water given IV over 1 minute q48h for total dose of 8–15 mg/kg.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Seriously ill dogs—start antimonial drugs at lower doses.
- Renal insufficiency—treat before giving antimonial drugs; prognosis depends on renal function at the onset of treatment.
- Amphotericin B—nephrotoxicity can occur.



FOLLOW-UP

- Treatment efficacy—monitor by clinical improvement and identification of organisms in repeat biopsies.
- Relapses—a few months to a year after therapy; recheck at least every 2 months after completion of treatment; identified by detecting a rise in blood globulin levels or reappearance of clinical signs.
- Prognosis for a cure—guarded.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Leishmaniasis is a notifiable disease reportable to the CDC.
- Advise owner of zoonotic potential.

ABBREVIATIONS

- ELISA = enzyme-linked immunosorbent assay
- IFA = immunofluorescent antibody test
- PCR = polymerase chain reaction

Suggested Reading

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LENS LUXATION



BASICS

OVERVIEW

- Total dislocation of the lens from its normal location. • Anterior—forward displacement through the pupil into the anterior chamber.
- Posterior—backward displacement into the vitreous. • Occurs when the lens capsule separates 360° from the zonules that hold the lens in place. • Subluxation—partial separation of the lens from its zonular attachments; the lens remains in a normal or near-normal position in the pupil. • Primary (hereditary) luxation—due to a gradual zonular breakdown; usually inherited in dogs; often bilateral. • Congenital luxation—often associated with other congenital anomalies.
- Secondary luxation—due to chronic inflammation, buphthalmia, intraocular neoplasia, senile zonular degeneration or trauma.

SIGNALMENT

- Primary—usually seen in adult dog (typically 3–8 years old); commonly affected breeds include terriers, Chinese crested and Shar-Pei; rare in cats. • Secondary—dog and cat; any age/breed.

SIGNS

- Lens instability and subluxation—fibrils of liquefied vitreous in the anterior chamber; abnormally shallow or deep anterior chamber; abnormal iris curvature; phacodenesis (tremor of the lens with globe movement); iridodonesis (tremor of the iris with globe movement); aphakic crescent (crescent-shaped area of the pupil that is lacking the lens). • Lens luxation—anterior when the lens is in the anterior chamber; posterior when the lens sinks into the vitreous. Can have same signs as lens subluxation. • Acute or chronically painful eye with episcleral injection and diffuse or central corneal edema. • Glaucoma more common in anterior lens luxation.
- Uveitis. • Cataracts. • Retinal detachment.

CAUSES & RISK FACTORS

- Primary—associated with *ADAMTS17* gene mutation in some breeds; inheritance pattern uncertain in others. • Primary luxation and primary glaucoma—may occur simultaneously in some breeds. • Uveitis, especially chronic lens-induced uveitis.
- Intraocular neoplasia—may physically luxate the lens or cause chronic inflammation, leading to zonular degeneration. • Trauma—rarely causes a normal lens to luxate without signs of severe uveitis or hyphema.
- Cataracts—when intumescent or resorptive, can cause tension and breakage of lens zonules.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Uveitis, glaucoma—also cause painful, red eyes with corneal edema and may be concurrent. • Buphthalmia may cause lens luxation. • Corneal endothelial dystrophy or degeneration—may also cause corneal edema.
- Diagnosis made by careful ophthalmic examination and history.

CBC/BIOCHEMISTRY/URINALYSIS

Normal, unless sequela of a systemic disease that causes uveitis or neoplasia.

IMAGING

- Thoracic radiographs and abdominal ultrasonography—may be indicated if secondary to intraocular neoplasia. • Ocular ultrasonography—useful if corneal edema or cloudy ocular media preclude examination.

DIAGNOSTIC PROCEDURES

- Complete ophthalmic examination, including tonometry. • Genetic DNA test is available for some breeds predisposed to lens luxation.



TREATMENT

- Potentially visual eyes—consider referral for surgical removal of the lens. • Manual transcorneal reduction of anterior lens luxation followed by medical management of a posterior luxation has been described.
- Often, topical miotic therapy can keep a posteriorly luxated lens behind the pupil and surgery can be avoided in some cases.
- Irreversibly blind eyes can be treated by enucleation or evisceration with intrascleral prosthesis; if secondary to neoplasia, enucleation is the best choice for therapeutic and diagnostic purposes.



MEDICATIONS

DRUG(S)

- Initiate the following medications, and if the eye has the potential for vision, refer the patient to a veterinary ophthalmologist immediately for possible intracapsular lens extraction. • Topical miotics—demecarium bromide or prostaglandin analogs (latanoprost) q12h; indicated if the lens is primarily subluxated or posteriorly luxated.
- If the pupil is blocked due to anterior lens luxation, tropicamide may allow the pupil to dilate, releasing the lens and decreasing the risk for pupillary block glaucoma. • Mannitol 1 g/kg IV over 20 minutes; indicated for high

IOP (> 40 mmHg). • Carbonic anhydrase inhibitors—topical dorzolamide q8h; indicated for high IOP. • Topical anti-inflammatory—0.1% dexamethasone sodium phosphate or 1% prednisolone acetate (q6–24h) if inflammation is present.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Topical miotics—contraindicated if the lens is in the anterior chamber. • Client must verify location of lens prior to applying a miotic.



FOLLOW-UP

- Medically treated primary posterior luxation—IOP rechecked 24 hours after starting treatment and frequently thereafter; once IOP is stable, re-examine patient 3 or 4 times/year. • Monitor for secondary glaucoma and retinal detachment. • If only one lens is involved at the time of examination, the other lens may eventually become involved; the ophthalmologist may choose to perform prophylactic phacoemulsification in the contralateral eye if not yet luxated.

L



MISCELLANEOUS

ABBREVIATION

- IOP = intraocular pressure

Suggested Reading

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LEPTOSPIROSIS



BASICS

DEFINITION

- Caused by pathogenic members of genus *Leptospira*.
- Acute and chronic diseases of dogs (mainly nephritis and hepatitis) and other animals, including, rarely, cats.
- Dogs—serovars causing disease vary by geographic area; US recent serovars of concern—*L. grippotyphosa*, *L. autumnalis*, and *L. pomona*; vaccines should include representative serovars found in area.

PATOPHYSIOLOGY

- *Leptospira*—penetrate intact/cut skin/mucous membranes; rapidly invade bloodstream (4–7 days); spread to all parts of body (2–4 days).
- Invasion leads to fever, leukocytosis, transitory anemia (hemolysis), mild hemoglobinuria, and albuminuria.
- Fever and bacteremia soon resolve.
- Capillary and endothelial cell damage; occasionally results in petechial hemorrhages.
- Liver—hepatitis and jaundice.
- Kidney—leptospiruria; *Leptospira* localize in damaged renal tubules; organism replicates readily in tubular epithelial cell.
- Early serum antibodies appear about the time bacteremia ceases.
- Death—usually a result of interstitial nephritis, vascular damage, renal failure; may result from acute septicemia or DIC.

SYSTEMS AFFECTED

- Cardiovascular—endothelial cell damage; hemorrhage
- Hepatobiliary—hepatitis; dysfunction; necrosis
- Nervous—meningitis
- Renal/Urologic—focal interstitial nephritis; hemoglobinuric nephrosis; tubular damage/failure
- Respiratory—vasculitis; interstitial pneumonia

Chronic Disease

- Ophthalmic—anterior uveitis
- Renal/Urologic—chronic renal failure
- Reproductive—abortion; weak puppies
- Reproductive—linked to feline stillbirth

INCIDENCE/PREVALENCE

- Reported incidence (dogs)—falsely low; most infections are inapparent and remain undiagnosed.
- Prevalence (dogs)—recent surveys have noted increasing disease in urban dogs; hospital prevalence rates have been increasing since the 1990s.

GEOGRAPHIC DISTRIBUTION

- Worldwide, especially in warm, wet climates/seasons.
- *L. canicola* and *L. icterohaemorrhagiae*—usual serovars; clinical disease in dogs; *L. canicola* most common worldwide; *L. icterohaemorrhagiae* most common in Australia.
- *L. bratislava*—has yet to be confirmed by culture as a serovar in dogs in the United States.
- Standing water and neutral or slightly alkaline soil promote presence in environment.

SIGNALMENT

Species

Dog and rarely cat

Mean Age and Range

- Young dogs without passive maternal antibody—more likely to exhibit severe disease.
- Old dogs with adequate antibody titer levels—seldom exhibit clinical disease unless exposed to a serovar not in the vaccine.

Predominant Sex

Traditionally, male dogs more commonly affected; disputed by recent reports.

SIGNS

General Comments

- Vary with age/immune status, environmental factors that affect *Leptospira* survival, and virulence of infecting serovar.
- Primary reservoir host—may spread particular serovar via urine; may have no clinical signs or less severe disease (acute diffuse to chronic interstitial nephritis, e.g., *L. canicola* in dogs with relatively weak antibody response).
- Incidental (accidental) host—acute severe disease (e.g., *L. icterohaemorrhagiae* in dogs with strong antibody response).

Historical Findings

Peracute to Subacute Disease

- Fever
- Sore muscles
- Stiffness
- Shivering
- Weakness
- Anorexia
- Depression
- Vomiting
- Rapid dehydration
- Diarrhea: with/without blood
- Icterus
- Spontaneous cough
- Difficulty breathing
- PU/PD progressing to anuria
- Bloody vaginal discharge
- Death—without clinical signs

Chronic Disease

- No apparent illness
- Fever of unknown origin
- PU/PD—chronic renal failure

Physical Examination Findings

Peracute to Acute Disease

- Tachypnea
- Rapid irregular pulse
- Poor capillary perfusion
- Hematemesis
- Hematochezia
- Melena
- Epistaxis
- Injected mucous membranes
- Widespread petechial and ecchymotic hemorrhages
- Reluctance to move, paraspinal hyperesthesia, stiff gait
- Conjunctivitis
- Rhinitis
- Hematuria
- Mild lymphadenopathy

CAUSES

- Dogs—*L. canicola*, *L. icterohaemorrhagiae*, *L. pomona*, *L. grippotyphosa*, *L. copenhagenii*, *L. australis*, *L. autumnalis*, *L. ballum*, and *L. bataviae*
- Cats—*L. canicola*, *L. grippotyphosa*, *L. pomona*, and *L. bataviae*

RISK FACTORS

Transmission

- Direct—host-to-host contact via urine, post-abortion discharge, fetus/discharge, sexual contact (semen).
- Indirect—exposure (via urine) to a contaminated environment (vegetation, soil, food, water, bedding) under conditions in which *Leptospira* can

survive.

- Disease agent—*Leptospira* serovar, each with its own virulence factors, infectious dose, and route of exposure.
- Disease in companion animals is often the result of spillover from diseased wildlife (many different types of mammals) that may be maintenance hosts for different serovars.

Host Factors

- Vaccine—protection is serovar-specific; may not prevent kidney colonization and urine shedding; new vaccines available of “subunit” type; research has shown promise of panvalent antigen that cross-protects against many serovars.
- Outdoor animals or hunting dogs—exposure of mucous membranes to water; exposure of abraded or water-softened skin increases risk of infection.

Environmental Factors

- Warm and moist environment; wet season (high rainfall areas) of temperate regions; low-lying areas (marshy, muddy, irrigated); warm humid climates of tropical and subtropical regions.
- Temperature range—7–10°C (44.6–50°F) to 34–36°C (93–96°F).
- Water—organism survives better in stagnant than flowing water; in neutral or slightly alkaline pH.
- Organism survives 180 days in wet soil and longer in standing water.
- Dense animal population—kennels/urban settings; increases chances of urine exposure.
- Exposure to rodents and other wildlife.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Subacute to Acute Disease

- Dogs—heartworm disease; immune-mediated hemolytic anemia; bacteremia/septicemia; infectious canine hepatitis virus; canine herpesvirus; hepatic neoplasia; trauma; lupus; Rocky Mountain spotted fever; ehrlichiosis; toxoplasmosis; renal neoplasia; renal calculi.
- Cats—hemotropic mycoplasmosis; drugs (acetaminophen); bacteremia/septicemia; FIV- and FeLV-associated diseases; cholangitis; toxoplasmosis; FIP; hepatic neoplasia; autoimmune disease; trauma; renal calculi; renal neoplasia.

Reproductive/Neonatal Disease

- Dogs—brucellosis; distemper; herpes.
- Cats—FIP; FeLV; panleukopenia; herpesvirus; toxoplasmosis; salmonellosis.

CBC/BIOCHEMISTRY/URINALYSIS

- PCV and total plasma solids—high owing to dehydration; rarely PCV low (hemolysis)
- Leukocytosis with left shift—leukopenia initially during leptospiremic phase
- Thrombocytopenia
- Increased fibrin degradation products
- BUN and creatinine—high; mainly renal
- Electrolyte alterations—depend on degree of renal and gastrointestinal dysfunction
- Hyponatremia
- Hypochloremia
- Hypokalemia

(CONTINUED)

LEPTOSPIROSIS

hyperkalemia with kidney failure
 • Hyperphosphatemia • Hypoalbuminemia
 • Acidosis—serum bicarbonate low • Alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, alkaline phosphatase—high • Proteinuria • Isosthenuria—acute renal failure

OTHER LABORATORY TESTS

Serology (*Microscopic Agglutination Test*)

- Test serum in acute stage and also 3–4 weeks later (convalescent)
- Unvaccinated patients—titers may be low initially (1:100–1:200); may be higher in the convalescent serum (1:800–1:1,600 or higher) if a homologous *Leptospira* serovar is tested; several serovars may cross-react in the MAT test, especially if there are high titers to a single serovar.
- Vaccinated patients, older whole cell bacteria—expect high titers (for up to 12–16 weeks post-vaccination), then drop off to <1:400; new subunit vaccines—titers rise to ≥ 1:1,600 for 12 weeks for serovars *L. canicola* and *L. icterohaemorrhagiae*; titers for other subunit vaccine serovars are more variable (*L. pomona* and *L. grippotyphosa*).
- Run all serum samples (acute and convalescent) at the same time, if possible.

Darkfield Microscopy of Urine

- Often inconclusive • Difficult to read
- Requires fresh urine

Fluorescent Antibody Test of Urine

- More conclusive. • *Leptospira* not need to be viable; submit urine to lab on ice by overnight courier.
- Pretreat with furosemide 15 minutes before urine collection to increase success rate.
- Correlate results with clinical history.

PCR Test of Urine and Tissue

- Promising but still experimental

DIAGNOSTIC PROCEDURES

- Culture of body fluids antemortem (urine, blood, aqueous humor) and tissues post-mortem (kidney, liver, fetus, placenta)—usually not practical due to fastidiousness of *Leptospiras*; contact laboratory for the proper transport medium.
- Fluorescent antibody test—done on tissues submitted for post-mortem workup, especially kidney and liver.
- Special stains (Warthin-Starry silver)—attempt immunohistochemistry with monoclonal antibodies on formalin-fixed sections of kidney, liver, and fetal/placental tissue.
- PCR—some labs have protocols for urine/tissue specimens.

PATHOLOGIC FINDINGS

- Degree of kidney and liver disease depends on serovar and the host's immunity.
- Cats—generally less severe lesions.
- Dogs (acute disease)—lungs may be edematous; kidneys pale and enlarged; liver enlarged, may be friable with multifocal necrosis/hemorrhage; gastrointestinal tract may hemorrhage.



TREATMENT

NURSING CARE

- Dehydration and shock—parenteral, balanced, polyionic, isotonic intravenous solution (lactated Ringer's).
- Severe hemorrhage—blood transfusion may be needed in association with treatment for DIC.
- Oliguria or anuria—initially rehydrate; then give intravenous osmotic diuretics or tubular diuretics; peritoneal dialysis may be necessary.

CLIENT EDUCATION

Inform client of zoonotic potential from contaminated urine of affected dogs and their environment.



MEDICATIONS

DRUG(S) OF CHOICE

- Procaine penicillin G 40,000–80,000 U/kg IM q24h or divided q12h until kidney function returns to normal.
- Dihydrostreptomycin—10–15 mg/kg IM q12h for 2 weeks to eliminate organism from kidney interstitial tissues; try streptomycin if no renal failure; drug not available everywhere.
- Doxycycline 5 mg/kg PO or IV q12h for 3 weeks; use alone to clear both leptospiremia and leptosporuria.

PRECAUTIONS

- Aminoglycoside—carefully monitor patients with renal insufficiency.
- Penicillins (dogs)—adjust doses with renal insufficiency.

ALTERNATIVE DRUG(S)

- Ampicillin or amoxicillin—instead of penicillin (ampicillin 22 mg/kg PO q6–8h for 3 weeks; amoxicillin (22 mg/kg PO q8–12h for 3 weeks).
- Azithromycin—20 mg/kg PO q24h for 3 weeks.



FOLLOW-UP

PREVENTION/AVOIDANCE

- Vaccine (dogs)—whole cell bacterin vaccines contain serovars *L. canicola*/*L. icterohaemorrhagiae* (newer also include *L. pomona*/*grippotyphosa*); promotes immunity to homologous serovars and protection from overt clinical disease; may not prevent colonization of the kidneys, resulting in chronic carrier state; serovar-specific; does not promote protection against other serovars present in nature.
- Newer subunit vaccine contains *L. pomona*, *L. icterohaemorrhagiae*, *L. grippotyphosa*, and *L. canicola*; claims made that subunit provides protection from clinical disease/prevents kidney colonization.
- Vaccines—vaccinate dogs per current label recommendations;

bacteria-induced immunity lasts only 6–8 months and is serovar-specific (no cross-protection outside of the serogroup); revaccinate at least yearly; vaccinate high-risk dogs (hunter, show dogs, dogs with access to water/ponds) every 4–6 months, especially in endemic areas.

- Kennels—strict sanitation to avoid contact with infected urine; control rodents; monitor/remove carrier dogs until treated; isolate infected animals during treatment.
- Activity—limit access to marshy/muddy areas, ponds, low-lying areas with stagnant surface water, heavily irrigated pastures, access to wildlife.
- Environmental contamination: *Leptospira* shedding in urine is intermittent; *Leptospira* survive in urine in the environment but do not multiply; cells survive until either drying, UV light exposure or freeze-thaw has killed the *Leptospira*.

POSSIBLE COMPLICATIONS

- DIC
- Permanent liver/kidney dysfunction
- Uveitis
- Abortion

EXPECTED COURSE AND PROGNOSIS

- Most infections subclinical or chronic
- Prognosis guarded for acute severe disease



MISCELLANEOUS

AGE-RELATED FACTORS

Severe clinical disease in young dogs (non-vaccinated or lacking maternal antibody)

ZOONOTIC POTENTIAL

- High; spread in urine of infected animals.
- Strict kennel hygiene and disinfection of premises (iodine-based disinfectant or stabilized bleach solutions).
- Acutely infected and carrier animals must be treated.

PREGNANCY/FERTILITY/BREEDING

- Possible abortion.
- Antimicrobial therapy—consider effect of drug on developing fetus.

ABBREVIATIONS

- DIC = disseminated intravascular coagulation
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- PCR = polymerase chain reaction
- PCV = packed cell volume
- PU/PD = polyuria/polydipsia

INTERNET RESOURCES

<http://www.cfsph.iastate.edu/DiseaseInfo/disease.php?name=leptospirosis&lang=en>

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Client Education Handout
available online

L

LEUKEMIA, ACUTE LYMPHOBLASTIC



BASICS

OVERVIEW

• Lymphoproliferative disorder defined as the proliferation of neoplastic prolymphocytes and lymphoblasts in the bone marrow; most are of B-cell origin. • Leads to displacement and/or depression of normal hematopoietic cells (myelophthisis). • Neoplastic lymphoblasts are usually, but not always, circulating in the blood. • May infiltrate other organs including spleen, liver, and lymph nodes.

SIGNALMENT

• Dog—no significant sex predilection; with a mean age in one report 7.4 years old (range, 2–12 years), preponderance of large- and giant-breed dogs. • Rare in cat (also younger animals, especially with FeLV infection).

SIGNS

• Often nonspecific, can include anorexia, weight loss, and lethargy.
• Hepatosplenomegaly. • Mild to moderate lymphadenomegaly. • Petechial or ecchymotic hemorrhages.

CAUSES & RISK FACTORS

• Dogs—genetic factors, ionizing radiation, oncogenic viruses, and chemical agents including alkylating chemotherapy drugs are suspected, but unproven; missense mutations and tandem duplications have been identified in oncogenes such as Flt3, c-kit, and N-ras in dogs with ALL. • Cats—FeLV infection.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Acute or chronic infection—toxoplasmosis; canine distemper; ehrlichiosis. • Aplastic anemia. • Metastatic neoplasia. • Multicentric lymphoma with bone marrow involvement and circulating lymphoblasts can be difficult to distinguish from ALL. Lymphoma is typically characterized by bulky peripheral disease and minor bone marrow and peripheral blood involvement, whereas ALL has significant bone marrow and peripheral blood involvement and mild to moderate lymphadenopathy. • Other leukemias and myeloproliferative disorders.

CBC/BIOCHEMISTRY/URINALYSIS

• CBC—normocytic, normochromic, nonregenerative anemia (98%); neutropenia (78%); thrombocytopenia (90%); all present in > 75% of cases. • CBC may also show lymphoblastic lymphocytosis, leukopenia, or both. • Serum chemistry profile—elevated liver enzyme activities.

OTHER LABORATORY TESTS

• Careful bone marrow cytopathology—expansion of neoplastic lymphoblasts (> 30%) is the hallmark. Can also see low numbers of myeloid/erythroid precursors and megakaryocytes depending on extent of bone marrow involvement, cell type of origin, and differentiation. • Bone marrow core biopsy with immunohistochemical or enzymatic biochemical studies can be helpful if bone marrow cannot be obtained. • Enzymes include peroxidase and chloroacetate ester. • Flow cytometry using monoclonal antibodies against cell surface antigens on bone marrow aspirates and/or blood is typically used to characterize disease. • Useful antibodies include CD45 (all hematopoietic cells beside erythrocytes), CD34 (progenitor cells), CD18 (leukocytes), CD79a (B cells), and CD3 (T cells). • The majority of ALL cells are CD34+, while the majority of lymphoma cells are CD34-. • PCR for antigen receptor rearrangements (PARR) can confirm a clonally expanded population if bone marrow cytology and/or flow cytometry results are equivocal.

IMAGING

Radiography and ultrasonography often reveal hepatomegaly and splenomegaly.

DIAGNOSTIC PROCEDURES

Bone marrow aspirate and biopsy



TREATMENT

• Usually outpatient, unless supportive care required. • Transfusions—as indicated, to restore RBCs, platelets, or coagulation factors. • Consult a veterinary oncologist for updated treatment approaches. Allogenic bone marrow transplantation (using CD34+ cells harvested from a DLA-matched donor) is an option if initial remission can be achieved using chemotherapy, but is only available at a limited number of veterinary oncology specialty practices.



MEDICATIONS

DRUG(S)

• L-asparaginase (400 IU/kg IM/SC after pre-treating with diphenhydramine); usually used as initial induction agent.
• Combination chemotherapy—prednisone (20–30 mg/m² PO q12h), vincristine (0.5–0.7 mg/m² IV weekly), and cyclophosphamide (200–250 mg/m² divided PO weekly); may result in partial or short-lived complete remission. • Cytosine arabinoside (400–600 mg/m² IV weekly); administer as constant rate infusion over 6–8 hours, can cause thrombocytopenia or

other myelosuppression. • More aggressive chemotherapeutic agents may be used after lymphocytosis has lessened and cytopenias have resolved.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Acute tumor lysis syndrome (life-threatening bradycardia secondary to an acute increase in serum potassium and phosphorus levels following induction chemotherapy) can be seen in ALL dogs with high neoplastic cell counts. Consider high-rate fluid diuresis or peripheral blood leukoreduction using an apheresis machine.



FOLLOW-UP

PATIENT MONITORING

Monitor peripheral blood count and bone marrow—judge success and toxicity of treatment.

POSSIBLE COMPLICATIONS

Hemorrhage from thrombocytopenia—major cause of death in dogs.

EXPECTED COURSE AND PROGNOSIS

Most dogs will have a short-lived complete or partial remission with induction chemotherapy. Prognosis is grave with most dogs succumbing to resistant disease within a few weeks to months.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Chemotherapy—contraindicated in pregnant animals

ABBREVIATIONS

• ALL = acute lymphoblastic leukemia
• FeLV = feline leukemia virus • PCR = polymerase chain reaction • RBC = red blood cell

Suggested Reading

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LEUKEMIA, CHRONIC LYMPHOCYTIC



BASICS

OVERVIEW

- Uncommon, lymphoproliferative disorder.
- Slowly progressive over months to years.
- Circulating neoplastic lymphocytes are mature and well differentiated. • May originate in spleen or bone marrow.

SYSTEMS AFFECTED

- Hematopoietic • Lymphatic

SIGNALMENT

- More frequent in dog than cat. • Dogs—mean age, 10 years (range, 1.5–15 years); male-to-female ratio approaches 2:1. • Cats—median age 12.5 years (range, 5–20); male-to-female ratio 2:1.

SIGNS

- Nonspecific, often no clinical signs of illness
- Lethargy, decreased appetite, chronic weight loss • Lymphadenomegaly, splenomegaly
- Fever • Polydipsia and polyuria

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Lymphoma—may have a leukemic phase (stage V). • Acute lymphoblastic leukemia.
- Immune-mediated hematologic diseases.
- Chronic antigenic stimulation (reactive lymphocytosis)—ehrlichiosis, leptospirosis, leishmaniasis. • Acute viral infection associated lymphocytosis.

CBC/BIOCHEMISTRY/URINALYSIS

- Lymphocytosis—range, 5,000–> 500,000 cells/ μ L, typically small, mature lymphocytes.
- In dogs, more than 60% have large granular lymphocyte (LGL) morphology. • Larger cells may be observed, especially with progression to blast crisis (advanced stage). • Mild-to-moderate normocytic, normochromic anemia (nonregenerative). • Normal-to-low platelet count (less than 20% cases). • Normal-to-mildly increased serum globulins.

OTHER LABORATORY TESTS

- Cytologic examination (bone marrow aspirate or core biopsy)—may show high numbers of mature lymphocytes (especially B-cell CLL); crowding out of normal cell lines in advanced stages. • Immunocytochemistry, flow cytometry, PCR for antigen receptor rearrangement (PARR) to determine cell lineage. • If hyperglobulinemia, serum protein electrophoresis to detect monoclonal gammopathy. • Direct Coombs' test—may be positive with secondary immune-mediated hemolytic anemia. • Serology for *E. canis*.

IMAGING

Radiography and ultrasonography may reveal splenomegaly or internal lymphadenomegaly.

DIAGNOSTIC PROCEDURES

- Bone marrow aspiration (cytology) or biopsy (histopathology). • Lymph node and spleen cytology or histopathology.



TREATMENT

- Usually outpatients treated with oral therapy. • Splenectomy may be considered when spleen is involved and appears to be primary site of neoplastic lymphocytes.
- Treatment should be instituted when patient demonstrates clinical signs of illness (including weight loss, lethargy), lymphadenomegaly or organomegaly, cytopenias, or with lymphocyte count above 50,000/ μ L. • Consult a veterinary oncologist for updates in treatment.



MEDICATIONS

DRUG(S)

- Chlorambucil 6 mg/m² PO q24h for 7–14 days; then 6 mg/m² PO q48h and eventually (maintenance) 2–4 mg/m² q48h, adjusted based on response and CBC (dogs); 2 mg q2–4 days (cats). • Prednisone 40 mg/m² PO q12h (dogs); 5–10 mg/cat q24h (cats; use prednisolone); in combination with chlorambucil; may be tapered or discontinued when lymphocyte count normalizes. • Alternative chemotherapy agents and protocols to be considered when resistance or blast crisis develops over time, consult with an oncologist.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Chemotherapy may have toxic side effects; seek advice with oncologist before starting treatment if you are unfamiliar with cytotoxic drugs.



FOLLOW-UP

PATIENT MONITORING

Initially, biweekly examination of CBC—response to treatment and disease progression.

POSSIBLE COMPLICATIONS

Chronic chemotherapy-induced myelosuppression; may need to alter dosage, depending on neutrophil and platelet counts.

EXPECTED COURSE AND PROGNOSIS

- Variable course, but eventually progressive to blast crisis or becomes resistant to therapy.

- Median survival time with therapy approaches 18 months in dogs with B-cell CLL, and surpasses 24 months in dogs with T-cell CLL. • Median survival time with therapy in cats was > 14 months in one study.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Chemotherapy contraindicated in gestating animals

ABBREVIATIONS

- CLL = chronic lymphocytic leukemia
- LGL = large granular lymphocyte • PCR = polymerase chain reaction

Suggested Reading

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Vernau W, Moore PF. An immunophenotypic study of canine leukemias and preliminary assessment of clonality by polymerase chain reaction. *Vet Immunol Immunopathol* 1999, 69:145–164.

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Author Louis-Philippe de Lorimier

Consulting Editor Timothy M. Fan

LEUKOENCEPHALOMYELOPATHY IN ROTTWEILERS



BASICS

OVERVIEW

- Neurodegenerative disorder that affects the white matter of young adult rottweilers leading to chronic progressive ataxia of the limbs.
- The clinical signs are primarily associated to involvement of the cervical spinal cord, but white matter lesions are also present in the brainstem, cerebellum, and subcortical white matter.
- Occurs worldwide.
- Probably autosomal recessive inheritance.

SIGNALMENT

Rottweiler—either sex; onset in adult dogs 1.5–4 years old

SIGNS

- Insidious, non-painful, progressive onset.
- Cervical spinal cord signs prevail despite widespread demyelinating process.
- Proprioceptive ataxia of the thoracic (delayed protraction with overreaching of the limb) and pelvic limbs, with upper motor neuron weakness.
- Front limbs are more severely affected than hind limbs. Mild asymmetry between right and left limbs may be present.
- Nail scuffing in all limbs.
- Proprioceptive positioning and hopping delayed to absent in all limbs.
- Spinal reflexes normal to exaggerated.

CAUSES & RISK FACTORS

- Autosomal recessive inheritance suspected
- Inbreeding



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cervical compressive lesions such as cervical vertebral spondylomyelopathy (wobbler), cervical subarachnoid diverticula, fibrotic stenosis, spinal cord tumors—difficult to differentiate on clinical signs alone; all can have an insidious onset; MRI necessary for diagnosis.
- Neuroaxonal dystrophy and distal sensorimotor polyneuropathy—neurologic disorders reported in rottweilers; differentiated on the basis of neurologic deficits; neuroaxonal dystrophy: deficits relate to the cerebellum; distal sensorimotor polyneuropathy: tetraparesis associated with lower motor neuron signs.

- Discospondylitis, fracture/luxation, intervertebral disc disease—neck pain; disc disease rarely seen in large-breed dogs at a young age.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

N/A

IMAGING

- Spinal cervical survey radiographs normal.
- MRI—on T2W transverse images of the cervical spine, bilateral and symmetrical well-demarcated, ovoid in shape, intra-axial hyperintensities in the white matter of the dorsolateral funiculi, extending contiguously from the cervicomедullary junction to the sixth cervical vertebral body. Symmetrical hyperintensities also observed in pyramids and ventral aspect of the crus cerebri in the brain. No contrast enhancement.

DIAGNOSTIC PROCEDURES

CSF analysis normal.

PATHOLOGIC FINDINGS

- Although the most severe lesion is located in the white matter of the cervical spinal cord, it extends caudally into the thoracic spinal cord and rostrally into the brainstem.
- Macroscopic examination: in the dorsal aspect of the lateral funiculi of the cervical spinal cord and in the pyramidal tracts of the medulla oblongata, presence of well demarcated whitish opaque foci located bilaterally and symmetrically, corresponding to myelin loss.
- Microscopy: in the cervical spinal cord, the lesion affects the cervical spinal cord white matter in the dorsal portion of the lateral funiculi (dorsal spinocerebellar, lateral corticospinal, reticulospinal, and rubrospinal tracts). In the brain, the lesion affects the pyramidal tracts, crus cerebri, medial lemniscus, caudal cerebellar peduncle, trapezoid body, spinal tracts of the trigeminal nerve, and optic tracts; multifocal lesions are also observed in the cerebellar folia.
- The myelin loss exceeds axon loss with extensive astrogliosis and astrocytosis. Normal appearing axons observed in areas of severe demyelination.
- Lesion bilateral with some asymmetry.



TREATMENT

- Outpatient, unless the severity of neurologic deficits precludes nursing care at home.
- Activity—whatever can be tolerated.

- Diet—ensure proper intake of food; patient may have difficulty reaching the feeding area.
- Neurologic status—slowly and progressively deteriorates; eventually, the patient is unable to walk or get up.



MEDICATIONS

DRUG(S)

N/A



FOLLOW-UP

- Neurologic examination—monitor monthly to assess progression.
- Avoid bed sores and urine and fecal scalding by keeping the patient on a clean, dry, and cushioned pad (e.g., synthetic sheepskin).
- Severe tetraparesis—within 6–12 months after onset of clinical signs.
- Euthanasia—because of severe debility.



MISCELLANEOUS

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- MRI = magnetic resonance imaging
- T2W = T2-weighted

Suggested Reading

Davies DR, Irwin PJ. Degenerative neurological and neuromuscular disease in young rottweilers. J Small Anim Pract 2003, 44(9):388–394.

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Hirschvogel K, Matiasek K, Flatz K et al. Magnetic resonance imaging and genetic investigation of a case of Rottweiler leukoencephalomyopathy. BMC Vet Res 2013, 9:57.

Author Joane M. Parent

Consulting Editor Joane M. Parent

L-FORM BACTERIAL INFECTIONS



BASICS

OVERVIEW

Caused by bacterial variants with defective or absent cell walls.

L-Form Bacteria

- Isolated from humans, animals, and plants.
- Named for Lister Institute (London), where discovered in 1935.
- Also called L-organisms, cell wall deficient (CWD)-forms.
- Differ from the *Mycoplasma* by lack of sterols in their membranes (similar to bacteria).
- Soft, fragile, pleomorphic, spherical, and osmotically fragile; structurally equivalent to protoplasts and spheroplasts, which cannot divide.
- Can grow and replicate by cell fission in an irregular manner, yielding daughter cells that differ in size, nucleic acid content, and amount of cytoplasm.
- Formed as spontaneous variant of bacteria or when cell wall synthesis is inhibited or impaired by antibiotics (e.g., penicillin), specific immunoglobulins, or lysosomal enzymes that degrade cell walls.
- Can be induced from virtually all gram-positive and -negative bacteria under suitable conditions.
- May revert to normal cell wall strain in a suitable host or favorable medium.
- Encompasses both unstable (can revert to normal walled bacteria) L-forms with reversible loss of cell wall organization due to phenotypic variants of bacteria and stable (not able to revert) L-forms with irreversible loss of cell wall due to genomic mutations.
- Usually no pathogenicity.

SIGNALMENT

- Sporadic in cats and dogs
- Most common in free-roaming cats of all ages

SIGNS

- Dogs—arthritis.
- Cats—penetrating wound (usually cat bite); infected surgical site; cellulitis; fever; arthritis; synovitis.

CAUSES & RISK FACTORS

- Bites, scratches, or trauma may allow organism to enter skin and subcutaneous tissue.
- Environmental reservoir unknown.

- Formation encouraged by antibiotic treatment of host, resistance of host, suitability of in vivo site for establishment of infective locus, and relatively low to moderate virulence of the infecting bacterium.
- Greatly reduced infectivity but may revert and display the pathogenic properties of the original bacterium.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- *Mycoplasma*—differentiate by phase microscopy, electron microscopy, or measuring penicillin-binding proteins.
- Suppurative skin infections caused by mycobacteria, yeast, or fungi.
- Arthritis caused by immune-mediated disease, bacteria, spirochetes, *Mycoplasma*, *Rickettsia*, *Chlamydia*, viruses, or fungus.

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilia with left shift
- Monocytosis
- Lymphocytosis
- Eosinophilia
- Mild normochromic, normocytic anemia
- High serum total protein

OTHER LABORATORY TESTS

- Cytology—exudate from draining lesions contains macrophages and neutrophils.
- Joint fluid—high neutrophil count.
- Culture—difficult; requires special media (Hayflick); “fried-egg” appearance of colonies on solid agar (center portion embedded in agar; thin vacuolated growth on agar surface).
- Light microscopy—difficult to demonstrate.
- Electron microscopy—may show characteristic pleomorphic, cell-wall-deficient organisms in phagocytes.
- Precise characterization and speciation—the organism must revert to the parental cell-walled state (may take years).

IMAGING

Radiographs—periarticular soft tissue swelling; periosteal proliferation.

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

- Biopsy—pyogenic cellulitis; panniculitis; chronic pyogranulomatous arthritis; tenosynovitis.
- Stains—neither conventional (H&E) nor specialized (gram, acid-fast, silver, PAS) reveal organisms.



TREATMENT

- Gentle cleaning degrades fragile organisms.
- Allow open wounds to heal by secondary intention.



MEDICATIONS

DRUG(S)

- Variable antibiotic sensitivity.
- Tetracycline 22 mg/kg PO q8h for at least 1 week after signs disappear.
- Fever usually breaks within 24–48 hours.
- β -lactam antibiotics—inhibit cell wall synthesis; not effective.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

Arthritic changes persist

L



MISCELLANEOUS

- Public health significance unknown
- Ubiquitous; therefore, role in disease questioned
- May play a role in recurrent infections or chronic diseases

ABBREVIATIONS

- H&E = hematoxylin and eosin
- PAS = periodic acid-Schiff

Suggested Reading

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LILY TOXICOSIS



BASICS

OVERVIEW

- Plants in the *Lilium* and *Hemerocallis* genera—widely used ornamental plants; very toxic to cats; *Lilium*—Easter lilies, tiger lilies, Japanese show lilies, rubrum lilies, numerous *Lilium* hybrids; *Hemerocallis*—daylilies.
- Ingestion of leaves or flowers—results in a severe nephrotoxic syndrome; as little as 2–3 leaves reported to be lethal.
- Toxic principle(s) not elucidated, but found to be in the water-soluble plant fraction.

SIGNALMENT

- Cats—systemic poisoning.
- Dogs—only mild gastrointestinal upset, even after ingestion of large quantities of plant material.
- No age or breed predilections noted.

SIGNS

- Sudden onset of vomiting—gradually subsides within 2–4 hours.
- Depression and anorexia—onset about the same time as vomiting; both persist throughout the syndrome.
- Polyuria and dehydration—by 12–24 hours; leads to anuric renal failure.
- Vomiting—recurs by 36 hours; accompanied by progressive weakness.
- Recumbency—by 2–4 days.
- Death—by 4–7 days post-ingestion.

CAUSES & RISK FACTORS

- Plants—Easter lilies; tiger lilies; Asiatic hybrid lilies; Japanese show lilies; *Lilium* hybrids; daylily; primarily when used in cut-flower arrangement or as household potted plants.
- All ingestions by cats of plant material from the *Lilium* and *Hemerocallis* genera should be considered potentially lethal.
- Exclusively indoor cats—predisposed to ingestion of newly introduced plants.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Nephrotoxins

- Aspirin and other NSAIDs
- Zinc
- Boric acid
- Ethylene glycol
- Mercury
- Nephrotoxic antibacterials—aminoglycosides
- Melamine/cyanuric acid poisoning

Systemic Diseases

- Acute presentation of chronic renal failure
- Urinary obstruction
- Immune-mediated renal disease
- Leptospirosis
- Pyelonephritis
- Lymphoma

CBC/BIOCHEMISTRY/URINALYSIS

- Stress leukogram.
- Moderate to severely high BUN, phosphate, and potassium.
- Creatinine—severe increase common; usually 15–29 mg/dL; may be into the 40s.
- Increased AST, ALT, and ALP late in disease.
- Severe proteinuria, glucosuria, and low specific gravity; numerous tubular epithelial casts. Early in the syndrome, tubular cell detail can be seen in the casts.
- Crystalluria—not caused by ingestion of these plants.
- Increased amylase and lipase may occur with very large ingestions.

OTHER LABORATORY TESTS

N/A

DIAGNOSTIC PROCEDURES

- If possible, examine plant to verify that it has been chewed.
- Have plant positively identified by a professional horticulturist or other expert if necessary.

PATHOLOGIC FINDINGS

- Gross—swollen kidneys; empty gastrointestinal tract; moderate to severe perirenal edema.
- Histologic—severe acute renal tubular necrosis with intact basement membranes; mild to severe interstitial edema; severe cast formation in the collecting ducts; later in the syndrome may note evidence of mitotic figures in the remaining tubular epithelium.



TREATMENT

- Early decontamination—lessens duration and severity of signs. Emesis not generally useful as vomiting is common. Endoscopy has been used to remove plant pieces.
- Fluid therapy—initiation within 18 hours of ingestion prevents anuric renal failure; intravenous normal saline at 2–3 times maintenance for 24 hours.
- Anuric renal failure—dialysis is the only effective treatment; 7 days of therapy has resulted in a return of renal function.



MEDICATIONS

DRUG(S)

- Decontamination—activated charcoal (2 g/kg PO).
- Cathartic—sorbitol (2.1 g/kg PO) or magnesium sulfate (0.5 g/kg PO).

CONTRAINdications/POSSIBLE INTERACTIONS

- Avoid fluids containing potassium.
- Avoid drugs eliminated by renal clearance.
- Diuretics (mannitol, hypertonic fluids, furosemide, thiazides) are not effective at initiating urine production once anuric renal failure has occurred.



FOLLOW-UP

PATIENT MONITORING

Periodically follow serum chemistries to ensure normal renal function; especially important after dialysis.

EXPECTED COURSE AND PROGNOSIS

- Dehydration from polyuric renal failure; required for the disease to progress to anuria.
- Prevention of dehydration (early fluids) prevents the progression of the syndrome to anuria. Prevention of anuria generally allows a gradual return to normal over 24–48 hours.



MISCELLANEOUS

SEE ALSO

- Poisoning (Intoxication) Therapy
- Renal Failure, Acute

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

Hall JO. Lily poisoning. In: Peterson ME, Talcott PA, eds., Small Animal Toxicology, 3rd ed. Philadelphia: W.B. Saunders, 2013, pp. 617–620.

Rumbeisha WK, Francis JA, Fitzgerald S, et al. A comprehensive study of Easter lily poisoning in cats. J Vet Diagn Invest 2004, 16(6):527–541.

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Consulting Editor Lynn R. Hovda



BASICS

OVERVIEW

- Lipomas are benign tumors of adipocytes (fat cells). Their appearance is that of mature adipocytes with no cellular or nuclear atypia, identical to cells that form adult fat.
- These tumors are reported to occur in approximately 16% of dogs and 12% of cats; however, their true incidence is probably higher, since many lipomas are diagnosed by clinical appearance without histology.
- This tumor may occur anywhere on the body, although the subcutaneous areas of the chest, abdomen, limbs, and axillae may be most commonly affected. Lipomas have also been reported within the chest and abdominal cavities, uterus, orbit, and bone.

SIGNALMENT

- Most common in middle-aged to older dogs; rarely seen in cats.
- There is no breed predisposition, although Labrador retrievers, Doberman pinschers, miniature schnauzers, cocker spaniels, dachshunds, and Weimaraners have been reported to be at increased risk.
- Obese animals may be more susceptible.
- Female dogs are predisposed.
- Lipomas in cats may occur more frequently in neutered males.

SIGNS

- Usually solitary, but multiple lipomas may occur in the same individual.
- Variable size, shape (often round), and growth rate (usually slow).
- Animals are often asymptomatic unless the mass becomes large enough to cause functional difficulties commonly with ambulation. Lipomas enlarge by expansion and not invasion. They may compress adjacent organs when they occur in the thoracic or abdominal cavity.
- Lipomas usually feel soft, but those that develop between muscle planes may feel firm and may be mistaken for infiltrative lipomas or soft tissue sarcomas. The caudal thigh region is a common place for intermuscular lipomas (between the semimembranosus and semitendinosus muscles).
- In many cases, the tumor is present for a long period of time (1 year or more) before presentation to a veterinarian.

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infiltrative lipoma.
- liposarcoma or other soft tissue sarcomas (e.g., myxosarcoma, fibrosarcoma, hemangiopericytoma).

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

N/A

IMAGING

Radiography—reveals fat density tissue/mass surrounded by soft tissue density structures. Macroscopic fat is also readily identified with CT or MRI techniques.

DIAGNOSTIC PROCEDURES

Fine-needle aspiration cytology—reveals normal, mature adipocytes; fat tends to coalesce into droplets that wash off the slide during staining, leaving a fairly acellular specimen.

PATHOLOGIC FINDINGS

Histologically consistent with normal adipose tissue, which may be subclassified if other tissue elements are present, e.g., cartilage (chondrolipoma), blood vessels (angiolipoma), hematopoietic elements (myelolipoma), or collagen (fibrolipoma); no tumor infiltration into surrounding structures (e.g., muscle).



TREATMENT

- Complete surgical excision is curative as these tumors are well encapsulated, but should only be considered if symptomatic.
- Intermuscular lipomas (most common in caudal thigh and axilla) extend deep between muscle planes but do not invade adjacent structures can be successfully treated with surgical resection.
- Liposuction has also been described with success for tumors up to 15 cm in diameter; however, regrowth occurs in a high proportion of cases.
- Intralesional triamcinolone acetonide has also recently been described, with complete regression in 9 of 15 cases.



MEDICATIONS

DRUG(S)

Medical therapy is unnecessary and unlikely to be effective.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

Have owner monitor for recurrence, which is rare and may be addressed successfully with a second surgery. If tumor recurs, consider the possibility of an infiltrative lipoma or soft tissue sarcoma.

PREVENTION/AVOIDANCE

No specific preventive measures, except possibly avoidance of obesity.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

Cure with complete surgical excision is expected. Recurrence may occur with incomplete removal. Surgery is best performed before the tumor interferes with function or mobility. Development of other primary lipomas in other locations may occur. Presence of other tissue elements within the tumor, such as cartilage, collagen, or hematopoietic cells, occurs rarely and does not appear to impact surgical outcome or prognosis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Possibly obesity

AGE-RELATED FACTORS

No specific factors, except general predisposition to tumor development with increasing age.

PREGNANCY/FERTILITY/BREEDING

Surgery can likely be delayed until after whelping

SEE ALSO

Lipoma, Infiltrative

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging

Suggested Reading

Case JB, MacPhail CM, Withrow SJ. Anatomic distribution and clinical findings of intermuscular lipomas in 17 dogs (2005–2010). J Am Anim Hosp Assoc 2012, 48:245–249.

Author Anthony J. Mutsaers

Consulting Editor Timothy M. Fan

LIPOMA, INFILTRATIVE



BASICS

OVERVIEW

- Invasive, non-encapsulated, lipoma variant that does not metastasize.
- A benign neoplasm that infiltrates soft tissues, particularly muscles, and including fasciae, tendons, nerves, blood vessels, salivary glands, lymph nodes, and joint capsules, and occasionally bones.
- Muscle infiltration typically extensive.
- Surgical cure—difficult to obtain.
- Occurs much less frequently than does lipoma.

SIGNALMENT

- Usually middle-aged dogs.
- No breed predilection definitively demonstrated; Labrador retrievers—possibly overrepresented.
- May be more common in females than in males.

SIGNS

- Large, diffuse, soft tissue mass.
- Clinically appears as localized muscle swelling and/or distended abdomen if abdominal component.
- Infiltration of pelvic, thigh, shoulder, sternal, and lateral cervical musculature—most common; recent evidence suggests no clear site prediction.

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Soft tissue sarcoma, particularly liposarcoma, hemangiopericytoma, myxosarcoma, rhabdomyosarcoma, and fibrosarcoma.
- Lipoma.
- Intermuscular lipoma.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

N/A

IMAGING

- Radiography—reveals fat dense tissue between soft tissue dense structures.

• CT or MRI imaging—allows adequate discrimination of tumor for surgery and/or radiation treatment planning; however, differentiation of normal fat from infiltrative lipoma can be problematic.

DIAGNOSTIC PROCEDURES

- Cytologic examination of aspirate reveals mature adipocytes with no cellular or nuclear atypia, identical to cells that form adult fat.
- Tissue biopsy is required to definitively classify as infiltrative lipoma.

PATHOLOGIC FINDINGS

- Histologic examination—well-differentiated adipocytes; may be indistinguishable from normal adipose tissue.
- Distinctive feature—tumor infiltration into and between muscle bundles and other tissues.



TREATMENT

SURGICAL CONSIDERATIONS

- Characteristic invasiveness makes excision extremely problematic; difficult to distinguish between tumor and normal adipose tissue.
- Poorly defined tumor margins—may contribute to the observed high recurrence rate after surgical excision.
- 36–50% of patients have recurrence within 3–16 months, except with limb amputation for appendicular tumor.
- Amputation of an affected limb is recommended only when quality of life is affected; tumor causes little inconvenience unless it interferes with movement, causes pressure-related pain, or develops in a vitally important anatomic site. However, amputation must be performed before growth of proximal extent of tumor crosses attainable surgical margin.

EXTERNAL BEAM RADIOTHERAPY

- Beneficial for long-term tumor control—median survival 40 months in a retrospective study of 13 dogs, with only 1 dog (7.7%) euthanized owing to tumor-related signs (versus 26.7% with surgery alone).
- Dogs with measurable disease may only have stabilization of the tumor.
- Cytoreductive surgery to microscopic disease prior to radiation may result in long-term disease control.



MEDICATIONS

DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Focus—whether and when to recommend surgery and adjunctive radiation therapy for incomplete surgical margins.
- Reevaluations—schedule as dictated by tumor growth and choice of therapy.

POSSIBLE COMPLICATIONS

Temporary acute side effects (e.g., moist dermatitis and alopecia) expected with radiation therapy, and consultation with a radiation oncologist is recommended regarding specific, anatomic site-related side effects.

EXPECTED COURSE AND PROGNOSIS

- Long-term control of tumor growth may be attained with external beam radiation therapy alone or in combination with surgery.
- Lack of metastatic potential affords a very good prognosis upon control of local tumor growth.
- If liposarcoma diagnosed, behavior is similar to other soft tissue sarcomas, therefore consult relevant literature on these tumors.



MISCELLANEOUS

SYNONYMS

- Lipomatosis
- Has been (mistakenly) referred to as well-differentiated liposarcoma

SEE ALSO

Lipoma

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging

Suggested Reading

McEntee MC, Page RL, Mauldin GN, et al. Results of irradiation of infiltrative lipoma in 13 dogs. Vet Radiol Ultrasound 2000, 41:554–556.

Author Anthony J. Mutsaers

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LIVER FLUKE INFESTATION



BASICS

OVERVIEW

- Platynosomum concinnum* infection occurs in cats in Florida, Hawaii, and other tropical-semitropical areas. One report of infection in a cat from Ohio and 1 from Illinois. Most common trematode infection affecting the liver of companion pets in North America.
- Infestation acquired from ingestion of infected intermediate host (e.g., lizard or frog).
- Estimated 15–85% of cats with intermediate host access are infected in endemic areas.
- Metorchis conjunctus* also may infect the liver and biliary structures of cats.
- Flukes reported in dogs: *Heterobilharzia americana* (North America); raccoon is the natural definitive host and most important reservoir host; *Metorchis conjunctus*; *Clonorchis sinensis* (China), *Schistosoma japonicum* (Philippines), *Metorchis bilis* and *Opisthorchis felineus* (Germany) in sled dogs fed a diet including raw fish.

SIGNALMENT

Platynosomum concinnum: young (6–24 months) cat with access to local fauna.

SIGNS

- Depend on severity of infection.
- Most infested cats lack clinical signs.
- With severe infestation: jaundice, emaciation, anorexia, vomiting, mucoid diarrhea, hepatomegaly, abdominal distention, malaise, fever.

CAUSES & RISK FACTORS

P. concinnum

- Adults reside in bile ducts and gallbladder; life cycle requires two intermediate hosts and tropical or semitropical climate.
- Embryonated eggs—pass in cat's feces; ingested by first intermediate host: a land snail.
- Miracidia—hatch from eggs in the snail penetrating host tissue and develop sporocysts.
- Mature daughter sporocysts—emerge from the snail and thereafter are ingested by a second intermediate host: usually an anole lizard (but also skinks, geckos, frogs, and toads); enter bile ducts where they reside until host ingested as prey by the cat.
- Cercariae—released in the upper digestive tract of the cat; migrate to the bile ducts where they mature and shed eggs within 8 weeks.
- Risk factors for infection—tropical or subtropical climate; appropriate intermediate hosts; access to an outdoor or indoor/outdoor environment; successful hunting skills; consumption of infected intermediate host.

Metorchis conjunctus

- Cats—may infect the liver and biliary structures initially causing watery blood-tinged diarrhea and later evidence of biliary tree invasion; eggs are passed in feces 17 days from initial infection.
- Infection typically associated with increased liver enzyme and may be associated with transient eosinophilia.

Heterobilharzia americana

- Eggs containing fully developed miracidium are passed in feces of final host. In fresh water, eggs hatch, release miracidia that penetrate snail hosts, where sporocysts develop. Cercariae released from snail host 25 days after infection; these infect vertebrate host (dog, human) by skin penetration.
- Adult flukes develop in liver and migrate to mesenteric veins where eggs disseminate to various viscera, including liver, pancreas, mesenteric lymph nodes, spleen, and intestines, where they initiate granulomatous inflammation and sclerotic vascular lesions.
- Eggs appear in feces 68 days after infection.

Schistosoma haematobium

- Adult fluke and eggs disperse to splanchnic organs, including liver and pancreas; in portal or hepatic veins eggs and adults associate with encapsulated fibrotic granulomatous foci.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cholangiohepatitis; hepatic lipidosis; bile duct carcinoma; hepatic lymphoma; choleliths and any disorder causing major bile duct occlusion.
- Identified by finding trematode eggs in feces, rarely observing anechoic ovoid structures with echoic center in biliary tree by ultrasound, cytologic examination of bile or hepatic aspirates; most definitively from histopathology of biopsied liver, biliary structures, or pancreas.

CLINICOPATHOLOGIC FEATURES

Best defined for *Platynosomum concinnum* in cats.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—variable; eosinophilia beginning 3 weeks after infection; persists for months; not all infected cats demonstrate eosinophilia.
- Biochemistry—high liver enzyme activities, especially ALT and AST; ALP may be normal or only slightly increased initially.
- Bilirubin—increased; markedly high in advanced severe disease.
- Urinalysis—bilirubinuria.

OTHER LABORATORY TESTS

- Fasting/postprandial bile acid—increased.
- Fecal examination—noninvasive definitive diagnostic test: *P. concinnum* eggs detected in only 25% of infected cats.

- Fecal egg retrieval—sedimentation most successful; formalin-ether or sodium acetate most reliable (demonstrates eight-fold more eggs than direct fecal examination).

- Patients with few parasites (one to five flukes)—may shed only two to ten eggs/g of feces; thus, may not discover eggs by fecal testing.
- Serial fecal examinations—may be necessary.

IMAGING

- Abdominal radiography—may show mild hepatomegaly.
- Abdominal ultrasonography—differentiates biliary obstruction from hepatocellular disease; shows one or more of the following: (1) biliary obstruction: dilated gallbladder, common bile duct (> 2 mm), and intrahepatic ducts; (2) gallbladder sediment with flukes (oval hypoechoic structures with echoic center), mildly thick gallbladder wall with a double-layered appearance (cholecystitis); (3) hypoechoic hepatic parenchyma with prominent hyperechoic portal areas (ducts) associated with cholangiohepatitis.

DIAGNOSTIC PROCEDURES

- Fecal examination for trematode eggs
- Cholecystocentesis—discloses fluke eggs
- Liver biopsy—reveals signs of infection

PATHOLOGIC FINDINGS

- Gross—liver may appear large and yellow-green with dilated bile ducts; may see flukes in bile ducts or gallbladder; increased size and tortuosity of bile ducts on cut section.
- Histologic lesions—depend on the number of flukes and duration of infestation; *early stage* (4–6 weeks): enlarged bile ducts and periductal areas infiltrated with inflammatory cells, especially eosinophils; *mid-stage* (4 months): severe adenomatous hyperplasia of bile duct epithelium and coincident periductal inflammation; *late stage* (6 months): extensive peribiliary fibrous connective tissue that may cause bile duct stenosis.



TREATMENT

Outpatient versus inpatient—depends on severity of illness

INPATIENT

- Balanced polyionic fluids with supplemental potassium chloride—20–40 mEq/L; as appropriate; based on serum electrolytes.
- Nutritional support—avoid development of hepatic lipidosis; feed high-protein calorically dense food and ensure food intake; use feeding tubes if needed to ensure adequate food intake in inappetent cats; rarely, severe clinical signs may require parenteral nutrition; rarely hepatic encephalopathy necessitates protein restriction.

LIVER FLUKE INFESTATION

(CONTINUED)

- B vitamin supplementation—important for anorectic and ill cats on fluid therapy; 2 mL B-soluble vitamins/L fluids.



MEDICATIONS

DRUG(S)

- Praziquantel 20 mg/kg SC q24h for 3–5 days is treatment of choice for cats; eggs may pass in feces for up to 2 months after treatment. Praziquantel at 30 mg/kg PO once and 50 mg/kg SC once cleared a dog symptomatic for *Heterobilharzia americana*.
- Prednisolone—initial dose for cats showing eosinophilia, significant inflammation on biopsy or having severe clinical signs: 1–2 mg/kg/day for 2–4 weeks; then tapered in 50% decrements every 2 weeks.
- Ursodeoxycholic acid 10–15 mg/kg q24h PO; tablet form and divided dose administered with feeding achieves best bioavailability; avoid if evidence of extrahepatic bile duct obstruction.
- Broad-spectrum antibiotic coverage to protect against retrograde biliary tree infection with enteric organisms introduced by parasite; infection encouraged by fluke death in tissues.
- Antioxidant therapy—suggested by necroinflammatory tissue injury; vitamin E (10 IU/kg day PO) and S-adenosyl-l-methionine (SAMe; Denosyl-SD4 has proven

bioavailability in cats as a GSH donor): 20 mg/kg PO daily, enteric coated tablets, until liver enzymes normalize.

- Antiemetic—metoclopramide (0.2–0.4 mg/kg PO, SC q6–8h or by constant rate infusion 1–2 mg/kg/day); ondansetron (0.5 mg/kg q12h, IV or PO 30 minutes before feeding); maropitant (1.0 mg/kg [5 mg/cat] IV, SC or PO once per day; maximum of 5 days).

CONTRAINDICATIONS

Pregnancy—use caution with drug use.



FOLLOW-UP

PATIENT MONITORING

- Monitor clinical signs, appetite, body condition and weight, liver enzymes, bilirubin, and fecal sedimentation.
- Watch for signs of biliary tree occlusion after administration of praziquantel.

PREVENTION/AVOIDANCE

- Restrict outdoor access if endemic parasite.
- Praziquantel prophylaxis—every 3 months; outdoor cats in endemic, tropical climates.

POSSIBLE COMPLICATIONS

- Death from liver failure; untreated symptomatic disease.
- Biliary tree obstruction.
- Pancreatitis.

- Pancreatic exocrine insufficiency—with chronic infection.
- Cholangitis/cholangiohepatitis (suppurative or nonsuppurative).

EXPECTED COURSE AND PROGNOSIS

Uncomplicated recovery with treatment expected in most patients.



MISCELLANEOUS

ZOONOTIC POTENTIAL

None

SEE ALSO

- Bile Duct Obstruction
- Cholangitis/Cholangiohepatitis Syndrome
- Hepatic Lipidosis

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- GSH = glutathione

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Author Julie R. Pembleton-Corbett

Consulting Editor Sharon A. Center

LIZARD VENOM TOXICOSIS



BASICS

OVERVIEW

- Poisonous lizards—found only in the US Southwest and Mexico; *Heloderma suspectum* (Gila monster—indigenous to Arizona, New Mexico, extreme Southern California, extreme Southern Utah, southwestern Nevada) and *H. horridum* (Mexican beaded lizard—not indigenous to the USA); tenacious bite with considerable mechanical trauma in addition to envenomation; deliver venom from secretory glands on the lower jaw by aggressive chewing action and distributing venom over grooved venom-conducting teeth; non-aggressive; animal envenomations rare.
- Venom components—multiple enzymatic components: kallikrein-like enzymes (helodermatine), acidic neurotoxin (gilatoxin), and phospholipase A₂.
- Envenomation may result in generalized weakness, pain, wound cyanosis, tongue swelling, hypotension, tachycardia, and ventricular arrhythmias. Coagulopathy is rare.

SIGNALMENT

Dogs and cats

SIGNS

Historical Findings

- Sudden onset of pain.
- Bite—usually on the face, especially the lower lip; lizard may still be attached to patient (pathognomonic).

Physical Examination Findings

- Bleeding from bite site
- Hypotension
- Extremely painful bite site
- Localized swelling; edema slower to develop than rattlesnake bite
- Excessive salivation
- Excessive lacrimation
- Frequent urination and defecation
- May note aphonia in cats
- Wound discoloration (bluish appearance)

CAUSES & RISK FACTORS

Outdoor activities in indigenous area



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Trauma; other animal bites or puncture-type trauma.
- Venomous snake bite—single or multiple punctures; pain; local wound discoloration and swelling; lacking (or including) hemolytic, hemorrhagic, and clotting abnormalities.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Electrocardiography—may detect arrhythmias.



TREATMENT

- Remove lizard—place a prying instrument between the jaws; push into the back of the mouth; a flame held underneath the jaw often releases grip; if attached to extremity, completely submerging lizard and limb in warm water may cause release.
- Inpatient—monitor and treat hypotension, as necessary, with crystalloid fluid therapy.
- Bite site—flush with lidocaine; probe to identify and remove fragments of lizard teeth (if not removed, they will become sequestra and abscess); soak with Burrow's solution or similar solution every 8 hours.



MEDICATIONS

DRUG(S)

- Control pain—can use narcotics (if severe)
- Broad-spectrum antibiotics indicated

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Corticosteroids—not generally used by the author; authorities differ on the value of corticosteroids.
- Antihistamines—not useful.



FOLLOW-UP

- Electrocardiogram—monitor for arrhythmias
- Bite site—monitor for infection



MISCELLANEOUS

Suggested Reading

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Author Michael E. Peterson

Consulting Editor Lynn R. Hovda

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LOWER URINARY TRACT INFECTION, BACTERIAL



BASICS

DEFINITION

Adherence and replication of bacteria within the urinary bladder.

PATHOPHYSIOLOGY

Urinary tract defenses against bacterial infection include anatomic and functional barriers that prevent retrograde urethral ascent of pathogens, the inherent antibacterial properties of normal urine, and local (i.e., mucosal) and systemic immune responses. Bacterial colonization and persistence within urine or on urothelial surfaces requires impairment of one or more of these defense mechanisms. The mucosal inflammatory response promotes leukocyte infiltration into the bladder wall, resulting in dysuria, pollakiuria, and hematuria.

SYSTEMS AFFECTED

Renal/Urologic

INCIDENCE/PREVALENCE

- Prevalence of UTIs in animals with predisposing conditions is more clinically relevant than total population frequencies.
- Prevalence of UTIs in dogs:
 - Without urinary tract-associated clinical signs: 2.1%
 - With diabetes mellitus, at initial diagnosis: 7.7%
 - With diabetes mellitus, at any point in time: 37%
 - With hyperadrenocorticism, at initial diagnosis: 46%
 - With thoracolumbar intervertebral disc extrusion: 20.0–38.5%
 - With indwelling urinary catheters while hospitalized: 63.8%
- Prevalence of UTIs in cats:
 - Without lower urinary tract-associated clinical signs: 0.9%
 - With lower urinary tract-associated clinical signs: 3.4–12.0%
 - With ureteral calculi: 8.4%
 - With chronic kidney disease, at any point following diagnosis: 16.9–29.1%
 - With diabetes mellitus, at any point following diagnosis: 12.2–12.8%
 - With uncontrolled hyperthyroidism, referred for I¹³¹ treatment: 12.2%
 - With perineal urethrostomies, at any point following surgery: 22%.

SIGNALMENT

Species

More common in dogs than cats

Breed Predilections

None

Mean Age and Range

- UTIs may occur in any age animal.
- Male dogs: mean, 8.0 ± 0.1 years; female dogs 7.7 ± 0.1 years. Relative risk of UTI diagnosis increases with age.

- Cats: Median, 7.7 yrs (range, 0.2–17 years).

Predominant Sex

- Dogs: female dogs more commonly affected than male dogs.
- Cats: male and female cats affected in approximately equal numbers.

SIGNS

Historical Findings

- Patients may be asymptomatic.
- May have variable severity of:
 - Pollakiuria, dysuria, hematuria, stranguria, urgent need to urinate (which may progress to urinary incontinence), urinating in inappropriate locations, and excessive licking at or discharge from the genitalia.
- Systemic clinical signs (anorexia, generalized discomfort) occur infrequently.

Physical Examination Findings

- Unremarkable in most animals.
- Abnormalities occasionally noted with urinary bladder palpation:
 - Bladder wall thickening or crepitus
 - Stimulation of micturition, regardless of bladder urine volume
 - Pain reactions.

CAUSES

- Commensal skin, mucosal, or gastrointestinal bacteria adhere to the urethral epithelium, and ascend retrograde.
- Urine cultures identify aerobic bacterial species in > 99% of UTIs. A single bacterial species is isolated in 75–95% of cases.
- *Escherichia coli*, *Staphylococcus* spp., or *Proteus* spp. are isolated from approximately 50% of animals.
- Eight species of bacteria (*E. coli*, *Staphylococcus*, *Proteus*, *Streptococcus*, *Klebsiella*, *Enterococcus*, *Pseudomonas*, and *Corynebacterium*) account for approximately 95% of UTIs.

RISK FACTORS

- Systemic immune dysfunction (e.g., suppressed immunity in dogs with hyperadrenocorticism).
- Nidus for bacterial adherence and defense mechanism avoidance (e.g., indwelling urinary catheters, uroliths).
- Altered composition of urine (e.g., persistently dilute urine, glucosuria).
- Compromise of barriers that inhibit retrograde bacterial movement (e.g., loss of urethral tone, ectopic ureters, incomplete bladder emptying).
- Disrupted urinary tract mucosal defenses (e.g., urolith-associated mucosal trauma).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Dysuria, pollakiuria, hematuria, and stranguria occur with most lower urinary tract

diseases of dogs and cats. UTI cannot be diagnosed or excluded based on clinical signs.

- Cystolithiasis and lower urinary tract neoplasia commonly induce clinical signs identical to those expected with UTIs. Diagnosis is further complicated by the increased risk of UTIs associated with these conditions. Clinical signs in cats with idiopathic cystitis (i.e., interstitial cystitis) are likewise indistinguishable from those induced by UTIs.
- Diagnostic evaluation and treatment differs for patients with “uncomplicated” vs. “complicated” UTIs. Uncomplicated UTIs are spontaneous infections diagnosed without identifiable breaches in urinary tract defense mechanisms. Complicated UTIs refer to: infections associated with impaired systemic or local urinary tract defenses, or three or more UTIs over a 12-month interval.
- Recurrent infections are subclassified as: reinfection—UTIs resolve with appropriate therapy; bacterial isolates may vary with successive infections; or relapse—UTIs appear to resolve; however, subsequent urine cultures confirm persistence of the original bacterial isolate.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC and biochemistry are unremarkable.
- Urinalysis
 - Pyuria is present in most animals with UTIs; but is not synonymous with infection. Dipstick leukocyte pads are inaccurate in dogs (many false negatives) and cats (many false positives).
 - Hematuria and proteinuria are common.
 - Alkaluria (pH > 7.0) occurs with urea-splitting bacterial UTIs.
 - Magnesium ammonium phosphate (struvite) crystalluria can occur in healthy dogs and cats, and may be absent in patients with UTIs.
 - Presence of “bacteria” in unstained urine sediment preparations incorrectly identifies UTIs in > 20% of cases. Stained sediment preparations improve accurate bacterial identification.

OTHER LABORATORY TESTS

Urine Culture

- Definitive diagnosis requires aerobic culture of a urine sample.
- Cystocentesis is the gold standard method for collecting urine culture specimens. Bacterial growth > 10³ cfu/mL is diagnostic for UTI in cystocentesis-collected urine samples from both dogs and cats.
- Urine samples obtained by catheterization are often contaminated by the normal flora of the distal urethra. Bacterial growth > 10⁴ cfu/mL in male dogs, > 10⁵ cfu/mL in female dogs, and > 10³ cfu/mL in cats, is diagnostic for UTI in catheter-obtained urine samples. Indwelling catheters may be colonized without concurrent UTI; therefore, sample collection from urinary catheters

(CONTINUED)

LOWER URINARY TRACT INFECTION, BACTERIAL

- should be avoided; catheter tip cultures are of questionable value.
- Culturing voided midstream urine samples should be avoided.
- Urine from non-sterile surfaces (i.e., “table top” samples) should not be cultured.

Antibiotic Sensitivity Testing

- Most antibiotics are concentrated and excreted in urine. Antibiotic sensitivity is accurately predicted by use of the isolate’s “sensitive” vs. “resistant” profiles.

IMAGING

Usually unremarkable. May be abnormal with predisposing diseases (ectopic ureters, urolithiasis, urinary tract neoplasia, etc.), or UTI complications (polypoid cystitis, emphysematous cystitis, struvite urolithiasis, pyelonephritis, etc.).

**TREATMENT****APPROPRIATE HEALTH CARE**

Outpatient treatment is appropriate; inpatient treatment may be necessary with UTI complications or associated conditions (e.g., urinary tract obstruction, acute pyelonephritis).

ACTIVITY

Unrestricted.

DIET

Dissolution protocols for infection-induced struvite uroliths include temporary feeding of a calculolytic diet.

CLIENT EDUCATION

Prognosis is excellent with uncomplicated UTIs. Prognosis in patients with complicated UTIs may depend on resolution of any risk factors.

SURGICAL CONSIDERATIONS

Management of struvite uroliths, resistant polypoid cystitis, and infection niduses may require surgical intervention.

**MEDICATIONS****DRUG(S) OF CHOICE**

- “First-line” antimicrobials are excreted in active form at high concentrations, bactericidal, effective against most isolates, and inexpensive. “Second-line” antimicrobials lack some of these characteristics, and should be reserved for resistant isolates.
- When urine culture has not been performed, or pending culture results, then empiric treatment with a first-line antimicrobial is preferred.
- When susceptibility data is available, the lowest-tier antimicrobial should be selected.

- First-line antimicrobials:
 - Amoxicillin (11–15 mg/kg PO q8h)
 - Trimethoprim-sulfadiazine (15 mg/kg PO q12h)
- Second-line antimicrobials:
 - Amoxicillin-clavulanate (12.5–25 mg/kg PO q12h)
 - Enrofloxacin/marbofloxacin/orbifloxacin
 - Cefovecin (8 mg/kg SC)
- Third-line antimicrobials:
 - Amikacin (dogs, 15–30 mg/kg IV or SC q24h; cats, 10–14 mg/kg IV or SC)
 - Chloramphenicol (dogs, 40–50 mg/kg PO q8h; cats 12.5–20 mg/kg PO q12h)
 - Meropenem/imipenem-cilastatin
 - Nitrofurantoin (4.4–5.0 mg/kg PO q8h)
- Antibiotic treatment of uncomplicated infections is recommended for 7–10 days.
- Complicated infections may require treatment for 4–6 weeks.
- Shorter duration treatment (3–4 days) of uncomplicated infections may be sufficient, but cannot yet be routinely recommended.

**FOLLOW-UP****PATIENT MONITORING**

- Uncomplicated UTIs: resolution can be assumed if there is no recurrence of clinical signs after therapy is completed.
- Complicated UTIs: continue therapy for at least 7–10 days beyond resolution of clinical signs, pyuria, and bacteriuria. Resolution should be confirmed by repeating urine culture 7–10 days after end of therapy.

PREVENTION/AVOIDANCE

- Diagnosis and control of predisposing conditions is the most effective method for preventing UTIs.
- Ancillary therapies can be considered with recurrent infections:
 - Methenamine—converted into formalin when urine pH is <7.0. Concurrent administration of ascorbic acid (vitamin C) promotes urinary acidification.
 - Prophylactic antibiotics—once-daily administration of antibiotics may lengthen infection-free intervals; however, multidrug resistance is more likely in subsequent isolates.
 - Cranberry extract—may inhibit *E. coli* attachment to the bladder mucosa.

POSSIBLE COMPLICATIONS

UTIs may lead to pyelonephritis, struvite urolith formation, or polypoid cystitis.

EXPECTED COURSE AND PROGNOSIS

- Prognosis for patients with uncomplicated UTIs is good to excellent. The prognosis for patients with complicated infections is determined by successful control or resolution of predisposing conditions.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Struvite urolithiasis
- Polypoid cystitis
- Pyelonephritis
- Emphysematous cystitis

AGE-RELATED FACTORS

- Juvenile animals with recurrent UTIs should be evaluated for ectopic ureters, urolithiasis, or other urinary tract malformations, regardless of whether urinary incontinence has been reported.
- Adult cats with UTIs should be evaluated for chronic kidney disease, diabetes mellitus, and hyperthyroidism.

SYNONYMS

- Bacterial cystitis
- Urethritis
- Urethrocystitis

SEE ALSO

- Pyelonephritis
- Urolithiasis, Struvite—Cats
- Urolithiasis, Struvite—Dogs

L

ABBREVIATION

- UTI = urinary tract infection

Suggested Reading

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Author Barrak M. Pressler

Consulting Editor Carl A. Osborne



Client Education Handout
available online

LOWER URINARY TRACT INFECTION, FUNGAL



BASICS

OVERVIEW

- Infecting fungi/yeasts are usually normal commensal flora of the skin and mucosa, or environmentally ubiquitous organisms.
- Candida albicans* is the most common fungal isolate; other *Candida* spp. are less common, and non-*Candida* spp. fungi are least common. • Urinary shedding of fungal organism may occur with systemic fungal infections that have disseminated to the kidneys. This appears to be common in dogs with systemic *Aspergillus* spp. infection, and cats with *Cryptococcus neoformans*. • Organ system affected: renal/urolologic. • Uncommon in dogs and cats.

SIGNALMENT

- Dog and cat • No breed, age, or sex predilection

SIGNS

- Typical signs of lower urinary tract disease: dysuria and pollakiuria; gross hematuria is rare. • Many animals are asymptomatic.

CAUSES & RISK FACTORS

Suspected risk factors: diabetes mellitus, urinary tract stenosis (e.g., perineal urethrostomy, cystotomy tubes, indwelling urinary catheters), lower urinary tract disease (e.g., bladder transitional cell carcinoma, chronic bacterial urinary tract infection), recent or chronic antibiotic or glucocorticoid administration.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Isolated fungal lower urinary tract infections must be differentiated from systemic infections with secondary appearance of fungi in the urine. • Lower urinary tract fungal infections may rarely progress to pyelonephritis.
- Contamination of urine samples during collection may occur in animals with cutaneous or mucocutaneous yeast overgrowth (i.e., ventral abdominal or perivulvar dermatitis or balanoposthitis).

CBC/BIOCHEMISTRY/URINALYSIS

- CBC and biochemistry usually unremarkable. If infection has ascended to the upper urinary tract or has systemically disseminated then abnormalities will reflect those organs involved. • Yeast/fungi may be visible within urine sediment. However, low numbers of organisms may necessitate concentrated sediment preparations for visualization. • Fungal species cannot be determined solely based on cytologic appearance.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Urine Culture

- Candida* spp. usually grow within 3 days on standard blood agar. • Other fungi may grow more slowly and thus will not be detected by standard urine culture protocols. • If fungal urinary tract infection is suspected or confirmed, a fungal culture should be requested. Organism identification is based on growth characteristics and morphologic features on Sabouraud's dextrose agar.

Antifungal Sensitivity Testing

- C. albicans* is usually sensitive to fluconazole; therefore, antifungal sensitivity testing is not necessary at the time of initial diagnosis. • Non-*albicans* species of *Candida* are more commonly resistant to fluconazole, and thus sensitivity testing should be considered. • Susceptibility testing should be performed on non-*Candida* spp. organisms and with *Candida* spp. infections that fail to resolve despite 4–6 weeks of appropriate antifungal therapy.



TREATMENT

- Identify and correct any concurrent risk factors. • Urinary alkalinization has been historically recommended for treatment of funguria, but is of unknown benefit.



MEDICATIONS

DRUG(S)

- Oral fluconazole (5–10 mg/kg PO q12h) is the initial treatment of choice. • Itraconazole or ketoconazole may be effective in some patients, but are not recommended because of poor urinary excretion of active drug. • In patients with persistent infection despite 4–8 weeks of fluconazole, intravesicular (bladder) infusion of 1% clotrimazole (1% solution in PEG 400) may be considered.
- Intravesicular 1% clotrimazole infusion protocol: catheterize and empty the bladder. Infuse 7.5–10 mL/kg of 1% clotrimazole solution (volume should be determined by bladder palpation during infusion). Infused fluid should be retained for a minimum of 15–30 minutes; most cats will retain the infused drug if not allowed access to a litter box or urination area, whereas in dogs, balloon catheters may be required to prevent premature voiding. Repeat infusion q7 days for a minimum of three treatments. Repeat fungal urine culture approximately 1 week after third treatment to determine whether additional infusions are required. Oral

fluconazole therapy should be continued throughout the infusion protocol.

- Amphotericin B (intravenous or intravesicular) treatment has been attempted in sporadic cases, but efficacy is unknown.
- Benign neglect and regular monitoring may be considered in asymptomatic patients with persistent infections despite repeated treatment attempts. However, ascending infection (i.e., fungal pyelonephritis) and systemic dissemination may occur.

CONTRAINdications/POSSIBLE INTERACTIONS

- Intravesicular clotrimazole appears to be safe but has not been fully investigated.
- Intravesicular clotrimazole should be avoided in animals with recent bladder surgery or urethral trauma.



FOLLOW-UP

- Treatment should be continued until two successive urine cultures 14–21 days apart result in no fungal growth. • Fungal urine culture should be repeated approximately 60 days after cessation of therapy and at regular intervals thereafter.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Diabetes mellitus • Transitional cell carcinoma

SEE ALSO

- Aspergillosis chapters • Cryptococcosis

Suggested Reading

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Author Barrak M. Pressler

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LUMBOSACRAL STENOSIS AND CAUDA EQUINA SYNDROME



BASICS

DEFINITION

- Lumbosacral stenosis refers to narrowing of the lumbosacral vertebral canal and/or L7-sacral intervertebral foramina, causing compression of L7, sacral, or caudal nerves.
- Cauda equina syndrome implies pain or other clinical signs related to dysfunction of these nerves.

PATHOPHYSIOLOGY

- Congenital—abnormal vertebral development causing narrowing of the lumbosacral vertebral canal. Transitional vertebrae and other malformations are common at this site and may contribute to (early) disease progression.
- Acquired—bony and soft tissue degenerative changes, most commonly affecting the L7 intervertebral disc, that cause stenosis of the vertebral canal and/or intervertebral foramina. Specific syndrome of sacral osteochondrosis dissecans recognized in young German shepherds.

SYSTEMS AFFECTED

Nervous—specifically nerves from L7 caudally

GENETICS

No known genetic basis

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

- Reasonably common in dogs
- Uncommonly reported in cats but suspected with increasing frequency

Breed Predilections

- Congenital—small to medium dogs; border collies
- Acquired—any medium-large dog; frequently German shepherds, boxers, rottweilers

Mean Age and Range

- Congenital—3–8 years.
- Acquired—mean age at onset 6–7 years. Sacral osteochondrosis signs often appear ~ 1 year old.

Predominant Sex

- Congenital—none
- Acquired—male

SIGNS

- Lumbosacral pain—salient feature; may be the only clinical sign; may be evident in reluctance to jump or climb stairs. Pain on pressure on, or dorsiflexion of, the lumbosacral vertebral column (often also induced during extension of hip joints).

- Pelvic limb lameness—caused by lumbar 7th and/or sacral nerve dysfunction; may progress to pelvic limb weakness, muscle wasting, and postural reaction deficits.
- Urinary and/or fecal incontinence—caused by S1–3 nerve dysfunction.
- Abnormal tail carriage, tail weakness or paralysis—results from dysfunction of caudal nerves.
- Self-inflicted lesions—most often associated with congenital lesions or cauda equina inflammation.

CAUSES

- Congenital vertebral malformation, including transitional vertebrae, or osteochondrosis of the cranial sacrum.
- Intervertebral disc herniation (types I and II).
- Hypertrophy or hyperplasia of the interarcuate ligament.
- Proliferation of the articular facets and/or peri-articular soft tissues.
- Subluxation at the lumbosacral junction.
- Inflammatory or neoplastic disease of the vertebral canal can produce identical clinical signs (hence “cauda equina syndrome”).

RISK FACTORS

Dogs, especially German shepherds, with lumbosacral transitional vertebrae have increased risk to develop the syndrome.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hip dysplasia or other orthopedic disease (notably iliopsoas injury)—distinguish via thorough orthopedic examination ± imaging.
- Chronic discospondylitis, osteomyelitis, neoplastic disease—cannot be differentiated by clinical signs alone.
- Vertebral fractures and subluxations—acute; characterized by more bilateral signs.
- Localized meningo(my)ecephalitis or radiculoneuritis—usually more diffuse pain.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal.
- Urinalysis—may reveal lower urinary tract infection secondary to urinary incontinence, or associated with discospondylitis.

OTHER LABORATORY TESTS

If images suggest the need, CSF analysis may aid in diagnosing inflammatory (or infectious or neoplastic) disease.

IMAGING

- Radiology—commonly exhibit spondylosis at the lumbosacral junction; narrowing of the L7–S1 disc space; ventral displacement of the sacrum relative to the lumbar vertebrae; BUT interpret with caution because all these can be observed in clinically normal animals.

- CT and MRI—modalities of choice. Apparent abnormalities must be interpreted with regard to the whole clinical picture because many are also observed in normal animals.

DIAGNOSTIC PROCEDURES

- Electromyography—denervation may be detected in muscles innervated by the nerves L7 to caudal; denervation confirms localization of the lesion but is not specific for compressive lesions.
- Slowed sciatic-tibial nerve conduction or prolongation of F wave latencies may be detected.

PATHOLOGIC FINDINGS

- May see one or more of the following features:
 - Type II disc disease with bulging of dorsal annulus
 - Hypertrophy of the interarcuate ligament
 - Stenosis of the intervertebral foramen by soft tissue or bony proliferation compressing L7 nerve(s)
 - Ventral displacement of the sacrum in relation to lumbar vertebrae
 - Proliferation of articular facets and hypertrophy of joint capsule
 - Congenitally shortened pedicles
 - Thickened and sclerotic laminae and articular processes
 - Various vertebral malformations (not only transitional vertebrae).
- Cauda equina syndrome can also be associated with neoplasia, inflammation, infection.

L



TREATMENT

APPROPRIATE HEALTH CARE

- Urinary incontinence—in-patient for initial management.

NURSING CARE

- Urinary incontinence—manual expression or catheterize the bladder until adequate voluntary control returns; monitor for urinary tract infection and administer appropriate antibiotics following culture and sensitivity.

ACTIVITY

- Nonsurgical treatment—confinement and restricted leash walks, alone or combined with systemic anti-inflammatory drugs or analgesics, or epidural injection of corticosteroids, frequently alleviate pain; clinical signs may return with increasing levels of exercise.
- If treated surgically, restrict for 6–12 weeks; then gradual return to athletic function.

DIET

Avoid obesity; excess weight increases biomechanical stress on the spine.

LUMBOSACRAL STENOSIS AND CAUDA EQUINA SYNDROME (CONTINUED)

CLIENT EDUCATION

- Inform client that there may be progressive neurologic impairment of the pelvic limbs, urinary and fecal incontinence, and paralysis of the tail.
- Inform client that pelvic limb lameness and self-inflicted lesions result from pain associated with nerve root irritation and/or compression.
- Discuss surgical treatment which is appropriate for cases with severe pain and may be suitable for cases with neurologic deficits (especially incontinence, which may be difficult to reverse).
- Medical management is frequently successful for animals with mild pain and/or mild neurologic deficits only.

SURGICAL CONSIDERATIONS

Several options, each focused on alleviating the specific source of the problems defined by imaging—dorsal laminectomy, lateral foraminotomy or fixation-fusion may all be effective in specifically selected cases.



MEDICATIONS

DRUG(S) OF CHOICE

- NSAIDs—e.g., carprofen 2 mg/kg q12h for 5–7 days then reducing doses until used as required.
- Gabapentin—frequently used at ~ 20–30 mg/kg q8h may be effective (side effect: sedation).
- Epidural corticosteroid—methylprednisolone acetate 1 mg/kg (< 0.5 mL total volume).

CONTRAINDICATIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Syndrome progression, increasingly severe neurologic signs.
- Seroma formation—frequent sequela to surgery; can be effectively managed by cage rest and surgical drainage. Prevent by careful soft tissue closure.
- Adhesions between nerves and surrounding soft tissues after surgery.

- Recurrence of clinical signs following medical (commonly) or surgical (uncommonly) intervention.
- Failure of fixation-fusion implant.
- Fracture of articular process after excessive lateral bone excision at surgery.
- Infection (especially if an implant is used for surgery).

EXPECTED COURSE AND PROGNOSIS

- Vary with the severity of neurologic injury.
- Majority are successfully managed medically, but need to ensure outcome matches requirements for dog's way of life; surgery remains an option.
- If low lumbar pain and mild neurologic deficits—good prognosis after surgery; 70–80% have an excellent or good outcome.
- If fecal and urinary incontinence—guarded prognosis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Lower urinary tract infections frequently accompany urinary incontinence.

AGE-RELATED FACTORS

- If a lumbosacral transitional vertebra is present, syndrome may develop 1–2 years earlier than the average dog.
- Older large-breed dogs may have concomitant diseases that also cause neurologic deficits: type II disc protrusions at other sites, degenerative peripheral nerve disease (especially Labradors), degenerative myelopathy (especially German shepherds).

SYNOMYS

- Lumbosacral instability
- Lumbosacral malarticulation or malformation
- Lumbosacral spondylolisthesis
- Lumbosacral spondylopathy

SEE ALSO

- Discospondylitis
- Intervertebral Disc Disease, Thoracolumbar
- Intervertebral Disc Disease—Cats

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug

INTERNET RESOURCES

<http://veterinarymedicine.dvm360.com/vetmed/Medicine/Degenerative-lumbosacral-stenosis-in-dogs/Article-Standard/Article/detail/169902>

Suggested Reading

- De Risio L, Sharp NJ, Olby NJ, et al. Predictors of outcome after dorsal decompressive laminectomy for degenerative lumbosacral stenosis in dogs: 69 cases (1987–1997). *J Am Vet Med Assoc* 2001, 219(5):624–628.

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Client Education Handout
available online

LUNG LOBE TORSION



BASICS

OVERVIEW

- Twisting of lung lobe(s) at the hilus with occlusion or narrowing of the bronchus, lymphatics, vein, and (finally) arteries.
- Affected lobes—right middle lobe most commonly affected (especially in large dogs); other lobes can twist singly or in pairs. Occasionally torsion occurs in midlobar area. Pugs—left cranial lobe most common.
- Initially, the lobe becomes engorged with blood and enlarges; infarction and necrosis may follow; hemorrhagic pleural effusion typically develops, chylothorax also possible.
- Chronic survivors—may note shrinkage and fibrosis of the lobe.

SIGNALMENT

- Dogs and less commonly cats.
- More common in large, deep-chested dogs but small breed dogs can be affected.
- Afghans (with chylothorax).
- Any age.
- Spontaneous syndrome in pugs typically ≤ 4 years old.
- More common in males.

SIGNS

- Tachypnea, acute or chronic respiratory distress
- Lethargy
- Anorexia
- Fever
- Pain
- Orthopnea
- Cough, hemoptysis
- Retching
- Ventral thoracic dullness
- Tachycardia
- Pale mucous membranes
- Cyanosis
- Shock

CAUSES & RISK FACTORS

- Inconsistently found with preexisting conditions (e.g., trauma, neoplasia, and chylothorax; asthma/bronchitis in the cat). Atelectasis and/or pleural effusion seem to be predisposing factors.
- Thoracic or diaphragmatic surgery.
- Spontaneous or idiopathic.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pulmonary contusion or atelectasis
- Diaphragmatic hernia
- Pulmonary abscess or infarction
- Neoplasia, lymphomatoid granulomatosis
- Coagulopathy
- Pneumonia, embolization or thrombosis
- Congestive heart failure
- Pleural effusion and compression atelectasis

- Fungal or foreign body granuloma
- Lobar consolidation or bronchial obstruction from a foreign body
- Feline steatitis

CBC/BIOCHEMISTRY/URINALYSIS

Neutrophilia and anemia common. Neutropenia may carry poorer prognosis.

OTHER LABORATORY TESTS

Fluid analysis—pleural effusion can be hemorrhagic; with chronicity or preexisting effusions, the effusion may be a modified transudate or chylous.

IMAGING

Radiography

- Opacification of affected lobe with loss of visible lobar vessels and truncation of bronchus.
- Initially may reveal air bronchograms with proximal narrowing or disorientation of the torqued bronchus. Small gas bubbles with “sponge appearance” can be scattered throughout affected lobe (vesicular gas pattern); seen in 87% of one series.
- Progressive pleural effusion—suggested by ventral leafing and interlobar fissure lines.
- Consolidation and occasional swelling of the torqued lobe with possible displacement or rotation of the heart, trachea, or carina. Mediastinal shift can be contralateral or ipsilateral. Other lobes can be displaced.
- Thoracentesis provides therapeutic benefits and can improve visualization of intrathoracic structures.

Ultrasonography

- Thoracic ultrasound prior to fluid removal often allows better resolution of internal structures.
- Hypoechoic periphery with scattered reverberating foci (bronchial cartilage) centrally.
- Rounded edges of lobes.

Computed Tomography

Preoperative computed tomography may be helpful. Requires apnea induced by hyperventilation or breath-hold.

DIAGNOSTIC PROCEDURES

- Thoracentesis—obtain pleural fluid for analysis (modified transudate, exudate, hemorrhage, or chylous effusion possible).
- Bronchoscopy—may reveal occlusion or twist of the associated bronchus.
- Surgical exploration—for definitive diagnosis and treatment.



TREATMENT

- Thoracentesis or chest tube placement as needed.
- Intravenous fluid administration for support.
- Administer oxygen and treat for shock—when indicated.

- Anesthesia—requires adequate ventilatory support; carefully monitor patient.
- Surgical removal of the involved lobe(s)—only effective treatment; do not untwist lobe and attempt to salvage—may lead to recurrence or necrosis; in situ ligation of the vessels or clamping with non-crushing forceps has been advocated to avoid reperfusion problems such as acidosis; consider use of surgical stapling device; closely inspect remaining thoracic structures for any abnormalities; perform culture and pathologic examination of excised specimen.
- Post-surgery—monitoring; supportive care; tube drainage. Torsion of a second lung lobe may occur.



MEDICATIONS

DRUG(S)

- Antibiotics—perioperatively
- Treatment for shock—when indicated
- Pain control

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A

L



FOLLOW-UP

- Observe for recurrence of pleural effusion.
- Reexpansion pulmonary edema—can be a serious problem (especially in cats) if large volumes of pleural fluid are withdrawn quickly or if chronically compressed lungs are acutely inflated at surgery.
- Thoracic radiographs—before discharge; as needed thereafter.
- Prognosis—fair to good if no underlying abnormality remains.



MISCELLANEOUS

Suggested Reading

D'Anjou M, Tidwell AS, Hecht S.

Radiographic diagnosis of lung lobe torsion. Vet Radiol Ultrasound 2005, 46:478–484.

Neath PJ, Brockman DJ, King LG. Lung lobe torsion in dogs: 22 cases (1981–1999). J Am Vet Med Assoc 2000, 217:1041–1044.

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LUPUS ERYTHEMATOSUS, CUTANEOUS (DISCOID)



BASICS

OVERVIEW

- Considered to be a benign variant of systemic lupus erythematosus.
- One of the most common immune-mediated skin diseases in dogs.
- Predominantly involves the nasal planum, face, and ears with rare lesions beyond the head.

SIGNALMENT

- Dogs and cats.
- Very uncommon in cats.
- Predominant breeds—collie, German shepherd dog, Siberian husky, Shetland sheepdog, Alaskan malamute, chow chow, and their crosses.
- No age predilection.

SIGNS

- Initial symptom: depigmentation of nasal planum and/or lips.
- Depigmentation progresses to erosions and ulcerations.
- Loss of normal “cobblestone” architecture of the nasal planum.
- Tissue loss and scarring can occur.
- Chronic lesions are fragile and may easily hemorrhage; rarely severe hemorrhage from arteriole damage.
- May also involve pinnae and periocular region; rarely feet and genitalia.

CAUSES & RISK FACTORS

- Exact mechanism undetermined; actinic radiation may alter antigenic nature of keratinocytes.
- Seasonal and geographic exacerbation—associated with increased actinic radiation.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Major Considerations

- Other immune-mediated diseases (PF, PE, SLE)
- Drug reaction
- Dermatomyositis
- Nasal dermatophytosis
- Mucocutaneous pyoderma
- Insect bite hypersensitivity

Other (Rare) Considerations

- Contact allergy
- Zinc-responsive dermatosis
- Trauma
- Superficial necrolytic dermatitis
- Epitheliotropic cutaneous T-cell lymphoma
- Squamous cell carcinoma

CBC/BIOCHEMISTRY/URINALYSIS

Normal unless due to an underlying cause

OTHER LABORATORY TESTS

ANA, LE preparation, and Coombs' tests—usually normal or negative except in SLE.

OTHER DIAGNOSTIC PROCEDURES

- Biopsy and histopathology will differentiate DLE from other disorders.
- Biopsies of early lesions: depigmented areas, mild erosions, or mildly crusted lesions are preferable for diagnosis.

PATHOLOGIC FINDINGS

- Histopathology is characterized by interface-lichenoid dermatitis with prominent basal cell apoptosis, varying degrees of epidermal atrophy, and pigment incontinence.
- Not easily differentiated from mucocutaneous pyoderma by histopathology (treatment with antibiotics prior to sampling is helpful).
- Avoid sampling severely crusted, ulcerative lesions if possible.
- Immunopathologic examination may be done but is usually not necessary.



TREATMENT

- Not life-threatening but may be disfiguring.
- Avoid direct solar exposure; apply waterproof sun blocks.



MEDICATIONS

DRUG(S)

- Topical therapy:
 - Glucocorticosteroids—initially, a potent fluorinated product (e.g., 0.1% fluocinolone) q24h for 14 days; then q48–72h; once in remission switch to less-potent product (e.g., 0.5% or 2.5% hydrocortisone) if possible.
 - Tacrolimus ointment (0.1%) q12–24h initially then taper to q24–72h once in remission.
 - Systemic therapy:
 - Tetracycline and niacinamide—250 mg each PO q8h for dogs < 10 kg; 500 mg PO q8h for larger dogs (alternatives include doxycycline 10 mg/kg PO q24h and minocycline 5 mg/kg PO q12h).
 - Prednisone—consider for severe or non-responsive cases; 2–4 mg/kg/day either solely or in combination with azathioprine 2 mg/kg PO q48h; taper prednisone to 0.5–1 mg/kg PO q48h for long-term maintenance.
 - Cyclosporine—5–10 mg/kg PO q24h as alternative immunosuppressive therapy.
 - Consider systemic antibiotic treatment for a minimum of 3–4 weeks prior to systemic immunosuppressive therapy to differentiate from mucocutaneous pyoderma.
- Vitamin E 10–20 IU/kg PO q12h; may help reduce inflammation and protect the skin.
- Hydroxychloroquine—5 mg/kg q24h; antimalarial drug that has been used in human cases.



FOLLOW-UP

PATIENT MONITORING

- Recheck 2–4 weeks after initiating treatment to evaluate for clinical response.
- CBC and biochemistry—every 12 months if using topical therapy and every 3–6 months if using systemic therapy.
- CBC and platelet

counts—every 2 weeks for the first month; then every 3–6 months while on azathioprine.

PREVENTION/AVOIDANCE

Affected animals should avoid ultraviolet light exposure.

POSSIBLE COMPLICATIONS

- Scarring
- Secondary pyoderma
- Hemorrhage
- Disfigurement

EXPECTED COURSE AND PROGNOSIS

Progressive but not usually life-threatening if left untreated.

- With proper treatment, expect remission in majority of cases.
- Cases requiring chronic immunosuppressive therapy have a more guarded prognosis, but remissions are common with more aggressive therapy.



MISCELLANEOUS

SYNOMYMS

- Collie nose
- Nasal solar dermatitis

ABBREVIATIONS

- ANA = antinuclear antibody
- DLE = discoid lupus erythematosus
- LE = lupus erythematosus
- PE = pemphigus erythematosus
- PF = pemphigus foliaceus
- SLE = systemic lupus erythematosus

Suggested Reading

Griffies JD, Mendelsohn CL, Rosenkrantz WR, et al. Topical 0.1% tacrolimus for the treatment of discoid lupus erythematosus and pemphigus erythematosus in dogs. J Am Anim Hosp Assoc 2004; 40:29–41.

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LUPUS ERYTHEMATOSUS, SYSTEMIC (SLE)



BASICS

DEFINITION

A multisystem auto-immune disease characterized by the formation of antibodies against a wide array of self-antigens. Pathogenic antibodies, circulating immune complexes, and auto-reactive T-cells are the primary mediators of tissue injury.

PATOPHYSIOLOGY

- Cause unknown. • Antibodies directed toward a broad range of membrane, cytoplasmic, and nuclear antigens are produced, resulting in Type II hypersensitivity. • Antigen-antibody complexes are formed and deposited in a variety of sites including blood vessels, renal glomeruli, synovial membrane, choroid plexus, and skin, resulting in Type III hypersensitivity. • Production of auto-reactive T-cells causes Type IV hypersensitivity.
- Tissue injury is caused by activation of complement by circulating immune complexes, infiltration of inflammatory cells, and direct cytotoxicity of auto-antibodies against membrane-bound antigens. • Clinical manifestations depend on localization of the immune complexes and specificity of the auto-antibodies. • Genetic, environmental, pharmacologic, and infectious factors may be triggers for disease.

SYSTEMS AFFECTED

- Musculoskeletal—deposition of immune complexes in the synovial membranes. • Skin/Exocrine—deposition of immune complexes in the skin. • Renal/Urologic—deposition of immune complexes in the glomeruli.
- Hemic/Lymphatic/Immune—auto-antibodies against RBCs, leukocytes, platelets, or bone marrow precursors. • Other organ systems—if there is deposition of immune complexes or antibodies (muscle, nerve, eye, for example).

GENETICS

Heritable although not by simple autosomal mechanisms. Breeds that are predisposed include the German shepherd dog, Shetland sheepdog, collie, beagle, and poodle. Several colonies of dogs with a high predisposition toward SLE have been established, and there is an association with MHC (DLA) type. An immune-mediated disease in the Nova Scotia duck tolling retriever characterized by immune-mediated arthropathy and steroid-responsive meningitis-arteritis has been reported and is termed SLE-related disease in this breed.

INCIDENCE/PREVALENCE

Uncommon in dog, rare in cat

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Medium to large breeds. • German shepherd, poodle, and beagle overrepresented.
- German shorthaired pointers are predisposed to exfoliative cutaneous lupus erythematosus. • Rough collies and Shetland sheepdogs are predisposed to vesicular cutaneous lupus erythematosus. • Siamese and Persian cats may be at increased risk of SLE.

Mean Age and Range

The mean age is 5 years, range 6 months to 13 years.

Predominant Sex

Male dogs overrepresented in one study only.

SIGNS

Historical Findings

- Lethargy. • Anorexia. • Shifting-leg lameness. • Skin lesions. • Fever. • Weakness.
- Other findings depend on the organ(s) affected. • Onset of clinical signs may be acute or insidious. • Disease often has a waxing and waning course. • Different clinical manifestations are often sequential rather than concurrent.

Physical Examination Findings

- Swollen and/or painful joints are the major presenting sign in most patients. Joints are often swollen but not deformed (non-erosive).
- Cutaneous lesions may be symmetric or focal—erythema, scaling, ulceration, depigmentation, vesicles, ulcerated or draining nodules, and/or alopecia may be observed. • Ulceration of mucocutaneous junctions and oral mucosa. • Persistent or cyclic fever—especially in the acute phase.
- Lymphadenopathy. • Hepatosplenomegaly.
- Muscle pain or atrophy. • Neurologic signs.

CAUSES

Definitive cause not identified. T suppressor cells may be defective in dogs with SLE.

RISK FACTORS

Exposure to ultraviolet light may exacerbate the cutaneous lesions.



DIAGNOSIS

- Definitive diagnosis—positive ANA or LE test (or both), and two major signs or one major *and* two minor signs. • Probable diagnosis—positive ANA or LE cell test (or both) and one major *or* two minor signs.
- Major signs—polyarthritis, glomerulonephritis, skin lesions, hemolytic anemia, thrombocytopenia, polymyositis.
- Minor signs—fever of unknown origin, oral ulcers, peripheral lymphadenopathy, pleuritis, pericarditis, myocarditis, neurologic signs (seizures, neuropathy).

DIFFERENTIAL DIAGNOSIS

- Neoplastic diseases may be associated with circulating immune complexes; patient may have signs similar to those of SLE.
- Infectious diseases such as ehrlichiosis, leishmaniasis, and bartonellosis. Differentiation is important because SLE is treated with immunosuppressive drugs.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—may reveal anemia, leukopenia, leukocytosis, or thrombocytopenia; anemia may be moderate and nonregenerative (e.g., anemia of chronic disease) or severe and regenerative (e.g., hemolytic).
- Biochemistry—results vary widely, depending on the organ(s) affected.
- Urinalysis—repeatable elevated protein:creatinine ratio (> 1) with benign sediment and negative culture supports pathologic proteinuria due to glomerulonephritis.

OTHER LABORATORY TESTS

- ANA test—detects antibodies directed against nuclear antigens. False-positive results may be seen in normal dogs and cats and in those with infectious, inflammatory, or neoplastic diseases or those being treated with certain drugs (e.g., penicillins, sulfonamides, tetracyclines). Antinuclear antibodies are detected in 10–20% of dogs with seroreactivity to *Bartonella vinsonii*, *Erblichia canis*, and *Leishmania infantum*. False negatives also occur. • LE test—identifies phagocytized nuclear material within neutrophils and macrophages; positive result supports diagnosis of SLE; time-consuming to perform. • Direct antiglobulin (Coombs') test—identifies complement or antibody on the surface of RBCs; test should only be run in patients with anemia.

IMAGING

- Radiographs of affected joints reveal soft-tissue swelling consistent with non-erosive arthritis. • Thoracic and abdominal radiographs may demonstrate hepatomegaly or splenomegaly

DIAGNOSTIC PROCEDURES

- Arthrocentesis—high cell count with nondegenerate neutrophils and monocytes and low viscosity are characteristic findings.
- Bacterial culture of synovial fluid—negative.
- Blood culture in animals with fever—negative. • Skin biopsy—in patients with skin lesions; save specimen in 10% buffered formalin (for histopathologic examination) and Michel's solution (for immunofluorescence testing).

PATHOLOGIC FINDINGS

- Non-erosive polyarthritis with infiltration of synovial membranes by neutrophils and lymphocytes; no pannus formation.
- Membranous or membranoproliferative glomerulonephritis. • Mononuclear interface dermatitis with hydropic degeneration of

LUPUS ERYTHEMATOSUS, SYSTEMIC (SLE)

(CONTINUED)

keratinocytes and eosinophilic round bodies representing apoptotic basal keratinocytes.

- Vasculitis and panniculitis in some patients.
- Immunofluorescence—deposition of immune complexes along the basement membrane of the dermal-epidermal junction.
- Vasculitis may be seen in any organ, especially myocardium, pericardium, and meninges. • Reactive lymphoid hyperplasia in the lymph nodes and spleen.



TREATMENT

APPROPRIATE HEALTH CARE

- Hospitalization—may be necessary for initial management (e.g., in a patient with hemolytic crisis).
- Outpatient management—often possible.

NURSING CARE

Supportive care varies with systems affected.

ACTIVITY

- Enforced rest—during episodes of acute polyarthritis.
- Avoid sunlight if photosensitization suspected.

DIET

Restricted protein, high-quality protein diet with n-3 fatty acid supplementation is recommended in animals with glomerulonephritis.

CLIENT EDUCATION

- Discuss the progressive and unpredictable course of the disease.
- Discuss the need for long-term, immunosuppressive therapy and its side effects.
- Discuss heritability of the disease.

SURGICAL CONSIDERATIONS

None



MEDICATIONS

DRUG(S) OF CHOICE

- Corticosteroids—to control the abnormal immune response and reduce inflammation; e.g., prednisone (1–2 mg/kg PO q12h).
- Cytotoxic immunosuppressive drugs—add when prednisone fails to improve the condition after 7–10 days or if the patient is steroid intolerant.
- Azathioprine (dogs, 2 mg/kg PO q24h until remission, then q48h).
- Chlorambucil (cats, 0.1–0.2 mg/kg PO q24h initially, then q48h).
- Cyclosporine—microemulsion, e.g., Atopica—dogs, 5–10 mg/kg/day PO divided twice daily; cats, 0.5–3 mg/kg PO q12h.

Measurement of trough cyclosporine concentration recommended.

- Gradually taper doses (no more often than every 3–4 weeks) once remission is achieved.

PRECAUTIONS

- Cats are susceptible to azathioprine toxicity and the drug is not recommended for use in this species.
- Azathioprine and chlorambucil may both cause bone marrow suppression.
- Treatment with immunosuppressive drugs can increase the risk of severe infection.
- Cyclosporine may cause gastrointestinal upset, papillomatosis, and gingival hyperplasia.

POSSIBLE INTERACTIONS

Concurrent use of aspirin and prednisone increases the risk of gastrointestinal ulceration.

ALTERNATIVE DRUG(S)

- Levamisole: dogs, 2–5 mg/kg PO every other day for 4 months (max 150 mg per patient) combined with prednisone 0.5–1.0 mg/kg PO q12h. The prednisone is tapered over 1–2 months and the levamisole continued for 4 months.
- Other immunosuppressive drugs can be considered depending upon the clinical manifestations exhibited (mycophenolate mofetil for immune-mediated hemolytic anemia, leflunomide for immune-mediated hemolytic anemia, polyarthritis, and myasthenia gravis).



FOLLOW-UP

PATIENT MONITORING

- Physical examination—weekly.
- CBC and biochemical analysis—to monitor the side effects of cytotoxic immunosuppressive drugs; day 7 then every 2–4 weeks.
- ANA—often remains elevated during remission but may fall as patient improves clinically.

PREVENTION/AVOIDANCE

Do not breed affected animals.

POSSIBLE COMPLICATIONS

- Renal failure and nephrotic syndrome secondary to glomerulonephritis.
- Bronchopneumonia, urinary tract infection, or sepsis secondary to immunosuppression.

EXPECTED COURSE AND PROGNOSIS

Prognosis is guarded. The presence of hemolytic anemia and glomerulonephritis and the development of bacterial infection warrant a poor prognosis.



MISCELLANEOUS

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

The use of cytotoxic immunosuppressive drugs in pregnant animals is contraindicated.

SEE ALSO

- Anemia, Immune-Mediated
- Glomerulonephritis • Polyarthritis, Non-erosive, Immune-Mediated
- Thrombocytopenia, Primary Immune-Mediated

ABBREVIATIONS

- ANA = antinuclear antibody • LE = lupus erythematosus • RBC = red blood cell
- SLE = systemic lupus erythematosus

INTERNET RESOURCES

<http://www.vin.com>

Suggested Reading

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Client Education Handout
available online

LYME BORRELIOSIS



BASICS

DEFINITION

- One of the most common tick-transmitted zoonotic diseases in the world.
- In man caused by spirochete species of the *Borrelia burgdorferi* sensu lato complex (e.g., *B. burgdorferi* sensu stricto, *B. afzelii*, *B. bavariensis*, *B. garinii*, and others).
- Dominant clinical feature (dogs)—recurrent lameness due to arthritis; sometimes anorexia and depression; may develop renal disease.
- Reported in humans, dogs, horses, and sporadically in cats.

PATHOPHYSIOLOGY

• Arthritis—caused by the presence of migrating spirochetes in tissue and subsequent cellular and humoral immune responses of the host.

- Local skin infection after a tick bite is followed weeks to months later by a generalized infection of predominantly connective tissue in joints, tendons, muscles, and lymph nodes.
- While an *erythema migrans* (EM) may be observed at the site of *Bb* inoculation, this lesion is unique to human. The EM is not seen in dogs.
- Immune complexes with *Bb*-specific antigens have been demonstrated in dogs and can be deposited in the kidneys; viable *Bb* organisms are not found in the kidneys.
- The incubation period in experimentally infected dogs is 2–5 months.

SYSTEMS AFFECTED

- Persisting *Bb* organisms—found in tissues with a high content of collagen (skin, joints, tendons, pericardium, peritoneum, meninges, muscle, heart, and lymph nodes); rarely found in body fluids (blood, CSF, and synovial fluid).
- Pathologic changes—with few exceptions restricted to joints, draining lymph nodes; in rare cases involvement of the kidneys.

GENETICS

Certain dog breeds are reported to develop severe renal failure (e.g., Bernese mountain dogs, Labrador, Golden retriever).

INCIDENCE/PREVALENCE

- Seroprevalence in dogs within a population varies greatly with exposure to infected ticks in endemic areas; in the upper Midwest and northeast of the United States and in central Europe seroprevalence is 2–10%.
- Clinically apparent LB develops in a fraction of infected individuals; mechanisms unclear; however, co-infections with other organisms (e.g., *Anaplasma phagocytophilum*) may impact on clinical outcome.

GEOGRAPHIC DISTRIBUTION

- Northern hemisphere (North America, Europe, Asia).
- United States—the majority of cases have been reported in the Mid-Atlantic to New England coastal states, northeastern states, and upper midwestern states. Ecologic

conditions supporting LB exist in adjacent states and also on the West Coast.

- Europe—absent or less frequent in areas bordering to the Mediterranean basin.

SIGNALMENT

Species

Dog and rarely cat

Mean Age and Range

Experimentally, young dogs (pups) appear to be more susceptible than adult dogs.

SIGNS

- Recurrent lameness due to arthritis.
- Experimentally, acute form lasts for only 3–4 days; reoccurs days to weeks later in the same or other limbs (shifting lameness); one or more joints may be swollen and warm; a pain response is elicited by palpation; responds well to antibiotic treatment.
- Affected dogs may refuse to walk or stand or walk stiffly with an arched back and may be sensitive to touch.
- Chronic non-erosive polyarthritis found in animals with prolonged infection without adequate treatment; may persist despite antimicrobial therapy.
- Fever, anorexia, and depression may accompany arthritis.
- Superficial lymph nodes close to the infecting tick bite may be swollen.
- Kidneys—reported glomerulonephritis with immune-complex deposition in the glomeruli leading to fatal renal disease; patients may present with renal failure (vomiting, diarrhea, anorexia, weight loss, polyuria/polydipsia, peripheral edema or ascites); protein loss (protein-losing nephropathy); hypoalbuminemia.

CAUSES

- *Bb*—transmitted by hard-shelled tick species of the genus *Ixodes* (e.g., *I. scapularis*, *I. pacificus*, *I. ricinus*, *I. persulcatus*).
- Infection—only after a tick (nymph or adult female) has been attached to the host for at least 18 hours.

Ixodes Ticks

- Have a 2- to 3-year life cycle depending on availability of hosts.
- Uninfected eggs are deposited in midsummer.
- Larvae—hatch a few weeks later; become infected by feeding on small mammals or birds that carry *Bb* organisms.
- Nymphs—larvae molt into nymphs in the spring of the following year; stay infected or become infected by feeding again on mammals, birds, or lizards.
- Adults—nymphs molt into adults in summer and stay infected; females mate and feed on larger mammals (e.g. deer); drop off and hide under leaves until the following summer, when they each lay about 2,000 eggs; males usually do not attach and do not feed.

RISK FACTORS

Canine LB is a peri-domestic disease due to expansion of housing into tick habitat; outdoor activities; roaming in and travel to endemic areas places dogs at risk.



DIAGNOSIS

Diagnosis of LB is a clinical conclusion made on the basis of compatible clinical signs, response to antibiotic therapy, exclusion of other diagnoses, appropriate laboratory data (particularly antibody testing), and history of exposure to an epidemiologic environment that provides the opportunity for infection with *Bb*.

DIFFERENTIAL DIAGNOSIS

- Lyme arthritis—differentiate from other inflammatory arthritic disorders.
- Bacteria—anaplasmosis; ehrlichiosis; Rocky Mountain spotted fever; others.
- Immune-mediated diseases—idiopathic, lupus erythematosus, rheumatoid arthritis.
- Specific breed diseases—Akita arthritis, shar-pei fever.
- Rule-out other disorders with serologic assays and immune testing (anticellular antibodies; lupus erythematosus preparations).

CBC/BIOCHEMISTRY/URINALYSIS

- With arthritis only—unremarkable.
- With protein-losing glomerulopathy—uremia, proteinuria, hypercholesterolemia, hyperphosphatemia, and hypoalbuminemia usually occur.

L

OTHER LABORATORY TESTS

- Fluid from affected joints—high WBC counts (up to 75,000/ μ L; up to 97% PMNs).
- Detection of specific antibodies indicates only exposure to *Bb* antigens; Western blotting/line immunoassay/fluorescent bead-based multiplex assay allow differentiation between vaccination and infection; cross-reaction with antibodies induced by other bacterial infections is only problematic in tests with lysate antigen preparations.
- The membrane ELISA in-house test (SNAP 3Dx or 4Dx, IDEXX Labs, Westbrook, ME) detects a subgroup of antibodies against the outer surface protein VlsE of *Bb* using the C6 peptide; convenient test that only indicates infection and does not respond to vaccine-induced antibodies—C6-specific antibodies normally drop or may even disappear approximately 4–6 months after antibiotic therapy. Low to moderate pre-therapy levels do not drop significantly.

IMAGING

Radiographs—help identify effusions in the joint; may help distinguish erosive from non-erosive joint disease; rule out trauma.

DIAGNOSTIC PROCEDURES

- Organisms can be demonstrated regularly in tissue samples taken from skin or synovium after experimental infections with PCR or culture; however, under field conditions these tests are time-consuming and unreliable (not recommended).
- Blood samples particularly are typically negative when tested with PCR or culture.

LYME BORRELIOSIS

(CONTINUED)

PATHOLOGIC FINDINGS

Gross

- Swollen joints with excess synovial fluid.
- Sometimes enlarged lymph nodes.

Histopathology

- Acute, clinically apparent arthritis—fibrinopurulent synovitis.
- Other joints—may have mild synovitis with infiltration of lymphocytes and plasma cells.
- Lymph nodes—may show cortical hyperplasia with multiple enlarged follicles and expanded parafollicular areas.
- Skin near tick bite site—shows perivascular infiltrates of plasma cells, lymphocytes, and some mast cells in the superficial dermis.
- Renal lesions—glomerulonephritis, diffuse tubular necrosis with regeneration, and interstitial inflammation.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient

NURSING CARE

Keep patient warm and dry.

ACTIVITY

Reduced activity until clinical signs improve.

DIET

No change needed

CLIENT EDUCATION

- Inform client of importance of regular application of antibiotics as prescribed.
- A case of diagnosed canine LB should prompt a discussion of the risk to humans living in the same area as the dog.

SURGICAL CONSIDERATIONS

Aspiration of synovial fluid—may be considered for diagnostic purposes.



MEDICATIONS

DRUG(S) OF CHOICE

- Most commonly used antibiotics—doxycycline (5–10 mg/kg PO q12h; with food; vomiting and gastritis possible), amoxicillin (20 mg/kg PO q8–12h) or azithromycin (25 mg/kg PO q24h).
- Doxycycline—preferred when a co-infection with *Anaplasma phagocytophilum* occurs.
- Antibiotics—do not terminate the infection completely; consequently, persistent infection with a very low bacterial burden remains; treatment significantly improves clinical signs and pathology.
- Recommended treatment period—4 weeks.

CONTRAINDICATIONS

Consider potential side effects of applied drugs.

PRECAUTIONS

Doxycycline can be used in young (<6 months old) animals.

ALTERNATIVE DRUG(S)

- Corticosteroids—may initially ameliorate signs; mask effects of antibiotics for diagnostic purposes; enhance clinical signs later by immunosuppression.
- Nonsteroidal pain medications—use judiciously to avoid masking signs.



FOLLOW-UP

PATIENT MONITORING

- Improvement—in acute Lyme arthritis seen within 2–5 days of antibiotic treatment.
- If no improvement or if signs exacerbate—consider a differential diagnosis.

PREVENTION/AVOIDANCE

- Mechanical removal of ticks—groom animals daily.
- Prevention of tick attachment—acaricides and repellents (do not use permethrin on cats) supplied as spot-on, sprays, collars or pills/chewables.
- Vaccines—all vaccines currently available depend predominately on the effect of antibodies against the spirochetes' outer surface protein A (OspA). These antibodies prevent the spirochetes' migration within the feeding tick from the gut into the salivary glands. Commercially available vaccines for dogs contain non-adjuvanted recombinant OspA or OspA and numerous antigens (e.g., OspC) in adjuvants (bacterins) produced from inactivated cultured *Bb* organisms. Studies have shown that the protection rate improves over time due to booster immunizations that induce higher and longer-lasting vaccine antibody titers.
- Tick population control in the environment—restricted to small areas; limited success by reducing deer and/or rodent population.

POSSIBLE COMPLICATIONS

Fatal renal failure

EXPECTED COURSE AND PROGNOSIS

- Recovery from acute lameness expected 2–5 days after initiation of antibiotic treatment.
- Disease may be recurrent with intervals of weeks to months; responds again to antibiotic treatment.



MISCELLANEOUS

AGE-RELATED FACTORS

- Young pups appear to be more susceptible than adult dogs under experimental conditions.
- Disease can occur in dogs of all ages.

ZOONOTIC POTENTIAL

- Occurs in humans; source of infection is infected ticks.
- Dogs can transport unattached ticks, which later attach to humans—however, *Ixodid* are not intermittent feeders; once tick starts feeding on a dog, it usually feeds to repletion and does

not change hosts.

- LB cannot be transmitted directly from dogs to humans.

PREGNANCY/FERTILITY/BREEDING

- Although possible, there is no convincing evidence that *Bb* infection is transmitted *in utero* in dogs.
- Pregnant animals tolerate antibiotic treatment; do not use tetracyclines.
- Maternal C6-specific antibodies can be passed from dams to puppies.

SYNOMYMS

- Lyme arthritis • Lyme disease

ABBREVIATIONS

- *Bb* = *Borrelia burgdorferi*
- CSF = cerebrospinal fluid
- ELISA = enzyme-linked immunosorbent assay
- IFAT = immunofluorescence antibody test
- LB = Lyme borreliosis
- PCR = polymerase chain reaction
- PMN = polymorphonuclear neutrophil
- WBC = white blood cell

INTERNET RESOURCES

- Centers for Disease Control and Prevention: <http://www.cdc.gov/lyme>
- European Centre of Disease Prevention and Control: http://www.ecdc.europa.eu/en/healthtopics/emerging_and_vector-borne_diseases/tick_borne_diseases/lyme_disease
- European Union Concerted Action on Lyme Borreliosis: <http://www.eucalb.com>
- National Institutes of Health: <http://www.niaid.nih.gov/topics/lymedisease>

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**Client Education Handout
available online**



BASICS

DEFINITION

- Inflammation of one or more lymph nodes characterized by active migration of neutrophils, macrophages, or eosinophils into the node.
- Lymphoid hyperplasia is not a form of lymphadenitis.

PATOPHYSIOLOGY

- Usually the result of an infectious agent gaining access to a lymph node and establishing infection; because of the filtration functions of lymph nodes, they are likely to be exposed to infectious agents.
- Many organisms can cause inflammation, but agents such as fungi and mycobacteria that reside within macrophages and elicit a granulomatous inflammatory response are especially prone to establishing infection within lymph nodes.
- Non-infectious—occurs infrequently; an example is eosinophilic lymphadenitis that occurs as an occasional component of eosinophilic inflammatory diseases.

SYSTEMS AFFECTED

- Hemic/Lymphatic/Immune.
- May be a component of a more widespread infectious disease.

GENETICS

- No known genetic basis.
- Exception—rare cases of immunodeficiency; e.g., the familial susceptibility of certain basset hounds to mycobacteriosis, of which lymphadenitis is a frequent manifestation; Rottweilers may be predisposed to idiopathic hypereosinophilic syndromes causing eosinophilic lymphadenitis.

INCIDENCE/PREVALENCE

- Frequent manifestation of a number of infectious diseases.
- Precise incidence is unknown.

GEOGRAPHIC DISTRIBUTION

Same as for systemic fungal infections such as histoplasmosis (central United States) and blastomycosis (central and eastern United States) and, less commonly, leishmaniasis (southern and southwestern United States).

SIGNALMENT

Species

Dogs and cats

Breed Predilections

None

Mean Age and Range

Because of their susceptibility to infection, neonates may have a higher rate of occurrence than older animals.

Predominant Sex

None

SIGNS

General Comments

- Complications of infection in another organ—usually relate to that organ rather than to the inflamed lymph node.
- Component of systemic infection—associated with systemic inflammatory disease: fever, malaise, and anorexia.

Historical Findings

- Seldom causes lymph node enlargement that is severe enough to be observed by owners.
- Systemic signs of inflammatory disease or organ dysfunction.

Physical Examination Findings

- Inflamed lymph nodes are typically large and firm and may be painful.
- Bacterial—animal may develop abscesses within the nodes that may open to the exterior and present as draining tracts.
- Animals may also have fever and other systemic signs of infection.

CAUSES

Bacteria

- Most pathogenic aerobic and anaerobic species have occasionally been reported.
- More likely agents—*Pasteurella*, *Bacteroides*, and *Fusobacterium* spp.
- A few, such as *Yersinia pestis* (bubonic plague) and *Francisella tularensis* (tularemia), have a particular affinity for lymph nodes and are especially likely to be manifest as lymphadenitis, especially in cats.
- Bartonella vinsonii* infection may cause granulomatous lymphadenitis in dogs. *Bartonella* spp. can cause lymphoid hyperplasia in cats; however, organisms are not detected with routine stains.

Fungi

- Infections commonly include lymphadenitis as one manifestation of systemic disease.
- Likely organisms include *Blastomyces*, *Cryptococcus*, *Histoplasma*, *Coccidioides*, and *Sporothrix*.
- Many other mycotic agents have occasionally been reported.

Viruses

- Many viral infections implicated because of lymphoid hyperplasia.
- Coronavirus (FIP).
- Mesenteric lymph nodes are most commonly affected.

Other

- Protozoa—animals with toxoplasmosis and leishmaniasis frequently have lymphadenitis, although it is unlikely to be the most obvious clinical finding.
- Algae—lymphadenitis is often one manifestation of canine protothecosis.
- Non-infectious (e.g., associated with pulmonary or systemic eosinophilic disease)—usually unknown.

RISK FACTORS

- Animals with compromised immune function are susceptible to infection and, therefore, to lymphadenitis.
- FeLV and FIV are among the more common causes of immune compromise in veterinary patients.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Must ascertain that a palpable or visible mass is actually a lymph node and not a neoplastic mass or inflammatory process such as sialoadenitis.
- Frequently cannot be distinguished on the basis of clinical findings from other causes of lymphadenomegaly, such as lymphoid hyperplasia, lymphoma, and metastatic neoplasia.
- Fever and painful lymph nodes are likely to be associated with lymphadenitis.
- Lymphoma and lymphoid hyperplasia are more common causes of generalized lymph node enlargement than is lymphadenitis.

CBC/BIOCHEMISTRY/URINALYSIS

- Although affected animals may have an inflammatory leukogram, the absence of such changes does not exclude the diagnosis.
- Some animals with systemic causes of lymphadenitis (e.g., fungal infections, leishmaniasis) may have marked hyperglobulinemia.
- Circulating eosinophilia, often severe, is a relatively consistent finding in animals with eosinophilic diseases that are extensive and severe enough to cause lymphadenitis.
- Biochemistry results may reflect the degree of organ involvement from the underlying disease process.

OTHER LABORATORY TESTS

Serologic tests for the various systemic fungal diseases and possibly *Bartonella* spp. can be useful for identification, although these tests are best used only when attempts to demonstrate the organisms fail.

IMAGING

Radiography and ultrasonography—involve of internal nodes, such as those in the thoracic and abdominal cavities, in patients with systemic inflammatory disease; valuable in assessing involvement of other organs, e.g., pneumonia in a patient with blastomycosis or histoplasmosis.

DIAGNOSTIC PROCEDURES

- Fine-needle aspiration cytology is sufficient to diagnose most cases; a simple hematologic (Romanowsky) stain (e.g., Diff-Quik) is usually suitable.
- Gram staining can be performed in patients suspected of bacterial infection.

LYMPHADENITIS

(CONTINUED)

- Cytologic findings—high proportion of neutrophils, macrophages, eosinophils, or some combination of those cell types, which are only rarely seen in normal lymph nodes.
- Bacteria, fungal agents, protozoa, and algae—often present in fine-needle aspirates of lymph nodes from animals with those infections; cytologic examination frequently is the most efficient means of detecting and identifying specific infectious agents in animals with either lymphadenitis of an isolated node or systemic infection.
- When a diagnosis is not made by cytologic examination, a lymph node biopsy may be indicated; specimens can be used for both histopathologic evaluation and culture.

PATHOLOGIC FINDINGS

- Although affected lymph nodes may be grossly normal, they are more frequently large and firm; the extent of enlargement varies widely and often distorts the shape of the node.
- Severe lymphadenitis may extend through the capsule of the node into adjacent tissues.
- On cut surface, affected nodes are often hyperemic and may have poorly defined nodules; in extreme examples of purulent lymphadenitis, abscesses may develop.
- Histologic lesions of purulent lymphadenitis include diffuse or multifocal infiltration of the affected node by neutrophils; the normal cortical-medullary architecture of the node may be disrupted.
- Granulomatous lymphadenitis—accumulations of activated macrophages involving the parenchyma of the node.
- Eosinophilic lymphadenitis—large numbers of eosinophils both within sinuses and in the cortical parenchyma.
- Necrosis common in all forms.



TREATMENT

APPROPRIATE HEALTH CARE

- Because lymphadenitis is a lesion rather than a specific disease, no single set of therapeutic recommendations is appropriate.
- The characteristics of the inflammation and the causative agent dictate appropriate treatment.

NURSING CARE

N/A

ACTIVITY

N/A

DIET

N/A

CLIENT EDUCATION

N/A

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

- Effective drug therapy requires identification of the causative agent.
- Purulent lymphadenitis of a single lymph node is likely to be of bacterial cause and can be treated with broad-spectrum systemic antibiotics if no organism is detected on initial cytologic evaluation.

PRECAUTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PREVENTION/AVOIDANCE

N/A

EXPECTED COURSE AND PROGNOSIS

N/A



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Multiple affected lymph nodes—frequently a manifestation of systemic infection that also affects many other organs.
- Detection of fungi, protozoa, or algae in any inflamed node should alert one to the possibility of systemic infection by that agent.

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

- Bubonic plague, tularemia, and mycotic organisms present some risk of human infection.
- Specimens from affected animals should be handled cautiously.

PREGNANCY/FERTILITY/BREEDING

N/A

ABBREVIATIONS

- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus

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LYMPHADENOPATHY



BASICS

DEFINITION

Abnormally large lymph nodes, generalized or localized to a single node or group of regional nodes

PATOPHYSIOLOGY

- Can result from hyperplasia and reactivity of lymphoid elements, inflammatory infiltration, or neoplastic proliferation within the lymph node.
- Because of their filtration function, lymph nodes often act as sentinels of disease in the tissues they drain; inflammation of any tissue is often accompanied by enlargement of the draining nodes, which most likely results from reactive lymphoid hyperplasia but may also be caused by extension of the inflammatory process into the nodes (lymphadenitis).
- Reactive hyperplasia involves proliferation of lymphocytes and plasma cells in response to antigenic stimulation; hyperplasia alone involves proliferation of lymphocytes only and is an early stage of reactive hyperplasia.
- Lymphadenitis—implies active migration of neutrophils, activated macrophages, or eosinophils into the lymph node.
- Infectious agents may be involved.
- Neoplastic proliferation may be either primary (malignant lymphoma) or metastatic.

SYSTEMS AFFECTED

Hemic/Lymphatic/Immune

SIGNALMENT

- Dogs and cats
- No breed, sex, or age predilection

SIGNS

- Typically does not cause clinical signs.
- Severe—may cause mechanical obstruction and interference with the function of adjacent organs, signs of which depend on the affected lymph node and may include dysphagia, regurgitation, respiratory distress, dyschezia, and limb swelling.
- Dogs and cats may be systemically ill from the underlying disease process.

CAUSES

Lymphoid Hyperplasia/Reactivity

- Localized or systemic infection caused by infectious agents of all categories (i.e., bacteria, viruses, fungi, protozoa, and algae) when infection does not directly involve the node.
- Some infectious agents may produce lymphadenitis of certain lymph nodes with concurrent hyperplasia of other nodes that are not directly infected.
- Other infectious agents (e.g., rickettsia, *Bartonella* spp., and *Brucella canis*)—hyperplasia without overt lymphadenitis.
- FIV and FeLV infection—generalized hyperplasia, although lymphoid depletion may occur late in the course of the disease;

lymphadenitis can develop with a secondary infection.

- Antigenic stimulation by factors other than infectious agents (e.g., allergens).
- May develop in animals with immune-mediated disease (e.g., SLE and rheumatoid arthritis).

Lymphadenitis

- Bacteria—capable of causing purulent lymphadenitis, which may progress to abscessation; a few (e.g., *Mycobacterium* spp., *Bartonella* spp.) induce granulomatous lymphadenitis; other agents include aerobic and anaerobic organisms, *Pasteurella*, *Bacteroides*, *Fusobacterium*, *Yersinia pestis*, and *Francisella tularensis*.
- Fungi—systemic infections from histoplasmosis, blastomycosis, cryptococcosis, and sporotrichosis.
- Uncommon—protozoa, algae, and metazoan parasites.
- Several involved lymph nodes—frequently a manifestation of systemic infection, such as histoplasmosis or blastomycosis.
- Although primary infection of the lymph nodes does occur, lymphadenitis is usually accompanied by (and often results from) infection of other tissues being drained by the affected node.
- Eosinophilic—may be associated with allergic inflammation of the organ being drained by the affected lymph node (e.g., skin affected with flea allergy dermatitis); may be encountered in a patient with multisystemic idiopathic eosinophilic disease, such as feline and canine hypereosinophilic syndromes, or in a lymph node draining a mast cell tumor.
- Lymphadenitis and reactive hyperplasia often occur together.

Neoplasia

- Cats—neoplastic transformation of lymphocytes by FeLV.
- Dogs—lymphoma, cause unknown.
- Most tumors that metastasize to the lymph nodes—unknown.

RISK FACTORS

- Impaired immune function predisposes to infection and, therefore, to lymphadenitis.
- Animals with allergic diseases are likely to develop lymph node hyperplasia or eosinophilic lymphadenitis.
- Lymphoma (cats)—infection with FeLV, FIV.
- Lymphadenomegaly caused by metastatic neoplasms—vary with the type of primary neoplasm.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- A mass in a location characteristic of a lymph node usually can be assumed to be

one; cytologic evaluation of a fine-needle aspirate usually resolves any doubt.

- Palpable lymph nodes in normal dogs—mandibular, prescapular, axillary, superficial inguinal, and popliteal nodes; facial, retropharyngeal, and iliac nodes are palpable when larger than normal.
- Severe lymph node enlargement (> 5 times normal size)—most likely to develop in patients with abscessation (lymphadenitis) and lymphoma.
- Lesser degrees of enlargement—attributable to reactive hyperplasia, lymphadenitis, or neoplasia.
- Extent of enlargement in patients with metastatic disease varies widely.
- Multiple lymph nodes affected throughout the body—likely the result of lymphoma or systemic infection that causes either lymphadenitis or lymphoid hyperplasia.
- Abscessation and metastatic neoplasms usually affect a single lymph node.

CBC/BIOCHEMISTRY/URINALYSIS

- Cytopenias—seen with lymphoma, anemia of chronic disease, stress, splenic disease, or neoplastic infiltration of the bone marrow; also seen with rickettsial or viral disease.
- Lymphocytosis—suggests rickettsial disease (dogs) and lymphoid neoplasia (dogs and cats); atypical lymphocytes in the blood help establish a diagnosis of lymphoid neoplasia.
- Eosinophilia—may occur in animals with lymphadenopathy due to allergic or parasitic skin disease.
- Neutrophilia, with or without a left shift—may develop in patients with lymphadenitis, lymphoid hyperplasia, or neoplasia.
- Hypercalcemia—relatively common in dogs and rare in cats with lymphoma.
- Hyperglobulinemia—may develop in patients with chronic inflammatory disease or lymphoid neoplasia.

OTHER LABORATORY TESTS

- Cats—test for FeLV antigen and FIV in animals with large lymph nodes; infected animals may have lymphoma, lymphoid hyperplasia, or even lymphadenitis caused by immunosuppression.
- Serologic tests for antibodies against systemic fungal agents such as *Blastomyces* and *Cryptococcus* or bacteria such as *Bartonella* spp. may help establish those diagnoses.

IMAGING

- Radiography and ultrasonography—involve lymph nodes within the body cavity.
- Lesions associated with lymph node enlargement may be detected in other organs (e.g., diffuse pneumonia in dogs with blastomycosis, and primary tumor in animals with lymphadenomegaly caused by metastatic neoplasia).

LYMPHADENOPATHY

(CONTINUED)

DIAGNOSTIC PROCEDURES

Cytologic Examination

- Aspirates from affected lymph nodes help determine the major category of lymphadenomegaly (i.e., hyperplasia, inflammation, or neoplasia) and may provide a specific diagnosis in patients with certain infectious diseases or neoplasms; a standard hematologic (Romanowsky) stain (e.g., Diff-Quik) is suitable in most cases.
- Gram staining can be performed in animals suspected of bacterial lymphadenitis.
- Aspirates from reactive and hyperplastic lymph nodes contain a mixed cell population in which small lymphocytes predominate along with large lymphocytes, plasma cells, occasional neutrophils, and perhaps a few eosinophils and mast cells.
- Aspirates from lymph nodes affected by lymphadenitis contain high proportions of neutrophils, macrophages, and/or eosinophils, depending on the cause of the inflammation; specific infectious agents, such as bacteria and systemic fungi, may be evident.
- Frequently the means of diagnosis in animals with systemic fungal infection, such as blastomycosis and cryptococcosis.
- Aspirates from lymph nodes affected by lymphoma typically contain a high proportion (usually > 50%) of large lymphocytes. These are usually blasts with clearly recognizable nucleoli.
- Aspirates from lymph nodes containing metastatic neoplasia contain populations of cells that are not seen in normal nodes; the appearance of such cells varies widely, depending on the type of neoplasm.

Other

- In cats, severe lymphoid hyperplasia has been misdiagnosed as lymphoma; thus a biopsy is essential for animals with lymphadenomegaly.
- When a diagnosis cannot be made by cytologic examination, a surgical biopsy may be needed; excisional biopsy is preferable to needle biopsy.
- The cytologic diagnosis of lymphoma should be confirmed by histopathologic examination of an excised lymph node for accurate grading and to obtain potential prognostic information.



TREATMENT

- Because of the many disease processes and specific agents that can cause lymphadenomegaly, treatment depends on establishing the underlying cause.
- In animals suspected of lymphoma, corticosteroids should not be administered before completing staging tests if chemotherapy may be instituted.



MEDICATIONS

DRUG(S) OF CHOICE

Appropriate medications vary with the cause of lymph node enlargement.

CONTRAINDICATIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

Lymph node size to assess efficacy of treatment.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Lymph node hyperplasia and lymphadenitis are often components or manifestations of systemic disease.
- Lymphoma may involve other organs (e.g., liver, spleen, intestines, kidneys, and meninges) with a variety of clinical consequences.
- Clinical disease in animals with metastatic neoplasms in the lymph nodes is usually attributable to the primary tumor rather than

to the metastasis; however, exceptions are dogs with tonsillar carcinoma, who may have massively large mandibular lymph nodes, and dogs with adenocarcinoma of the anal sac, who often have dramatically large sublumbar lymph nodes.

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

- Direct transmission of diseases that cause lymphadenitis to humans is unlikely, with the exception of systemic mycotic disease, sporotrichosis, tularemia, plague, and *Bartonella* spp.

- Caution should be exercised when performing fine-needle aspiration in animals that may have systemic fungal disease.

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Lymphadenitis
- Lymphoma—Cats
- Lymphoma—Dogs

ABBREVIATIONS

- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- SLE = systemic lupus erythematosus

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Authors Kenneth M. Rassnick and Alan H. Rebar

Consulting Editor Alan H. Rebar

LYMPHANGIECTASIA



BASICS

DEFINITION

An obstructive disorder of the lymphatic system of the gastrointestinal tract resulting in lymphatic hypertension and protein-losing enteropathy.

PATOPHYSIOLOGY

- Lymphatic obstruction results in dilation and rupture of intestinal lacteals with subsequent loss of lymphatic contents (plasma proteins, lymphocytes, and chylomicrons) into the intestinal lumen.
- Although some of the proteins may be digested and reabsorbed, excessive enteric loss of plasma proteins will ultimately result in panhypoproteinemia.
- Hypoproteinemia causes a decrease in plasma oncotic pressure, which, if severe, will lead to edema, ascites, and/or pleural effusion.

SYSTEMS AFFECTED

- Gastrointestinal—diarrhea
- Respiratory—pleural effusion
- Skin—subcutaneous edema
- Systemic—ascites
- Vascular—thromboembolic disease

GENETICS

A familial tendency for protein-losing enteropathy has been reported for soft-coated Wheaten terriers, basenjis, Yorkshire terriers, and Norwegian Lundehunds, but the actual genetic cause has not been identified for any of these breeds.

INCIDENCE/PREVALENCE

Uncommon

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog

Breed Predilections

Increased prevalence in soft-coated Wheaten terrier, Basenji, Norwegian lundehund, and Yorkshire terrier.

Mean Age and Range

Dogs of any age can be affected. Most common in middle-aged dogs.

Predominant Sex

An increased prevalence has been reported in female soft-coated Wheaten terriers; no sex predilection has been reported for other breeds.

SIGNS

- Clinical signs are variable.
- Diarrhea—chronic, intermittent, or continuous, watery to semisolid consistency (typically small bowel type diarrhea); however, not all animals have diarrhea.
- Ascites.
- Subcutaneous edema.

- Dyspnea from pleural effusion.
- Weight loss.
- Flatulence.
- Vomiting.

CAUSES

Primary or Congenital Lymphangiectasia

- Focal—intestinal lymphatics only.
- Diffuse lymphatic abnormalities (e.g., chylothorax, lymphedema, chyloabdomen, thoracic duct obstruction).

Secondary Lymphangiectasia

- Right-sided congestive heart failure
- Constrictive pericarditis
- Budd-Chiari syndrome
- Neoplasia (lymphosarcoma)

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Lymphangiectasia must be differentiated from other causes of protein-losing enteropathy.
- PLE must be differentiated from other causes of hypoalbuminemia.

CBC/BIOCHEMISTRY/URINALYSIS

- Hypoalbuminemia and hypoglobulinemia (panhypoproteinemia)
- Hypocholesterolemia
- Hypocalcemia
- Hypomagnesemia
- Lymphopenia

OTHER LABORATORY TESTS

Tests to Differentiate PLE from Other Causes of Hypoalbuminemia

- Serum chemistry profile and pre- and post-prandial serum bile acids concentrations to rule out hepatic failure.
- Urine protein:creatinine ratio to rule out protein-losing nephropathy.
- Occult fecal blood test to rule out gastrointestinal blood loss (requires animal being fed a vegetarian diet for 72 hours to prevent false-positive results from meat protein).
- Fecal α_1 -protease inhibitor concentration to help confirm intestinal protein loss, although this test is not necessary in most dogs with lymphangiectasia.

Tests to Differentiate Other Causes of Excessive Protein Loss into the GI Tract

- Fecal smear and flotation to rule out intestinal parasites.
- Serum cobalamin and folate concentrations to rule out small intestinal dysbiosis or cobalamin deficiency, which could be associated with excessive intestinal protein loss. While cobalamin deficiency does not cause PLE it is an indicator of long-standing and severe distal small intestinal disease,

which in turn could be associated with excessive protein loss.

If an infectious enteritis is suspected, fecal culture for diagnosis of specific enteric pathogens (e.g., *Salmonella* spp.), PCR for enteropathogenic *Campylobacter* spp., and a *Clostridium* enterotoxin test (ELISA) if infectious enteritis is suspected.

Fluid analysis of body cavity effusions—the effusion associated with lymphangiectasia is usually a transudate, but chyloabdomen and chylothorax can occasionally be observed.

IMAGING

- Survey thoracic radiographs to rule out cardiac disease and neoplasia.
- Abdominal radiographs to rule out mechanical intestinal disease (obstruction or partial obstruction) and other causes of PLE.
- Abdominal ultrasound to rule-out mechanical intestinal disease and other causes of PLE.
- Cardiac ultrasound to rule out right-sided congestive heart failure.
- Abdominal ultrasonography can show hyperechoic mucosal striations extending from the lumen to the submucosal layer of the bowel. One study suggested that corn-oil given orally 60–90 minutes before abdominal ultrasonography improves the diagnostic yield.

DIAGNOSTIC PROCEDURES

- Endoscopy allows intestinal mucosal visualization and biopsy. Ileal biopsies should be procured in animals that have hypcobalaminemia.
- Laparotomy allows visualization of dilated intestinal lymphatics and biopsies of intestines (full thickness) and lymph nodes, but may be contraindicated in patients with severe hypoproteinemia.
- An ECG can aid in evaluating the heart in animals suspected of having right-sided congestive heart failure.

PATHOLOGIC FINDINGS

- Gross findings at laparotomy may include dilated lymphatics that are visible as a web-like network throughout the mesentery and serosal surface.
- May see small yellow-white nodules and foamy granular deposits adjacent to lymphatics.
- Histopathology findings include ballooning distortion of villi, caused by markedly dilated lacteals.
- Villi can be edematous; some have a blunted appearance.
- Usually associated with mucosal edema or diffuse or multifocal accumulations of lymphocytes and plasma cells in the lamina propria.

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LYMPHANGIECTASIA

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

May need hospitalization if complications due to hypoalbuminemia develop.

NURSING CARE

N/A

ACTIVITY

Normal

DIET

- Low-fat diet with high-quality protein. Avoid diets that are excessively high in fiber.
- Dogs with concurrent lymphangiectasia and IBD may benefit from a commercial hypoallergenic hydrolyzed protein diet that is moderately restricted in dietary fat.
- Long-chain triglycerides stimulate intestinal lymph flow and may lead to increased intestinal protein loss.
- Diets fortified with medium-chain triglycerides may be beneficial.
- May feed MCTs to supplement fat and increase caloric intake.
- Commercial sources of MCTs—MCT oil or Portagen (Mead Johnson, Evansville, IN).
- Supplement with fat-soluble vitamins—A, D, E, and K.
- Elemental diets can also be used.

CLIENT EDUCATION

Discuss unpredictable disease progression and response to therapy.

SURGICAL CONSIDERATIONS

- When intestinal lymphangiectasia is secondary to an identifiable lymphatic obstruction, consider surgery to relieve the obstruction.
- Pericardectomy may be indicated in cases of constrictive pericarditis.
- Patients that benefit from surgical intervention are rare.



MEDICATIONS

DRUG(S) OF CHOICE

• Try corticosteroids if dietary therapy alone is unsuccessful (however, such therapy is not intended to treat lymphangiectasia but rather concurrent gastrointestinal inflammation). Oral prednisone or prednisolone at a dose of 1–2 mg/kg q12h for 5–7 days, followed by 1 mg/kg q12h for at least 6 weeks. In large-breed dogs the starting dose should be more conservative than in small-breed dogs. After remission of the disease, dosage can be slowly

tapered to the lowest dose effective at controlling the disease. Alternatively, may consider the use of a locally-effective corticosteroid (e.g., budesonide), or other immunomodulators such as azathioprine or cyclosporine.

- If the patient is cobalamin deficient, cobalamin must be supplemented to achieve therapeutic response: 250–1,500 µg/dog SC once a week for 6 weeks, then one dose 1 month later. Follow with a recheck a month after the last dose to determine the need for continued supplementation.
- If secondary small intestinal dysbiosis is suspected the patient should be treated with tylosin at 10–20 mg/kg q12h for 6 weeks.
- Magnesium sulfate should be supplemented parenterally (IV) at 1 mEq/kg/day in dogs that are hypomagnesemic before oral supplementation with magnesium oxide, magnesium citrate, or magnesium carbonate.
- Diuretics such as furosemide (1 mg/kg q12h) and spironolactone (1 mg/kg q12h) in animals with severe ascites to improve patient comfort.

CONTRAINdications

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Body weight, serum total protein, albumin, and globulin concentrations, and evidence of recurrent clinical signs (pleural effusion, ascites, and/or edema).
- Patients need to be reevaluated depending on the severity of the disease process.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Respiratory difficulty from pleural effusion
- Severe protein-calorie depletion
- Intractable diarrhea

EXPECTED COURSE AND PROGNOSIS

- Prognosis is guarded.
- Some animals fail to respond to treatment.
- Remissions of several months to more than 2 years can be achieved in some patients.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Soft-coated Wheaten terriers may have concurrent protein-losing nephropathy.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

Protein-Losing Enteropathy

ABBREVIATIONS

- ECG = electrocardiogram
- MCT = medium chain triglycerides
- PLE = protein-losing enteropathy

Suggested Reading

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Author Jörg M. Steiner

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Client Education Handout
available online



BASICS

OVERVIEW

- Abnormal accumulation of protein-rich lymph fluid into interstitial spaces, especially subcutaneous fat.
- Chronic lymphedema causes tissue fibrosis.
- May be congenital or acquired.

SIGNALMENT

- More common in dog than in cat.
- Congenital in bulldogs and reported to be hereditary/congenital in a family of poodles and whippets; possible breed predilection in Labrador retrievers and Old English sheepdogs.

SIGNS

Historical Findings

- Primary/congenital—usually peripheral limb swelling at birth or develops in first several months.
- Swelling typically starts at distal extremity and slowly advances proximally.

Physical Examination Findings

- Most common in limbs, especially pelvic limbs; may be unilateral or bilateral.
- Less common in ventral thorax, abdomen, ears, and tail.
- Pitting, non-painful; temperature of affected area is normal.
- Pitting quality lost with chronicity as fibrosis occurs.
- Lameness and pain uncommon unless cellulitis develops.

CAUSES & RISK FACTORS

- Hereditary/congenital malformation of the lymphatic system—aplasia, valvular incompetence, and lymph node fibrosis.
- Excessive interstitial fluid production secondary to venous hypertension (associated with congestive heart failure and obstruction of venous drainage) or increased vascular permeability (associated with infection, trauma, heat, and irradiation).
- Secondary damage to lymphatic vessels or lymph nodes—associated with trauma, infection (e.g., *Brugia pahangi* lymphatic filarial infection—Southeast Asia), neoplasia (e.g., lymphoma, lymphangiosarcoma [rare]), and thoracic duct ligation (rare).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Edema caused by venous stasis (e.g., congestive heart failure and cirrhosis); look for varices, hyperpigmentation, and

ulceration.

- Arteriovenous fistulae—listen for machinery murmur; feel for pulsatile vessels; confirm with angiogram.
- Edema caused by hypoproteinemia—protein-losing nephropathy or enteropathy, hepatic failure, serum loss from burns or hemorrhage; check serum protein concentration.
- Trauma—review history; look for bruising and lacerations.
- Neoplasia—if swelling is firm, obtain aspirate for cytologic examination.
- Cellulitis—look for fever, pain, and warm swelling.
- Insect bites.

CBC/BIOCHEMISTRY/URINALYSIS

Results normal

OTHER LABORATORY TESTS

Serologic tests for tick-borne infections, including *Bartonella* spp.

IMAGING

Lymphography useful in documenting abnormalities within the lymphatic system; best results obtained with an injection of water-based contrast media directly into a lymphatic vessel. See "Suggested Reading" for detailed description of the technique.

DIAGNOSTIC PROCEDURES

- Biopsy of affected tissues to rule out lymphangiosarcoma.
- Culture and sensitivity when lymphangitis is present.



TREATMENT

- No curative therapy—a number of surgical and medical treatments may be tried.
- Rest and massage of the affected limbs does not help.
- Conservative care—long-term use of pressure wraps, coupled with skin care and use of antibiotics to treat cellulitis and lymphangitis; may be successful in some patients.
- Surgical procedures—can be attempted when conservative care and medications fail; lymphangioplasty, bridging techniques, lymphaticovenous shunts, superficial and deep lymphatic anastomosis, and excisional procedures; none is consistently beneficial, and excisional procedures have been reported only in dogs.
- In humans—microwave heating of affected areas appears beneficial and adds to the effect of benzopyrones (see "Drugs").
- Diets severely restricted in long-chain triglycerides are being investigated in humans.



MEDICATIONS

DRUG(S)

- Benzopyrones reduce high-protein edema by stimulating macrophages to release proteases; beneficial effects have been recorded in experimental studies in dogs. Rutin, 50 mg/kg PO q8h, may benefit. A study in humans showed combined usage of oral and topical benzopyrones to be more effective than either alone.
- Diuretics, steroids, anticoagulants, and fibrinolytic agents have been used, but no confirmed benefit.
- Treat underlying cause where possible (e.g., ivermectin for *Brugia pahangi* infection).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Diuretics—initially reduce swelling but increase protein content of interstitial fluid, resulting in further tissue damage and fibrosis.



FOLLOW-UP

- Puppies with severe lymphedema may die.
- Resolution seen in some puppies with pelvic limb involvement only.
- Prognosis with lymphangiosarcoma is poor.



MISCELLANEOUS

Suggested Reading

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- Author** Francis W.K. Smith, Jr.
Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

LYMPHOMA—CATS



BASICS

DEFINITION

Malignant transformation of lymphocytes

PATHOPHYSIOLOGY

Viral (FeLV) or chemical (tobacco smoke) oncogenesis

SYSTEMS AFFECTED

- Gastrointestinal
- Hemic/Lymphatic/Immune
- Nervous—most common spinal cord tumor in cats
- Ophthalmic
- Renal (high rate of relapse in central nervous system)
- Respiratory—nasal, thoracic cavities

GENETICS

N/A

INCIDENCE/PREVALENCE

- About 90% of hematopoietic tumors and 33% of all tumors in cats.
- Prevalence—41.6–200 per 100,000 cats.

GEOGRAPHIC DISTRIBUTION

Regional differences may relate to differences in FeLV prevalence.

Breed Predilections

Siamese/Oriental breeds overrepresented in some studies

Mean Age and Range

- FeLV-positive cats—3 years.
- FeLV-negative cats—7 years.
- Median age of cats with localized extranodal lymphoma—13 years.
- Most cats with Hodgkin's-like lymphoma are older than 6 years.

Predominant Sex

None

SIGNS

General Comments

Depend on anatomic form.

Historical Findings

- Mediastinal form—open-mouthed breathing; coughing; regurgitation; anorexia; weight loss.
- Alimentary form—anorexia; weight loss; lethargy; vomiting; constipation; diarrhea; melena; hematochezia. SCL typically more chronic signs compared to LCL.
- Renal form—consistent with renal failure.
- Nasal form—nasal discharge or epistaxis, facial swelling, ocular signs, respiratory noise, sneezing, anorexia.
- Multicentric form—possibly none in early stages; anorexia, weight loss, and depression with progression of disease.
- Spinal form—quickly progressing posterior paresis may be seen.
- Cutaneous form—pruritic, hemorrhagic, or alopecic dermal masses may be seen.

Physical Examination Findings

- Mediastinal form—non-compressible cranial thorax, dyspnea, tachypnea.
- Alimentary form—thickened intestines or abdominal masses.
- Renal form—large, irregular kidneys.
- Nasal form—purulent or mucoid nasal discharge, facial deformity, epiphora, exophthalmos, poor globe retropulsion.
- Multicentric form—generalized lymphadenomegaly, possible hepatosplenomegaly.
- All forms—fever; dehydration; depression; cachexia in some patients.

CAUSES

FeLV

RISK FACTORS

- FeLV exposure.
- Exposure to environmental tobacco smoke (relative risk 2.4, increases linearly with duration and quantity of exposure).
- FIV infection.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Mediastinal form—congestive heart failure; cardiomyopathy; chylothorax; pyothorax; hemothorax; pneumothorax; diaphragmatic hernia; allergic lung disease; thymoma; ectopic thyroid carcinoma; pleural carcinomatosis; acetaminophen toxicity.
- Alimentary form—foreign body ingestion; intestinal ulceration; intestinal fungal infection; inflammatory bowel disease; intussusception; lymphangiectasia; other gastrointestinal tumor.
- Renal form—pyelonephritis; amyloidosis; glomerulonephritis; chronic renal failure; polycystic kidneys; feline infectious peritonitis.
- Multicentric form—systemic mycotic infection; immune-mediated disease; toxoplasmosis; lymphoid hyperplasia; hypersensitivity reaction; plague (specifically if prominent cervical lymphadenopathy as with Hodgkin-like form).

CBC/BIOCHEMISTRY/URINALYSIS

- May see anemia (negative prognostic factor), leukocytosis, and lymphoblastosis.
- May find high creatinine, high serum urea nitrogen, high hepatic enzyme activity, hypercalcemia (rare), and monoclonal gammopathy.

OTHER LABORATORY TESTS

FeLV testing: usually negative in older cats and in cats with (LGLL), usually positive in younger cats and those with mediastinal (85%) or CNS lymphoma, renal (45% positive), multicentric (20%), intestinal (15%).

IMAGING

- *Thoracic radiography*—may see mediastinal mass, pleural effusion, abnormal pulmonary parenchymal patterns (rare), perihilar or retrosternal lymphadenomegaly.
- *Abdominal ultrasonography*—may see diffuse echotexture changes in the liver, spleen, and kidneys, focal or diffuse thickening of the intestines and the gastric wall, abdominal lymphadenopathy, intestinal/gastric mass.
 - Hypoechoic subcapsular thickening is associated with renal lymphoma.
 - Despite thickening of intestines, layering may be preserved.
- *Computed tomography*—space-occupying mass effect in affected area, especially used for nasal lymphoma.

DIAGNOSTIC PROCEDURES

- Aspiration or biopsy of a mass or lymph node.
- Aspirate often sufficient to diagnose LCL, biopsy often required for SCL.
- Can be challenging to distinguish SCL from IBD.
- PARR testing can be done to determine if lymphocyte population is monoclonal (consistent with lymphoma) or not; sensitivity for detecting T-cell and B-cell LSA is 78% and 50%, respectively.
- Staging: CBC/Chemistry profile/Urinalysis/FeLV/FIV testing, thoracic radiographs, abdominal ultrasound, regional lymph node aspirates for localized lesions, ± bone marrow aspirate depending on CBC findings serum cobalamin level in SCL.

PATHOLOGIC FINDINGS

- Gross—usually white to gray in color with areas of hemorrhage and necrosis.
- Cytologic—monomorphic population of lymphoid cells, sometimes with prominent, multiple nucleoli and coarse nuclear chromatin.
- Histopathologic—vary; several morphologic classification schemes in use.
 - Nasal lymphoma is most often immunoblastic B-cell origin.
 - Hodgkin's-like lymphoma is characterized by Reed-Sternberg cells and few neoplastic cells in a background of a reactive T-cell population with histiocytes and granulocytes.
 - LGL lymphoma most commonly affects the intestine and mesenteric lymph nodes.
 - B-cell most common in stomach (100%) and large intestine (88%), T-cell most common in small intestine (52%, most common location in gut).
 - In GI lymphoma, LCL more common than SCL when both cytologic and histopathologic samples are evaluated.

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient whenever possible, supportive care if needed.

NURSING CARE

Fluid therapy, antiemetics, appetite stimulants, thoracocentesis, etc. when indicated.

ACTIVITY

Normal

DIET

No change, can add n-3 fatty acids to diet (fish oil origin).

CLIENT EDUCATION

- Emphasize that side effects are treatable and should be addressed promptly.
- Inform client that the goal is to induce remission and achieve a good quality of life for as long as possible.

SURGICAL CONSIDERATIONS

- To relieve intestinal obstructions or perforations and remove solitary masses.
- To obtain specimens for histopathologic examination.

RADIATION THERAPY

Possible option for localized lesions, such as nasal cavity or mediastinum.



MEDICATIONS

DRUG(S) OF CHOICE

- Chemotherapy—there are many variations of similar combination protocols, all with similar efficacy.
- High-grade lymphoma can respond to CHOP-based protocols (cyclophosphamide, doxorubicin, vincristine, prednisone/prednisolone) such as the University of Wisconsin–Madison protocol (alternating drugs in repeated sequence) or COP-based protocols (cyclophosphamide, vincristine, prednisone/prednisolone).
- Vinblastine has similar efficacy but less GI toxicity compared to vincristine.
- SCL can respond to oral chlorambucil (either low dose daily/every other day or high dose pulsed) and prednisone/prednisolone.
- Consult a veterinary oncologist for doses, schedules, and to help assess best option(s) for treatment.

CONTRAINdicATIONS

Avoid doxorubicin in cats with preexisting renal failure as high-cumulative dosages have been demonstrated to potentially be nephrotoxic.

PRECAUTIONS

- Myelosuppression secondary to chemotherapy—more in FeLV-positive cats.

- Seek advice before initiating treatment if you are unfamiliar with cytotoxic drugs. Some drugs such as vincristine and doxorubicin are vesicants and can cause tissue sloughing if leaked outside the vein.

POSSIBLE INTERACTIONS

None



FOLLOW-UP

PATIENT MONITORING

- Physical examination and CBC—before each chemotherapy treatment and 1 week after each new drug is administered, or if there are concerns about low cell counts.
- Diagnostic imaging—as necessary depending on location to assess response to therapy.

PREVENTION/AVOIDANCE

Avoid exposure to or breeding FeLV-positive cats.

POSSIBLE COMPLICATIONS

- Leukopenia/neutropenia.
- Sepsis.
- Anorexia, vomiting, weight loss; may need imaging tests to distinguish between chemotherapy side effects and lymphoma progression.

EXPECTED COURSE AND PROGNOSIS

- Depends on initial response to chemotherapy, anatomic type, FeLV status, and tumor burden.
- Median survival according to treatment (overall 50–70% response rate):
 - Prednisone alone—1.5–2 months.
 - COP/CHOP-based chemotherapy—6–9 months.
 - Doxorubicin-based and lomustine rescue therapy reported for refractory LSA.
 - Median survival according to FeLV status:
 - Negative = 7 months (17.5 months if low tumor burden).
 - Positive = 3.5 months (4 months if low tumor burden).
- Median survival according to anatomic location:
 - Renal—FeLV-negative, 11.5 months; FeLV-positive, 6.5 months.
 - Nasal = 1.5–2.5 years with radiation and chemotherapy.
 - Chemotherapy may not improve survival over radiation alone.
 - Higher radiation doses (> 32 Gy) result in longer survival.
- Mediastinal—about 10% of patients live > 2 years.
- Alimentary—8 months.
- Peripheral multicentric—23.5 months.
- If localized (median remission time)—114 weeks.
- Median survival according to histology (tumor grade or subtype):

LYMPHOMA—CATS

- SCL of gastrointestinal tract with or without additional visceral involvement: 95% overall response to chlorambucil and prednisone for median survival of approximately 2 years (longer in complete vs. partial remission).
- LGLL~30% response for median survival 57 days.
- Cats with Hodgkin-like lymphoma can do well for extended periods of time, even without treatment (months to years).
- Weight loss during first month of treatment of LCL associated with shorter survival.
- Clinical response after 1 cycle of COP chemotherapy associated with longer survival.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Hypoglycemia (rare)
- Monoclonal gammopathy (rare)
- Hypercalcemia (10–15%)

AGE-RELATED FACTORS

Young cats with lymphoma are generally FeLV-positive.

ZOONOTIC POTENTIAL

None

L

PREGNANCY/FERTILITY/BREEDING

Do not use chemotherapy in pregnant animals.

SYNONYMS

- Lymphosarcoma
- Malignant lymphoma

ABBREVIATIONS

- CNS = central nervous system
- FeLV = feline leukemia virus
- GI = gastrointestinal
- IHC = immunohistochemistry
- LCL = large cell lymphoma
- LGLL = large granular lymphocyte lymphoma
- LSA = lymphoma
- PARR = PCR (polymerase chain reaction) for antigen receptor rearrangement
- SCL = small cell lymphoma

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Client Education Handout
available online

LYMPHOMA—DOGS



BASICS

DEFINITION

- Clonal proliferation of B, T, or non-B-/non-T-type (null cell) lymphoblasts found primarily in enlarged peripheral lymph nodes.
- Cells can spread systemically to invade bone marrow, peripheral blood, CNS, and visceral organs.

PATOPHYSIOLOGY

- ~85% of cases are multicentric (involving more than one lymph node).
- ~75% are B-cell in origin and ~25% are T-cell in origin.
- T-cell LSA is usually associated with hypercalcemia.
- Multicentric T-cell LSA includes aggressive (PTCL-NOS) and indolent (TZL, FL) subtypes.
- Multicentric B-cell lymphoma is an aggressive disease.
- Aggressive lymphomas respond to treatment quickly, but have a shorter overall survival.

SYSTEMS AFFECTED

- Lymphatic (~85%)—generalized peripheral lymphadenopathy with or without splenic, hepatic, peripheral blood, and/or bone marrow involvement.
- Gastrointestinal (~5–7%)—focal or diffuse infiltration of intestines, and associated lymph nodes.
- Mediastinal (~5%)—proliferation of neoplastic lymphocytes in mediastinal lymph nodes, thymus, or both.
- Skin—divided into cutaneous non-epitheliotropic B- and T-cell LSA and mycosis fungoides (epitheliotropic T-cell LSA).
- Hepatosplenitis ($\gamma\delta$ T-cell LSA (rare)—liver/spleen sinusoidal infiltration of T-cells with eventual bone marrow infiltration.
- Intravascular LSA (rare)—typically T- or null cell proliferation in lumen or wall of blood vessel.

COMPARATIVE CYTOGENETICS AND GENE EXPRESSION PROFILING

- Some chromosome copy number aberrations are shared between human and canine lymphomas.
- Gene expression profiling can be used to separate distinct subtypes of human and canine lymphoma.
- Canine diffuse large B-cell lymphoma and marginal zone lymphoma may be a continuum of the same disease.

INCIDENCE/PREVALENCE

- 20–107 LSA cases per 100,000 dogs.
- LSA comprises up to 24% of all canine neoplasms and 83% of all canine hematopoietic malignancies.

SIGNALMENT

Breed Predilections

- Boxer, basset hound, golden retriever, Saint Bernard, Scottish terrier, Airedale terrier, and bulldog—reported high-risk breeds.
- Dachshund and Pomeranian—reported low-risk breeds.
- Breed determines relative risk for B-cell or T-cell disease: ~85% of

boxer LSAs are T-cell in origin, while golden retrievers develop both B- and T-cell LSA in a ~50:50 ratio.

Median Age

Historically, 6–9 years

SIGNS

History

- Multicentric—from no clinical signs to anorexia, lethargy, vomiting, diarrhea, weight loss, fever, polydipsia and polyuria secondary to hypercalcemia.
- Gastrointestinal—vomiting, diarrhea, anorexia, weight loss, malabsorption.
- Mediastinal—respiratory distress, pleural effusion, coughing, difficulty swallowing, caval syndrome.
- Skin:
 - Cutaneous LSA—lesions usually generalized or multifocal: nodules, plaques, ulcers, focal alopecia and hypopigmentation.
 - Mycosis fungoides—initial scaling, alopecia, pruritus progressing to thickened, ulcerated, exudative lesions. Later stages include proliferative plaques and nodules with progressive ulceration. Oral mucosa many times involved.
- Extranodal—vary with the anatomic site: ocular—photophobia and conjunctivitis; CNS—neurologic deficits, paresis, paralysis, seizures; hepatosplenitis—lethargy, inappetance, weakness, icterus.

Physical Examination Findings

- Multicentric—generalized, painless, enlarged peripheral lymph node(s) with or without hepatosplenomegaly.
- Gastrointestinal—unremarkable to palpable thickened gut loops and/or abdominal mass, rectal mucosal irregularities, ascites.
- Mediastinal—dyspnea; tachypnea; muffled heart sounds secondary to pleural effusion, pitting edema of head, neck, forelimbs.
- Skin—raised plaques that may coalesce, patch lesions, and erythematous, exudative lesions.
- Extranodal—ocular—anterior uveitis, retinal hemorrhages, and hyphema; CNS—dementia, seizures, and paralysis.

CAUSES

Suggested causes include heritable breed risks, chromosomal aberrations, increased telomerase activity, germline and somatic genetic mutations, epigenetic changes, retroviral infection, Epstein-Barr virus infection, and environmental factors.



DIAGNOSIS

Differential Diagnosis

- Multicentric—disseminated infections, metastatic disease, immune-mediated disorders, other hematopoietic tumors.
- Gastrointestinal—other GI tumors, foreign body, enteritis, GI ulceration, systemic mycosis.
- Mediastinal—other tumors (thymoma, chemodectoma, ectopic thyroid), infectious disease.
- Skin—infestive

dermatitis, pyoderma, immune-mediated dermatitis, histiocytic or mast cell disease.

- Extranodal—depends on affected site.

STAGING

CBC/Biochemistry/Urinalysis

- Anemia of chronic disease, thrombocytopenia, lymphocytosis, lymphopenia, neutrophilia, monocytosis, circulating blasts, hypoproteinemia (gastrointestinal).
- Hypercalcemia, increased liver enzymes with hepatic involvement, increased BUN or creatinine with renal involvement.
- Urinalysis usually normal.

Imaging

- Thoracic radiography—sternal or tracheobronchial lymphadenopathy, widened mediastinum, pulmonary densities, and pleural effusion.
- Abdominal ultrasonography—abdominal lymphadenopathy, hepatosplenic involvement, thickened bowel loops, other visceral organ involvement, ascites.

Diagnostic Procedures

- Fine-needle aspirate cytology of enlarged lymph nodes or other affected organs—for cytopathologic confirmation.
- Lymph node biopsy or resection—for accurate histopathologic classification.
- Bone marrow cytology—for accurate prognosis.
- CSF analysis—if patient has neurologic signs.
- ECG—identify arrhythmias before doxorubicin administration.

Other Laboratory Tests

- Immunohistochemistry (LN biopsy/resection)—to determine immunophenotype.
- Flow cytometry or PCR for antigen receptor rearrangements (PARR) (LN or affected organ fine-needle aspirates)—to determine immunophenotype.

Pathologic Findings

- Multicentric—effacement of LN parenchyma with large, neoplastic CD3+ T cells (PTCL-NOS) or small, CD3+ cell proliferation between fading follicles (indolent TZL). Effacement of LN parenchyma with large, neoplastic CD79a+ B cells (high-grade DLBCL) or perifollicular proliferation of CD79a+ cells (MZL) or CD79a+ cell proliferation that maintains follicle architecture (FL).
- Gastrointestinal infiltration of neoplastic lymphocytes throughout mucosa and submucosa, with occasional transmural infiltration.
- Skin—CD79a+ B-cells infiltrating mucosa and submucosa, but sparing the epidermis (non-epitheliotrophic) LSA or CD3+ T-cells invading the epidermis—Pautrier's microabscesses (mycosis fungoides).
- Hepatosplenitis—sinusoidal infiltration of erythrophagocytic CD3+ T-cells.

Staging

- I—one enlarged LNII—regionally enlarged LNs
- III—generalized LN involvement
- IV—visceral organ involvement
- V—blood

(CONTINUED)

or bone marrow involvement • Substage a—not sick • Substage b—sick



TREATMENT

CURRENT STANDARDS OF CARE

- High-grade LSAs are exquisitely sensitive to both chemotherapy and radiation.
- Systemic multi-agent chemotherapy—therapy of choice.
- Radiation therapy—for refractory lymphadenopathy, large mediastinal masses, and solitary cutaneous areas.
- Surgery—rarely used unless an acutely obstructive gastrointestinal mass is identified or to remove a refractory lymphadenopathy.
- Autologous and allogeneic bone marrow transplantation can be considered.

OTHER TREATMENTS

Fluid therapy—for advanced disease to treat clinically ill, azotemic, and/or dehydrated patients. Also to prevent tumor lysis syndrome and/or reduce calcium levels.

CLIENT EDUCATION

- Canine LSA is a treatable, but rarely curable disease.
- Side effects of chemotherapy drugs include reversible gastrointestinal tract and bone marrow toxicities.
- The vast majority of dogs receiving chemotherapy enjoy an excellent quality of life.



MEDICATIONS

DRUG(S) OF CHOICE

- Always consult a veterinary oncologist to discuss various treatment options, precautions, chemotherapy dosing schedules, and potential side effects.
- Consider combination chemotherapy protocols to treat intermediate and high-grade diseases and single agent protocols to treat indolent diseases.
- Most multi-agent protocols have superior remission and survival times when compared to single agent protocols.
- Corticosteroids alone can induce significant multi-drug resistance.

Intermediate and High-Grade Lymphomas

- L-CHOP—L-asparaginase 10,000 IU/m², vincristine (Onvcovin) 0.7 mg/m² IV, cyclophosphamide (Cytoxan) 250 mg/m² IV or PO, doxorubicin (Adriamycin) 30 mg/m² IV, prednisone 30, 20, 10 mg/m² PO q24h tapering for 3 weeks. Consult a veterinary oncologist concerning the treatment schedule.
- COP—vincristine 0.7 mg/m² IV, cyclophosphamide (Cytoxan) 250 mg/m² IV or PO, prednisone 30, 20, 10 mg/m² PO q24h tapering for 3 weeks. Each drug given weekly.

Single Agent

- Any drug of L-CHOP can be used as a single agent, but expect shorter overall

survival than multiagent.

- Doxorubicin (Adriamycin) 30 mg/m² IV every 3 weeks (1 mg/kg for dog < 15 kg) 5–6 treatments.
- CCNU (lomustine) 70 mg/m² PO every 3 weeks, prednisone 2 mg/kg PO daily.

Low-Grade Lymphomas

- Chlorambucil (Leukeran) 6 mg/m² PO daily for 7–14 days, prednisone 2 mg/kg PO daily. Consider reducing chlorambucil dose to 3 mg/m² for maintenance.
- CCNU (lomustine) as above.

PRECAUTIONS

- Doxorubicin—use dextrazoxane (Zinecard) in conjunction with doxorubicin or substitute epirubicin for dogs with cardiac issues.
- Always use a freshly placed catheter when administering intravenous doxorubicin.
- L-asparaginase and doxorubicin—pretreat with diphenhydramine (1–2 mg/kg SC) 15 minutes before administration.

POSSIBLE INTERACTIONS

Most chemotherapy drugs have overlapping gastrointestinal and bone marrow toxicities. Consider anti-diarrheal (metronidazole, loperamide) and antiemetics (metoclopramide, maropitant, ondansetron) to abrogate these effects.

ALTERNATIVE (RESCUE) PROTOCOLS

- Many published rescue protocols have been reported; therefore always consult with a medical oncologist.
- MOPP—methchlorthamine (Mustargen), vincristine, procarbazine, and prednisone.
- DMAC—dexamethasone, melphalan, actinomycin-D, and cytosine arabinoside.
- CCNU ± L-asparaginase, prednisone, or DTIC (dacarbazine).
- Mitoxantrone alone or Adriamycin/DTIC.



FOLLOW-UP

PATIENT MONITORING

- Weekly physical examination to assess response and CBC to gauge bone marrow toxicities.
- If neutropenia (neutrophils < 1,500 cells/mm³) is noted, reduce dosage (20–25%) of drug when given again.

MOST COMMON COMPLICATIONS

- Reversible neutropenia 4–7 days after chemotherapy.
- Temporary vomiting, diarrhea, and anorexia 2–5 days after chemotherapy.
- Alopecia in certain dog breeds (poodle, Shih Tzu, etc.).
- Febrile neutropenia (treated with broad-spectrum antibiotics).

EXPECTED COURSE AND PROGNOSIS

- > 80% of dogs will go into clinical remission during the first month of induction chemotherapy.
- Stage, substage, and immunophenotype are important prognostic indicators.
- Expect median survivals of ~12–14 months and ~6–9 months in dogs

LYMPHOMA—DOGS

with high-grade multicentric B- and T-cell LSA, respectively, when treated with a multi-agent protocol. Dogs with indolent disease can live years. Gastrointestinal, mediastinal (T-cell ± hypercalcemia), and mycosis fungoides are associated with poorer response to treatment and an overall shorter survival time.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Treatment of pregnant dogs is usually contraindicated.

SYNONYMS

- Lymphosarcoma • Malignant lymphoma

SEE ALSO

- Hypercalcemia • Leukemia, Acute Lymphoblastic • Leukemia, Chronic Lymphocytic

ABBREVIATIONS

- CNS = central nervous system
- DLBCL = diffuse, large B-cell lymphoma
- FL = follicular LSA
- LN = lymph node
- LSA = lymphoma
- MZL = marginal zone lymphoma
- PTCL-NOS = peripheral T-cell lymphoma—not otherwise specified
- TZL = T-zone lymphoma

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Client Education Handout
available online

L

LYMPHOMA, CUTANEOUS EPITHELIOTROPIC



BASICS

OVERVIEW

- Cutaneous epitheliotropic lymphoma (CEL)—most common form of cutaneous T-cell lymphoma.
- An uncommon malignant neoplasia of dogs and cats.
- Sézary syndrome—rare; cutaneous lesions, invasion of peripheral lymph nodes by neoplastic lymphocytes, and leukemia occur simultaneously.
- Pagetoid reticulosis—rare; the lymphoid infiltrate is confined to the epidermis and adnexal structures in the early stages of the disease and extends to the dermis in the late stages.

SYSTEMS AFFECTED

- Hemic/Lymphatic/Immune
- Skin/Exocrine

SIGNALMENT

- Dogs and cats—most common in dogs.
- Age range 6–14 years—mean 8.6 years.
- No apparent breed or sex predilection.

SIGNS

Historical Findings

- Chronic skin disease—months before diagnosis
- Rarely acute
- Mimics other inflammatory dermatoses
- None to severe pruritus

Physical Examination Findings

- Four clinical categories of presentation:
- Exfoliative erythroderma: generalized erythema, scaling, depigmentation, alopecia
- Mucocutaneous: depigmentation, erythema, erosion, and ulceration affecting mucocutaneous junctions
- Tumoral: solitary or multiple erythematous and scaly plaques, nodules, and masses
- Oral mucosal ulceration of gingiva, palate, and/or tongue.
- Lesions—typically throughout the skin; marked tendency for involvement of mucocutaneous junctions or oral cavity; lesions can be limited to the mucocutaneous junctions or oral mucosa.
- Exfoliative erythroderma; progression to the tumor stage is very rapid in dogs compared to humans.
- Mucocutaneous form and oral mucosa form: tend to merge with chronicity.
- Rarely nodules develop without a preexisting patch or plaque stage (d'emblee form).
- Nodular stage may occasionally progress to a disseminated form with lymph node involvement, leukemia, and rarely other organs.

CAUSES & RISK FACTORS

None identified; possible risk of development of chronic antigenic stimulation (including allergy) theorized.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Dermatophytosis, demodicosis, feline

thymoma-associated exfoliative dermatitis—alopecia, erythema, scaling.

- Allergic dermatitis and sarcoptic acariasis—generalized pruritus, erythema, scaling.
- Discoid lupus erythematosus, erythema multiforme, mucocutaneous pyoderma—mucocutaneous depigmentation/ulceration.
- Non-neoplastic stomatitis—infiltrative and ulcerative oral mucosal disease.
- Cutaneous neoplasia—nodule or mass formation.

CBC/BIOCHEMISTRY/URINALYSIS

- Laboratory abnormalities—vary depending on the stage and form of CEL, and whether or not the disease has disseminated.
- Generally unremarkable if only the skin or mucosa is affected.
- Sézary cells—neoplastic lymphocytes (8–20 μm) with convoluted nucleus and cerebriform appearance are present in peripheral blood of Sézary syndrome patients.

IMAGING

Radiographs and ultrasound—imaging if signs of systemic disease present and/or for tumor staging.

DIAGNOSTIC PROCEDURES

- Skin scrapings and fungal culture—demodicosis and dermatophytosis.
- Skin biopsy—definitive diagnosis; sample multiple different-appearing lesions, avoid eroded/ulcerated and infected lesions.

PATHOLOGIC FINDINGS

- Infiltrate of neoplastic lymphocytes—into epidermis, hair follicle epithelium, and adnexa; distributed diffusely or as discrete Pautrier microaggregates.
- Dermal infiltrate—polymorphous; malignant lymphocytes may obscure the dermoepidermal junction; patch and plaque stages, limited to the superficial dermis; nodular stage, extends to the deep dermis and subcutis.
- Immunohistochemical tissue staining reveals a predominance of CD8+ cytotoxic T-cells (dogs).



TREATMENT

- Goal is to maintain a good quality of life.
- Therapy is rarely curative.
- Rarely, solitary nodules can be surgically excised.
- Radiation therapy: total skin electron beam therapy or orthovoltage radiation is well tolerated and may be beneficial in some cases.



MEDICATIONS

DRUG(S)

- Chemotherapy—several protocols used with limited to no success.
- Lomustine (CCNU)—overall response rate of 80% with remission achieved in about 25% of cases (60–70 mg/m² PO every 3–4 weeks for a mean of 3 to 5

treatments).

- Dacarbazine—1000 mg/m²; complete and durable remission after 3 cycles in a dog with nodal involvement.
- Pegylated liposomal doxorubicin—44% response rate in dogs (average dose, 1 mg/kg IV every 3 weeks).
- Combination protocol with cyclophosphamide, doxorubicin, vincristine, and prednisolone—partial to complete response in a few dogs that failed lomustine therapy.
- High doses linoleic acid (e.g., sunflower oil)—3 mL/kg orally twice weekly; good improvement in 7/10 dogs for up to 2 years.
- Topical chemotherapy—mechlorethamine (nitrogen mustard); some success in managing early lesions; however, lack of long-term efficacy: carcinogenic potential for owner and veterinary staff.
- Corticosteroids—topical and/or systemic may result in some symptomatic relief.
- Retinoids—isotretinoin (3 mg/kg/day) or acitretin (2 mg/kg/day) may be beneficial; cost can be a limiting factor.
- Imiquimod—a topical immunomodulator with antineoplastic and antiviral effects may be useful for localized disease. No published reports in veterinary literature.

CONTRAINdications/POSSIBLE INTERACTIONS

- Depend on the chemotherapeutic or treatment protocol.
- Seek advice from a veterinary oncologist or dermatologist before initiating therapy if you are unfamiliar with cytotoxic drugs and/or to learn about the most recent treatment protocols.



FOLLOW-UP

- Prognosis grave.
- Average survival time for dogs depends upon stage of disease at diagnosis, therapeutic choice, and response to therapy; varies from a few weeks to longer than 18 months.
- Rarely, dogs and cats may live for longer than 2 years after the diagnosis is made.
- Death is usually the result of euthanasia.



MISCELLANEOUS

SYNONYMS

- Lymphoma, epidermotropic
- Mycosis fungoïdes

Suggested Reading

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Author Sheila M. F. Torres

Consulting Editor Alexander H. Werner

LYMPHOMATOID GRANULOMATOSIS



BASICS

OVERVIEW

- Lymphomatoid granulomatosis is a rare lymphoproliferative disorder predominantly involving the lungs.
- Rare pulmonary disease of dogs and cats characterized by angiocentric and angiodestructive proliferation and infiltration by atypical lymphoid cells.

SIGNALMENT

- Dog and cat
- Median age—5.75 years (range, 1.5–14 years) in dogs
- No breed predilection but more common in large breeds and pure breeds
- No gender predisposition

SIGNS

- Progressive respiratory signs including cough and dyspnea
- Serous nasal discharge
- Exercise intolerance
- Weight loss
- Anorexia
- Fever in 50% of patients
- Duration—days to weeks

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Mycotic, bacterial, or aspiration pneumonia
- Primary or metastatic pulmonary neoplasia
- Atypical pulmonary lymphoma

CBC/BIOCHEMISTRY/URINALYSIS

- No consistent abnormalities
- Neutrophilic leukocytosis, eosinophilia, and basophilia may be common

OTHER LABORATORY TESTS

Some dogs have concurrent heartworm disease and/or test positive for heartworms.

IMAGING

- Radiography—reveals lobar pulmonary consolidation (e.g., mass lesions), hilar lymphadenomegaly, and pleural effusion.
- Lesions—unilateral or bilateral.

DIAGNOSTIC PROCEDURES

- Biopsy—for definitive diagnosis (adequate tissue sample size required for accurate diagnosis).
- Immunohistochemistry is required on the biopsied tissue (CD3, CD20, CD79).

PATHOLOGIC FINDINGS

- Gross—multiple pulmonary nodules with a predilection for the caudal lung lobes with metastasis or involvement of hilar lymph nodes.
- Histologic—characterized by sheets of atypical lymphoid and plasmacytoid cells admixed with fewer eosinophils and small lymphocytes in the pulmonary blood vessels. The lymphocytes can be of B-cell and T-cell lineage, with Reed-Sternberg-like cells reported.
- Cytologic—may appear as sterile eosinophilic and neutrophilic inflammation with reactive macrophages.
- Systemic spread is possible—to liver, heart, kidneys, spleen, pancreas, adrenal gland, and other organs.



TREATMENT

- Cytotoxic drugs combined with surgical excision when appropriate.
- Always consult a veterinary oncologist.



MEDICATIONS

DRUG(S)

Combination protocol—CHOP or other combination protocol suitable for lymphoma. No standard treatment protocol has been systemically evaluated.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Myelosuppression—caused by cytotoxic drugs
- Hemorrhagic cystitis—caused by cyclophosphamide



FOLLOW-UP

PATIENT MONITORING

Same as for lymphoma treated by chemotherapy

POSSIBLE COMPLICATIONS

- Dyspnea as disease progresses
- Depression
- Anorexia
- Myelosuppression caused by chemotherapy

EXPECTED COURSE AND PROGNOSIS

Median survival in dogs with systemic chemotherapy has been reported to be approximately 12 months; however, range for survival may be broad based upon initial response to therapy. The reported survival is compounded by the difficulty of accurately diagnosing the disease.



MISCELLANEOUS

ASSOCIATED CONDITIONS

No known definitive associations

SYNOMYMS

- Eosinophilic pulmonary granulomatosis
- Granulomatosis
- Lymphoid granulomatosis
- Lymphoproliferative angiitis

ABBREVIATION

CHOP = cyclophosphamide, hydroxydaunorubicin (doxorubicin), vincristine (Oncovin), and prednisone

Suggested Reading

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L

LYSOSOMAL STORAGE DISEASES



BASICS

OVERVIEW

- Inherited disorders caused by partial or complete deficiency of a lysosomal enzyme or an enzyme-activator protein, which leads to intracellular accumulation (storage) of the substrate of that enzyme.
- Storage products—proteins, carbohydrates, lipids, or a combination.
- Classes of diseases—proteinoses, glycoproteinoses, oligosaccharidoses, sphingolipidoses, mucopolysaccharidoses.
- Many different types reported in dogs and cats.
- Inheritance is autosomal recessive.

SIGNALMENT

- Dog—German shepherd, German shorthaired pointer, English setter, beagle, cairn terrier, bluetick hound, West Highland white terrier, Sydney silky terrier, English springer spaniel, Portuguese water dog, Japanese spaniel, Labrador retriever, American bulldog, Irish setter, mixed-breed dogs, many others.
- Cats—Persian, Siamese, Korat, Balinese, domestic shorthair.
- Most affected animals <1 year old; a few adult-onset diseases described, with onset as late as 2 years old, or older.

SIGNS

General Comments

- Vary with severity of the enzyme deficiency.
- In certain diseases, carrier animals can be affected with a milder form of the disease.
- Many organ systems are affected, but neurologic signs tend to predominate.

Historical Findings

- Affected animals are normal at birth.
- Fail to thrive and may manifest skeletal malformations, particularly in the mucopolysaccharidoses.
- Neurologic signs within the first few months of life suggest multifocal neurologic disease.

Physical/Neurologic Examination Findings

- Cerebellar dysfunction common—intention tremor, nystagmus, dysmetria.
- Peripheral neuropathy occurs in some diseases—weakness, hyporeflexia or areflexia, wasting.
- Other neurologic signs—ataxia; exercise intolerance; seizures; behavioral changes; visual deficits, deafness, stereotypical behaviors, proprioceptive deficits, tremors.
- Non-neurologic signs—may see organomegaly or skeletal malformations.
- Ocular pathology in some diseases—corneal opacification, cataract formation.

CAUSES & RISK FACTORS

- Genetic—deletion or mutation involving a single gene that causes an absolute or partial deficiency of a lysosomal enzyme or activator protein; deficient production of enzymes that

do not have normal biologic activity.

- Susceptible breed.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Metabolic encephalopathy—usually episodic clinical signs; results of CBC, biochemistry, and urinalysis often diagnostic.
- Toxicities—acute onset of clinical signs; history of exposure.
- Cerebellar hypoplasia—onset at 3–6 weeks of age; non-progressive.
- Cerebellar abiotrophy—deficits limited to the cerebellum; may be difficult to differentiate in the early stages without specific tests.
- Prenatal or neonatal infections (especially viral) resulting in meningoencephalomyelitis—differentiated by CSF analysis; may be other signs, such as chorioretinitis.
- Metabolic diseases—especially organic and amino acidurias.

CBC/BIOCHEMISTRY/URINALYSIS

- Regular blood smears and CSF analysis—cytoplasmic vacuolation of leukocytes caused by accumulation of storage products is present in some cases.
- Urine—may find abnormal accumulation of substances (e.g., oligosaccharide in a-mannosidosis).

OTHER LABORATORY TESTS

N/A

IMAGING

- Radiography—bony malformation may be present in diseases in which skeletal pathology is a feature (e.g., mucopolysaccharidoses).
- Magnetic resonance imaging—used in one case to reveal diffuse white matter pathology in the brain of a dog with globoid cell leukodystrophy.

DIAGNOSTIC PROCEDURES

- Molecular genetic testing—available for the diagnosis of many lysosomal storage diseases; may be used to identify potential carriers.
- Aspirates or biopsies of parenchymal organs, particularly the liver and spleen, may reveal intracellular storage material.
- Biochemical tests—diagnosis may be made by demonstrating low enzyme activity or presence of accumulated substrate or metabolic intermediates in preparations of serum, brain, viscera, leukocytes, or skin fibroblasts.
- Electromyography and nerve conduction studies—abnormal in diseases in which peripheral neuropathy or myopathy is a feature.
- Biopsy of peripheral nerve or skeletal muscle may demonstrate specific pathology.



TREATMENT

- Outpatient—unless severe deficits preclude nursing care at home.
- Activity—restrict to

safe areas; avoid stairs.

- Diet and fluids—ensure proper intake in patients often debilitated; parenteral fluid therapy and enteral or parenteral nutritional support may be needed with severe disease.
- Bone marrow transplantation—used experimentally with some success.
- Gene therapy—area of intense research that may offer hope for specific treatment.
- Enzyme replacement therapy—intrathecal enzyme replacement has shown some efficacy in an experimental setting.
- Primary treatment—preventive; control of breeding; genetic counseling.
- Patients may be at risk of developing secondary infection; initiate appropriate treatment if infection develops.



MEDICATIONS

DRUG(S)

N/A



FOLLOW-UP

- Progressive; ultimately fatal.
- Pedigree analysis—useful in diagnosis; important for identification of potential carrier animals.



MISCELLANEOUS

ABBREVIATION

- CSF = cerebrospinal fluid

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MALASSEZIA DERMATITIS



BASICS

OVERVIEW

- *Malassezia pachydermatis* (syn. *Pityrosporum canis*)—yeast; commensal of the skin, ears, and mucocutaneous areas; can overgrow causing dermatitis, cheilitis, and otitis externa.
- *M. pachydermatis* is lipid-loving, others are lipid-dependent. • Yeast numbers in diseased areas are usually excessive, although this is a variable finding. • The transformation from harmless commensal to pathogen related to allergy, seborrheic conditions, and congenital and hormonal factors.

SYSTEMS AFFECTED

Skin/Exocrine

SIGNALMENT

- Dog—any breed; West Highland white terrier, poodle, basset hound, cocker spaniel, and dachshund predisposed. • Cat—less common; associated with internal neoplasia in aged cats; affects all breeds; however, young Rex cats are predisposed. • No gender predilection. • *Malassezia* dermatitis and *Malassezia*-associated seborrheic dermatitis—common worldwide.

SIGNS

- Pruritus variable; erythema, alopecia, scale, and greasiness of lips, ears, feet, axillae, inguinal area, and ventral neck; malodor.
- Hyperpigmentation and lichenification—chronic cases. • Concurrent black waxy to seborrheic otitis—frequent. • Frenzied facial pruritus—uncommon but characteristic.
- Often an allergy history that worsens and develops glucocorticoid tachyphylaxis.
- Concurrent bacterial folliculitis, hypersensitivity, endocrine and seborrheic dermatitis.

CAUSES & RISK FACTORS

- High humidity and temperature—may increase the frequency. • Concurrent hypersensitivity disease (particularly atopy, flea allergy, and some food allergy/intolerances)—may be a predisposing factor.
- Seborrheic dermatitis (young dogs)—in predisposed breeds. • Endocrinopathy—suspected predisposing factor. • Genetic factors—in predisposed dog breeds and Rex cats. • Concurrent increase in cutaneous *Staphylococcus pseudintermedius* and bacterial folliculitis—confirmed finding; in some cases, canine seborrheic dermatitis with overgrowth of both; treatment of one produces partial resolution and unmasks the other; antiyeast treatment only resolves signs of *Malassezia* dermatitis. • Cats have a young and an adult-age disease, and can be allergy-associated. In Rex cats, genetic factors of the skin and/or their predisposition to a mast cell

abnormality called urticaria pigmentosa are speculative risk factors. Aged cats: *Malassezia* dermatitis associated with thymomas and carcinomas of the pancreas and liver.



DIAGNOSIS

Diagnosis by demonstrating excessive numbers of the organism on diseased skin, and a significant improvement in clinical signs following removal of the yeast.

DIFFERENTIAL DIAGNOSIS

- Allergic dermatitis—including flea allergy, atopy, and cutaneous adverse reaction to food
- Superficial bacterial folliculitis • Primary and secondary seborrhea (keratinization defect)
- Acanthosis nigricans—dachshund

CBC/BIOCHEMISTRY/URINALYSIS

Normal unless affected by underlying cause

OTHER LABORATORY TESTS

- Fungal culture—use contact plates (small agar plates made from bottle lids and filled with Sabouraud agar or modified Dixon agar, especially in the cat); press plates onto the affected skin surface; incubate at 32–37°C for 3–7 days; count the distinctive yellow or buff, round, domed colonies (1–1.5 mm); provides semi-quantitative data. • Non-quantitative culture methods—no value because *Malassezia* is a normal commensal.

DIAGNOSTIC PROCEDURES

- Skin cytology—touch, cotton swab, or cellophane tape preparation stained with Diff-Quik; apply stain as a drop directly onto the slide (yeast may wash off during staining); pass a flame under the slide to improve stain penetration and visualization. • Greasy and/or scaly areas are most likely to produce positive results.



TREATMENT

- Identify and treat any predisposing factors or diseases. • Topical therapy—yeast is principally located in the stratum corneum.
- Shampoo treatment—to remove scale and exudation. • Topical therapies (based on trial data)—miconazole and chlorhexidine shampoo most effective; selenium sulfide shampoo less effective but useful; twice-weekly treatments. • Other topical antifungal and antibacterial shampoo treatments (e.g., ketoconazole) also of value if given with suitable systemic medications.
- Alternative combinations—topical keratolytic shampoo treatment with systemic antiyeast and antibacterial drugs.



MEDICATIONS

DRUG(S)

- Localized cases—may respond to creams and lotions containing imidazole compounds.
- Ketoconazole 10 mg/kg q24h for 2–4 weeks in widespread or chronic lichenified cases. Fluconazole 10 mg/kg q24hr. Itraconazole 5 mg/kg q24hr. • Other imidazoles also effective. • Chronic lichenified cases—ketoconazole (7–10 mg/kg q24h) as a short diagnostic for 7–10 days with effective topical antimycotic shampoo treatment; a good response confirms the diagnosis; response may be slow in chronic cases in which yeasts are buried deep in epidermal folds. • Topical antimicrobial antibacterial shampoo—to maintain remission in chronic cases.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Ketoconazole—rarely may cause hepatic reaction; masks signs of hyperadrenocorticism and interferes with adrenal function tests due to blocking of cortisol production (via inhibition of P450) in the adrenal gland; contraindicated in cats with hepatic and severe debilitating internal malignancy as they may not be able to metabolize the drug.



FOLLOW-UP

- Physical examination and skin cytology—after 2–4 weeks, to monitor therapy. • Treat until only rare organisms can be demonstrated or 7 days after a complete response is achieved. • Pruritus and odor—usually noticeably improved within 1 week.
- Recurrences—common when underlying dermatoses are not well controlled; regular bathing with antifungal antibacterial shampoo combinations helps decrease recurrence.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Ketoconazole contraindicated

Suggested Reading

Miller WH, Griffin CE, Campbell KL. Fungal and Algal Skin Diseases. In: Kirk's Small Animal Dermatology, 7th ed. St. Louis, MO: Elsevier, 2013, pp. 243–249.

Author Kenneth V. Mason

Consulting Editor Alexander H. Werner

MALIGNANT FIBROUS HISTIOCYTOMA



BASICS

OVERVIEW

- Name based on histologic features of fibroblast- and histiocyte-like cells.
- A group of primitive pleomorphic mesenchymal neoplasms, but definitive cellular origin unknown; likely possibilities include fibroblasts, histiocytes, and undifferentiated mesenchymal cells.
- Several histologic variants.
- Storiform-pleomorphic and giant cell—two major variants; both locally invasive; firm, subcutaneous, or visceral masses on examination.
- Despite previous reports to the contrary, metastatic potential in dogs appears to be moderate to high.
- Have been reported as injection site-related sarcomas of cats.

SIGNALMENT

- More commonly reported in cat than in dog.
- Similar biologic behavior in both species.
- Mean age—cats: 9 years (range, 2–12 years); dogs: 8 years (range, < 1–10 years).
- No proven breed or sex predilection, although flat-coated retrievers, rottweilers and golden retrievers appear overrepresented and may be predisposed.

M

SIGNS

Historical Findings

- Anorexia, weight loss, and lethargy may occur.
- Dependent upon on site of involvement.

Physical Examination Findings

- Firm, invasive tumor arising in subcutaneous tissue.
- May exhibit deep extension into underlying skeletal muscle.
- May develop adjacent to bone and induce bone destruction and proliferation.
- Most common sites—dorsal thoracic and scapular area, limbs, and pelvic region.
- May also be a primary splenic tumor in dogs; palpable splenomegaly may be found.
- Distant metastasis—common.

CAUSES & RISK FACTORS

- Unknown
- Can be induced with carcinogens in laboratory animal species
- Injection sites in cats



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other soft tissue sarcoma (e.g., fibrosarcoma, leiomyosarcoma)
- Chondrosarcoma
- Osteosarcoma (extraskeletal)
- Liposarcoma
- Peripheral nerve sheath tumors
- Histiocytic diseases, such as histiocytic sarcoma or systemic histiocytosis
- Mast cell neoplasia

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—may vary; may be normal; may see regenerative or nonregenerative anemia.
- Biochemistry—variably abnormal.
- Urinalysis—usually normal.

OTHER LABORATORY TESTS

Cytologic examination of aspirate—may reveal histiocyte- and fibroblast-like cells.

IMAGING

- Radiography—reveals soft tissue dense mass; may note bone proliferation or destruction.
- Three-view thoracic radiography to check for lung metastasis.
- MRI or CT may be superior for delineating extent of tumor invasion into surrounding tissues.
- Ultrasonography may detect abnormalities consistent with abdominal metastasis (most common in lymph nodes and liver).

DIAGNOSTIC PROCEDURES

Histologic examination of biopsy specimen—necessary for definitive diagnosis.

PATHOLOGIC FINDINGS

- Classification—considerable debate exists among pathologists, which may account for the apparent differences in behavior reported in the literature.
- Storiform-pleomorphic (may be called inflammatory) and giant cell (also called osteoclast-like) are the two major variants reported. Myxoid variant also described.
- Many are histologically high grade.
- Specialized immunohistologic stains, such as CD18, vimentin, desmin, alpha-smooth muscle actin, extra domain 1 (ED1), and/or azan (for collagen) may aid classification. Definitive staining patterns have not been clearly identified.
- Recent report of considerable overlapping histopathologic characteristics with histiocytic diseases in the splenic form.



TREATMENT

- Surgical excision—difficult owing to local invasive nature; recurrence rate is high.
- Amputation of an affected limb—may be appropriate; thoracic and abdominal radiographs and abdominal ultrasound critical for evaluating detectable metastasis before amputation.
- Radiotherapy may be helpful as adjuvant treatment for localized tumor not amenable to complete surgical resection. Expected local tumor control rates may be similar to other high-grade soft tissue sarcomas.



MEDICATIONS

DRUG(S)

Chemotherapy—may be helpful in residual, high-grade tumor or metastatic disease setting; doxorubicin-based protocols are most commonly instituted (dose for canine patients > 10 kg, 30 mg/m² IV every 3 weeks; patients < 10 kg, 1 mg/kg IV every 3 weeks).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

Reexamination—metastatic potential would suggest physical examination and possible imaging; monthly for 3 months, then every 3 months thereafter.

POSSIBLE COMPLICATIONS

Temporary acute side effects (e.g., moist dermatitis and alopecia) may be expected with radiation therapy, and consultation with a radiation oncologist is recommended regarding specific, anatomic site-related side effects.



MISCELLANEOUS

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging

Suggested Reading

Fulmer AK, Mauldin GE. Canine histiocytic neoplasia: An overview. Can Vet J 2007, 48:1041–1050.

Author Anthony J. Mutsaers

Consulting Editor Timothy M. Fan

MALOCCLUSION—SKELETAL AND DENTAL



BASICS

DEFINITION

- **Malocclusion:** any deviation from normal occlusion due to abnormal positioning of a tooth (dental malocclusion) or due to asymmetry or deviation of bones that support the dentition (skeletal malocclusion).
- **Ideal occlusion:**
 - Maxillary incisors positioned rostral to the mandibular incisors.
 - Mandibular canine is inclined labially and bisects the space between the opposing maxillary third incisor and canine.
 - Maxillary premolars do not contact the mandibular premolars; mandibular premolar crowns are positioned lingual to the maxillary premolars; mandibular premolar crown cusps bisect the interdental spaces rostral to the corresponding maxillary premolar.
 - Maxillary fourth premolar mesial cusp is lateral to the space between the mandibular fourth premolar and first molar.

Terms of Malocclusion (American Veterinary Dental College Nomenclature)

- Neutroclusion (Class 1): a normal rostral-caudal relationship of the maxillary and mandibular dental arches with malposition of one or more individual teeth (dental malocclusion); rostral (anterior) crossbite; mesioversion ("lance tooth") linguoversion ("base-narrow mandibular canine) and caudal (posterior).
- Mandibular distoclusion (Class 2): an abnormal rostral-caudal relationship in which the mandibular arch occludes caudal to its normal position relative to the maxillary arch (skeletal malocclusion).
- Mandibular mesioclusion (Class 3): an abnormal rostral-caudal relationship in which the mandibular arch occludes rostral to its normal position relative to the maxillary (skeletal malocclusion).
- Asymmetrical skeletal malocclusion: maxillary-mandibular asymmetry that can occur in a rostro-caudal direction (unilateral abnormal relationship), in a side-to-side direction (loss of midline alignment), or in a dorso-ventral direction with abnormal vertical space between opposing dental arches (open bite).
- "Wry bite": a nonspecific term used to describe a variety of unilateral occlusal abnormalities.

SIGNALMENT

Species

Dogs and cats

Breed Predilections

Breed predilection for certain malocclusions

Mean Age and Range

Malocclusion usually apparent after eruption of teeth (permanent or deciduous).

SIGNS

- Vary greatly according to type, extent, and consequent injuries caused by the

malocclusion.

- May be associated with open or closed bites or overcrowding of the teeth.
- Periodontal disease—from crowding or misalignment of teeth.
- Soft tissue defects—from traumatic tooth contact; may be seen in the floor of the mouth and palate; palatal trauma may eventually result in oronasal fistula formation.
- Fractures or attrition (wear) of teeth—may result from improper tooth contact.

Class 1 Malocclusions

- Rostral (anterior) crossbite—palatally displaced maxillary incisors or labially displaced mandibular incisors; level bite—maxillary and mandibular cusps contact directly.
- Base-narrow canines—tips of mandibular canines touch palate lingual to normal contact point, just labial to the diastema between corner incisor and maxillary canine (linguoversion).
- Lance teeth—mesioversion of maxillary canine(s); the diastema between the corner incisor and this canine is often diminished and may force the mandibular canine into an abnormal position. dolichocephalic breeds (e.g., shelties and collies).
- Caudal (posterior) crossbite—most are due to reversal of the relationship (labial/lingual) between the upper and lower carnassial teeth; more common in dolichocephalic breeds (e.g., collies, shelties, some sight hounds).

CAUSES

- Congenital or hereditary factors—skeletal malocclusions (Classes 2, 3, and 4) and breed predilection.
- Impediment to tooth eruption—operculum; retention of soft tissue covering.
- Delayed eruption of deciduous or permanent teeth.
- Retention (persistent) or delayed loss of deciduous teeth; permanent mandibular canines will erupt lingual to persistent deciduous teeth.
- Traumatic injury affecting the jaws or teeth.

RISK FACTORS

Hereditary predispositions



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Tooth displacement—due to trauma, oral masses, or other causes.
- Mechanical block—due to jaw fractures, luxated or subluxated teeth, or foreign bodies causing open bite.
- Examine breed standards to determine what might be acceptable for the breed.

CBC/BIOCHEMISTRY/URINALYSIS

Generally normal

IMAGING

- Oral photography—pre-, peri-, and post-therapy.
- Intraoral radiography—to evaluate roots and abnormalities, jaw anatomy, root maturity

DIAGNOSTIC PROCEDURES

- Complete oral examination to assess other oral abnormalities, including persistent deciduous teeth.
- Impressions and models—for evaluation and appliance manufacture.



TREATMENT

APPROPRIATE HEALTH CARE

- The accurate assessment of abnormalities of occlusion will help determine if treatment is warranted and what treatment is appropriate.
- Extraction of offending teeth can many times be an effective alternative to more classic orthodontic treatments.
- Not every malocclusion needs orthodontic correction. If the bite is functional and non-traumatic to the animal, treatment may not be necessary.
- Additionally, extraction (or crown reduction with pulp capping) of offending teeth often can be an effective alternative to more classic orthodontic treatments.
- Orthodontic treatment is usually based on prevention of improper contact trauma, wear, or injury to hard or soft tissues, and should only be performed by a trained individual.

DIET

Soft diet with appliances

CLIENT EDUCATION

Home Care with Appliance

- Examine the appliance twice daily.
- Flush the mouth with an oral hygiene solution or gel.
- Prevent chewing of items and provide a soft diet until the appliance is removed.

SURGICAL CONSIDERATIONS

Permanent Tooth Class 1 Malocclusion

- Treatment primarily involves tipping movements of the teeth, although extrusion may be required to provide proper retention.
- Rostral crossbite—arch crowding; may require odontoplasty to thin teeth (to allow room for movement).
 - Movement can be accomplished but is likely complicated and should be handled by a specialist.
- Base-narrow canine teeth—treatment is aimed at prevention of contact trauma, pain and discomfort, and oronasal fistula formation.
 - The diastema (space between the maxillary third incisor and canine) must be sufficient for the mandibular canine to fit; once occluding correctly in the diastema, the closed bite serves as a natural retainer.
 - If the mandibular canines have just started to erupt into a lingual position, manual manipulation or "ball therapy" may influence a more buccal eruption sequence; the deciduous teeth and roots must be completely absent.
 - A hard rubber ball (hand ball, etc.) can be placed in the mouth and of a size that will help "slide" the canines laterally; apply the ball with gentle

MALOCCLUSION—SKELETAL AND DENTAL

(CONTINUED)

mouth closing pressure two to three times daily, a few minutes at a time, and encourage play with the ball. • If the tip of the mandibular canine barely touches the edge of the maxillary mucosa, gingivoplasty or gingivectomy in the diastema may release the contact. • Moderate cases may be easily managed by building a false crown extension with composite material that will splay the false tip lateral to the gingival margin, with eventual correction of the positioning. • More severe cases (extreme linguoversion, inadequate diastema or rostral or distal deviation of the mandibular canine) may require an orthodontic appliance (incline plane): • Movement can be accomplished but is likely complicated and should be handled by a specialist. • Mandibular canine extraction or crown reduction with vital pulpotomy can provide the patient with a comfortable bite. • Maxillary canine mesioversion (Lance tooth): • Movement can be accomplished but is likely complicated and should be handled by a specialist. • Caudal (posterior) crossbite—in most cases, no treatment is necessary, as the bite is typically functional; in traumatic situations, extraction of one of the offending teeth; orthodontic correction is long and tedious and requires more advanced orthodontic appliances and blocking the bite open.

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Permanent Tooth Class 2, 3, and Asymmetrical Malocclusion

- Based on providing a functional, non-traumatic occlusion for the animal's medical health; treatment may not be necessary.
- May require advanced orthodontic and surgical procedure and is generally best handled by a specialist.

Deciduous Tooth Class 1 Malocclusion

Careful and gentle extraction of the maloccluded deciduous tooth (interceptive orthodontics) to remove inappropriate physical impediment in hopes that the permanent tooth will erupt in the appropriate position; when performed at least 4 weeks prior to permanent tooth eruption, success rate > 80% is not uncommon.

Deciduous Tooth Class 2, 3, and 4 Malocclusion

Careful and gentle extraction of the maloccluded deciduous tooth in hopes that the short jaws will be released from the bite interlock, allowing it to grow (if the genetic potential is present), prior to eruption of permanent teeth and reestablishment of bite interlock; performed at least 6 weeks prior to permanent tooth eruption, success rate < 20% is common.



FOLLOW-UP

PATIENT MONITORING

- For the corrected occlusion to be stable, it needs to be self-retaining or it may tend to revert to malocclusion; examine at 2 weeks, 2 months, and 6 months after the treatment is complete to see if desired outcome is stable.
- It is advisable at around 6 months post-therapy for radiographs to be taken and compared to the pretreatment films to determine if all teeth still appear vital (alive) and to evaluate any root changes that may have occurred due to the pressures of tooth and root movement during orthodontics.

PREVENTION/AVOIDANCE

- Careful selection of puppies, with oral and general examination, as well as examination and history of sire and dame, prior to purchase.
- Selective breeding based on preferred breed characteristics.
- Careful monitoring of deciduous and permanent tooth eruption for early detection and treatment, if required.

POSSIBLE COMPLICATIONS

- Selective extraction of deciduous tooth—potential for injury to underlying permanent tooth buds either by direct injury with extraction instruments or subsequent traumatic inflammation affecting tooth growth and maturity; injuries may result in tooth buds dying, teeth becoming non-vital as they erupt, root dysplasia or dilaceration, crown hypoplasia, or hypomineralization.
- Orthodontic movement of permanent teeth—several conditions may result, including root resorption, root ankylosis, or non-vitality of the tooth; these conditions are uncommon in properly managed orthodontic procedures.

EXPECTED COURSE AND PROGNOSIS

- Course of treatment may vary with the type of malocclusion and the animal's nature and habits (e.g., inappropriate chewing).
- Generally, most cases take 1–7 months for movement and retention phase, depending on severity and if extrusion of tooth/teeth is required for stabilization of the bite. Prognosis is good to excellent in most treated patients.
- Prognosis is fair to good in most untreated malocclusions.
- Complications in untreated cases—periodontal disease; attrition or fractures of teeth; trauma to soft tissues;

oronasal fistula formation; drying or desiccation of exposed tooth surfaces, resulting in beige to brown discoloration.

- Some cases DO NOT need or require orthodontic intervention; only routine observation for early detection and treatment of any secondary complications (e.g., periodontal disease, worn or chipped teeth) is advised.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Lack of head symmetry
- Oral soft tissue trauma
- Chipped teeth
- Desiccation of exposed tooth surfaces
- Periodontal disease

PREGNANCY/FERTILITY/BREEDING

Although animals have the medical right to as functional and correct an occlusion as can be reasonably provided by therapy, animal club rules, professional association principles, and state and national laws may conflict with an animal's right to proper medical therapy. Some kennel club rules disqualify animals with modification to natural appearance (with certain exceptions), and owners should be made aware of this. If hereditary involvement is suspected, inform the owner. If treatment is being considered, the owner or agent should acknowledge his or her responsibility to inform anyone who has the right to know of such alterations. Additionally, the possibility of removing the animal from the genetic pool by appropriate methods should be discussed.

INTERNET RESOURCES

<http://www.avdc.org/Nomenclature.html>.

Suggested Reading

Lobprise HB. Blackwell's Five-Minute Veterinary Consult Clinical Companion—Small Animal Dentistry. Ames, IA: Blackwell, 2007 (for additional topics, including diagnostics and techniques).

Wiggs RB, Lobprise HB. Veterinary Dentistry: Principles and Practice. Philadelphia: Lippincott-Raven, 1997, pp. 457–463.

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Consulting Editor Heidi B. Lobprise

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**Client Education Handout
available online**

MAMMARY GLAND HYPERPLASIA—CATS



BASICS

OVERVIEW

Benign enlargement of one or more mammary glands

SIGNALMENT

- Young, intact, cycling, or pregnant queens.
- Cats of either gender after gonadectomy (rare in tom).
- Cats of either gender that are receiving exogenous progestagen (e.g., megestrol acetate).
- Less often in older (9–12 years) pregnant queens.

SIGNS

- Localized or diffuse rapid (2–5 weeks) enlargement of one or more mammary glands.
- Firm and non-painful masses in uncomplicated cases.
- No concurrent signs of systemic illness; tachycardia, lethargy and anorexia possible with complications.

CAUSES & RISK FACTORS

- Exaggerated proliferation secondary to an endogenous progesterone influence (pregnancy, pseudopregnancy) or exogenous progestagens (megestrol or medroxyprogesterone acetate).
- May develop after gonadectomy; pathogenesis may involve progesterone, growth hormone, prolactin, insulin-like growth factors. Suspect ovarian remnant syndrome.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Mastitis—lactating queen; mammary glands erythematous and painful; systemic illness with fever and immature neutrophilia; inflammatory cells and bacteria in fluid expressed from the affected gland(s).
- Mammary neoplasia—old queens (> 6 years); gross appearance may be indistinguishable; irregular shape and margins, heterogeneous echogenicity on ultrasound; differentiated by biopsy of affected tissue.

CBC/BIOCHEMISTRY/URINALYSIS

Normal; leukocytosis possible with secondary mastitis.

OTHER LABORATORY TESTS

Progesterone analysis—confirm exposure or ovarian remnant syndrome.

IMAGING

- Transabdominal ultrasonography—rule out pregnancy.

- Ultrasonography of affected gland(s)—homogeneous parenchyma, round or oval with regular margins.

DIAGNOSTIC PROCEDURES

- Cytologic examination of fluid expressed from affected glands—non-inflammatory.
- Excision biopsy—benign fibroglandular proliferation with no inflammation or necrosis.



TREATMENT

- Hyperplasia owing to high endogenous progesterone—regresses when progesterone falls at the end of false pregnancy or gestation; consider ovariohysterectomy if preservation of fertility is not desired.
- Hyperplasia owing to exogenous progestagens—regresses when medication is withdrawn.
- Hyperplasia developing after gonadectomy—suspect ovarian remnant; surgical removal of ovarian remnants.
- In uncomfortable animals, may attempt progesterone receptor blockers (aglepristone), prolactin inhibitors (bromocriptine, cabergoline), testosterone.
- Mastectomy, systemic antibiotics or supportive care may be needed with complications.



MEDICATIONS

DRUG(S)

- Bromocriptine mesylate 0.25 mg (per cat) PO q24h for 5–7 days; not approved for use in cats; may cause nausea.
- Cabergoline 5 µg/kg PO q24h for 5–7 days.
- Nausea—metoclopramide (0.2 mg/kg PO q6–8h) or divided bromocriptine dose (give twice daily).
- Aglepristone (10–15 mg/kg SC on 2 consecutive days or 20 mg/kg SC once a week until resolution); not approved for use in cats, not readily available in the United States (mifepristone, a related compound, available in United States as human product; dose for cats undefined).
- Testosterone cypionate or testosterone enanthate (2 mg/kg IM once); not approved for use in cats.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Aglepristone—pregnant animals will abort. May see dermatitis at the site of injection.
- Dopamine agonists—pregnant animals will abort; may cause vomiting.



FOLLOW-UP

AGE-RELATED FACTORS

Young queens

EXPECTED COURSE AND PROGNOSIS

- Remission within 4 weeks after the end of pseudopregnancy or gestation, withdrawal of progestins, ovarioectomy, or aglepristone treatment.
- Likelihood of recurrence in cats left intact—unknown.
- Correlation with other abnormal conditions of the reproductive tract—unknown.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Fertility not affected after aglepristone treatment.

SYNOMYS

- Benign mammary hyperplasia
- Fibroglandular mammary hyperplasia
- Mammary fibroadenomatosis
- Fibroepithelial mammary hyperplasia
- Fibroadenomatous hyperplasia

SEE ALSO

Ovarian Remnant Syndrome

M

Suggested Reading

Burstyn U. Management of mastitis and abscessation of mammary glands secondary to fibroadenomatous hyperplasia in a primiparous cat. J Am Vet Med Assoc 2010, 236:326–329.

Gimenez F, Hecht S, Craig LE, et al. Early detection, aggressive therapy: Optimizing the management of feline mammary masses. J Feline Med Surg 2010, 12:214–224.

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Johnston SD, Root Kustritz MV, Olson PN. Disorders of the mammary glands of the queen. In: Canine and Feline Theriogenology. Philadelphia: Saunders, 2001, pp. 474–485.

Authors Maria Soledad Ferrer and Lynda M.J. Miller

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MAMMARY GLAND TUMORS—CATS



BASICS

DEFINITION

Malignant and benign tumors of the mammary glands in cats

PATHOPHYSIOLOGY

- 5–15% of tumors are histologically benign.
- 85–95% of tumors are malignant, and most are carcinomas; sarcomas are rare (see "Pathologic Findings").
- Inflammatory carcinomas are rarely diagnosed. These are anaplastic carcinomas with considerable inflammatory cell infiltrates, and are associated with extensive local ulceration, edema, and pain, as well as rapid metastasis.
- Pulmonary metastasis is identified in up to 80% of cats, and regional lymph node metastasis in up to 50%. Other sites for metastasis include the liver, spleen, kidney, adrenal gland, pleura, peritoneum, heart, thyroid gland, and bone. At necropsy, metastasis is identified in > 90% of cats.

SYSTEMS AFFECTED

- Reproductive—mammary glands.
- Metastasis can affect any organ system, especially the respiratory and lymphatic systems.

M

GENETICS

The high incidence of mammary tumors in Siamese cats suggests a genetic component to this disease, but specific genes have not been identified to date.

INCIDENCE/PREVALENCE

- Third most common neoplasia in cats (after hematopoietic and skin tumors).
- The estimated incidence is 12.8–25.4 per 100,000 cats.

SIGNALMENT

Species

Cat

Breed Predilections

- Domestic shorthair and longhair breeds are affected most commonly, but this likely reflects the popularity of these breeds rather than a true predilection.
- Siamese cats have twice the risk of other breeds for developing mammary tumors.

Mean Age and Range

- Mean—10–12 years.
- Range—9 months to 23 years; most are > 5 years of age.
- Siamese cats tend to develop mammary tumors at a younger age, and the incidence begins to plateau around 9 years of age.

Predominant Sex

- Females predominate.
- While being intact increases the risk of mammary tumors (see "Risk Factors"), most cats diagnosed with mammary tumors are spayed.
- 1–5% of mammary carcinomas occur in male cats.

SIGNS

Historical Findings

- Most cats present for evaluation of a palpable ventral abdominal mass.
- Cats with advanced metastatic disease may present for general signs of illness (e.g., lethargy or anorexia) or for signs attributable to a specific site of metastasis (e.g., dyspnea due to pulmonary metastasis or pleural effusion).
- The duration of clinical signs can vary from days to several months.

Physical Examination Findings

- Mammary masses can be discrete or infiltrative, soft or firm. Smaller masses often are freely moveable, whereas larger masses can adhere to the underlying abdominal musculature.
- The overlying skin can be intact, but frequently it is ulcerated.
- The associated nipple may be inflamed and exude serous fluid.
- Any gland can be affected, although the caudal two glands are affected more commonly. Left and right sides are affected with equal frequency.
- Up to half of cats will have multiple tumors affecting glands on the same and/or opposite sides.
- Axillary or inguinal lymphadenopathy (reactive or metastatic) may be present.
- As tumor cells spread via the lymphatics, linear beaded chains of tumor nodules can form in lymphatic vessels within the mammary tissue.
- Cats with inflammatory carcinomas present with severe ulceration, erythema, pain, and edema in the ventral abdomen and pelvic limbs.

CAUSES

Unknown

RISK FACTORS

- Compared to intact cats, those spayed at < 6 months of age are 11 times less likely to develop mammary carcinomas, and those spayed at 6–12 months are 7 times less likely, suggesting that hormonal influence is significant in the pathology of mammary gland carcinoma.
- There is no obvious protective effect when cats are spayed at > 12 months of age.
- Exogenous progestins (e.g., medroxyprogesterone acetate) increase the risk of benign and malignant mammary tumor development in female and male cats. In one study, 8 of 22 male cats with mammary carcinomas had a history of exogenous progestin therapy.
- Parity has not been shown to affect mammary tumor development.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Fibroepithelial hyperplasia—especially in young (< 2 years) intact female cats, and older or spayed cats receiving exogenous progestins.

- Mastitis.
- Other cutaneous or subcutaneous tumors.
- Inguinal or axillary lymphadenopathy (reactive or neoplastic).
- Inguinal hernia.
- Large/prominent inguinal fat pad.

CBC/BIOCHEMISTRY/URINALYSIS

Usually unremarkable

OTHER LABORATORY TESTS

Coagulation profile recommended for cats with suspected inflammatory carcinomas due to the high incidence of secondary disseminated intravascular coagulopathy.

IMAGING

- Three-view thoracic radiographs are recommended to screen for pulmonary metastasis and/or pleural effusion. Pulmonary metastases are most commonly associated with ill-defined interstitial nodules or a diffuse pulmonary pattern, although well-defined interstitial nodules are seen occasionally. Malignant pleural effusion is common, and can obstruct adequate visualization of pulmonary parenchyma.
- Abdominal ultrasound is recommended to screen the medial iliac lymph nodes and other abdominal visceral organs for metastases.
- Ultrasound also can be used to try to visualize non-palpable axillary or inguinal lymph nodes, as well as to look for additional small masses within the mammary glands.

DIAGNOSTIC PROCEDURES

- Cytology can be useful for ruling out other non-mammary malignancies. However, it is not useful for distinguishing between benign and malignant mammary masses.
- Histopathologic evaluation is needed to reach a definitive diagnosis. Since most mammary tumors are malignant, this is usually performed on tissue removed during radical mastectomy (see "Treatment"). While not contraindicated, incisional biopsies are routinely recommended only for cats with advanced-stage disease that are not candidates for aggressive local surgery.
- All tissue removed must be submitted for histopathologic evaluation. This allows for the most accurate diagnosis, and also allows for evaluation of surgical margins for completeness of excision.
- The ipsilateral draining lymph nodes (axillary and inguinal) should be removed whenever possible and submitted separately for histopathologic evaluation, even if grossly normal.
- Cytology of pleural fluid can be useful for confirming intrathoracic metastasis.

PATHOLOGIC FINDINGS

- The most common histologic subtypes are tubulopapillary, cribriform, and solid carcinomas.
- Histologic subtype has not consistently been shown to affect prognosis, but there is some evidence that tubulopapillary carcinomas carry a better

(CONTINUED)

prognosis. • Tumor grade, based on degree of tubule formation, nuclear and cellular pleomorphism, and mitotic index, is predictive of survival after surgery. • Vascular and lymphatic invasion is associated with more advanced clinical stage and shorter disease-free interval after treatment.

- Mammary sarcomas are rare but potentially slow to metastasize.



TREATMENT

APPROPRIATE HEALTH CARE

- Surgery is recommended for cats with gross disease confined to the mammary glands with or without regional lymph node involvement.
- Adjuvant chemotherapy is recommended after the cat has recovered from surgery.
- Chemotherapy can be used as a sole treatment modality for cats with non-surgical local disease and/or distant metastasis, although long-term control would not be expected to be durable. • Radiation therapy has not been evaluated. • Palliative pain therapy is recommended for cats with non-resectable local disease or gross metastasis, or when definitive therapy is declined.

CLIENT EDUCATION

- Stress the benefits of early ovariohysterectomy (< 6 months of age) in non-breeding cats. • Stress the importance of early detection and aggressive treatment.

SURGICAL CONSIDERATIONS

- Radical mastectomy of the affected mammary chain(s) is recommended. This significantly reduces the risk of local tumor recurrence as well as recurrence in the lymphatic vessels coursing through the mammary tissue. • Bilateral radical mastectomies are usually staged 2–4 weeks apart; however, some studies suggest that unilateral radical mastectomy is sufficiently effective to control local disease in a subset of patients. • The inguinal and (if possible) axillary lymph nodes should be removed at the same time, regardless if they are normal in size. • In cats with advanced metastatic disease, palliative local mastectomy can be considered to remove an ulcerated or infected tumor.



MEDICATIONS

DRUG(S) OF CHOICE

- Doxorubicin (25 mg/m² IV q3 weeks) alone or in combination with cyclophosphamide (100 mg/m² IV or PO divided over 4 days).
- Mitoxantrone, carboplatin, and docetaxel might have activity. • Consult with an oncologist for current chemotherapy recommendations.
- Palliative analgesics and antibiotics should be considered for cats with tumors that are painful and/or ulcerated.

CONTRAINdications

Use doxorubicin with caution in cats with renal or hepatic insufficiency.

PRECAUTIONS

If you are unfamiliar with chemotherapy, consult an oncologist before administering.



FOLLOW-UP

PATIENT MONITORING

- Thorough physical examination conducted monthly for the first 3 months, then every 2–3 months thereafter is recommended. Palpation of the previous incision line, the remaining mammary glands, and regional lymph nodes should be emphasized during examination. • Three-view thoracic radiographs every 2–3 months for detection of metastases.

PREVENTION/AVOIDANCE

Ovariohysterectomy prior to 6 months of age can reduce the risk of developing mammary carcinoma by 11 times.

POSSIBLE COMPLICATIONS

Malignant pleural effusion may develop rapidly causing life-threatening dyspnea.

EXPECTED COURSE AND PROGNOSIS

- Most cats die from local recurrence and/or metastasis. • Tumor size is strongly predictive of prognosis. For tumors ≤ 2 cm in diameter median survival is > 4.5 years (14 months in males), for tumors 2–3 cm it is 1–2 years (5–6 months in males), for tumors > 3 cm it is 4–6 months (1–2 months in males).
- Radical mastectomy significantly reduces the risk for local tumor recurrence. The impact on survival is not as consistent because

of the high metastatic rate associated with this tumor. • In retrospective studies, adjuvant chemotherapy (doxorubicin with or without cyclophosphamide) has not consistently improved disease-free interval or survival. However, chemotherapy has proven efficacy against nonresectable and metastatic feline mammary tumors (gross disease), and given the high metastatic rate of these tumors adjuvant chemotherapy is still strongly recommended. • For cats with advanced-stage disease treated with chemotherapy alone, response rates are around 50%. Survival times are 6–12 months for cats that do have a positive response to treatment, < 6 months for those that do not.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

- Given the possible genetic contribution to this disease, particularly in Siamese cats, breeding affected cats is not recommended.
- Chemotherapy is not recommended in pregnant queens, particularly during the early stages of pregnancy.

Suggested Reading

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Author Dennis B. Bailey

Consulting Editor Timothy M. Fan



Client Education Handout
available online

M

MAMMARY GLAND TUMORS—DOGS



BASICS

DEFINITION

Benign or malignant tumors of the mammary glands in dogs

PATHOPHYSIOLOGY

- Estrogen can exert direct genotoxic effects on mammary epithelium leading to mutations and aneuploidy.
- Progesterone may increase growth hormone and growth hormone receptor expression by the mammary gland leading to increased insulin-like growth factor-1 (IGF-1) which is associated with proliferation and survival.
- Most dogs develop multiple tumors due to entire mammary tissue exposed to sex hormones during puberty, i.e., "field carcinogenesis."
- Mammary gland tumors are a continuum from benign to malignant.
- Obesity decreases sex hormone-binding globulin leading to increased concentration of free estrogen.

SYSTEMS AFFECTED

- Reproductive
- Metastasis—lymphatic, respiratory, skeletal, nervous, and other systems

M

GENETICS

Germline mutations of *BRCA-1* and -2 genes reported in English springer spaniels.

INCIDENCE/PREVALENCE

50–70% of all tumors in female dogs. 71% of all female Beagles developed at least one mammary neoplasm.

SIGNALMENT

Breed Predilections

Toy and miniature poodle, English springer spaniel, Brittany spaniel, cocker spaniel, English setter, boxer, English pointer, German shepherd, Maltese, Doberman, and Yorkshire terrier

Mean Age and Range

Uncommon in dogs < 5 years; mean age 9–11 years (malignant) and 7–9 years (benign).

SIGNS

- 70% of patients have multiple tumors.
- Caudal mammary glands more commonly affected.
- Discrete, well-circumscribed mass in systemically healthy patient.
- Inflammatory carcinoma: diffuse edematous, warm, painful mammary chains.
- Inflammatory carcinoma associated with distant metastasis and systemic illness.

CAUSES

Unknown; likely hormonal

RISK FACTORS

- Age
- Breed: small breeds more common than large breeds

- Hormone influence (see "Prevention")
- Obesity during puberty increases risk. Underweight at 9–12 months of age associated with protective effect.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Lipoma
- Mast cell tumor
- Mammary hyperplasia
- Mastitis

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

N/A

IMAGING

- Thoracic radiography may detect metastasis and three views are advised.
- CT is more sensitive for detection of pulmonary metastasis than are plain radiographs.
- Abdominal radiography may detect metastasis to regional lymph nodes or vertebrae.
- Abdominal sonography to evaluate for regional or distant metastasis.

DIAGNOSTIC PROCEDURES

- Fine-needle aspirate cytology: 67.5–93% correlation with histopathology; 88% sensitivity and 96% specificity for malignancy.
- Fine-needle aspirate cytology of local lymph node(s).
- Histologic evaluation for definitive diagnosis. Request margin evaluation.

PATHOLOGIC FINDINGS

- There is a wide histologic spectrum of mammary tumors. Dogs may have concurrent benign and malignant tumors. Histologic examination of all excised masses is indicated.
- Histologic grading 1 (well-differentiated) to 3 (poorly differentiated) based on tubule formation, nuclear pleomorphism, and mitotic index valid for epithelial tumors only.
- Stromal invasion, vascular/lymphatic invasion, and lymph node status important.



TREATMENT

APPROPRIATE HEALTH CARE

- Surgery—primary mode of treatment.
- Chemotherapy—may be effective and indicated for patients with high risk of metastasis or recurrence: histologic high-grade, lymphatic/vascular invasion, stage III or higher.

CLIENT EDUCATION

- Advise client that a mammary lump should be evaluated by a veterinary health professional.

- Inform client that early surgical intervention is best.

- Advise ovariohysterectomy before first estrus.

SURGICAL CONSIDERATIONS

- Type of surgery determined by therapeutic intent. Curative intent with wide excision, preventative with chain mastectomy, palliative intent for advanced disease.
- Consider age, tumor size, number of tumors, history of prior tumors, and clinical stage.
- Most patients with inflammatory carcinoma are poor surgical candidates due to profound diffuse microscopic disease, advanced stage, systemic illness, and local coagulopathies.
- 58% of dogs treated with regional mastectomy will develop a new tumor in the ipsilateral chain. Increased risk if initial tumor is malignant (> 70%).
- Current recommendations for single tumor of unknown histology: wide excision to achieve complete removal is the adequate surgical "dose," i.e., 2-cm lateral margins and 1 fascial plane deep.
- Ovariohysterectomy (OHE) within 2 years prior to or concurrent with tumor removal may have survival benefit.
- Remove tumor following abdominal closure if performing concurrent OHE to avoid tumor seeding of abdomen or incision.



MEDICATIONS

DRUG(S) OF CHOICE

- Always consult a veterinary oncologist for updated information.
- Doxorubicin 30 mg/m² IV (dogs > 15 kg) every 21 days.
- NSAID ± chemotherapy for inflammatory carcinoma.

CONTRAINDICATIONS

Doxorubicin—myocardial failure

PRECAUTIONS

Chemotherapy may be toxic; seek advice before treatment if you are unfamiliar with cytotoxic drugs.

POSSIBLE INTERACTIONS

Doxorubicin—potential side effects include myelotoxicity, vomiting, diarrhea, and cardiac damage.

ALTERNATIVE DRUG(S)

- Carboplatin, gemcitabine, 5-FU, cyclophosphamide have been reported with varying impact on clinical outcome.
- Perioperative desmopressin for grade 2–3 carcinoma may improve survival.
- Tamoxifen—helpful in some humans with breast cancer; ineffective in dogs and has serious side effects (e.g., pyometra); do not use in dogs.

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FOLLOW-UP

PATIENT MONITORING

Physical examination, abdominal sonography, and thoracic radiographs—1, 3, 6, 9, and 12 months after treatment.

PREVENTION/AVOIDANCE

- Spayed before first estrous cycle—0.5% lifetime risk of developing tumor.
- Spayed before second estrous cycle—8.0% lifetime risk.
- Spayed after second estrus—26% lifetime risk.
- Spayed after 2.5 years of age—no sparing effect on risk.

POSSIBLE COMPLICATIONS

- Infection or dehiscence with surgery
- Myelosuppression with chemotherapy
- DIC with some (especially inflammatory carcinomas) types

EXPECTED COURSE AND PROGNOSIS

- 50% of canine mammary tumors are malignant.
- 50% of malignant tumors metastasize.
- 58–70% of dogs will develop another tumor in the ipsilateral chain.
- Tumor size, lymph node status, and proposed WHO clinical stage (I–V) are most consistent prognostic factors.
- Presence of lymphatic invasion, incomplete surgical margins may be independent prognostic factors.
- Mammary sarcoma carries worse prognosis.

- Inflammatory carcinoma median survival time < 3 months.
- WHO clinical stage may be applicable to non-inflammatory epithelial tumors.
- Stage I: Tumor size < 3 cm, no regional or distant metastasis—complete excision has excellent prognosis.
- Stage II: Tumor 3–5 cm, no regional or distant metastasis—complete excision has excellent prognosis.
- Stage III: Tumor > 5 cm, no regional or distant metastasis—median survival 10 months with surgery alone.
- Stage IV: Any tumor size, lymph node metastasis, no distant metastasis—median survival time 5–10 months with surgery.
- Stage V: Any tumor size, any lymph node status, evidence of distant metastasis—median survival time < 6 months.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Hypertrophic osteopathy
- Metastasis to lymph nodes, lungs, and CNS

PREGNANCY/FERTILITY/BREEDING

- Treatment with progestin increases the chance of tumor development at a younger age.
- Treatment with progestin increases risk of development of benign tumor.
- Treatment with progestin and estrogen increase risk of malignant tumor development.

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Client Education Handout
available online

M

MARIJUANA TOXICOSIS



BASICS

OVERVIEW

- Marijuana (*Cannabis sativa*) is the most common illicit drug exposure in companion animals.
 - The major psychoactive agent, δ -9-tetrahydrocannabinol (THC), is most concentrated in the leaves and buds. Dried plants are much more potent than fresh.
 - THC binds two cannabinoid receptors, CB1 (CNS) and CB2 (peripheral), resulting in clinical signs.
 - The minimum lethal dose of THC is greater than 3 g/kg for dogs.
 - The THC content in marijuana can range from 0.4% to 20% depending upon the cultivation techniques.
- Commonly affected organ systems
- Cardiovascular • Gastrointestinal • Nervous
 - Ophthalmic • Respiratory • Renal/Urologic

SIGNALMENT

Younger animals may be overrepresented due to an increased tendency to ingest foreign items.

SIGNS

- M**
- Often begin 1–2 hours after ingestion. May begin in minutes following inhalation.
 - Ataxia and incoordination, hypersalivation, vomiting, glazed eyes, mydriasis, depression, hypothermia, trembling, urinary incontinence.
 - Higher doses may cause bradycardia, hypotension, and coma. Nystagmus, vocalization, sinus tachycardia, seizures, and hyperthermia may also occur.

CAUSES & RISK FACTORS

- Intoxication occurs via ingestion (most often) or inhalation of marijuana smoke. Pets in homes of recreational or medical marijuana users are at greater risk for exposure.
- Ingestion of plant material is most common but homemade or commercial foods laced with concentrated marijuana ("medibles") are gaining popularity. Examples include brownies, cookies, gummy candy, soda/other drinks, pizza, ice cream, caramel corn, chocolates, bread, snack mixes, and more.
- Regions with medical marijuana dispensaries may correlate to increased exposures.
- Police dogs may be at higher risk.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other illicit drugs—LSD, PCP, hallucinogenic mushrooms.

- Opioids (greater cardiac/respiratory depression, miosis, reversed with naloxone), benzodiazepines, muscle relaxants, ethanol, ethylene glycol (metabolic acidosis, crystalluria), methanol, diethylene glycol, propylene glycol, tranquilizers, depressants, xylitol (hypoglycemia).

CBC/BIOCHEMISTRY/URINALYSIS

No specific abnormalities but should be used to rule out other causes.

OTHER LABORATORY TESTS

- Human urine drug tests are unreliable and may result in false negatives. A positive result can be considered a true positive.
- Stomach contents and/or urine may be submitted to veterinary diagnostic lab for confirmatory testing.

IMAGING

No specific abnormalities but abdominal radiography is useful if an obstruction is suspected (e.g., ingestion of a baggie containing marijuana, packaging of a food product).

DIAGNOSTIC PROCEDURES

None



TREATMENT

- Mildly affected patients may not require intervention and can be kept in a low-stimulatory, protective environment.
- Treatment is focused on decontamination and supportive care. Induce emesis following recent (< 2 h) ingestion in asymptomatic patients only if they have not already vomited. If symptomatic, gastric lavage should be considered for very large ingestions or if concentrated products (i.e. butter, foods) were ingested.
- Activated charcoal q8h for 2–3 doses if severe signs.
- Warming/cooling measures as needed.
- IV fluid support if poor perfusion parameters or dehydration.
- Oxygen if respiratory depression.
- Provide ocular lubricant and rotation to comatose animals.



MEDICATIONS

DRUG(S)

- Antiemetics (e.g., maropitant 1 mg/kg SQ q24h for dogs or cats) as needed.
- Diazepam (0.25–0.5 mg/kg IV PRN for dogs or cats) for CNS stimulation, anxiety, agitation.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Use acepromazine cautiously due to risk of hypotension.
- Use phenobarbital cautiously due to the risk of severe sedation and respiratory depression.



FOLLOW-UP

PATIENT MONITORING

Monitor temperature, pulse, and respiration q2–3h until normal. Monitor blood pressure in severe cases (hypotension).

PREVENTION /AVOIDANCE

- Educate pet owners about the risks of leaving marijuana or laced food products accessible to pets. Stress that pets will readily consume such products.
- Keep pets confined during parties.
- Keep police dogs muzzled if indiscriminate eaters.

EXPECTED COURSE AND PROGNOSIS

- Clinical signs may last up to 24 hours in mild cases and may be monitored at home.
- Clinical signs may persist for several days in severe cases, especially if a large dose were ingested.
- The prognosis is excellent with appropriate care.
- Death is rare but has been reported in dogs ingesting foods made with marijuana butter.



MISCELLANEOUS

ABBREVIATIONS

- CNS = central nervous system
- THC = δ -9-tetrahydrocannabinol

INTERNET RESOURCES

- <http://www.aspca.org/pet-care/animal-poison-control/toxic-and-non-toxic-plants/marijuana>
- <http://www.petpoisonhelpline.com/poison/marijuana/>

Suggested Reading

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Client Education Handout available online

MARKING, ROAMING, AND MOUNTING BEHAVIOR—CATS



BASICS

OVERVIEW

Urine Marking

- Depositing of urine on vertical (spraying) or horizontal (novel items) surfaces for communication purposes (territorial, sexual, or agonistic situations).
- Marking can account for 30% of feline behavior problems.

Roaming

- Escape or wandering activity for the purpose of seeking mates, defining territory, obtaining food, or sensory stimulation/enrichment.
- Urine marking and roaming behavior are normal but undesirable feline behaviors in companion cats.

Mounting

- Mating behavior
- Mounting of inanimate objects for the purpose of masturbation.

SIGNALMENT

- Common in intact males, especially if estrus females are present.
- Can also occur in intact females or neutered individuals of either gender.
- No age or breed predilection for marking or roaming.
- Mounting can also be seen in sexually deprived, intact male cats mounting other males, females, kittens, people, and inanimate objects.

SIGNS

- Urine marking is characterized by the cat backing up to object with an erect and quivering tail and projecting a stream of urine backward and upward toward the object.
- May also occur with the cat assuming a squatting posture and depositing urine on horizontal surfaces, notably personal or novel items in the environment.
- Urine marking is thought to be characterized by the deposition of small amounts of urine, on multiple surface types, in conjunction with normal litter box use for toileting of urine and fecal material.
- Mounting of other cats, people, or objects.

CAUSES AND RISK FACTORS

- Urine marking may function to delineate territory, aggressive intent, or reproductive goals between cats or may be a response to anxiety.
- Likelihood of urine marking within the household appears to increase with density of cats in the household; however, urine marking may occur in households with only 1 or 2 cats.
- Agonistic (aggressive) relationships between cats in the same household and the presence of outdoor cats are correlated with an increase in the likelihood of marking behavior.

- Roaming is a normal feline exploratory behavior with cats seeking environmental enrichment, food, or sexual activity.
- Roaming is more likely with outdoor cats being housed indoors, in intact male cats, and in cats with a barren indoor environment (resulting in increased motivation to explore the outdoors).
- Mounting can be seen in deprived males or isolated males or if males are housed in pairs.
- Roaming, marking, and mounting may be seen in 5–10% of neutered males.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Rule out causes of lower urinary tract disease.
- Urine marking must be distinguished from inappropriate urination for the purpose of emptying the bladder. The latter problem is characterized by elimination on a consistent surface or location, may involve feces, and is usually associated with a decrease in litter box use. Cats can continue to use the litter for fecal elimination while avoiding it for urination, and the reverse is also possible. Cats that urine mark will continue to use the litter box for toileting of urine and feces.
- Roaming behavior may occur due to any disease process that might cause a cat to seek isolation due to illness.
- For marking and mounting also consider neonatal testosterone exposure, treatment with anabolic steroids or testosterone or retained or residual testicular tissue.

CBC/BIOCHEMISTRY/URINALYSIS

- Rarely do cats with roaming or mounting behaviors display abnormalities in lab work.
- CBC/biochemistry tests can provide helpful information to rule out coexisting conditions and provide baseline data prior to initiating drug therapy.
- Urine marking may be associated with underlying urinary tract disorders.

OTHER LABORATORY TESTS

- Unless indicated from baseline data, no further lab tests are necessary.
- In neutered and spayed females, rule out potential hormonal effects from retained or residual testicular tissue which might be associated with secondary sexual characteristics such as penile barbs and elevated testosterone in males or estrus like behaviors in females.
- Urine marking may be associated with medical conditions that might contribute to increased irritability such as hyperthyroidism.

IMAGING

Radiographs and ultrasound if laboratory data indicates a need to further explore the urinary tract.

DIAGNOSTIC PROCEDURES

None indicated



TREATMENT

FOR URINE MARKING

- Neuter and spay intact animals. When possible, reduce numbers of cats in the household to reduce density if overcrowding a factor.
- Provide alternate marking options such as scratching posts, scratch boxes, facial marking combs (Cat-A-Comb). Given that urine marking is a normal behavior, for some cats the use of a urine marking station (empty litter box placed vertically at location where marking occurs) may be appropriate.
- Multiple feeding stations and litter stations in multiple locations (one litter box per cat plus one additional).
- Manage litter hygiene so that boxes are scooped daily and completely cleaned weekly (clay litters) or monthly (clumping type litters) using hot water only (no cleansers).
- Increase perching and hiding opportunities (especially elevated locations) in each room of the home.
- Isolate cat from area being marked.
- Make urine marked areas aversive by using double-stick tape, mothballs, bubble wrap, etc.
- Manage stress factors in household (alter routine in home, address relationship issues between cats in the home, manage interactions between cats and people in home to increase positive relationships by encouraging play and positive reinforcement-based training).
- Reduce exposure to outdoor cats by blocking visual access, decrease number of cats in yard (use of fencing, motion-activated sprinkler, remove bird feeders, etc.).
- Increase (or decrease) time allowed outdoors.
- Use of synthetic facial pheromone (F3 fraction).

FOR ROAMING BEHAVIOR

- Neuter if intact.
- Use double barriers at exits (for example, screen doors) or confine away from doors (e.g., room).
- Alternately, allow controlled access to outdoors using cat fencing or screened areas or outdoor access while walked on a leash and harness.
- Enrich home environment with increased food access, random treats, and increased play opportunities. Feed the cat as soon as it returns home.
- Remove outdoor reinforcements such as outdoor cats through the use of fencing, motion-activated water sprinklers, removing

MARKING, ROAMING, AND MOUNTING BEHAVIOR—CATS

(CONTINUED)

bird feeders, and insuring neighbors not feeding.

- ID cat (tags, tattoo, or microchips).

FOR MOUNTING BEHAVIOR

- Neuter if intact.
- Interrupt the behavior and redirect to more desirable behaviors such as play.
- Identify and remove any triggers which initiate the behavior.
- Provide alternative outlets for play/enrichment.

**MEDICATIONS****DRUGS****For Urine Marking**

- Fluoxetine 0.5–1.0 mg/kg PO q24h; Side effects: sedation, anorexia, irritability, urine retention, constipation.
- Clomipramine 0.5–1.0 mg/kg PO q24h; Side effects: sedation, anticholinergic effects, arrhythmias, and GI disturbances.

For Roaming Behavior

No medications are recommended for roaming behavior

For Mounting Behavior

- Medications might be a consideration if a stress/anxiety component identified.
- Fluoxetine or clomipramine as in urine marking.
- Lorazepam 0.25–0.50 mg per cat PO q12–24h; Side effects sedation, hyperphagia and possible hepatic disease.

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CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Use caution when prescribing clomipramine in cats with seizures.
- Do not use fluoxetine or clomipramine with MAO inhibitors such as selegiline.
- Caution in using TCAs, such as clomipramine, when treating cats with diabetes, glaucoma, or cardiac disease.
- Do not combine a TCA and an SSRI; serotonin syndrome possible.

**FOLLOW-UP****PATIENT MONITORING**

- Telephone follow-up within 2 weeks after consultation, repeat as needed to monitor progress and assess response to treatment.
- Electrocardiogram if concerns about cardiac status.
- CBC and biochemistry profile 3–4 weeks after initiating medical therapy and then q6–12 months while on medication.

EXPECTED COURSE AND PROGNOSIS

- Response to therapy by diminished urine marking within 4 weeks.
- Continue drug therapy for a minimum of 8 weeks if response noted; continue 1 month beyond resolution.
- When the behavior is stable, wean dose by 25% per week.
- If behavior reoccurs, reinstitute lowest effective dose.
- Some animals may need to be maintained on medication indefinitely.

**MISCELLANEOUS****SEE ALSO**

Housesoiling—Cats

ABBREVIATIONS

- GI = gastrointestinal
- MAO = monoamine oxidase
- SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant

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MARKING, ROAMING, AND MOUNTING BEHAVIOR—DOGS



BASICS

DEFINITION

- Marking, roaming, and mounting behavior fall within the normal behavioral repertoire for the dog. However, they are objectionable to owners if the behavior is shown to excess, in an inappropriate context, or in a sexually altered dog.
- Normal behaviors with multiple causes—may be maladaptive owing to stimuli in the dog's environment.
- Marking—generating a signal for conspecifics with either a visual mark or leaving scent (urine, feces, anal sacs, or sebaceous glands) on an object or to define territory.
- Roaming—free wandering for exploration or in search of potential mates, food, or social contact.
- Mounting—primarily a component of mating behavior but also shown in social contexts and play (especially in pre-pubertal dogs).

GENETICS

None known but objectionable expression of these behaviors may be more common in familial lines.

INCIDENCE/PREVALENCE

Not known

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog

Breed Predilections

- Seen in any breed

Mean Age and Range

- Age at onset—sexual maturity (around 1 year of age)
- Mounting may occur in prepubertal puppies

Predominant Sex

- Males
- Most common in intact males, or intact females in estrus
- Also exhibited by castrated males and spayed females

SIGNS

Historical Findings

- Marking—deposition of urine and/or fecal matter in locations unacceptable to owners; occurs inside and outside of the home.
- Roaming—wandering behavior that takes the dog away from its home.
- Mounting—a behavior in which a dog raises the cranial part of its body onto other dogs, animals, people or objects while wrapping forelimbs around the target with or without pelvic thrusting.

Physical Examination Findings

- Physical examination findings are typically unremarkable unless a medical etiology is suspected (especially for marking behavior).
- For inappropriate mounting of other dogs, it is advisable to also perform a physical examination of the target of the mounting.

CAUSES

- Normal dog behaviors. Urine marking occurs most commonly in novel areas rather than in the home environment. Female dogs rarely mark in the home.
- Hormonally regulated; intact males likely to roam, mark, and mount.
- Learned components possible; reproductive status not sole variable.

Roaming

- Anxiety • Curiosity • Reproduction • Social contact and play

Marking

- Medical. • Communication with conspecifics; communicates social rank, sexual status, territorial boundaries, or general information, not related to the need to empty the bladder or bowel. • Anxiety

Mounting

- Sexual (including courtship and masturbation) • Play • Social status or cohesion • Attention-seeking • Anxiety
- Compulsive disorder

RISK FACTORS

- Intact males more likely to roam, mark, and mount.
- Marking on walks; learned behavior.
- Mounting only in front of owners; attention-seeking.
- Intact bitches, or females spayed after first heat.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Define the cause of the behavior as either normal or a sign of another diagnosis.

Roaming

- Sexually motivated behavior • Testosterone-producing tumors • Hunger/searching for food • Separation anxiety • Noise phobias
- Territorial behavior • Social facilitation
- Predatory behavior • Escaping from enclosure—play/investigative behavior

Marking

- Sexually motivated behavior • Testosterone-producing tumors • Territorial behavior
- Social status behavior • Conflict behavior
- Anxiety • Housesoiling; incomplete or loss of housetraining • Urinary tract disease • Any medical condition that causes PU/PD
- Constipation or diarrhea • Anal sac disease

Mounting

- Sexually motivated behavior • Testosterone-producing tumors • Social status behavior
 - Endocrine disease • Urinary tract disease
- If target of mounting is another dog, look at target for:
- Estrogen-producing tumors
 - Infections of anal sacs, uterus, vagina, or urinary tract

CBC/BIOCHEMISTRY/URINALYSIS

If abnormal, address medical issues.

OTHER LABORATORY TESTS

As indicated:

- Thyroid testing if roaming due to hunger
 - Blood testosterone levels in neutered animals showing intact male behaviors
 - Urine culture and sensitivity
 - Vaginal cytology to determine estrus status
- If target of mounting is another dog, exam target for:
- Blood estrogen levels (reproductive tumors)
 - Urine culture and sensitivity
 - Vaginal cytology, culture and sensitivity

IMAGING

Radiographs or ultrasound if a medical etiology is suspected.

DIAGNOSTIC PROCEDURES

As applicable if a medical etiology is suspected

PATHOLOGIC FINDINGS

N/A

M



TREATMENT

APPROPRIATE HEALTH CARE

N/A

NURSING CARE

N/A

ACTIVITY

See "Client Education"

DIET

No special dietary considerations

CLIENT EDUCATION

Roaming

- Secure enclosure to prevent escape
- Leash walk
- Adequate exercise, attention, supervision, stimulation
- Doggie daycare

Marking

- Restrict access to targeted areas and provide adequate indoor supervision when the owner is home.
- Confinement if tolerated when home alone.
- Remove stimuli or triggers.
- Express anal sacs if necessary.
- Use Bellyband (male) or Puppy Pants (female).
- Clean marked areas with effective enzymatic cleaners.

MARKING, ROAMING, AND MOUNTING BEHAVIOR—DOGS (CONTINUED)

- Command-/reward-based interaction with dog.
- Consider counter-conditioning or systematic desensitization to trigger stimuli or for anxiety conditions.
- Consider remote punishment for marking (such as water sprayer, alarm, citronella spray).

Mounting

- Obedience training
- Command-/reward-based interaction with dog
- Consider counter-conditioning or systematic desensitization to trigger stimuli or for anxiety conditions
- Adequate exercise, attention, and stimulation
- Ignore behavior if an attention-seeking component
- Consider remote punishment

SURGICAL

- Neuter intact males.
- Spay females. For marking spay early before first estrus to prevent hormone effects.



MEDICATIONS

DRUG(S) OF CHOICE

- M**
- Medication is not necessary for roaming unless the primary problem (separation anxiety or noise phobias) warrants its use. Medical etiologies should be treated accordingly.
 - No drug is approved for the treatment of marking or mounting; informed owner consent is advised. Medication use is *only* appropriate if persistent anxiety is strongly suspected as a contributing motivation.
 - Medication should *only* be used in combination with a sound behavior modification plan.

Tricyclic Antidepressants (TCA)

- Amitriptyline 2–4 mg/kg PO q12h
- Clomipramine 1–3 mg/kg PO q12h
- Side effects include sedation, anticholinergic effects, cardiac conduction disturbances, and GI signs.

Selective Serotonin Reuptake Inhibitors (SSRI)

- Fluoxetine 0.5–2 mg/kg PO q24h
- Paroxetine 1–2 mg/kg PO q24h
- Sertaline 1–3 mg/kg PO q24h
- Side effects include sedation, inappetence, lethargy, irritability, urine retention, constipation.

Azapirone

- Buspirone 0.5–2 mg/kg PO q8–12h
- Side effects: GI signs

Benzodiazepines

In dogs with concurrent anxiety diagnoses—alprazolam 0.01–0.1 mg/kg PO q8–12h

CONTRAINDICATIONS

- TCAs are contraindicated in animals with cardiac conduction disturbances or glaucoma.
- TCAs and SSRIs are contraindicated for dogs with a history of seizures.

PRECAUTIONS

- When dispensing clomipramine and fluoxetine, clients should be advised that occasional cases of increased aggression have been reported.
- Use caution with all drugs if dog has hepatic or renal compromise.
- Use benzodiazepines with caution in aggressive dogs because of potential for disinhibition.

POSSIBLE INTERACTIONS

- TCAs and SSRIs should not be used together.
- Do not use TCAs or SSRIs with monoamine oxidase inhibitors, including amitraz products and selegiline

ALTERNATIVE DRUG(S)

Megestrol Acetate

- Outdated treatment used as a last resort only.
- Side effects include obesity, pyometra, polyuria/polydipsia, diabetes mellitus, mammary hyperplasia, and carcinoma.



FOLLOW-UP

PATIENT MONITORING

Follow-up is variable depending on the severity of the problem and whether medication is prescribed. Help may be needed implementing changes to the environment and behavior modification. Owners should be encouraged to keep logs or journals detailing episodes of marking, roaming, or mounting to assess treatment success or non-response. If medication is prescribed, follow-up and journals are essential to assess response. In urine marking, owners should be encouraged to supervise the dog indoors and to inspect areas daily for urine marks.

PREVENTION/AVOIDANCE

- Neutering males and spaying females reduces likelihood of marking, roaming, and mounting behavior.
- Client education via proper husbandry techniques is helpful.

POSSIBLE COMPLICATIONS

- Roaming—becoming lost or picked up by animal control; possible injury from car accidents or fighting with other animals.
- Marking—property damage when it occurs inside the home.
- Mounting—disruption of relationship with familiar dogs; possible fighting with other animals
- Pet relinquishment.

EXPECTED COURSE AND PROGNOSIS

- Prognosis is good if the correct cause is determined and the owner is compliant with the behavior protocols.
- Castration will decrease house marking by 90% or better in 40% of male dogs, while 80% of dogs will decrease marking by at least 50%. Castration has little to no effect on urine marking in outdoor areas.
- Castration decreases mounting in more than 65% of dogs but relatively few stop completely. Castration has its greatest effect when the target of mounting is human rather than dog-dog mounting.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

Intact animals older than sexual maturity.

ZOONOTIC POTENTIAL

Roaming exposes pet to other animals, including wildlife—rabies exposure possible.

PREGNANCY/FERTILITY/BREEDING

Listed medications should be avoided in pregnant animals.

SYNONYMS

N/A

SEE ALSO

Housesoiling—Dogs

ABBREVIATIONS

- GI = gastrointestinal
- PU/PD = polyuria/polydipsia
- SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant

INTERNET SOURCES

N/A

Suggested Reading

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Acknowledgment Tracy L. Kroll

MAST CELL TUMORS



BASICS

DEFINITION

- Malignant round cells derived of hematopoietic origin containing granules packed with many vasoactive substances including histamine, heparin, serotonin, dopamine, tryptase, and chymase.
- Most common malignant skin tumor in the dog, representing approximately 7–21% of all canine skin tumors.
- Second most common malignant skin tumor in the cat, representing approximately 20% of all feline skin tumors.
- Tumors may affect dermis, subcutis, spleen, liver, and intestines.

PATOPHYSIOLOGY

- Histamine release from MCTs affects a multitude of tissues.
- Histamine (H₂) receptors are primarily located within the stomach and histamine is thought to be one of the most significant stimulants of gastric acid secretion.
- In extreme cases, perforation of the gastrointestinal tract may occur, leading to peritonitis.
- Histamine release around a tumor leads to the production of wheals, hives, and erythema.
- Local release of heparin is also common, resulting in bleeding and subsequent bruising, which can be seen around the tumor.

SYSTEMS AFFECTED

- Skin—MCTs are the most common malignant cutaneous tumor of the dog.
- Gastrointestinal—on necropsy evaluation, 35–83% of dogs with MCTs have evidence of gastrointestinal ulceration.
- Hemic/Lymph/Immune—lymph node metastasis is common in high-grade tumors. Bone marrow metastasis is rare but can occur.
- Hepatobiliary—the liver and spleen are common distant sites of metastasis for high-grade MCTs.

GENETICS

The specific breed predilections indicate that a genetic predisposition exists.

INCIDENCE/PREVALENCE

- Most common malignant skin tumor in the dog, representing approximately 7–21% of all canine skin tumors.
- Primary visceral and intestinal MCTs are rare in the dog.
- Second most common skin tumor in the cat, accounting for 20% of cutaneous tumors.
- Most common splenic tumors of cats, comprising half of the MCTs diagnosed in cats.

SIGNALMENT

Species
Dog and cat

Breed Predilections

- Dogs—brachycephalic breeds, as well as golden retriever, Labrador, Rhodesian ridgeback, beagle, Staffordshire terrier, Weimaraner, Shar-Pei, and Australian cattle dog.
- Cats—Siamese.

Mean Age and Range

- Dogs—middle-aged, range 4 months–18 years.
- Cats—middle-aged (8–9 years for cutaneous mastocytic types) and older cats (intestinal and splenic); however, the histiocytic form of cutaneous MCTs affects young cats with a mean age of 2.4 years.

Predominant Sex

- Dogs—no predilection
- Cats—male Siamese

SIGNS

Dogs

- Mass is found in the subcutis or on the skin and may also be present within lipomas.
- Regional edema or a Darier's sign may be seen in the region around a tumor that has degranulated.
- Lymphadenopathy of regional lymph nodes may be seen in dogs with metastatic disease.
- History of intermittent progression and regression in size.
- Systemic illness with advanced local or systemic disease; vomiting, anorexia, weight loss, and melena.

Cats

- Visceral disease manifests as chronic weight loss, anorexia, diarrhea, and lethargy.
- Focal mass lesion may be palpated with primary intestinal MCT.

CAUSES

- Up to 30% of canine MCTs have been shown to contain a mutation in the c-kit oncogene, leading to constitutively activated receptor and unchecked cell division.
- Up to 56% of feline MCTs have a c-kit mutation, though these mutations do not appear to have any bearing on prognosis nor on protein expression.

RISK FACTORS

See above under "Breed Predilections" and "Causes"



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cutaneous forms—adenexal tumors, basal cell tumors, histiocytoma, lipoma, and soft tissue sarcoma.
- Visceral forms—lymphoma, histiocytic tumors, malignant fibrous histiocytomas, multiple myeloma, hemangiosarcoma, hemangioma, and erythroid myeloid hyperplasia.
- Intestinal forms—lymphoma, adenocarcinoma, leiomyoma,

leiomyosarcoma, gastrointestinal stromal tumors, and fungal infections.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia (regenerative secondary to gastrointestinal blood loss).
- Eosinophilia, mastocytosis, and thrombocytopenia.
- Identification of circulating mast cells is more common in the cat with visceral MCT than the dog.
- Increased BUN secondary to gastrointestinal bleeding and increased liver values secondary to metastasis.

OTHER LABORATORY TESTS

- Regional lymph node aspiration and cytology
- Liver and splenic aspiration and cytology
- Mast cell tumor prognostic panel
- C-kit PCR and immunohistochemistry staining

IMAGING

- Thoracic radiographs—intrathoracic or sternal lymph node metastasis
- Abdominal ultrasound—viscera assessment with emphasis on liver, spleen, and mesenteric lymph nodes

DIAGNOSTIC PROCEDURES

- Fine-needle aspirate and cytology for definitive diagnosis.
- Biopsy (incisional or excisional) for definitive diagnosis and histologic grading.

M

PATHOLOGIC FINDINGS

- Dogs—Patnaik grading scale:
 - Grade I (low-grade) tumors have a mostly benign behavior and represent ~36%.
 - Grade II (intermediate-grade) MCTs are the most common form and represent ~43%.
 - Grade III (high-grade) MCTs are the most aggressive form, are metastatic, and represent ~20%.
- Cats—Histologic forms of cutaneous MCTs:
 - Mastocytic form—single tumor and is the most common (compact or diffuse). There are two histologic varieties of mastocytic MCTs in the cat, compact and diffuse: compact—more benign behavior; diffuse—more undifferentiated and aggressive.
 - Histiocytic form—multiple lesions on the head and neck with relatively benign behavior.



TREATMENT

ACTIVITY

Limit for animals with heavy tumor burdens (such as cats with visceral MCTs or dogs with large tumors) until the mass has been treated appropriately.

MAST CELL TUMORS

(CONTINUED)

DIET

N/A

CLIENT EDUCATION

Owners of dogs with MCTs should be informed that 14–17% of dogs will develop additional MCTs. All new masses should be evaluated by a veterinarian.

SURGICAL CONSIDERATIONS

- Conventional recommendations (dogs)—2–3 cm margins and one fascial plane deep, maybe unnecessary with grade II MCTs in dogs as majority (70%) of “dirty” margins fail to locally regrow.
- Narrow margins (cats)—majority of tumors will not regrow following narrow surgical margins.
- Splenectomy (cats)—recommended in cats with massive visceral tumor burden despite the presence of metastases.

RADIATION THERAPY

- For incompletely excised mast cell tumors in locations that are not amenable to surgical re-excision or in cases where another surgery is not possible (dogs).
- Can be used in a gross disease setting, but severe systemic reactions (including death) are possible.



MEDICATIONS

DRUG(S) OF CHOICE

Dogs

- Vinblastine (2.0 mg/m² IV q7 days × 4, then q14 days × 4) and prednisone (1 mg/kg PO q24h).
- Vinblastine only (3.5 mg/m² IV q14 days).
- Lomustine (50–70 mg/m² PO q 21 days).
- Torceritinib (2.75 mg/kg PO MWF).
- Masitinib (12.5 mg/kg PO q24h).

Cats

- Lomustine (32–60 mg/m² PO q4–6 weeks).
- Vinblastine (2 mg/m² IV q7 days × 4, then q14 days × 4) and prednisone (1 mg/kg PO q24h).

CONTRAINDICATIONS AND PRECAUTIONS

- Vinblastine—use with caution in animals with liver disease; drug is also myelosuppressive and possesses vesicant properties.
- Lomustine is hepatotoxic and should be avoided in dogs with underlying liver disease; drug is extremely myelosuppressive and associated with refractory thrombocytopenia. Administer with Denamarin.
- Torceritinib and masitinib can cause gastrointestinal ulcers, myelosuppression, muscle pain, hypertension, proteinuria and gastrointestinal upset.

POSSIBLE INTERACTIONS

- Torceritinib and masitinib should be used with caution with other drugs that induce

gastric ulcers such as prednisone or NSAIDs, or in patients with gastric ulceration secondary to mast cell tumor.

- Lomustine should be used with caution with other hepatotoxic drugs such as NSAIDs.

ALTERNATIVE DRUG(S)

Symptomatic treatment—benadryl, prednisone, famotidine or other H₂ inhibitors, omeprazole, and sucralfate should be considered for any dog or cat with gross mast cell disease.



FOLLOW-UP

PATIENT MONITORING

Dogs

- Grade I or II—complete surgical resection should be curative in the majority of patients.
- Grade II (high)—complete surgical resection evaluated every 3 months for 1 year with physical examination, abdominal ultrasound, and lymph node assessment.
- High-grade tumors (grade III or those in a location associated with a negative prognosis)—physical examination, blood work, and abdominal ultrasound every 3 months for 1 year and then every 6 months for an additional 2 years.

Cats

Visceral or intestinal—abdominal ultrasound every 3 months for 1 year.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Chemotherapy-related myelotoxicity or hepatotoxicity

EXPECTED COURSE AND PROGNOSIS

- Complete excision of low-grade mast cell tumors in most locations is curative.
- Complete excision of high-grade mast cell tumors or those located in areas associated with a poor prognosis (mucocutaneous junctions, ± inguinal regions) often require adjuvant therapy with chemotherapy. Median survival times average approximately 11–12 months.
- Incomplete excision of a low-grade mast cell tumor may require additional local therapy with another surgery (often cured) or radiation therapy (93% disease-free at 3 years).
- Incomplete excision of a high-grade mast cell tumor requires additional local therapy in addition to systemic chemotherapy. Median survival times range from 6 to 12 months.
- Regional metastasis to a lymph node should be treated with surgical excision at the time of the primary tumor removal. Systemic chemotherapy is necessary. Median survival times are typically less than 9 months.
- Evidence of distant metastasis is often treated with systemic chemotherapy or

ancillary therapies alone with a median survival of 4 months or less.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Progressive and metastatic disease has the potential to cause excessive parietal cell production of hydrochloric acid with associated gastric ulceration, melena, and iron-deficiency anemia and gastric perforation.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

While on chemotherapy dogs should not be bred. There are no long-term studies regarding fertility in dogs or cats previously treated with lomustine, vinblastine, or RTKIs.

SYNONYMS

- Mastocytoma
- Systemic mastocytosis

ABBREVIATIONS

- MCT = mast cell tumor
- NSAID = nonsteroidal anti-inflammatory drug
- RTK = receptor tyrosine kinase
- RTKI = receptor tyrosine kinase inhibitor

INTERNET RESOURCES

- www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/
- www.vet.uga.edu/VPP/CLERK/Dahm/Index.php
- www.vetmed.wsu.edu/deptsOncology/owners/mastCell.aspx

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Client Education Handout
available online

MASTITIS



BASICS

OVERVIEW

- Bacterial infection of one or more lactating glands.
- Result of ascending infection, trauma to the gland, or hematogenous spread.
- *Escherichia coli*, *Staphylococci*, and β -hemolytic streptococci—most commonly involved. *Mycobacterium* and blastomycosis reported.
- Potentially life-threatening infection; may lead to septic shock.
- Sepsis—direct effect of mammary glands with systemic involvement.

SIGNALMENT

- Postpartum bitch and queen
- Pseudopregnant lactating bitch or queen (rare)

SIGNS

Historical Findings

- Anorexia
- Lethargy
- Neglect of puppies or kittens
- Failure of puppies or kittens to thrive

Physical Examination Findings

- Firm, swollen, warm, and painful mammary gland(s) from which purulent or hemorrhagic fluid can be expressed.
- Fever, dehydration, and septic shock—with systemic involvement.
- Abscessation or gangrene of gland(s) can result.

CAUSES & RISK FACTORS

- Ascending infection via teat canals.
- Trauma inflicted by puppy or kitten toenails and teeth.
- Poor hygiene.
- Systemic infection originating elsewhere (e.g., metritis).
- Rarely secondary to fibroadenomatous hyperplasia in queens.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Galactostasis—no systemic illness; cytologic examination and culture of milk help with differentiation.
- Inflammatory mammary adenocarcinoma—affected gland does not produce milk; differentiated by biopsy.

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis with left shift
- Leukopenia—with sepsis
- Mildly high PCV, total protein, and BUN—with dehydration

IMAGING

- Ultrasonography reveals loss of distinct layering of normal tissue in glands, decreased echogenicity, increased heterogeneity, and altered blood vessel density on color Doppler.
- Color Doppler can assist in prognosis—loss of blood vessels in inflamed areas predicts progression to gangrene.

OTHER LABORATORY TESTS

Culture—identification and sensitivity of microorganisms from milk of affected glands;

screening for methicillin-resistant *Staphylococcus aureus* recommended.

DIAGNOSTIC PROCEDURES

- pH of milk—normally slightly more acidic than serum, may become alkaline with infection.
- Cytology—neutrophils, macrophages, and other mononuclear cells can be observed in normal milk; the presence of large numbers of free and phagocytosed bacteria and degenerative neutrophils is noted with septic disease; bacterial culture to identify the organism and sensitivity pattern.



TREATMENT

- Inpatient until stable.
- Puppies and kittens—neonates may be allowed to continue nursing unless glands are necrotic or dam is systemically ill; affects choice of antibiotics; monitor weight gain in neonates: pups should gain 10% of birth weight per day, kittens should gain a minimum of 7–10 g/day.
- Dehydration or sepsis—intravenous fluid therapy.
- Correct electrolyte imbalances and hypoglycemia.
- Treat shock, if present.
- Apply warm compress and milk out affected gland(s) several times daily.
- Cover glands with friable tissue to prevent excoriation if nursing is allowed.
- Application of cabbage leaf wraps to affected glands may speed resolution.
- Abscessed or gangrenous glands—require surgical debridement, with or without negative pressure wound therapy.
- Open wound management may be needed after surgery in some cases; negative pressure wound therapy useful adjunctive modality postoperatively and for conservatively managed cases.



MEDICATIONS

DRUG(S)

- Acidic milk—weak bases; erythromycin (10 mg/kg PO q8h), lincomycin (15 mg/kg PO q8h), or trimethoprim-sulphadiazine (15–30 mg/kg PO q12h), for 21 days.
- Alkaline milk—weak acids; amoxicillin or cephalosporin (20 mg/kg q8h, dogs and cats); amoxicillin/clavulanic acid (13.75 mg/kg PO q12h, dogs; 62.5 mg/cat PO q12h, cats) for 21 days.
- Either alkaline or acidic milk—chloramphenicol (40–50 mg/kg PO q8h) or enrofloxacin (2.5 mg/kg PO q12h) for 21 days.
- May infuse affected gland(s) with 1% betadine solution by lacrimal cannula.
- Cabergoline (5 μ g/kg PO q24h, 5–7 days) to suppress lactation in unaffected glands in patients with sepsis; neonates must be hand reared.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Patient allowed to nurse—avoid tetracycline, enrofloxacin, and chloramphenicol; may use cephalosporins, amoxicillin, and amoxicillin with clavulanic acid.



FOLLOW-UP

PATIENT MONITORING

- Physical examination and CBC.
- Repeated ultrasonographic evaluation helps assess healing—normal distinct layering of tissues will appear with recovery.

PREVENTION/AVOIDANCE

- Clean environment
- Hair shaved from around mammary glands
- Toenails of puppies and kittens clipped
- Ensure neonates nurse from all glands.

POSSIBLE COMPLICATIONS

- Abscessation or gangrene—may cause loss of gland(s).
- Hand-raising puppies and kittens—requires considerable commitment by the owner, may affect behavioral outcome of offspring.

EXPECTED COURSE AND PROGNOSIS

Prognosis—good with treatment

M



MISCELLANEOUS

ABBREVIATION

PCV = packed cell volume

INTERNET RESOURCES

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MATERNAL BEHAVIOR PROBLEMS



BASICS

DEFINITION

Abnormal maternal behavior is either excessive maternal behavior in the absence of neonates or deficient maternal behavior in the presence of the dam's own neonates. The latter is more common in dogs, the former in cats.

PATHOPHYSIOLOGY

The pathophysiology of one type of excessive maternal behavior, pseudocyesis, appears to be elevated progesterone levels following estrus in unbred bitches followed by an abrupt drop in progesterone levels. The pathophysiology of refusal to accept puppies by females after caesarean section is the waning of factors, including oxytocin, needed during the sensitive period for acceptance of the neonate. The pathophysiology of other types of deficient maternal behavior is unknown.

SYSTEMS AFFECTED

Behavioral

GENETICS

There is no identified genetic predisposition, but a breed disposition for deficient maternal behavior in Jack Russell terriers indicates that there may be a genetic component. There are genetic models in mice. The genes responsible for deficient maternal behavior in mice are paternally imprinted. If this is true in dogs and cats, one would expect that rejecting mothers were normally mothered themselves, but their grandmother may have been deficient. The genetic basis should be investigated in dogs and cats.

INCIDENCE/PREVALENCE

The incidence of deficient maternal behavior has not been determined but seems to be low, less than 1% of cases in a behavior practice. Maternal behavior in cats and dogs that do not have offspring is more common.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dogs and cats

Breed Predilections

Poor maternal behavior may be more common in Jack Russell terriers and cocker spaniels, but there has been no quantitative study.

Mean Age and Range

There is no particular age at risk, but primiparous females and older bitches seem to be at risk of deficient maternal behavior.

Predominant Sex

Female generally, but some males may allow suckling behavior.

SIGNS

Deficient Maternal Behavior

Absent maternal behavior; the mother simply abandons her offspring. This is most apt to occur after caesarean section.

Poor Maternal Behavior

- The mother stays with her offspring but will not allow them to nurse.
- In other cases the mother may show inadequate retrieval of young, insufficient cleaning of the young, or failure to stimulate elimination.
- In another form of poor maternal behavior, the bitch carries the puppies from place to place without settling down or, in the most extreme form, kills some or all of her litter.

Abnormal Maternal Behavior

- The bitch or queen may allow her offspring to suckle but kills her offspring either at birth or over a period of days. Occasionally the bitch, or more rarely the queen, will abandon or attack her offspring if it has changed in odor or appearance. A female may be disturbed by another animal or by people and can redirect her aggression to her offspring.
- A bitch may accidentally disembowel or even consume offspring completely while eating the fetal membranes and umbilical cord. This should be distinguished from normal licking, which can be quite vigorous, even dislodging the pup from a teat.

Maternal Aggression

Cats with kittens may be aggressive to other animals, especially dogs in the same household. Bitches may be aggressive to unfamiliar humans or even to familiar humans, especially if they are hypocalcemic.

Excessive Maternal Behavior

- The pseudopregnant bitch or bitch spayed during the late luteal phase of the estrous cycle adopts, attempts to nurse, and guards inanimate objects (stuffed animals or even leashes). The pseudopregnant bitch may have mammary development and may be lactating.
- The newly spayed queen may steal kittens from a lactating queen. Queens post-spaying may also lactate if suckled.

CAUSES AND RISK FACTORS

- The presence of kittens in the environment of the recently spayed cat is a risk factor for excessive maternal behavior and kitten stealing.
- The risk of excessive carrying of pups, redirected aggression, or even cannibalism is increased if there are other dogs or too many people present in the nest area.
- Primiparous females or those subjected to caesarian section are at higher risk than multiparous or naturally delivering females.
- A large litter of kittens or sick offspring.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- The most important differential is between primary abnormal maternal behavior and poor maternal behavior secondary to mastitis or metritis.
- Lactation tetany can result in aggressive behavior, although this behavior is rarely directed at the puppies and occurs later in lactation, not at parturition.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal unless other medical conditions are present. Blood calcium levels will be low if the bitch is suffering from lactation tetany.

OTHER LABORATORY TESTS

Only as indicated by metabolic conditions of the bitch or queen.

IMAGING

Only as indicated by other problems.

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

Presence of milk in the mammary glands of females with excessive maternal behavior.



TREATMENT

APPROPRIATE HEALTH CARE

Normal health care

NURSING CARE

N/A

ACTIVITY

N/A

DIET

- Adequate diet for nursing bitches and queens to meet energy and calcium demands.
- Restricted diets for pseudocyesis to discourage lactation and diminish milk production.
- In the case of deficient maternal behavior, the bitch or queen should be fed ad libitum to encourage lactation.

CLIENT EDUCATION

Abnormal or Poor Maternal Behavior

- The bitch that is carrying her pups or exhibiting redirected aggression to them should be isolated in a quiet, dark area. The bitch that bites her pups should be muzzled. The owner must stimulate elimination of the puppies or kittens because the muzzled female cannot. An Elizabethan collar inhibits cannibalism in queens.
- The bitch should be attended at parturition and the pups removed temporarily if she is biting the pups themselves in addition to the umbilical cord.

(CONTINUED)

MATERNAL BEHAVIOR PROBLEMS

- Bitches and queens with poor maternal behavior may exhibit the same behavior with subsequent litters.

Excessive Maternal Behavior

- Cats that have stolen kittens should be separated from the biologic mother and kittens.
- The mothered objects should be removed from the pseudopregnant bitch.
- Food intake should be restricted to inhibit lactation.

Maternal Aggression toward Animals or Humans

The best treatment for excessive maternal aggression is to separate the kittens; weaning alone may not suffice because the presence of the kittens alone may sustain or even reinstate maternal aggression in a queen separated from her kittens for several weeks.

SURGICAL CONSIDERATIONS

- Delay spaying for 4 months post-estrus to avoid post-spaying maternal behavior and its accompanying aggression.
- Spaying avoids future excessive maternal behavior in the absence of young.

**MEDICATIONS****DRUG(S) OF CHOICE****Excessive Maternal Behavior**

- Mibolerone (Cheque Drops) was the drug of choice for pseudopregnant bitches or those exhibiting maternal behavior and lactation following spaying. The dose is 16 µg/kg PO once daily for 5 days. Mibolerone inhibits prolactin and thereby inhibits lactation. The drug is no longer available except at some compounding pharmacies.
- Bromocriptine (Parlodel) can be used to inhibit prolactin. The dose is 10 micrograms/kg for 10 days. Should not be administered to pregnant animals.
- Cabergoline is a prolactin antagonist shown to be effective for the treatment of pseudopregnancy in dogs. Dosage is 5 µg/kg PO q24h for 4–6 days. Some animals may require more than one course of treatment. Not commercially available in North America.

CONTRAINDICATIONS

Do not use mibolerone in cats because it has a narrow margin of safety in that species. It should not be administered to Bedlington terriers.

PRECAUTIONS

Mibolerone can cause masculinization that may include male sexual behavior, clitoral

hypertrophy, vulvovaginitis, and urinary incontinence in females. Bromocriptine can cause gastrointestinal vomiting, sedation, and hypotension as well as abortion.

POSSIBLE INTERACTIONS

- If tranquilizers are administered, care must be taken that the puppies or kittens are not sedated.
- Do not use estrogen or progesterones at the same time as mibolerone.

ALTERNATIVE DRUG(S)

Drugs are usually not needed.

Deficient Maternal Behavior

- Oxytocin may be administered either parenterally 1–5 units or by nasal spray (Syntocinon).
- Because prolactin appears to be necessary for maternal behavior in other species, a dopamine blocker, acepromazine (0.55–2.2 mg/kg PO), can be used. Dopamine inhibits prolactin release; therefore, a dopamine blocker would increase prolactin.

CONTRAINDICATIONS

Do not give oxytocin to pregnant animals or in combination with sympathomimetic agents.

**FOLLOW-UP****PATIENT MONITORING**

The puppies or kittens of females with deficient or poor maternal behavior should be monitored daily to be sure that they are gaining weight.

PREVENTION/AVOIDANCE

- Place a nursing female in quiet, comfortable quarters away from noise and disturbances by other animals or people.
- Do not rebreed females with poor maternal behavior. Determine whether any female offspring of the female with abnormal behavior have also exhibited poor maternal behavior. In other species, poor maternal behavior is a paternally imprinted gene; the father must contribute the gene for poor maternal behavior. The daughters of rejecting mothers will not reject, but the daughters of their sons may.
- Deficient maternal behavior can occur with each litter; do not rebreed.

POSSIBLE COMPLICATIONS

- Loss of offspring.
- Hand-reared puppies and kittens frequently have abnormal or deficient social behavior. This is due in part to insufficient suckling

time and to the consequences of lack of maternal licking, which adversely affects response to stress and reproductive behavior.

EXPECTED COURSE AND PROGNOSIS

- Excessive maternal behavior usually wanes around the time of normal weaning (6–8 weeks).
- Poor and deficient maternal behavior can occur with each litter.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

- Consider especially drug use and effect of disease on the fetus.
- Do not breed dogs with history of poor maternal behavior.

SYNONYMS

Mismothering

INTERNET RESOURCES

<http://www.ivis.org/advances/BehaviorHoupt/houpt-aberent/chapter>.

M

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Consulting Editor Gary M. Landsberg



Client Education Handout
available online

MAXILLARY AND MANDIBULAR FRACTURES



BASICS

DEFINITION

Fractures of the mandibles, maxillae, and associated structures are classified as to location, severity (i.e., tooth involvement, soft tissue tears, and type of bone fracture), and effects of the muscles of mastication on reduction.

PATHOPHYSIOLOGY

Effects of the Muscles of Mastication

- The muscles opening the mouth (e.g., digastric muscle) may help reduce or displace a fracture.
- Favorable—fracture reduced by muscles of mastication.
- Nonfavorable—fracture displaced by muscles of mastication.

Classification of Sympyseal Injury

- Type I—separation; no break in soft tissue.
- Type II—separation; break in soft tissue.
- Type III—separation; break in soft tissue and comminution of bone; broken teeth not unusual.
- Teeth involved may be maintained during osseous process (i.e., with endodontics or restoration). If required, they can be extracted following bone healing.
- Note: symphyseal laxity is a common clinical finding in geriatric cats and toy breed dogs.

Classification of Jaw Fracture by Location

- A—central incisors (mesial midline) to canine teeth (a symphysis is a common jaw fracture site in the cat)
- B—from canine to second premolar
- C—second premolar to first molar (carnassial tooth)
- D—from first molar to the angle of the mandible
- E—angle of the mandible
- F—coronoid process
- G—condylar process
- H—midline palate
- I—non-midline palate
- J—massive or combination of fractures

SIGNALMENT

Species

Dog and cat

SIGNS

- Vary greatly according to the location, type, extent, cause, and underlying risk factors resulting in the injury.
- Facial deformity, malocclusion, fractured teeth, oral or nasal bleeding, and inability to properly close the jaw are common signs.

CAUSES

Injury, trauma, and predisposing factors

RISK FACTORS

- High-risk environment or temperament.
- Oral infections (e.g., periodontal disease, osteomyelitis), neoplasia, or certain metabolic diseases (e.g., hypoparathyroidism)—may result in weaker jaws that are more prone to injury.
- Traumatic injury affecting the jaws or teeth.
- Congenital or hereditary factors resulting in weakened or deformed jaw bone.



DIAGNOSIS

A thorough and complete physical examination is very important in traumatic jaw injuries as many unseen or multiple injuries and complications are possible.

DIFFERENTIAL DIAGNOSIS

- Based on visualization, palpation, and radiographic findings.
- TMJ conditions—see Temporomandibular Joint Disorders.
- Tooth subluxation or luxation (i.e., interference with jaw closure).
- Endodontic disease (e.g., tooth abscess).
- Foreign body lodged in or near the oral cavity.
- Maxillary or mandibular nerve injury or disease.
- Eosinophilic myositis.
- Craniomandibular osteopathy.
- Neoplasia.

CBC/BIOCHEMISTRY/URINALYSIS

As required—to assess and treat shock from initial injury; to assess animal prior to surgery.

IMAGING

Radiography—*intraoral and extraoral; CT and MRI*

DIAGNOSTIC PROCEDURES

- Oral examination
- Neurologic examination
- Biopsy for histopathology, if indicated

PATHOLOGIC FINDINGS

- Non-unions
- Neoplasia
- Osteomyelitis
- Periodontal and/or endodontic disease



TREATMENT

SURGICAL CONSIDERATIONS

- Based on type of fracture, available equipment, supplies, and the doctor's knowledge, experience, and comfort level.
- Treatment selection is based on four major points: (1) Reduction of fracture and reasonable contact of fracture ends, if possible.
- (2) Reestablishment of natural occlusion, and avoidance of causing a malocclusion when the fracture is reduced.
- (3) Stabilization sufficient for proper healing.
- (4) Salvage condition (nonrepairable or non-stabilizable condition).

TYPICAL TYPES OF TREATMENTS FOR CLASSES OF FRACTURES

Interarch Stabilization (Typically for Classes D, E, F, G, and J)

- Tape muzzle
- Cross-arch wiring (maxilla to mandible)
- Composite fixation of cross-arch teeth; sometimes used in combination with dental pins (e.g., TMS, Whaledent, New York, NY)
- Bimaxillary encircling and retaining device (BEARD)
- Cross-arch buttons

Intra-Arch Stabilization (Typically for Classes H and I)

- Pin and wire combination
- Dental wiring
- Acrylic or composite splint

Intraoral Stabilization with Splint

(Typically for Classes A, B, C, H, I, and J)
Composite or acrylic splint

Intraoral Stabilization with Wire

(Typically for Classes A, B, C, H, I, and J)

- Interdental wiring—Ivy loop, Stout's multiple loop, Essig, and Risdon wiring techniques.
- Dental wiring—circumferential used for anchorage for composite and acrylic splints (pig tails, cerclage, or twists).
- Osseous wiring—circumferential; transosseous; transcircumferential.

Internal Fixation (for Most Classes of Fractures, but Must Be Used Selectively with Consideration of Teeth and Roots)

- Orthopedic wire; IM pins; plates; screws.
- Note: do NOT place an IM pin within the mandibular canal.

External Fixation (for Most Classes of Fractures, but Must Be Used Selectively with Consideration of Teeth and Roots)

IM pins with bars (stainless steel or carbon) or tubing (e.g., Penrose) reinforced with composite or acrylic.

Salvage Surgery (Typically for Class J Fractures)

- Condylectomy—non-repairable fractures of the TMJ.
- Cheiloplasty—salvage procedure to maintain reasonable mandibular support in certain nonunion conditions.
- Rostral (or other) mandibulectomy—used in certain non-union cases or with massive injury.

TECHNIQUES

Below are more commonly used techniques; more advanced options are beyond the scope of this chapter (see "Suggested Reading").

Initial Treatment

- Awareness of occlusion, tooth roots, and anatomy during treatment is critical.
- Patient should be intubated, and a pharyngostomy tube aids in occlusal checks intraoperatively.
- Teeth in the fracture line should be assessed and maintained by appropriate treatment until the fracture heals, if possible, as removal may result in instability.
- Bone graft—to re-establish structural stability: autograft (harvested from individual); allograft—(same species); Alloplast (artificial material).
- Treatment with composite/acrylic splints in association with wiring (Ivy loop, Stout's multiple loop) is generally very effective; may allow for improved occlusal reestablishment and less dental trauma.
- Assess soft tissue damage, debride and suture where appropriate.

Procedure

- Disinfect with chlorhexidine and clean and polish teeth (flour pumice without fluoride).
- Reduce fracture in proper occlusion.
- Coat adjacent teeth and soft tissue with petroleum jelly.
- Acid etch the teeth with a 37% phosphoric acid gel; leave on for 30–60 seconds; rinse off thoroughly and air dry the teeth.
- Apply splint.

(CONTINUED)

MAXILLARY AND MANDIBULAR FRACTURES**Materials****Acrylics**

Warning: Acrylics give off vapors that can be hazardous and should be used in well-ventilated areas. They also generate heat during the thermochemical reaction during setting that can result in thermal injury to the teeth (pulpitis).

- Place the powder and liquid in a salt-and-pepper fashion in small increments (to avoid hyperthermic reaction) until the desired shape and density of splint attained.
- Finish and smooth with acrylic bur on high-speed handpiece.

Composites (ProttempGarant-ESPE)

- Little exothermal reaction and fumes; more expensive.
- After acid-etching, use a dentinal bonding agent and apply a separator agent to opposing arcade to prevent composite from bonding to these teeth during occlusion check.
- With a new mixing tip, apply product to splint area, shaping it as it hardens.
- Finish and smooth with white stone bur and place a final layer of unfilled resin.

Circumferential Osseous Wiring or Suturing

- Wiring around the bone—used most commonly for symphyseal separations.
- 20- or 18-gauge needle—to pass wire.
- 24- to 28-gauge wire—in neonates, small dogs or cats, absorbable (long-acting—e.g., PDS) or non-absorbable 1- to 2-0 suture material can sometimes be substituted for wire.
- Run wire from stab incision (ventral intermandibular space) to vestibule; pass behind canines, down through vestibule on opposite side, and back down through the ventral incision.
- Tighten wire to reduce fracture, but do not overtighten the wire ends or the teeth may be pulled too far medially (base narrow, lingually displaced) and hit the palate.
- If teeth go base narrow, either loosen the wire ends or place a figure-8 wire looped around the canine teeth and under the jaw.

HOMECARE

- Orthodontic wax—soft, pliable wax sent with owner to periodically cover irritating wires.
- Oral irrigants—use twice daily for oral hygiene and to reduce bacteria; chlorhexidine solutions help reduce bacteria; zinc and ascorbic acid solutions (Maxi-Guard Gel, Addison Biological) help reduce bacteria and stimulate soft tissue healing.
- Diet—soft food or gruel may be required during healing.
- Nutritional and fluid maintenance required.
- Chewing exercise—avoid hard chew items during healing process.

**MEDICATIONS****DRUG(S)****Pain Management**

- Local anesthesia— intraoral local blocks; regional nerve blocks: mental n., mandibular

n., infraorbital n., palantine n., and maxillary n.

- Injectables—butorphanol tartrate; buprenorphine; nalbuphine.
- Transdermal patches—fentanyl.
- Oral—carprofen; butorphanol tartrate; hydrocodone.

Antibiotics

- Broad-spectrum based on history, health, and chemical profile.

**FOLLOW-UP****PATIENT MONITORING**

- Physical—recheck 2 weeks postoperative.
- Radiographic—recheck 4–6 weeks postoperative, then every 2 weeks until fracture is healed and/or appliance is removed.
- Fracture site may temporarily (1–2 weeks) be more at risk to refracture after the support of the appliance is removed.
- Once the fracture line is stable, compromised teeth may need additional endodontic treatment (e.g., root canal) or careful extraction.
- If the healing process results in a malocclusion—orthodontics, endodontics, and/or selective exodontia (extraction) may be required.
- Other considerations—stability of fracture and appliance; oral hygiene; oral intake of food and water; maintenance of weight; appropriate urination and defecation; indications of pain or swelling.

PREVENTION/AVOIDANCE

Try to minimize risk of trauma.

POSSIBLE COMPLICATIONS

- Malocclusion • Endodontic disease
- Osteomyelitis • Non-union • Sequestrum
- Dehiscence • Neurologic defects • Facial pain syndrome • Impaired mastication
- Temporary weight loss • Soft tissue trauma due to appliance or wires

POSSIBLE SEQUELAE**Impaired Mastication**

- TMJ arthritis—chronic or intermittent TMJ pain; may require condylectomy.
- Malocclusion—dental attrition; may require extractions.
- Non-union—may require partial or complete mandibulectomy or maxillectomy.
- Ankylosis of mandible at the TMJ or zygomatic arch area.

Facial Pain Syndrome

- Acute or chronic.
- Due to nerve trauma from injury or as a complication of surgery.

Nerve Damage

Affecting motor function

EXPECTED COURSE AND PROGNOSIS

- Generally good; however, predisposing factors, initiating force, location, type of fracture, quality of homecare, and selection of treatment modality all affect the healing outcome.
- 4–12 weeks to bony union.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Malocclusion • Mastication difficulty
- Lack of head symmetry • Soft tissue trauma
- Periodontal disease • Chipped, broken, luxated, or avulsed teeth

AGE-RELATED FACTORS

Fracture healing may be faster in younger animals.

SEE ALSO

Temporomandibular Joint Disorders

ABBREVIATIONS

- BEARD = bignathic encircling and retaining device
- CT = computed tomography
- IM = intramedullary
- MRI = magnetic resonance imaging
- TMJ = temporomandibular joint

INTERNET RESOURCES

<http://www.avdc.org/Nomenclature.html>.

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Client Education Handout
available online

M

MEDIASTINITIS



BASICS

OVERVIEW

- The mediastinum occupies the central portion of the chest and is defined anatomically by the thoracic inlet cranially, the diaphragm caudally, the mediastinal pleura laterally, the paravertebral gutters and ribs dorsally, and the sternum ventrally. It is lined on both sides by parietal pleura, contains the major organs in the central thorax, and separates these organs from the left and right lung lobes.
- Mediastinitis—an inflammatory process involving the mediastinal space, usually the result of bacterial or fungal infection.
- Acute disease—severe infection may be life-threatening and can spread to the pleural space; sepsis can occur.
- Chronic—mediastinal granuloma or abscess can develop and result in cranial vena cava syndrome or chronic smoldering internal abscessation.
- Systems affected—cardiovascular system through interference with venous return; respiratory system secondary to intrathoracic mass effect or pleural effusion; gastrointestinal system through esophageal obstruction.

M SIGNALMENT

Rare in dogs and cats

SIGNS

- Lethargy and weakness.
- Dysphagia and regurgitation.
- Edema of head, neck, and forelimbs.
- Polypnea, respiratory difficulty or obstructed breathing, and cough.
- The presence of a fever should raise the suspicion for an infectious process.

CAUSES & RISK FACTORS

- Acute disease—usually result of esophageal perforation, tracheal tear, foreign body migration, or neck wound; mediastinal abscesses can develop subsequent to infections or neoplastic disorders arising in the mediastinum or adjacent tissues.
- Chronic disease—usually result of a bacterial (e.g., *Actinomycetes* and *Nocardia* spp.) or fungal (e.g., *Coccidioides*, *Cryptococcus*, *Blastomyces*, and *Histoplasma* spp.) infection. *Spirocercus lupi* infection possible in certain geographic regions.
- Predisposing factors—esophageal foreign body; cervical or thoracic trauma.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Isolated pericarditis, pyothorax, and pneumonia.
- Cranial mediastinal mass—lymphosarcoma; thymoma, thyroid, or parathyroid tumor; neurogenic tumor; mesenchymal tumor; mediastinal cyst.

- Esophageal motor dysfunction, sliding hiatal hernia.
- Gastroesophageal disorders, causing gastroesophageal reflux, chronic vomiting, and other upper GI conditions.

CBC/BIOCHEMISTRY/URINALYSIS

- High WBC count with left-shift.
- PCV and total protein—may be high owing to volume depletion/dehydration.

OTHER LABORATORY TESTS

Additional laboratory tests to rule-out other possible causes of clinical signs.

IMAGING

- Thoracic radiographs—usually demonstrate a focal or diffuse widening of the mediastinum; can be accompanied by pneumothorax or bilateral pleural effusion, depending upon the underlying disease process.
- Esophageal contrast study—investigate esophageal perforation or other abnormality; use a water-soluble contrast medium with suspected perforation (i.e., iohexol or iopamidol).
- Thoracic ultrasonography—differentiate between mediastinal fluid accumulation (e.g., cyst and abscess), inflammatory reaction, and tumor.
- Computed tomography—more definitive than ultrasound.

DIAGNOSTIC PROCEDURES

- Cytology—thoracocentesis of any pleural effusion; transthoracic fine-needle aspirate or cutting-needle biopsy of a mediastinal mass that is not cardiac or vascular in origin.
- Ultrasound-guided aspirate or biopsy most helpful in accurate sampling of tissues.
- Submit samples for aerobic and anaerobic bacterial culture and sensitivity testing.



TREATMENT

- Antibiotic or antifungal therapy as indicated.
- Drainage and debridement of abscessed material.
- Inpatient therapy with restricted activity until infection is controlled and condition is stable.
- Pleural effusion of marked quantity or pyothorax of any degree—managed by tube thoracostomy or possibly surgery.
- Intravenous fluid therapy, parenteral nutrition or esophageal feeding tube—until oral water and food intake returns to normal or near normal.
- Esophageal perforation—surgical emergency; after surgery, use either parenteral nutrition or gastric tube feeding for 3–5 days.
- Chronic disease—surgical exploration needed when associated with an abscess or a granuloma.
- Tube thoracostomy—maintain post-surgery by continuous water seal suction or intermittent lavage and suction for 5–7 days or until negligible fluid is removed.



MEDICATIONS

DRUG(S)

- Broad-spectrum bactericidal antibiotic—based on bacterial culture and sensitivity testing; should be administered parenterally for at least the first week of treatment, then orally.
- Antifungal treatment—indicated for mycotic infection. Recommended agents include itraconazole, fluconazole, and amphotericin B; treatment usually required for 3–6 months.



FOLLOW-UP

PATIENT MONITORING

- Daily temperature recording.
- Hemogram—every 2–3 days during hospitalization (usually 7–10 days).
- Thoracic radiographs—at 7- to 10-day intervals (more often if drainage is needed).
- Antibiotics—generally continue for 1 week after hemogram and radiographs return to normal; with abscessation, continue an additional 4–6 weeks.

POSSIBLE COMPLICATIONS

- Pyothorax
- Sepsis
- Mediastinal fibrosis

EXPECTED COURSE AND PROGNOSIS

- Advise clients of guarded prognosis.
- With early diagnosis and aggressive treatment—prognosis fair to good.
- With mediastinal fibrosis—long-term prognosis guarded to poor.
- Recognized complications—esophageal dysmotility; compression of the cranial or caudal vena cava; phrenic or recurrent laryngeal nerve paralysis.



MISCELLANEOUS

ABBREVIATIONS

- GI = gastrointestinal
- PCV = packed cell volume
- WBC = white blood cell

Suggested Reading

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MEGACOLON**BASICS****DEFINITION**

A gastrointestinal disorder characterized by persistently increased large bowel diameter associated with chronic constipation/obstipation and low-to-absent colonic motility.

PATHOPHYSIOLOGY

- Acquired megacolon results from chronic colonic fecal impaction that leads to excessive absorption of fecal water and solidified fecal concretions.
- Prolonged distension of the colon results in irreversible changes in colonic motility that leads to colonic inertia.
- Congenital absence of colonic ganglionic cells (Hirschsprung's disease) is not clearly documented in small animals.
- The pathogenesis of idiopathic megacolon in cats likely involves a disturbance of normal colonic smooth muscle function.

SYSTEMS AFFECTED

Gastrointestinal

GENETICS

N/A

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT**Species**

- Idiopathic megacolon—cat
- Acquired megacolon—cat and dog

Breed Predilections

Some evidence for increased risk in Manx cat

Mean Age and Range

- Idiopathic megacolon—middle-aged to older cats (mean age, 4.9 years; range, 1–15 years).
- Acquired megacolon—none.

Predominant Sex

None

SIGNS**Historical Findings**

- Idiopathic megacolon—typically a chronic/recurrent problem; signs often present for months to years.
- Acquired megacolon—signs may be acute or chronic.
- Constipation/obstipation.
- Tenesmus with small or no fecal volume.
- Hard, dry feces.
- Infrequent defecation.
- Small amount of diarrhea (often mucoid) may occur after prolonged tenesmus.
- Occasional vomiting, anorexia, and/or lethargy with chronic fecal impaction.
- Weight loss.

Physical Examination Findings

- Abdominal palpation reveals an enlarged colon with hard feces.
- Digital rectal examination may indicate an underlying (obstructive) cause and confirms fecal impaction.
- Dehydration.
- Scruffy, unkempt hair coat.

CAUSES

- Idiopathic—cats.
- Mechanical obstruction—pelvic fracture malunion, foreign body or improper diet (especially bones), stricture, prostatic disease, perineal hernia, neoplasia, anal or rectal atresia.
- Causes of dyschezia—anorectal disease (anal sacculitis, anal sac abscess, perianal fistula, proctitis), trauma (fractured pelvis, fractured limb, dislocated hip, perianal bite wound or laceration, perineal abscess).
- Metabolic disorders—hypokalemia, hypocalcemia, severe dehydration.
- Drugs—vincristine, barium, antacids, sucralfate, anticholinergics.
- Neurologic/neuromuscular disease—congenital abnormalities of the caudal spine (especially Manx cats), paraplegia, spinal cord disease, intervertebral disc disease, dysautonomia, sacral nerve disease, sacral nerve trauma (e.g., tail fracture/pull injury), trauma to colonic innervation.

RISK FACTORS

- Conditions leading to inability to posture (limb and pelvic fractures, neuromuscular disease, etc.) or rectoanal pain.
- Prior pelvic fractures.
- Possible association with low physical activity and obesity.
- Perineal hernias.

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- Other causes of palpable colonic masses (e.g., lymphoma, carcinoma, intussusception)—distinguish on the basis of texture, rectal examination, imaging, and mucosal biopsy.
- Dysuria/stranguria—exclude by palpation of the bladder and colon, and by urinalysis.
- Tenesmus due to inflammation of the colonic mucosa (colitis)—exclude by palpation, rectal examination, and endoscopic imaging with mucosal biopsy.

CBC/BIOCHEMISTRY/URINALYSIS

- May show evidence of dehydration (elevated packed cell volume, total protein) and stress leukogram.
- Electrolyte abnormalities may develop depending on duration of obstipation; may be prerenal azotemia with dehydration.
- Urinalysis—no consistent changes; important to confirm normal renal function

in dehydrated animals and to rule out lower urinary tract disease as a differential diagnosis.

OTHER LABORATORY TESTS

N/A

IMAGING

- Abdominal/pelvic radiographs to identify any underlying causes.
- Can easily see the enlarged, fecal-filled colon on survey abdominal radiographs.
- Abdominal ultrasound may identify mural or obstructive masses.

DIAGNOSTIC PROCEDURES

May need colonoscopy to rule out mural or intraluminal obstructive lesions.

PATHOLOGIC FINDINGS

- The most severe dilation typically occurs in the transverse and descending colon, although the entire length of the colon can be involved.
- The colon is usually histologically unremarkable with megacolon.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Inpatient medical management; surgery may be indicated if recurrent/severe problem.
- Medical therapy—restore normal hydration, followed by anesthesia and manual evacuation of the colon using warm water enemas, water-soluble jelly, and gentle extraction of feces with a gloved finger or sponge forceps; do not traumatize the colonic mucosa.
- Continue long-term therapy at home.

NURSING CARE

- Most patients require parenteral fluid support to correct dehydration.
- Intravenous administration of balanced electrolyte solutions is the preferred route.

ACTIVITY

- Encourage activity and exercise.
- Restriction indicated in the postoperative period if surgery is performed.

DIET

- Many patients require a low-residue producing diet; bulk-forming fiber diets can worsen or lead to recurrence of colonic fecal distension.
- A high-fiber diet is occasionally helpful.
- A more palatable, maintenance-type diet can be supplemented with fiber-enriched foods (pumpkin) or products containing fermentable fiber such as Metamucil.

CLIENT EDUCATION

- In idiopathic disease or with severe colonic injury, medical therapy is often life-long and can be frustrating to clients.
- Increased activity of the cat with daily or alternate-day subcutaneous fluid therapy can help minimize recurrences in many cats.
- Recurrence of megacolon is common.

MEGACOLON

(CONTINUED)

- Surgery (subtotal colectomy) is indicated if medical therapy fails.

SURGICAL CONSIDERATIONS

- An underlying obstructive cause requires surgical correction.
- Avoid enema administration/colonic evacuation prior to subtotal colectomy.
- Subtotal colectomy with ileorectal or colorectal anastomosis—treatment of choice for idiopathic megacolon refractory to medical management.
- Colectomy may also be required with obstructive megacolon caused by irreversible changes in colonic motility.



MEDICATIONS

DRUG(S) OF CHOICE

- Can improve colonic motility in less severe cases with cisapride, a prokinetic gastrointestinal drug (dogs, 0.3–0.5 mg/kg PO q8–12h; cats, 2.5–10 mg/cat q8–12h). Metoclopramide does not affect colonic motility and should not be used in cats with megacolon.
- Stool softeners (e.g., lactulose, 1 mL/4.5 kg PO q8–12h to effect) are recommended in conjunction with cisapride and diet.
- Broad-spectrum antibiotics are recommended prior to surgery to reduce the potential for bacterial sepsis.

M

CONTRAINDICATIONS

- Sodium phosphate retention enemas (e.g., Fleet; C.B. Fleet Co., Inc.)—because of their association with severe hypocalcemia.
- Mineral oil and white petrolatum—because of danger of fatal lipid aspiration pneumonia due to lack of taste.

PRECAUTIONS

Common hairball laxatives (e.g., Laxatone, Cat-a-Lax) are typically ineffective.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Docusate sodium can be used as a stool softener in place of lactulose.



FOLLOW-UP

PATIENT MONITORING

- Following colonic resection and anastomosis—for 3–5 days check for signs of dehiscence and peritonitis.
- Clinical deterioration warrants abdominocentesis and/or peritoneal lavage to detect anastomotic leakage.
- Continue fluid support until the patient is willing to eat and drink.

PREVENTION/AVOIDANCE

- Repair pelvic fractures that narrow the pelvic canal.
- Avoid exposure to foreign bodies and feeding bones.

POSSIBLE COMPLICATIONS

- Recurrence or persistence—most common.
- Potential surgical complications include peritonitis, persistent diarrhea, fecal incontinence, stricture formation, and recurrence of obstipation.
- Traumatic perforation of the colon is a serious complication of overzealous fecal evacuation.

EXPECTED COURSE AND PROGNOSIS

- Historically, medical management has been unrewarding for the long term.
- Cisapride appears to improve the prognosis with medical management in some patients, but may not suffice in severe or long-standing cases.
- Postoperative diarrhea—expected; typically resolves within 6 weeks (80% of cats with idiopathic megacolon undergoing subtotal colectomy) but can persist for several months; stools become more formed as the ileum

adapts by increasing reservoir capacity and water absorption.

- Subtotal colectomy is well tolerated by cats; constipation recurrence rates are typically low.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Perineal hernia

AGE-RELATED FACTORS

Concurrent medical conditions (e.g., chronic renal insufficiency, hyperthyroidism) may occur with idiopathic megacolon, because many cats are old.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

- The effect of cisapride on the fetus is unknown.
- Patients would be at increased risk for dystocia if they carried a pregnancy to term.

SEE ALSO

- Constipation and Obstipation
- Dyschezia and Hematochezia
- Perineal Hernia

Suggested Reading

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Client Education Handout
available online

MEGAESOPHAGUS



BASICS

DEFINITION

A focal or generalized, diffuse dilation of the esophagus with decreased to absent peristalsis.

PATHOPHYSIOLOGY

- In the normal esophagus, the presence of a food bolus in the proximal esophagus stimulates afferent sensory neurons.
- Signals are transferred centrally, via the vagus and glossopharyngeal nerves to the tractus solitarius and nucleus ambiguus.
- Motor impulses travel back via the efferent neurons of the vagus nerve to stimulate striated muscle (canine) and striated and smooth muscle (feline) esophageal contraction.
- Lesions anywhere along this pathway may lead to megaesophagus and resultant retention of food and liquids.
- There is evidence that afferent nerve dysfunction is the most common lesion in idiopathic cases of megaesophagus. Focal megaesophagus is typically caused by esophageal obstruction distal to the dilated portion of esophagus.

SYSTEMS AFFECTED

- Gastrointestinal—dysphagia, regurgitation, weight loss.
- Musculoskeletal—weakness, weight loss, exercise intolerance, dysphonia.
- Nervous—possible manifestation of systemic neurologic/neuromuscular disorder.
- Respiratory—aspiration pneumonia, coughing.

GENETICS

- Congenital form—megaesophagus can be inherited in wirehaired fox terriers (autosomal recessive) and miniature schnauzers (autosomal dominant or 60% penetrance autosomal recessive).
- Other breeds reported include dachshund, German shepherd, Great Dane, Irish setter, Labrador retriever, pug, and Chinese shar-Pei.
- Myasthenia gravis may be congenital in Jack Russell terriers, springer spaniels, smooth fox terriers, dachshunds, and Samoyeds.
- Acquired form—many diseases, especially neuromuscular diseases, may have an association with megaesophagus. Genetic predispositions for such diseases are listed under each disease separately.

INCIDENCE/PREVALENCE

- Congenital forms—rare
- Acquired disease—uncommon in the dog and rare in the cat.

SIGNALMENT

Species

Dogs are more commonly affected than cats

Breed Predilections

- Dogs—see “Genetics”
- Cats—Siamese and Siamese-related cats

Mean Age and Range

- Congenital cases present soon after birth or at weaning during transition from liquid diets to solid foods.
- Acquired cases may be seen at any age, depending on the etiology.

SIGNS

Historical Findings

- Owners often report vomiting; the veterinarian must differentiate vomiting from regurgitation.
- Regurgitation (considered the hallmark sign); dysphagia; coughing/nasal discharge with aspiration pneumonia; ravenous appetite or inappetence; weight loss or poor growth; ptalism, and halitosis.
- Dysphonia may occur secondary to neuromuscular disease.
- Other signs depend upon underlying etiology.

Physical Examination Findings

- Cervical swelling may be noted, representing a distended cervical esophagus; ptalism; halitosis; increased respiratory noises, nasal discharge, and fever (if concurrent pneumonia); cachexia; weakness; weight loss.
- Assess for concurrent neurologic deficits that may indicate generalized disease. Special attention should be paid to cranial nerves IX, X, and XI. Muscle atrophy (if present) may be focal or generalized.

CAUSES

Congenital

Idiopathic megaesophagus; congenital MG (rare)

Acquired/Adult Onset

- Idiopathic (most common).
- Neuromuscular disease—MG, focal or generalized (25% of cases in dogs); SLE; myositis/myopathic disease; dysautonomia (more common in cats); botulism; vagal dysfunction/damage (bilateral); a possible association between laryngeal paralysis and esophageal dysmotility secondary to polyneuropathy has been identified.
- Brainstem disease—disease involving CN IX, X nuclei or peripheral nerves.
- Esophageal obstruction—vascular ring anomaly; esophageal or periesophageal neoplasia (e.g., lymphoma, leiomyoma); stricture; foreign body; granuloma.
- Toxicity—lead, thallium, anticholinesterase; acrylamide.
- Endocrine disease—hypoadrenocorticism, hypothyroidism (controversial). Thymoma is associated with MG and megaesophagus in approximately 25% of cats.
- Miscellaneous—gastric dilatation volvulus, hiatal hernia, gastroesophageal intussusception; esophagitis (gastroesophageal reflux, parasitic infection).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Must distinguish regurgitation from vomiting.
- Regurgitation—passive; little to no abdominal effort; no prodromal phase; regurgitated material has increased amounts of thick mucus.
- Vomiting—active process; prodromal phase; vomited material may have increased bile staining.
- The shape of the

expelled material, presence of undigested food, and length of time from ingestion to regurgitation or vomiting are less helpful to differentiate.

CBC/BIOCHEMISTRY/URINALYSIS

- May be normal.
- Inflammatory leukogram may be seen with pneumonia.
- Other changes may identify underlying etiology—basophilic stippling on red blood cells with lead toxicity; electrolyte disturbances with hypoadrenocorticism; hypercholesterolemia with hypothyroidism; elevated creatine kinase with myopathic disease.

OTHER LABORATORY TESTS

- Acetylcholine receptor antibody titer in all cases of megaesophagus (screen for MG). Approximately 2% of dogs with generalized MG are seronegative; testing should be repeated 2–3 months later, particularly if initial antibody titer is only slightly below the reference interval.
- ACTH stimulation test or baseline cortisol level for hypoadrenocorticism.
- Thyroid panel for hypothyroidism (may be affected by concurrent disease).
- Blood and urine lead levels.
- ANA titers for SLE.
- Blood cholinesterase levels for organophosphate toxicity.

IMAGING

Survey Thoracic Radiographs

- Dilated esophagus filled with air, fluid, or food. Interpret thoracic radiographs in anesthetized animals and anxious or painful animals with caution in light of aerophagia that can cause distention of the esophagus with air.
- Evidence of aspiration pneumonia.
- Ventral displacement of the trachea on lateral radiographs.
- Ventrodorsal radiographs may show lateral tracheal displacement.
- Evidence of underlying etiology: mediastinal mass (thymoma), hiatal hernia, neoplasia, etc.
- Radiographs do not differentiate dogs with megaesophagus due to MG from dogs with megaesophagus due to other etiologies.

Contrast Esophagram and Video-Fluoroscopy

- Barium liquid and barium meal may demonstrate abnormal pooling, poor motility, or structural lesions. Iohexol may be used if perforation is a concern.
- Use with caution in animals with megaesophagus due to risk of aspiration of contrast material.
- Exercise extreme caution in animals with radiographic evidence of pneumonia.
- Monitor animals closely after radiographs for signs of aspiration.
- Videofluoroscopy—may be used to assess primary and secondary esophageal peristalsis. May help determine the best food consistency for long-term management.

DIAGNOSTIC PROCEDURES

- Esophagoscopy—may be used for foreign body retrieval, evaluation of suspected obstructive lesions, neoplasia, or esophagitis.

MEGAESOPHAGUS

(CONTINUED)

Distal esophageal neoplasia may mimic idiopathic megaesophagus and may require endoscopy for diagnosis.

- Electrophysiology—in cases of suspected neuromuscular disease, may be used in conjunction with muscle and nerve biopsies.
- Additional tests—may be indicated in cases of CNS disease: CSF analysis, distemper titers, brain CT or MRI. • Fecal exam—may indicate *Spirocerca lupi* infection.

PATHOLOGIC FINDINGS

Depend upon underlying etiology and presence of complicating factors.



TREATMENT

APPROPRIATE HEALTH CARE

- Treat underlying etiology (when applicable).
- Most important aspects are meeting nutritional requirements and treating or preventing aspiration pneumonia.

NURSING CARE

• Aspiration pneumonia may require oxygen therapy, nebulization/coupage, fluid therapy with balanced electrolyte solution. • These animals may be recumbent and require soft bedding and should be maintained in sternal recumbency or turned to alternate down side every 4 hours.

ACTIVITY

Depending on etiology, restricted activity is not necessary.

DIET

- Calculate precise nutritional requirements, including degree of debilitation.
- Experimentation with different food consistencies is essential (e.g., liquid gruel, small meatballs, blenderized slurries). • Many cases benefit from gastrostomy tube placement for feeding; however, this does not prevent gastroesophageal reflux and potential aspiration or aspiration of saliva. • Feeding and drinking should be from an elevated position (45–90° from floor) and the upright position should be maintained for 10–15 minutes after eating or drinking. An upright position may be easier to attain with the use of a specific "chair" (e.g., Bailey chair).

CLIENT EDUCATION

- Most cases of megaesophagus require life-long therapy. Even if an underlying etiology is found and treated, prognosis for resolution of megaesophagus is guarded. Client dedication is important for long-term management. • Most animals succumb to or are euthanized because of aspiration pneumonia or progression of underlying disease.

SURGICAL CONSIDERATIONS

- Surgery is indicated for vascular ring anomalies, bronchoesophageal fistula, some foreign bodies and other obstructive lesions,

or thymectomy. • Balloon dilation is indicated for cases of esophageal stricture. • Surgical resection of megaesophagus is not recommended.



MEDICATIONS

DRUG(S)

- Antibiotics for aspiration pneumonia (ideally based on culture and sensitivity from transtracheal wash or bronchoalveolar lavage).
- Therapy for underlying etiology if indicated—immunosuppressives (use with caution if pneumonia present) for immune-mediated disease; pyridostigmine for MG, prednisone supplementation for hypoadrenocorticism • H₂ blockers for esophagitis—ranitidine (1–2 mg/kg PO, IV q12h), famotidine (0.5–1 mg/kg PO, SC, IM, IV q12–24h). Proton pump inhibitors may be used in severe cases—omeprazole (1 mg/kg PO q24h) or pantoprazole (1 mg/kg IV q24h).

Prokinetics

- The use of prokinetics in dogs and cats with diffuse megaesophagus is controversial and should be avoided because they will tighten the lower esophageal sphincter and possibly increase the risk of aspiration pneumonia. Prokinetics such as metoclopramide (1.0–2.0 mg/kg/day IV CRI or PO q6–8h) or cisapride (0.5 mg/kg PO q8–12h) are more effective for minimizing gastroesophageal reflux and esophagitis. Cisapride is more potent and effective than metoclopramide for increasing lower esophageal tone and enhancing gastric emptying, and can be used in animals with evidence of esophagitis but no evidence of megaesophagus, or in cats with esophageal dysmotility affecting the smooth muscle in the distal 1/3 of the esophagus.

PRECAUTIONS

- Absorption of orally administered drugs may be compromised. • Injectable forms should be used when applicable.
- Immunosuppression, if indicated, must be used with caution due to risk of aspiration pneumonia.



FOLLOW-UP

PATIENT MONITORING

- Thoracic radiographs when aspiration pneumonia is suspected (fever, cough, lethargy). • Cases of pneumonia may require CBC, blood gas analysis, and bronchoalveolar lavage. Repeat thoracic radiographs in animals with congenital megaesophagus as spontaneous resolution may occur. • Examine and weigh patients regularly to evaluate disease progression and ensure adequate nutritional intake.

PREVENTION/AVOIDANCE

If an esophageal foreign body is identified, remove as quickly as possible.

POSSIBLE COMPLICATIONS

- Aspiration pneumonia • Others, depending on etiology

EXPECTED COURSE AND PROGNOSIS

- Congenital cases have a guarded prognosis (20–40% recovery). • Miniature schnauzers may have better prognosis. • Prognosis may be improved with identification and treatment of specific etiology (e.g., hypoadrenocorticism, vascular ring anomaly).
- Roughly 50% cases of MG respond to therapy; however, megaesophagus may persist even if other signs of MG resolve. • Prognosis for idiopathic, adult onset disease is poor.
- Owner dedication is crucial.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Aspiration pneumonia

AGE-RELATED FACTORS

- Signs of regurgitation in very young animal or at weaning may indicate congenital lesion.
- Prognosis may be better in young animals.

ZOONOTIC POTENTIAL

- None for megaesophagus. • Rabies vaccination status should be determined in any animal with possible neurologic disease.

SYNOMYMS

- Esophageal aperistalsis • Esophageal dilatation

SEE ALSO

- Dysphagia • Esophageal Foreign Bodies
- Myasthenia Gravis • Pneumonia, Aspiration
- Pneumonia, Bacterial • Regurgitation

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- ANA = antinuclear antibody • CNS = central nervous system • CSF = cerebrospinal fluid • CT = computed tomography • MG = myasthenia gravis • MRI = magnetic resonance imaging • SLE = systemic lupus erythematosus

INTERNET RESOURCES

- <http://marvistavet.com/html/megaesophagus.html> • <http://www.baileychairs4dogs.com/>

Suggested Reading

Mace S, Shelton GD, Eddlestone S. Megaesophagus. Compend Contin Educ Vet 2012, 34(2):E1.

Authors Marguerite F. Knipe and Stanley L. Marks

Consulting Editor Stanley L. Marks



Client Education Handout
available online

MELANOCYTIC TUMORS, ORAL



BASICS

DEFINITION

Tumor of melanocytes arising in the oral cavity (gingiva, palate, tongue), most frequently malignant.

PATHOPHYSIOLOGY

- Locally invasive.
- Metastatic in > 75% cases in dogs (lymph nodes, lungs, other).
- When malignant, may invade into the underlying bone.

SYSTEMS AFFECTED

- Oral cavity (gingiva, palate, tongue)
- Metastatic sites—lymph nodes, lungs, bones, other

GENETICS

Unknown

INCIDENCE/PREVALENCE

- Dogs—most common malignant oral tumor, accounting for ~ 40% of neoplasms.
- Cats—third most common oral malignancy.

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dog more than cat

Breeds

- Dogs—cocker spaniel, miniature poodle, retriever breed, chow chow (tongue)
- Cats—none

Mean Age and Range

- Dogs—11 years (5–18 years)
- Cats—12 years (11–15 years)

Predominant Sex

- Dogs—male predisposed (in some studies)
- Cats—not reported

SIGNS

Historical Findings

- Excessive salivation
- Halitosis
- Dysphagia
- Bloody oral discharge
- Weight loss

Physical Examination Findings

- Oral mass (up to one-third are poorly pigmented or amelanotic), often friable
- Loose teeth
- Facial deformity (including exophthalmos)
- Regional lymphadenomegaly
- Pain or discomfort

CAUSES & RISK FACTORS

Overrepresented breeds



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other oral tumors (squamous cell carcinoma, fibrosarcoma)
- Epulides
- Gingival hyperplasia
- Tooth root abscess

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

Immunohistochemical markers—may help differentiate melanoma (especially amelanotic) from other tumors; may stain positive with vimentin, S-100, neuron-specific enolase, HMB-45 and Melan A (most specific, but somewhat less sensitive marker).

IMAGING

- High-detail skull radiography or dental radiographs—evaluate for osteolytic changes.
- Advanced imaging such as contrast-enhanced CT or MRI—better detail (especially maxilla) and helps with therapeutic planning (surgery or radiation therapy).
- Thoracic radiography or CT—evaluate lungs for metastasis.
- Abdominal ultrasonography—to complete clinical staging, occasional distant metastasis in abdominal visceral organs.

DIAGNOSTIC PROCEDURES

- Large and deep tissue biopsies—required to obtain definitive diagnosis via histopathology. Biopsies always taken from inside the mouth, not through the skin (would compromise local control with surgery).
- Fine-needle aspiration and cytology of regional lymph nodes (mandibular and retropharyngeal) recommended to evaluate for regional metastases, regardless of their size and consistency upon palpation.

PATHOLOGIC FINDINGS

Gross

- Masses—may be ulcerated and friable, often bleed when large and malignant.
- Amelanotic to dark brown, gray, or black.
- Varies greatly in size, often invasive in surrounding tissues.

Cytologic Findings

- Brown, rod-like intracellular granules (melanin) of various size and shapes.
- Pigment may be absent with amelanotic tumors.
- May see melanophages (phagocytic macrophages) with large intracytoplasmic vacuoles containing melanin, especially in lymph nodes.
- More cellular atypia observed in malignant tumors.

Histopathologic Findings

- Cells may vary in shape (e.g., epithelioid, fusiform, dendritic, and mixed), degree of pigmentation, and cytoplasmic morphology.
- Malignant—generally high mitotic index; nuclear and nucleolar pleomorphism (more atypia, less differentiation); invasive into surrounding tissues; amelanotic may pose a diagnostic challenge; immunohistochemistry and special stains may be particularly useful. Proliferation markers may help predict behavior.
- Immunohistochemistry (e.g., Melan-A, S100, HMB-45, vimentin)—may help confirm a diagnosis, especially if amelanotic (approximately one-third of cases).
- Histopathology report should include mitotic index (mitoses per 10 high-power field), degree of atypia/differentiation, invasiveness, and surgical margins if excisional biopsy.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient if undergoing aggressive oral surgery.

NURSING CARE

Pain management—multimodal analgesia (preemptive, intra- and postoperative) is mandatory with aggressive surgeries.

ACTIVITY

Restrict until sutures are removed and all surgical wounds are healed.

DIET

- Normal, but soft food recommended after aggressive oral surgery.
- Avoid toys and hard treats until oral tissues healed completely.

CLIENT EDUCATION

- Discuss importance of clinical staging.
- Discuss need for early aggressive approach with surgical removal.
- Warn caretaker that malignant melanoma frequently metastasize early in the course of the disease, resulting in a guarded prognosis.
- Adjuvant therapy is recommended to improve survival time and delay metastasis.
- Repeat clinical staging recommended after therapy.

SURGICAL CONSIDERATIONS

- Goal should be to remove all macroscopic tumor burden and obtain complete margins, in order to improve overall prognosis.
- Radical en bloc surgical excision—required (e.g., mandibulectomy or maxillectomy); well tolerated by most patients; surgical margins of at least 2 cm; improved survival when margins are free of neoplastic cells.

MELANOCYTIC TUMORS, ORAL

(CONTINUED)

- Surgical removal of the draining lymph node(s) is recommended when metastasis confirmed or suspected and no evidence of distant (e.g., lung) metastatic disease.

RADIATION THERAPY

CONSIDERATIONS

Three to six, weekly to twice weekly, large fractions of megavoltage radiation therapy—good response rate (> 80%) and may offer long-term control with inoperable tumors.



MEDICATIONS

DRUG(S)

- Carboplatin has been described for oral melanoma in dogs, with a response rate approximating 30% on measurable disease, but no clear survival advantage was demonstrated when used in the adjuvant setting.
- No effective chemotherapy described in cats.
- Multimodal analgesia recommended to control pain and discomfort.

IMMUNOTHERAPY

- Many immunotherapies have been attempted with varied success.
- A therapeutic vaccine is available that involves the injection of human cDNA (xenogeneic) coding for a melanocyte-specific protein, tyrosinase, and results in a measurable immune response in some patients.
- The tyrosinase vaccine is approved for the postoperative treatment of stage II and III oral malignant melanomas and results in improved survival times in comparison with historical control studies.

CONTRAINDICATIONS

Avoid the use of cisplatin in cats.

PRECAUTIONS

Seek advice from an oncologist before initiating treatment if you are unfamiliar with cytotoxic drugs (myelosuppression, specific toxicities, etc.).

POSSIBLE INTERACTIONS

Drug with overlapping toxicities should be avoided.

ALTERNATIVE DRUGS

Piroxicam may play a minor role for alleviating pain and slowing tumor progression.



FOLLOW-UP

PATIENT MONITORING

- Evaluate for local recurrence and regional metastasis—every 2–3 months following surgery or earlier if the owner believes the mass is returning; or if the patient is otherwise not normal.
- Thoracic radiography—at the time of rechecks and periodically thereafter.

PREVENTION/AVOIDANCE

None.

POSSIBLE COMPLICATIONS

- Poor wound healing, dehiscence, infection possible after aggressive surgery.
- Early radiation side effects, such as mucositis or dermatitis, may result from hypofractionated protocols.

EXPECTED COURSE AND PROGNOSIS

- Poor prognosis when untreated (median 2 months).
- Depends upon disease stage; better prognosis with stage I.
- Complete surgical excision (local and regional lymph node when positive) is essential to improve the prognosis. Median survival time with surgery alone varies with stage:
 - Stage I—over 18 months.
 - Stage II and III—5–12 months; prognosis of stage II and III canine oral melanoma may be improved to over 18 months with the adjuvant use of the recombinant xenogeneic tyrosinase vaccine.
 - Stage IV—less than 3 months.
- Survival with radiotherapy treatment alone (dogs)—6–10 months.
- Most common causes of death in dogs are metastatic disease and local tumor recurrence.
- Overall prognosis in cats—poor; most tumors are locally invasive and diagnosed late in the course of the disease; cause of death is often due to local disease progression. Median survival time of 146 days in 5 cats treated with hypofractionated radiation therapy.



MISCELLANEOUS

ASSOCIATED CONDITIONS

None

AGE-RELATED FACTORS

Older age at diagnosis (> 12 years) might predict a poorer prognosis in dogs.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Cytotoxic chemotherapy agents should not be used in pregnant or breeding animals.

SYNONYMS

Malignant—melanosarcoma (rarely used)

SEE ALSO

Melanocytic Tumors, Skin and Digit

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging

Suggested Reading

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MELANOCYTIC TUMORS, SKIN AND DIGIT



BASICS

OVERVIEW

- Benign or malignant neoplasm arising from melanocytes in the epidermis or the nail bed.
- Localized growth behavior with potential invasive characteristics.
- When malignant—occasionally invades bone (e.g., third phalanx) and metastasizes (lymph node, lungs, and other sites).

SIGNALMENT

- Dogs—around 10% of all skin tumors.
- Cats—< 5% of all skin tumors.
- Dogs, mean age 9 years, certain breeds more common—terriers (Scottish, Boston, and Airedale) schnauzers, cocker and springer spaniels, boxer, Irish setter, chow chow, Chihuahua, retriever breeds, and Doberman pinscher.
- Cats, mean age 10–12 years, no breed predilection.

SIGNS

- Skin mass with variable growth rates, pigmented or not (amelanotic), usually solitary.
- Lameness and pain if digit is involved.
- Develops anywhere; in dogs more common on face, trunk, feet, and scrotum, while in cats more common on head, digit, pinna, and nose.
- Draining regional lymph nodes—may be enlarged.
- Advanced disease—may cause respiratory signs secondary to diffuse pulmonary metastasis.

RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Distinguish amelanotic melanoma from poorly differentiated discrete cell tumors (mast cell tumors, lymphoma), various sarcomas (e.g., histiocytic), and carcinomas (especially basal cell).

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

Immunohistochemical markers—may help differentiate melanoma (especially amelanotic) from other tumors; may stain positive with vimentin, S-100, neuron-specific enolase, HMB-45, and Melan A.

IMAGING

- Thoracic radiography recommended for the detection of metastasis.
- Advanced imaging (CT scan) is more sensitive to detect smaller metastases.

- With digit melanoma, radiography of the lesion is recommended to determine if underlying bone (P3) is involved. Bone lysis is less common with nailbed melanoma (approximately 10%) than with squamous cell carcinoma (approximately 75%).

DIAGNOSTIC PROCEDURES

- Cytologic examination of fine-needle aspirates (primary mass, draining lymph node, other).
- Draining lymph nodes should be evaluated with cytology independently of their size or clinical appearance.

PATHOLOGIC FINDINGS

Gross

- Masses—may be ulcerated and friable when malignant.
- Benign—brown to black; varies from macules and plaques to firm, dome-shaped nodules, 0.5–2 cm in diameter, well demarcated.
- Malignant—amelanotic to dark brown, gray, or black, often > 2 cm in diameter and more invasive in surrounding tissues.
- Melanomas of the digit and mucocutaneous junctions tend to be malignant.

Cytologic findings

- Brown, rod-like cytoplasmic granules (melanin) in cells of various sizes and shapes.
- Pigment may be absent with amelanotic melanoma.
- May see macrophages (melanophages) with large intracytoplasmic vacuoles containing phagocytosed melanin.
- More atypia observed (e.g., large single nucleolus, mitotic figures) in malignant tumors.

Histopathologic Findings

- Both benign and malignant lesions may have cells that vary in shape (e.g., epithelioid, fusiform, dendritic, and mixed), degree of pigmentation, and cytoplasmic morphology.
- Malignant—generally high mitotic index; nuclear and nucleolar pleomorphism (more atypia, less differentiation); invasive into surrounding tissues; amelanotic may pose a diagnostic challenge; immunohistochemistry and special stains may be particularly useful. Proliferation markers may help predict behavior.



TREATMENT

SURGICAL CONSIDERATIONS

- Wide surgical excision—treatment of choice.
- Amputation of digit with nailbed localization.
- Lymphadenectomy of the draining lymph node indicated when metastasis confirmed or suspected and no evidence of detectable distant dissemination.



MEDICATIONS

DRUG(S)

- Adjunctive therapy—recommended with malignant melanoma, when surgical excision is incomplete, when the mass is non-resectable, or if metastasis is present.
- A study showed a xenogeneic murine tyrosinase vaccine, similar to the commercially available therapeutic vaccine approved for canine oral malignant melanoma, to be safe and potentially effective in the treatment of digit melanoma.
- In dogs and cats, the cytotoxic drugs with some reported efficacy include carboplatin (dogs and cats), cisplatin (dogs only), and doxorubicin. In general response rate is below 30%.
- Piroxicam may play a minor role in pain control and tumor control.
- Multimodal analgesia recommended to control pain and discomfort.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Drugs with overlapping toxicity should be avoided. Cisplatin is absolutely contraindicated in cats.

PRECAUTIONS

Veterinarians administering chemotherapeutics should follow published guidelines on the safe use of these drugs and should be familiar with potential side effects.



FOLLOW-UP

PATIENT MONITORING

- Evaluate for local recurrence and regional metastasis—every 2–3 months following surgery or earlier if the owner believes the mass is returning; or if the patient is otherwise not normal.
- Thoracic radiography—at the time of rechecks and periodically thereafter.

EXPECTED COURSE AND PROGNOSIS

Dogs

- Approximately 25% of cutaneous melanocytic tumors are reported to be malignant. Melanomas on the digit, footpad, scrotum, and mucocutaneous junctions are more frequently malignant.
- Prognosis with benign cutaneous melanomas is excellent.
- Median survival with malignant cutaneous or digit melanoma is 12 months.
- Breed differences in prognosis in some studies—majority of cutaneous melanomas in Doberman pinschers and miniature schnauzers behave in a benign fashion, and a majority of cutaneous melanomas in miniature poodles behave in a malignant fashion.

MELANOCYTIC TUMORS, SKIN AND DIGIT

(CONTINUED)

Cats

- 35–50% of melanomas reported to be malignant.
- Median survival with melanoma of the skin or digit not well documented and reported to be 4.5 months after surgery in one study of 57 cats.



MISCELLANEOUS

ASSOCIATED CONDITIONS

None

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Benign—melanocytic nevus; melanocytoma
- Malignant—melanosarcoma (rarely used)

Suggested Reading

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Consulting Editor Timothy M. Fan



Client Education Handout
available online



BASICS

DEFINITION

Presence of digested blood in the feces, causing a black, tarry appearance.

PATHOPHYSIOLOGY

Usually results from upper GI bleeding (esophagus, stomach, small intestine), but can be associated with ingested blood from the oral cavity or respiratory tract.

SYSTEMS AFFECTED

- Gastrointestinal
- Respiratory
- Coagulation

SIGNALMENT

- More common in dog than cat

SIGNS

Historical Findings

- Patients with upper GI tract hemorrhage may demonstrate vomiting (blood or “coffee grounds” appearance), inappetence, weight loss, weakness, and/or mucous membrane pallor.
- Patients with respiratory tract hemorrhage may demonstrate epistaxis, sneezing, hemoptysis, mucous membrane pallor, weakness, and/or dyspnea.
- Patients with abnormal coagulation may demonstrate petechia, ecchymosis, mucous membrane pallor, epistaxis, hematuria, hyphema, and/or weakness.

Physical Examination Findings

Depends on the underlying cause.

CAUSES

Primary GI Ulceration/Erosion

- Neoplasia—lymphoma, adenocarcinoma, sarcoma
- IBD (lymphoplasmacytic, eosinophilic, granulomatous, and/or histiocytic gastritis/enteritis)
- Benign polyps
- Infectious—Bacterial (*Salmonella* spp., *Clostridium perfringens*, *C. difficile*, *Helicobacter* spp.); fungal or fungal-like (pythiosis, histoplasmosis), parasitic (hookworms), viral (parvovirus, circovirus, distemper).
- Mechanical—foreign body
- Inflammatory—acute and chronic gastritis; hemorrhagic gastropathy,
- Drugs—NSAIDs, corticosteroids.

Metabolic/Other Diseases That Cause GI Ulceration

- Renal failure
- Hepatic disease/failure
- Pancreatitis
- Hypoadrenocorticism
- Neoplasia—gastrinoma, mast cell tumor
- Shock, poor perfusion

Ingestion of Blood

- Diet (raw foods)
- Esophageal lesion—neoplasia, esophagitis
- Oral or pharyngeal lesion—neoplasia, abscess
- Nasal lesion—neoplasia, fungal rhinitis, inflammatory rhinitis
- Respiratory lesion—lung lobe torsion, neoplasia, pneumonia, trauma (causing hemoptysis)

Coagulopathy

- Thrombocytopenia
- Thrombocytopathy—von Willebrand disease, thrombasthenia, thrombopathia, NSAIDs
- Clotting factor abnormalities—anticoagulant rodenticide ingestion, clotting factor deficiency
- Disseminated intravascular coagulation

RISK FACTORS

Arthritis or other conditions requiring use of NSAIDs or corticosteroids



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Medications that cause dark stool—bismuth subsalicylate, oral iron therapy, sucralfate
- Must distinguish intestinal from extraintestinal disease

CBC/BIOCHEMISTRY/URINALYSIS

- Microcytic, hypochromic, poorly regenerative anemia if chronic blood loss.
- Regenerative anemia in early blood loss—may be poorly regenerative if < 3–5 days.
- Panhypoproteinemia if significant blood loss.
- Thrombocytopenia, neutrophilia in some patients; pancytopenia in some.
- Biochemistry analysis may reveal extra-intestinal cause of melena—renal failure, hepatic disease, hypoadrenocorticism. Discordant increase in the BUN:creatinine ratio can be seen secondary to GI bleeding.
- Urinalysis may demonstrate hematuria in patients with coagulation defects.

OTHER LABORATORY TESTS

- Coagulation profile may reveal clotting abnormality.
- Buccal mucosal bleeding time may be prolonged and tests primary hemostasis.
- Fecal centrifugation flotation may reveal parasites.
- Diarrhea PCR panels for bacterial DNA and toxin genes in combination with ELISA testing for *C. perfringens* enterotoxin and *C. difficile* toxins A and B should be done judiciously in patients when indicated based on history, physical examination findings, environment, and risk factors.

- Rectal scraping may demonstrate fungal organisms (*Histoplasma* spp.).
- Resting cortisol and/or ACTH stimulation test abnormally low with hypoadrenocorticism.
- Gastric and intestinal histopathology, PCR, and urease testing for *Helicobacter* spp.

IMAGING

- Abdominal radiography may reveal a mass or foreign body, or abnormalities in renal or hepatic size/shape.
- Abdominal radiographs can be unremarkable with hepatic, and gastrointestinal dysfunction. Thoracic radiographs may identify pulmonary, tracheobronchial lesions.
- Nasal CT may demonstrate intranasal lesions.
- Ultrasonography may reveal a GI mass, loss of intestinal layering, alterations in hepatic echotexture and size, pancreatic changes suggestive of pancreatitis, or changes supportive of renal disease.
- Upper GI barium series may delineate gastric or upper small intestinal masses, ulceration, or filling defects; however, upper GI series is insensitive for detection of gastric and intestinal ulceration.

DIAGNOSTIC PROCEDURES

- Endoscopy allows visualization of masses and/or ulcers (esophageal, gastric, and/or duodenal), retrieval of GI foreign bodies, and procurement of biopsy samples.
- Rhinoscopy may allow visualization of nasal lesions (retroflexion of scope and choanal evaluation is helpful).
- Bronchoscopy allows visualization of airway lesions.
- Bone marrow aspiration and cytology indicated if pancytopenia is present.



TREATMENT

- Inpatient—most patients admitted for workup and management with exception of animals with melena secondary to intestinal parasites.
- Treat underlying disease—renal failure, hepatic disease, hypoadrenocorticism, respiratory disease, etc.
- Fluid replacement with balanced electrolyte solutions and potassium supplementation.
- Whole blood or packed red cell transfusions if anemia is severe.
- Whole blood or plasma transfusion if the patient has a coagulopathy.
- Temporarily discontinue oral intake if vomiting is intractable. Antiemetics may be needed in select cases with intractable vomiting.
- Surgery may be required for severe gastroduodenal ulceration, neoplasia, or foreign bodies.

MELENA

(CONTINUED)

**MEDICATIONS****DRUG(S) OF CHOICE**

- Mucosal protectants for gastroduodenal ulceration/erosion—H₂-receptor antagonists (e.g., ranitidine 1–2 mg/kg IV, SC, or PO q12h or famotidine 0.5–1 mg/kg IV, SC, or PO q12h); sucralfate 0.5–1 g PO q6–8h; misoprostol 3–5 µg/kg PO q8h.
- Triple therapy if *Helicobacter* suspected or confirmed (see *Helicobacter* spp.).

CONTRAINDICATIONS

Avoid corticosteroids and NSAIDs in patients with gastroduodenal ulceration/erosion.

ALTERNATIVE DRUG(S)

Proton pump inhibitors (omeprazole 0.7–1.5 mg/kg PO q12–24h) are superior to

H₂-receptor antagonists in animals with severe esophagitis or gastroduodenal ulceration.

**FOLLOW-UP****PATIENT MONITORING**

- PCV daily until anemia stabilized, then weekly.
- Hydration daily if patient vomiting.

POSSIBLE COMPLICATIONS

- Gastric or duodenal perforation resulting in peritonitis.
- Hypovolemic shock and death if severe, acute blood loss.

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

Helicobacter spp. and *Salmonella* spp. are potentially zoonotic.

SEE ALSO

Individual causative diseases

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- CT = computed tomography
- GI = gastrointestinal
- IBD = inflammatory bowel disease
- NSAID = nonsteroidal anti-inflammatory drug
- PCV = packed cell volume

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MENINGIOMA—CATS AND DOGS**BASICS****DEFINITION**

- Tumors of the meninges, most commonly found over the cerebrum.
- Most common tumor of the canine brain and spinal cord.
- Most common tumor of the feline brain, and second most common tumor of the feline spinal cord after lymphoma.

PATHOPHYSIOLOGY

- Primary tumor arising from the arachnoid cap cells.
- Intradural-extramedullary tumors.
- Usually solitary masses; occasionally multiple (cats > dogs).
- May occur as plaque-like masses on the floor of the calvaria, paranasally, or (rarely) in a retrobulbar location in dogs more than cats.
- Neurologic deficits secondary to the slow compression of the adjacent tissue, most commonly causing vasogenic edema, and occasionally obstructive hydrocephalus or infarction.
- Most are cytologically benign. In dogs, tend to be more invasive into brain parenchyma or surrounding vasculature, and can be considered *biologically* malignant, unless aggressive surgical resection is possible.

SYSTEMS AFFECTED

Nervous—primary effects (e.g., infiltration and compression of adjacent structures), and secondary effects (e.g., edema, increased ICP, brain herniation).

INCIDENCE/PREVALENCE

- Reported incidence of brain tumors is 14.5/100,000 dogs and 3.5/100,000 cats. Meningiomas account for approximately 22% of all canine brain tumors, and 59% of all feline brain tumors.
- 17% of cats with intracranial meningioma have > 1 tumor of the same type.
- Incidence of spinal tumors in dogs and cats—unknown; considerably less than that of brain tumors. Spinal meningiomas account for 14% of all canine meningiomas, and 4% of all feline meningiomas.

SIGNALMENT

Dog and cat

Dogs

- Boxers and golden retrievers most commonly affected; dolichocephalic breeds may have an increased risk of intracranial meningioma; mesocephalic breeds may have a higher incidence of paranasal meningioma.
- Most > 7 years of age; median 9 years, range 11 weeks–14 years; a spinal meningelial sarcoma was diagnosed in an 11-week-old rottweiler; slight predominance for females.
- Cystic meningiomas reported.

Cats

- No breed predilection.
- Most > 9 years of age; mean 12 years, range 1–24 years; slight predominance for males.

SIGNS**General Comments**

- Vary with tumor location.
- Typically chronic and insidiously progressive over weeks to months.
- May be acute if vascular invasion results in focal ischemia or if edema develops rapidly.
- Lateralizing deficits predominate.
- Elevated ICP, cerebral edema, or brain herniation may make localization of a focal lesion difficult.

Historical Findings

May be prolonged history of vague signs until compensatory mechanisms (e.g., decreased CSF and blood volume) are exhausted, followed by rapid progression of clinical signs.

Intracranial

- Dogs—late-onset seizures most common presenting sign.
- Cats—abnormal behavior and mentation most common presenting signs; nonspecific signs include lethargy, inappetence, and anorexia; seizures less common than in dogs.

Intraspinal

- Neck or back pain.
- Progressive incoordination and weakness—may worsen with exercise.

Physical Examination Findings**Intracranial**

- Cerebral disease is most common—abnormal behavior and mentation; circling or head-pressing; contralateral hemi-neglect, hemianopsia, facial paresis, facial and thoracic hypesthesia and conscious proprioceptive deficits; seizures.
- Brainstem—alterations of consciousness; abnormal gait; ipsilateral proprioceptive and cranial nerve deficits in CN III to XII; central vestibular abnormalities.
- Cerebellum—ataxia and dysmetria; intention tremors; truncal sway; broad-based stance; lack of menace responses with normal vision, and pupillary light and palpebral reflexes.
- Orbital—exophthalmos, orbital swelling, prolapsed globe; blindness in the affected eye; fundic abnormalities.

Intraspinal

- Paraspinal or radicular pain reflecting region of spinal column involved.
- Ataxia and paresis caudal to the lesion.

CAUSES

- Uncertain.
- Documentation in young cats with mucopolysaccharidosis type I suggests a causal relationship.

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- Metabolic or toxic encephalopathy—may also present with seizures or mentation changes and normal neurologic exam; differentiate with brain imaging.
- Other primary CNS (e.g., glioma, pituitary, nephroblastoma) or secondary (e.g., lymphoma, extensional, metastatic) tumors—may have more rapid onset and progression of signs; differentiate with brain or spinal imaging.
- Granulomatous meningoencephalitis—may cause progressive focal deficits in dogs; differentiate based on age; imaging and CSF analysis may be helpful.
- Nerve sheath tumors, gliomas, lymphoma, focal meningoencephalitis, type II intervertebral disc disease, degenerative myelopathy—differentiate by spinal cord imaging.
- *Cryptococcus* granuloma—reported to have same appearance on CT as a meningioma in a cat.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

N/A

M

IMAGING

- MRI—preferred imaging modality for intracranial and spinal disease.
- MRI—often hyperintense on T2WI, isointense on T1WI, and uniformly contrast-enhancing mass lesion of the brain or spinal cord; broad-based, with extra-axial attachment; a “dural tail” is a characteristic feature. If present, “dural tail” helps to differentiate an intraventricular meningioma from a choroid plexus tumor; spinal cord swelling may make the distinction between intradural-extramedullary and intramedullary difficult.
- CT—often homogeneous contrast enhancement of well-circumscribed mass lesion.
- Skull radiography and CT—may reveal hyperostosis of the calvaria adjacent to the meningioma and increased tissue density if the tumor is calcified; hyperostosis more commonly seen in cats.
- Spinal radiography—usually normal with intraspinal meningioma; can be helpful to rule out bony lesions.
- Myelography—typically reveals an intradural-extramedullary mass and interruption of the normal flow of contrast at the tumor; “golf tee” appearance makes differentiation from a nerve sheath tumor difficult without biopsy.

MENINGIOMA—CATS AND DOGS

(CONTINUED)

DIAGNOSTIC PROCEDURES

- CSF analysis—infrequently performed because of the characteristic results of diagnostic imaging; normal or high protein, sometimes with a neutrophilic or mixed pleocytosis. Should not be considered unless CT or MRI have been performed; if increased ICP is suspected, CSF collection is contraindicated; may increase risk of neurologic decompensation from brain herniation.
- Electroencephalography—reveals slow-wave, medium- to high-voltage activity indicating cortical depression; may show paroxysmal waveforms characteristic of seizure activity.
- Biopsy—remains necessary for definitive diagnosis; during surgery or using a CT-guided stereotactic system for intracranial tumors.



TREATMENT

APPROPRIATE HEALTH CARE

- M**
- Inpatient—necessary if dehydration, anorexia, disequilibrium, and/or frequent or life-threatening seizures.
 - Surgical excision—for definitive management; usually successful if the tumor is accessible; incomplete excision more common in intracranial meningiomas in dogs due to invasiveness, in intraspinal meningiomas in cats, and in tumors ventral to the spinal cord.
 - Fractionated conventional radiation therapy consisting of 15–20 treatments over 3–4 weeks—after incomplete excision, if excision not possible, or if a less invasive approach is desired; when combined with surgery, radiation is associated with prolonged survival time in canine intracranial and intraspinal meningiomas compared to surgery alone, and may contribute to prevention or delay of local recurrence. Feline intracranial meningiomas are believed to be radiation sensitive, but data are lacking due to the success of surgery.
 - SRS—delivers high dose of radiation to tumor with sub-millimeter accuracy; steep dose gradient limits exposure of normal tissue and reduces side effects of radiation; can be conducted on an outpatient basis in 1–5 treatments delivered on consecutive days; best candidates are those that are able to be stabilized with steroids prior to the procedure; shown to significantly decrease tumor volume, but occurs slowly. IMRT delivered in 3–5 fractions (hypofractionated IMRT) is sometimes mistakenly referred to as SRS; it is not as exact as SRS.
 - Chemotherapy—may be associated with prolonged survival after incomplete excision, post-radiation, or as sole agent. Hydroxyurea inhibits DNA synthesis, leading to cell death during the S phase of the cell cycle; shows

effectiveness in humans with intracranial meningiomas; commonly used in veterinary medicine, but controlled studies are lacking.

- Medical management—antiepileptic drugs and corticosteroids are only palliative; neither radiation nor chemotherapy aid in control of seizures or edema.

NURSING CARE

- Fluids—avoid overzealous administration; may exacerbate cerebral edema and neurologic deficits.
- Use caution with jugular compression during venipuncture or when positioning for surgery to avoid increases in ICP.



MEDICATIONS

DRUG(S)

Cerebral Edema

- Corticosteroids—improve neurologic deficits associated with vasogenic edema.
- Stuporous, severely ataxic, or showing signs of herniation—methylprednisolone sodium succinate (30 mg/kg IV) or dexamethasone sodium phosphate (0.25 mg/kg IV).
- Continued deterioration or no improvement—20% mannitol solution (0.5 g/kg IV over 15–20 minutes). Furosemide (2 mg/kg IV), has synergistic effects with mannitol and can be added if needed; hypertonic saline (3–5 mL/kg) may be used as an alternative to mannitol; dexamethasone (0.05–0.1 mg/kg q24h IV).
- Once patient is stable—dexamethasone (0.05–0.1 mg/kg q24h or in divided daily doses PO) or prednisone (0.25–0.5 mg/kg PO q12h); then taper to lowest effective dose.

Seizures

- Antiepileptic drugs—mandatory if isolated seizures > 1/month, cluster seizures, or status; recommended if any seizure activity in animal with meningioma, and possibly as preventive measure in animals with forebrain meningioma.
- Maintenance treatment—phenobarbital (first choice in dogs and cats) 2–3 mg/kg IV or PO q12h; or zonisamide 5–10 mg/kg q12h PO (dogs or cats); or levetiracetam 20–30 mg/kg q8h IV or PO; if extended release levetiracetam q12h PO (dogs or cats).
- Cluster seizures or status—diazepam 0.5 mg/kg/h CRI; or phenobarbital 4 mg/kg IV q2–6h until 12–16 mg/kg total loading dose; or midazolam 0.2–0.4 mg/kg/h CRI; or levetiracetam 60 mg/kg IV.

Chemotherapy

Hydroxyurea—150 mg/kg/week (dogs) and 75 mg/kg/week (cats).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Mannitol—monitor serum osmolality and electrolytes with repeated use; maintain osmolality at or below 320 mOsm/L to reduce risk of renal failure due to renal vasoconstriction.
- Corticosteroids—perform serial neurologic examinations; marked neurologic improvement possible within 24–48 h after initiation of corticosteroids.
- Antiepileptic drugs—evaluate serum phenobarbital levels 3 weeks after initiation of therapy; evaluate liver enzymes every 6 months while on phenobarbital.
- Hydroxyurea—monitor CBC with platelet count before starting, at 2 weeks, 6 weeks then CBC, chemistry profile every 3–4 months. May lead to GI effects, stomatitis, sloughing of nails, alopecia, and dysuria; most serious effects are bone marrow depression and pulmonary fibrosis.

EXPECTED COURSE AND PROGNOSIS

Cats

Intracranial

- Surgical excision—prognosis good; 75–80% of patients that undergo surgical excision are cured; reported mean survival time 22–27 months; seizure activity may persist despite successful excision. Recurrence usually occurs in same location.

- Medical management—neurologic deficits become more severe; may occur slowly over many months because meningiomas tend to be slow growing.

Intraspinal

- Surgical excision—survival time is shorter than that of cats with cerebral meningiomas; reported median survival times of 14.2 months in 16 cats, and 17.3 months in 26 cats.

- Corticosteroids—thoracolumbar disease progresses to paralysis and inability to control urination with urinary retention and possibly bladder atony and cystitis.

Dogs

Intracranial

- Surgical excision—outcome depends on surgical technique; reported median survival time is 7 months; increased with regional cerebral resection (16.5 months in 6 dogs), or with the use of a surgical aspirator (41.8 months in 17 dogs) or with endoscopy-assisted tumor removal (70.1 months with forebrain and 23.4 months with caudal brain meningioma in 33 dogs).

- Surgical excision with postoperative fractionated radiation therapy—reported median survival times of 16.5–30 months.

(CONTINUED)

MENINGIOMA—CATS AND DOGS

- Radiation therapy alone—reported median survival times of 5–12.5 months with conventional radiation.
- Chemotherapy using hydroxyurea—reported mean survival time of 7–8 months.
- SRS e.g., Frameless SRS, Varien Trilogy, Cyberknife—reported mean survival time of 16.4 months in 38 dogs, and 19.8 months in 20 dogs.
- Medical management—reported mean survival time of 3 months in dogs treated with palliative therapy alone.

Intraspinal

- Surgical excision—reported mean survival time of 19 months in 8 dogs.
- Surgical excision with postoperative radiation therapy—reported median survival time of 13.5 months in 6 dogs.

**MISCELLANEOUS****AGE-RELATED FACTORS**

Suspect brain tumor in dogs and cats > 5 years with recent onset of seizures and unremarkable extracranial diagnostic workup for seizures.

ABBREVIATIONS

- CN = cranial nerve
- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- GI = gastrointestinal
- ICP = intracranial pressure
- IMRT = intensity modulated radiation therapy
- MRI = magnetic resonance imaging
- SRS = stereotactic radiosurgery
- T1WI = T1-weighted images
- T2WI = T2-weighted images

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MENINGITIS/MENINGOENCEPHALITIS/MENINGOMYELITIS, BACTERIAL



BASICS

DEFINITION

- Meningitis—inflammation of the meninges.
- Meningoencephalitis—inflammation of the meninges and brain.
- Meningomyelitis—inflammation of the meninges and spinal cord.

PATHOPHYSIOLOGY

- Bacterial infection of the CNS can occur by direct extension from an infected extraneuronal site or less commonly when bacteria are introduced by penetrating trauma or a migrating foreign body.
- Hematogenous spread of bacteria to the CNS from mucous membrane colonization or a distant pyogenic focus can also occur. This is the most common cause in septicemic neonates and severely immunocompromised patients.
- Inflammation of the meninges commonly leads to secondary inflammation of the brain or spinal cord parenchyma, resulting in neurologic deficits.
- Inflammatory debris and scarring can obstruct CSF flow, leading to secondary hydrocephalus.

SYSTEMS AFFECTED

- Nervous—meninges, brain, or spinal cord.
- Multisystemic signs—may be present when the infection originates in an extraneuronal site or when the systemic inflammatory response is severe.

INCIDENCE/PREVALENCE

Rare

SIGNALMENT

Species

Dog and cat

Mean Age and Range

Any age

Predominant Sex

Males and females affected equally

SIGNS

General Comments

- Patients are often systemically ill.
- Depression, shock, hypotension, and DIC are often found in septicemic patients.
- CNS signs may be profound and rapidly progressive.

Physical Examination Findings

- Pyrexia in approximately 50%.
- Cervical rigidity and hyperesthesia—especially with meningitis.
- Neurologic deficits—reflect the location of the involved spinal cord or brain parenchyma (e.g., altered mentation, cranial nerve deficits, postural reaction deficits, ataxia, paresis, seizures).
- May find an extraneuronal site of underlying bacterial infection.
- Vomiting.
- Bradycardia with systemic hypertension suggests increased intracranial pressure.

CAUSES

- Meningoencephalitis—can be secondary to local extension from otitis media/interna or infection of the eye, retrobulbar space, sinuses, or nasal passages or due to direct inoculation by traumatic skull fractures or migrating grass awn or porcupine quill foreign bodies.
- Meningomyelitis—can be secondary to discospondylitis or vertebral osteomyelitis.
- Hematogenous spread of bacterial infection to the CNS can occur in neonates with omphalophlebitis, immunocompromised patients, or in dogs with bacterial endocarditis, prostatitis, discospondylitis, pneumonia, or severe gastroenteritis.
- The point of origin is not always found.

RISK FACTORS

- Untreated bacterial infection
- Immunocompromised state
- Injury involving the CNS or adjacent structures



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Infectious Meningitis (Non-bacterial)

- Canine distemper, toxoplasmosis, neosporosis, cryptococcosis, blastomycosis, neuroborreliosis, rickettsial organisms, West Nile virus, and feline infectious peritonitis all cause meningitis/meningoencephalitis that can be difficult to distinguish from bacterial disease.
- CSF—inflammatory with a variable lymphocytic, mixed mononuclear or neutrophilic pleocytosis depending on the specific infectious etiology.
- Antemortem diagnosis suspected based on typical clinical findings and identification of affected extraneuronal sites.
- Diagnosis is by identifying organisms in the CSF or in extraneuronal sites (using cytology, culture, or PCR) and by serology.

Steroid Responsive Meningitis-Arteritis (Aseptic Meningitis)

- Observed mainly in young (6–19 months) adult large-breed dogs but middle-aged and older dogs occasionally affected.
- Beagles, boxers, Bernese mountain dogs, German shorthaired pointers, Weimaraners, and Nova Scotia duck tolling retrievers are predisposed; any breed can be affected.
- Cervical pain without neurologic deficits is most common.
- Fever occurs in 60–80% of affected dogs.
- Signs may wax and wane initially.
- Affected dogs are systemically normal.
- Neurologic deficits may occur in chronically affected or inadequately treated dogs.
- CSF—increased nucleated cell count and protein.
- Neutrophilic pleocytosis in acute cases, mononuclear cells may predominate in chronic cases.
- Negative bacterial culture.
- Serum and CSF IgA increased.
- Dramatic response to corticosteroid administration.

Granulomatous

Meningoencephalomyelitis

- Idiopathic non-infectious inflammatory disease of the brain, spinal cord, and meninges in dogs.
- Meningoencephalitis of unknown origin (MUE) may be a more correct name for all of the non-infectious inflammatory disorders, because definitive diagnosis is not possible without post-mortem examination.
- Young adult and middle-aged dogs most often affected—poodles and terriers predisposed; any breed can be affected.
- Neurologic abnormalities reflect the location of the lesion(s).
- Cervical pain/fever in some dogs with disseminated form that involves the cervical spinal cord and meninges.
- CSF—mixed mononuclear pleocytosis with lymphocytes, monocytes, plasma cells, and large macrophages; may include 20% non-toxic neutrophils.
- CSF culture—negative.

Necrotizing Meningoencephalitis/Necrotizing Leukoencephalitis

- Breed-related idiopathic inflammatory disorders of the brain characterized by regional necrosis forming areas of cavitation.
- Signs reflect cerebral cortical damage (seizures, behavior change, circling) in pugs, Maltese terriers, Chihuahuas, Pekingese, Shih Tzus, and Lhaso apsos with NME.
- Yorkshire terriers with NLE have lesions in the cerebrum and in the brainstem resulting in seizures and abnormal mentation as well as abnormal gait, head tilt and cranial nerve abnormalities.
- No systemic signs.
- CSF—increased protein content and total nucleated cell count (NME and NLE).
- Small lymphocytes predominate in NME, while a mixed mononuclear pleocytosis is common in NLE.

Primary CNS Neoplasia

- History protracted; neurologic signs limited to the CNS; standard laboratory tests normal.
- Diagnosis by CT, MRI, CSF analysis, and biopsy.

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis is common; left-shift or toxicity may be seen. Thrombocytopenia may be present in septicemic patients.
- Biochemical evidence of other organ involvement (e.g., liver and kidney) may be seen in septicemic patients.
- Hyperglobulinemia may reflect chronic extraneuronal infection.
- Pyuria and bacteriuria occur in patients with underlying urinary tract or prostatic infection and in some bacteremic animals.

OTHER LABORATORY TESTS

- Serologic tests—may differentiate fungal, protozoal, rickettsial, and viral from bacterial disease; in cats, toxoplasma titer may be positive without clinical disease.
- Cytology of infected tissues—skin, eyes, nasal discharge, lymph node, tracheal wash; helps

MENINGITIS/MENINGOENCEPHALITIS/MENINGOMYELITIS, BACTERIAL

identify non-bacterial causative organisms, especially in patients with fungal disease.

- Blood culture—positive in 30% of dogs with bacterial meningitis.

IMAGING

- Thorax/abdominal radiography and abdominal ultrasound—to identify underlying infection or other significant disease.
- Spinal radiography—discospondylitis may be identified as a focus of infection.
- Head CT—may identify infected sinus, nasal cavity, or middle and inner ear as initiating site. Inflamed regions of brain parenchyma and meninges usually enhance with contrast.
- Echocardiography—performed when valvular endocarditis suspected based on murmur/arrhythmia.
- MRI with contrast—documents brain, spinal cord and meningeal inflammation and can identify extraneurial sites of infection (sinus, nasal, ear).

DIAGNOSTIC PROCEDURES

CSF Analysis

- Collection—a concern in animals with diminished mentation suggesting high intracranial pressure, because the procedure may precipitate brain herniation—pretreat with mannitol.
- Analysis—neutrophilic pleocytosis with high protein concentration; neutrophils may appear toxic or degenerated and intracellular bacteria are occasionally seen; often difficult to differentiate aseptic from bacterial meningitis cytologically.
- Culture—aerobic or anaerobic; may be positive (< 40%)—inoculation of CSF into broth enrichment media improves diagnostic yield.
- Universal bacterial PCR assay of CSF can be used to identify DNA from causative organisms when bacterial culture is negative.

PATHOLOGIC FINDINGS

- May note subdural empyema, or purulent material on the surface of the brain or spinal cord.
- Asymmetric diffuse or multifocal brain or spinal cord and meningeal suppurative inflammation common.
- Culture of affected neurologic tissue—positive in > 75% of patients.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient—treat aggressively; intensive care monitoring often necessary.

NURSING CARE

Fluid therapy and supportive care

ACTIVITY

Restricted

CLIENT EDUCATION

Inform client that rapid and aggressive treatment is important and that the prognosis for recovery is guarded.



MEDICATIONS

DRUG(S) OF CHOICE

Antibiotics

- Bactericidal agents that achieve therapeutic concentrations within CSF are most desirable—lipid-soluble drugs with small molecular size, low protein binding, and a low degree of ionization at physiologic pH recommended.
 - Cultures—CSF, blood, urine, primary site; determine drug sensitivity; until cultures identify the organism choose a broad-spectrum agent that penetrates the blood-brain barrier.
 - Recommended drugs include third-generation cephalosporins (moxalactam, ceftriaxone, cefotaxime), fluoroquinolones, trimethoprim-sulfonamides, doxycycline and metronidazole.
 - Penicillin, ampicillin, amoxicillin-clavulanate and carbapenems enter the CNS when there is inflammation and are a good choice to use in combination with another antibiotic that will continue to cross the BBB as inflammation resolves such as trimethoprim-sulfonamides. Ampicillin may achieve high CSF concentrations even without inflammation.
 - Metronidazole reaches high levels in CSF, brain parenchyma, and brain abscesses and demonstrates the best bactericidal activity against anaerobes.
 - Clindamycin is lipid soluble but does not readily cross the blood-brain barrier.
- Concentrations in brain and spinal cord are adequate for treatment of *Toxoplasma* and *Neospora* infections but insufficient for treating most CNS bacterial infections.
- Administer antibiotics intravenously for 3–5 days to achieve high CSF concentrations rapidly, then maintain on oral therapy.
 - Immediate IV therapy can be based on cytology; penicillin for Gram-positive infections, fluoroquinolone (enrofloxacin or ciprofloxacin) or third-generation cephalosporin for Gram-negative infections.

Antiepileptic Drugs

- Indicated for seizures • Diazepam initially and then phenobarbital

Corticosteroids

- Most CNS damage is due to inflammation.
- May administer dexamethasone (0.2 mg/kg) prior to antibiotic therapy and then every 12 hours for 2 days.

CONTRAINdicATIONS

- Aminoglycosides and first-generation cephalosporins—do not penetrate the blood-brain barrier even in the presence of inflamed meninges.
- Chloramphenicol reaches high CSF concentrations but is associated with a high relapse rate; do not use.



FOLLOW-UP

PATIENT MONITORING

Monitor for nervous system signs, fever, leukocytosis, and systemic signs.

PREVENTION/AVOIDANCE

Treat local infections adjacent to the CNS (e.g., infections of the eyes, ears, sinuses, nose, and spine) early and aggressively to prevent extension to the CNS.

POSSIBLE COMPLICATIONS

Damage to the brain and spinal cord may be irreversible.

EXPECTED COURSE AND PROGNOSIS

- Response to antibiotics—variable; prognosis guarded.
- Many patients die despite treatment.
- Some patients will have residual neurologic deficits.
- Treatment for at least 4 weeks after resolution of all signs is recommended.



MISCELLANEOUS

SEE ALSO

- Encephalitis • Meningoencephalitis of Unknown Origin
- Meningoencephalomyelitis, Granulomatous
- Steroid-Responsive Meningitis-Arteritis—Dogs

M

ABBREVIATIONS

- BBB = blood-brain barrier • CNS = central nervous system • CSF = cerebrospinal fluid
- CT = computed tomography • DIC = disseminated intravascular coagulation
- MRI = magnetic resonance imaging
- NLE = necrotizing leukoencephalitis
- NME = necrotizing meningoencephalitis
- PCR = polymerase chain reaction

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MENINGOENCEPHALOMYELITIS, EOSINOPHILIC



BASICS

OVERVIEW

Although eosinophilic meningoencephalomyelitis (EME) can be associated with meningitis, encephalitis, and myelitis as a result of CNS infection or parasitic migration, in most cases, no underlying cause can be found. Idiopathic EME occurs in young to middle-aged large-breed dogs and resolves in many cases following steroid treatment.

SIGNALMENT

- Dog and rarely cat. • Idiopathic EME—often larger dogs (> 25 kg); Rottweilers and golden retrievers predisposed. • Mean age—4 years (2 months–13 years).

SIGNS

- Vary with CNS location and severity.
- Neurologic deficits—most frequently associated with cranium, infrequently with spinal cord and rarely with cranial nerve involvement.

CAUSES & RISK FACTORS

- Idiopathic EME (unknown cause)—majority of reported cases. • Infectious—*Dirofilaria immitis* and cuterebral myiasis in cats; *Toxoplasma gondii*, *Neospora* spp., *Prototheca* spp., *Cryptococcus* spp., and nematode migration with *Baylisascaris procyonis* in dogs. • *Angiostrongylus*—dogs in Australia. • Intervertebral disc disease probably as allergic response to disc material.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cannot be differentiated from other encephalitides solely on clinical signs; CSF analysis must be done. • Idiopathic EME—negative serologic test results; marked CSF eosinophilic pleocytosis (20–95%); usually steroid-responsive. • Infectious diseases—identified on presence of systemic signs, blood work, fecal sample, CSF, serum/CSF serology, and imaging.

CBC/BIOCHEMISTRY/URINALYSIS

- Peripheral eosinophilia—may or may not be present. • Biochemistry and urinalysis—usually normal with idiopathic disease; eosinophilia, liver enzyme activity, and creatine kinase may be elevated in infectious diseases.

OTHER LABORATORY TESTS

- Serology—to rule out suspected infectious diseases. • Fecal flotation and sedimentation—to rule out migratory parasite.

IMAGING

- Thoracic radiography and abdominal ultrasound—to rule out systemic involvement. • MRI—variable; focal mass lesions, diffuse parenchymal abnormalities, post-contrast diffuse meningeal enhancement; abnormalities depend on cause and location of lesion.

DIAGNOSTIC PROCEDURES

CSF Analysis

- Eosinophilic pleocytosis significant when > 10%. • Presence of eosinophilic pleocytosis by itself cannot differentiate idiopathic EME from infection causing CSF eosinophilic pleocytosis. • Idiopathic EME—total nucleated cell count 4–3,880 cells/ μ L (median 99 cells/mL; reference < 0.003) with 22–95% eosinophils. • Infections—62–4,740 cells/mL (median 875 cells/mL) with 30–95% eosinophils.

CSF Serologic Testing

- If CSF eosinophils > 10%, look for parasitic and fungal disease. • Test for heartworm, *N. caninum*, *T. gondii*, and *C. neofmans*.

PATHOLOGIC FINDINGS

- CSF eosinophilic pleocytosis does not necessarily correlate with eosinophils observed in CNS parenchyma. • Wide variety of pathologic findings may indicate multiple causes, or the same disease taken at different times.



TREATMENT

- Usually inpatient, because of severity of clinical signs. • Activity—as tolerated.
- Regular diet.



MEDICATIONS

DRUG(S)

- Idiopathic disease—steroid administration; dexamethasone (0.2 mg/kg q24h for 1 day; then 0.15 mg/kg q24h for 6 days); follow with prednisone (0.5 mg/kg q24h for 8 weeks); then slowly wean patient off prednisone over 8 weeks–6 months depending on clinical response. • Protozoal disease—clindamycin, sulfonamides, and pyrimethamine. • Heartworm—microfilarial migration to the CNS is rare; no available treatment other than supportive.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Important to differentiate idiopathic EME from infection as treatment greatly differs—immunosuppressive dose of steroids versus anti-organism treatment. • Steroid should be used with caution if diagnosis has not been substantiated.



FOLLOW-UP

PATIENT MONITORING

Inpatient—repeat neurologic examination every 6 hours to monitor progress.

PREVENTION/AVOIDANCE

Steroid treatment should not be stopped even if the animal is back to normal within a few days. A minimum of 8 weeks followed by tapering of the medication over as many weeks is mandatory.

POSSIBLE COMPLICATIONS

- Recurrence may occur following cessation of medication. • Ensure treatment dosage is adequate and reinstate for a longer period.

EXPECTED COURSE AND PROGNOSIS

- Idiopathic disease—good prognosis in most cases with early treatment; improvement usually seen in the first 72 hours; full recovery in 2–6 months. Some patients continue to deteriorate despite steroids, and die.
- Protozoal and fungal diseases—poor-to-grave prognosis. • Larval migration—prognosis guarded to poor and depends on location of the lesion; signs may resolve, but larvae often continue to migrate and death may ensue. • Degradation of eosinophils is toxic to nervous tissue; patient may have permanent deficits from not only the primary disease but also cell death.



MISCELLANEOUS

AGE-RELATED FACTORS

Idiopathic EME is more frequent in young to middle-aged larger dog breeds (> 25 kg).

SEE ALSO

Encephalitis

ABBREVIATIONS

- CNS = central nervous system • CSF = cerebrospinal fluid • EME = eosinophilic meningoencephalomyelitis • MRI = magnetic resonance imaging

Suggested Reading

- Williams JH, Köster LS, Naidoo V, et al. Review of idiopathic eosinophilic meningitis in dogs and cats, with a detailed description of two recent cases in dogs. *J S Afr Vet Assoc* 2008, 79(4):194–204.
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MENINGOENCEPHALOMYELITIS OF UNKNOWN ORIGIN (MUO)



BASICS

DEFINITION

Meningoencephalomyelitis of unknown origin (MUO) refers to a broad term to describe inflammatory disorders that affects the CNS focally, diffusely, or multifocally. In the past, the majority of CNS inflammatory disorders were categorized as GME. As a result, multiple less serious viral and idiopathic disorders were frequently erroneously diagnosed as GME. The appropriate clinical term to describe cases in which CNS inflammation is suspected is now considered MUO or MUE.

PATOPHYSIOLOGY

- Unknown. Although a specific etiologic agent is not recognized, in the majority of cases, viral and immune causes are strongly suspected.
- Three clinicopathologic forms recognized—ocular, multifocal (brain or brain and spinal cord), and focal (single focus in the brain or spinal cord).

SYSTEMS AFFECTED

- Nervous
- Ophthalmic

GENETICS

Not proven

INCIDENCE/PREVALENCE

Unknown. Since brain biopsies are rarely obtained, a presumptive diagnosis is made in most cases. The condition is diagnosed and treated successfully with increasing frequency.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Breed Predilections

Any breed can develop MUO. Smaller toy breeds may be overrepresented and can be less responsive to therapy. However, the condition also occurs in medium and large-breed dogs.

Mean Age and Range

- Mean—5 years
- Range—6 months–10 years

Predominant Sex

Slightly higher prevalence in females

SIGNS

- Depend on the form of the disease and neuroanatomic localization.
- Cerebral form—frequently results in seizure activity.
- Ocular form—acute onset of blindness with dilated, unresponsive pupils.
- Focal form—*cerebral lesion*: disorientation, behavioral changes, seizures, cortical blindness, compulsive circling, head pressing; *brainstem lesion*: somnolence, cranial nerve deficits (most commonly facial and vestibular dysfunction), ipsilateral hemiparesis; *spinal cord*: neck pain, tetraparesis (C1–C5 or C6–T2 lesions) or paraparesis (T3–L3 or L4–S2 lesions) and proprioceptive ataxia.

CAUSES

Unknown

RISK FACTORS

- Unknown.
- Some dogs develop clinical signs within 5–15 days of vaccination.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- The combination of history, neurologic examination, CSF analysis, and MRI results usually lead to a presumptive diagnosis of inflammatory disease, but defining the cause of the inflammation can be problematic.
- Definitive diagnosis only by histopathologic studies. Some dogs with CNS inflammatory disease are successfully treated but data on these cases are lacking. Brain biopsies rarely performed to confirm the diagnosis. It is possible that some dogs surviving inflammatory CNS disease have lesions compatible with GME, but post-mortem studies not available to prove it. Alternatively, dogs who survive CNS inflammatory disease could have been suffering from other type of less serious viral or idiopathic inflammatory disease. Therefore the current accepted medical term to group these categories is MUO.
- Infectious inflammatory diseases—viral (distemper virus, other viruses); fungal (*Blastomycetes dermatitidis*, *Coccidioides* spp., *Cryptococcus neoformans*); rickettsial (*Rickettsia rickettsii*); bacterial (*Ehrlichia* spp., *E. coli*, *Streptococcus*); protozoal (*Neospora caninum*, *Toxoplasma gondii*).
- Other inflammatory disease—necrotizing encephalitis of the Yorkshire terrier, Maltese, and pug; immune-mediated steroid-responsive meningitis (beagles, Bernese mountain dogs, Nova Scotia duck tolling retrievers, Weimaraners, boxers).
- Sudden acquired retinal degeneration.
- Brain tumor—meningioma, glioma, choroids plexus papilloma, lymphoma.
- Subatlantoaxial luxation.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal.
- CBC—stress leukogram (elevated white blood cell count and segmented neutrophilia with lymphopenia) may be present.

OTHER LABORATORY TESTS

Serologic testing to rule out infectious CNS diseases.

IMAGING

MRI—method of choice; abnormalities are variable and consist of solitary, multiple, or circumscribed mass lesions. Multiple areas of heterogeneous contrast enhancement are frequent in the multifocal form of the disease. Other findings include mass effect with midline shift, obstructive hydrocephalus, white matter edema, and effacement of the

sulci. Usually MRI lesions are characterized as hypointense in T1-weighted and hyperintense in T2-weighted images. Necrotic lesions are recognized by a center of hypointensity with a peripheral ring of enhancement.

DIAGNOSTIC PROCEDURES

CSF Analysis

- Reference range—white cell count (0–3 cells/ μ L); protein concentration (0–30 mg/dL).
- Helps confirm presence of inflammatory disease but rarely demonstrates a definitive cause. The following are only guidelines, as significant overlap exists regarding CSF cytology of different inflammatory disorders.
- Inflammatory diseases—white cell count and protein concentration usually increased. Even with a normal cell count, presence of an abnormal cell population (e.g., macrophages) should be taken into consideration as evidence of pathology.
- Usually, mononuclear pleocytosis; however, polymorphonuclear pleocytosis, or a normal CSF can be present.
- Bacterial (rare in dogs)—marked polymorphonuclear pleocytosis.
- Fungal, protozoal infections—mixed pleocytosis (mononuclear and polymorphonuclear); rarely a fungal organism (*Cryptococcus neoformans* or *Blastomycetes dermatitidis*) is identified.
- Viral infections—mononuclear pleocytosis.

Brain Biopsy

Brain biopsy is the only procedure that can confirm conclusively a diagnosis of MUO. Due to morbidity, mortality, and cost associated with brain biopsy the test is not performed routinely. It is important to note that GME is NOT a clinical diagnosis but a term to describe findings at post-mortem. The term should not be used as clinical diagnosis, to avoid confusion.

PATHOLOGIC FINDINGS

- Hallmark feature—dense perivascular distribution of mononuclear infiltrates (lymphocytes, monocytes, and plasma cells).
- Macroscopically, discoloration and softening of affected tissue sometimes evident.



TREATMENT

APPROPRIATE HEALTH CARE

- Stable patients can be discharged with recommended treatment.
- Inpatient—for severely affected dogs; monitor patient closely for progression of neurologic deficits.
- In severe cases, sequential assessment of pupil size and reaction to light, and mentation are helpful to determine risk of herniation.

NURSING CARE

- Intravenous fluids for the anorexic patient. Take care not to overhydrate to exacerbate cerebral edema.
- Provide a padded cage for

MENINGOENCEPHALOMYELITIS OF UNKNOWN ORIGIN (MUO) (CONTINUED)

dogs with vestibular ataxia, severe dementia, or seizure activity. • Recumbent patients should be turned frequently (every 4 hours).

ACTIVITY

- Depends on severity of disease and lesion localization.
- Ataxic patients should be confined to a padded cage to avoid injury.

DIET

Ensure adequate caloric intake.

CLIENT EDUCATION

- Explain to the client that there is significant overlap of clinical signs among different inflammatory diseases. Insist on the importance of a diagnostic workup.
- Mortality rate is variable but clearly biased by older literature describing the severe cases that went to post-mortem as suffering from GME. Brain biopsies are rarely conducted. Clinical experience suggests that up to 70% of patients can respond to therapy, especially if initiated early in the course of the disease. However, treatment may be prolonged or could be required for life.
- Corticosteroid therapy may be necessary indefinitely.



MEDICATIONS

DRUG(S) OF CHOICE

- Dexamethasone 0.25 mg/kg IV or PO q24h for 4 days followed by prednisone 0.5–1.0 mg/kg PO q24h for 2 weeks. Dose is adjusted according to response and side effects. The goal is to find dosage that keeps the clinical signs controlled with minimal side effects. If deterioration of clinical signs noted when tapering steroids, immediately go back to previous dose that controlled the signs or consider adding other immunosuppressant listed below.
- To prevent gastrointestinal ulceration, combine steroid therapy with omeprazole 0.5 mg/kg PO q24h, famotidine 0.5–1 mg/kg IV or PO q12h. • If there is seizure activity—phenobarbital 2 mg/kg PO q12h, levetiracetam 20 mg/kg PO (ideally q8h but may be attempted q12h), or zonisamide 5–10 mg/kg PO q12h.
- Gabapentin 2–5 mg/kg PO q8–12h if compulsive circling is present.

CONTRAINDICATIONS

- Fungal, bacterial, and protozoal conditions can be exacerbated by the use of steroids. It is important to rule out these infectious disorders with proper diagnostic workup.
- Steroid should not be used in a patient treated or recently treated with NSAIDs.

PRECAUTIONS

Reduction in corticosteroid therapy can result in recrudescence of clinical signs that may not be controlled again as initially.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

- Azathioprine 2 mg/kg PO q24h.
- Cytosine arabinoside 50–100 mg/m² body surface area q12h for 2–3 days SC or IV. Repeat treatment every 3 weeks to 8 weeks pending clinical response.
- Cyclosporine 3–7 mg/kg PO q12h.
- Leflunomide 4 mg/kg PO q24h.
- Radiation therapy—alternative treatment in focal form of disease when other therapies have failed. Confirm diagnosis with histopathology before starting radiation therapy.



FOLLOW-UP

PATIENT MONITORING

- Repeat neurologic examination periodically (every 2–4 weeks).
- Evaluate CBC and biochemical profile regularly to monitor for leukopenia, thrombocytopenia, and liver and kidney function if alternative drugs are used.
- Monitor urine in patients on long-term steroid treatment—proteinuria or infection are frequent consequences. Patients receiving zonisamide may be at risk for KCS and immune-mediated conditions—hemolytic anemia, immune thrombocytopenia, and polyarthritis.

POSSIBLE COMPLICATIONS

- Deterioration of clinical signs despite aggressive treatment.
- Status epilepticus, dementia, brain herniation, and death.

EXPECTED COURSE AND PROGNOSIS

- Not all patients with CNS inflammatory disease have a poor prognosis.
- GME has been stereotyped as fatal without enough evidence. Uncertain if surviving dogs had GME as brain biopsies are rarely done.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Corticosteroid therapy can affect gestation

SYNOMYS

- Granulomatous encephalitis
- Granulomatous meningoencephalitis
- Meningoencephalitis of unknown etiology
- Meningomyelitis • Encephalitis • Myelitis

SEE ALSO

- Encephalitis • Encephalitis Secondary to Parasitic Migration • Meningitis/Meningoencephalitis/Meningomyelitis, Bacterial • Meningoencephalomyelitis, Eosinophilic • Necrotizing Encephalitis • Steroid-Responsive Meningitis-Arteritis—Dogs

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- GME = granulomatous meningoencephalomyelitis
- MRI = magnetic resonance imaging
- MUE = meningoencephalomyelitis of unknown etiology
- MUO = meningoencephalomyelitis of unknown origin
- NSAID = nonsteroidal anti-inflammatory drug

INTERNET RESOURCES

- <http://www.ivis.org>
- <http://www.vin.com>

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Client Education Handout
available online



BASICS

OVERVIEW

- Rare tumor in dogs and cats arising from the mesothelial cells of the serosal lining of the pleural, pericardial, or peritoneal cavities.
- Also has been reported in dogs to arise from the tunica vaginalis of the testes.

SIGNALMENT

- Older animals—dog and cat
- Sclerosing subtype more common in males
- German shepherds overrepresented

SIGNS

- Pleural effusion—dyspnea, tachypnea, exercise intolerance, coughing, gagging, cyanosis.
- Pericardial effusion—lethargy, anorexia, weakness, collapse, respiratory distress, exercise intolerance, distended abdomen, vomiting.
- Ascites—distended abdomen, anorexia, vomiting, lethargy, abdominal discomfort.
- Swollen testes.
- Sclerosing subtype signs are secondary to restriction around affected organs—vomiting, urinary issues.

CAUSES & RISK FACTORS

- Increased risk with asbestos exposure.
- Possible increased risk in golden retrievers with idiopathic hemorrhagic pericardial effusion.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other causes of effusions—hypoproteinemia, vasculitis, neoplasia (e.g., lymphoma, chemodectomas, hemangiosarcoma, carcinomatosis), idiopathic, congestive heart failure, liver disease, infectious/inflammatory.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

IMAGING

- Thoracic radiography—identification of pleural effusion, evaluation of cardiac silhouette (i.e., globoid heart consistent with pericardial effusion).

- Echocardiography—identification of pericardial effusion, rule out primary cardiac neoplasia.
- Thoracic and abdominal ultrasonography—evaluation of effusions.
- CT—identification of mass lesions and evaluation of lungs in the face of pleural effusion.

DIAGNOSTIC PROCEDURES

- Cytology of effusions to rule out infectious causes or lymphoma—difficult to diagnose mesothelioma on cytology as mesothelial cells are typically shed into effusions and can be highly reactive.
- Exploratory surgery (open or via thoracoscopic or laparoscopic examination) with biopsies.
- Fibronectin levels in effusions—not specific for mesothelioma but typically elevated in neoplastic effusions.



TREATMENT

- Pericardectomy or mass removal if possible.
- Symptomatic pericardiocentesis or thoracocentesis.



MEDICATIONS

DRUG(S)

- Intracavitary chemotherapy.
 - Cisplatin (dog only) 50–70 mg/m² every 3 weeks with saline diuresis.
 - Carboplatin (cat) 180–200 mg/m² every 3–4 weeks.
 - Carboplatin (dog) 300 mg/m² (dog) every 3 weeks.
 - Mitoxantrone (dog) 5.0–5.5 mg/m² every 3 weeks.
- Intravenous chemotherapy—doxorubicin 30 mg/m² (dog > 10 kg) or 1 mg/kg (dog < 10 kg or cat), or mitoxantrone (4.5–5.5 mg/m² dog and cat) once every 3 weeks.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Chemotherapy can cause gastrointestinal, bone marrow, cardiac, and other toxicities—seek advice if unfamiliar with cytotoxic drugs.
- Cisplatin in particular is nephrotoxic. Do not use in cats; causes fatal pulmonary edema.



FOLLOW-UP

PATIENT MONITORING

- Blood tests—especially CBC to monitor for bone marrow suppression secondary to chemotherapy and renal values to monitor for renal toxicity if treating with cisplatin.
- Serial thoracic radiography and/or ultrasounds of heart, thoracic cavity, or abdominal cavity to monitor for recurrence of effusions and to monitor tumor response.

EXPECTED COURSE AND PROGNOSIS

- Prognosis—variable and anecdotal.
 - Intracavitary cisplatin (dogs)—range 8 months to > 3 years.
 - Intracavitary carboplatin (cats) with piroxicam—6 months.
 - Surgery and intracavitary cisplatin and IV doxorubicin—> 27 months.
 - Reported survival with surgery alone—4–9 months.

M



MISCELLANEOUS

It is not recommended to breed animals with cancer. Chemotherapy is teratogenic—do not give to pregnant animals.

ABBREVIATION

- CT = computed tomography

Suggested Reading

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Author Rebecca G. Newman

Consulting Editor Timothy M. Fan

METALDEHYDE TOXICOSIS



BASICS

DEFINITION

- Metaldehyde is a polymeric form of acetaldehyde and primarily affects the nervous system. It is an ingredient of slug and snail baits, and sometimes found in solid fuel for camp stoves.
- Metaldehyde crosses the blood-brain barrier and disrupts GABAergic inhibitory action, facilitating neuronal excitation and increasing potential for convulsions.

SYSTEMS AFFECTED

- Neuromuscular—seizures and muscle tremors.
- Hepatobiliary—delayed hepatotoxicosis occasionally reported in dogs.
- Multiple organ failure may occur secondary to convulsions and hyperthermia.

INCIDENCE/PREVALENCE

Depends on presence and accessibility of toxicant.

GEOGRAPHIC DISTRIBUTION

More frequent in coastal and low-lying areas, where snails and slugs are common.

SIGNALMENT

Species

Dogs and cats (less often).

SIGNS

- So-called “shake and bake” toxicant due to characteristic tremors, seizures, and hyperthermia
- Signs typically develop within 4 hours of ingestion
- Anxiety and restlessness
- Salivation, vomiting, diarrhea
- Tachycardia
- Tachypnea
- Hyperthermia, often 106°F (41°C) or greater, leading to DIC and multi-organ failure if uncontrolled
- Ataxia
- Tremors
- Seizures, initially intermittent, progressing to continuous
- Hyperesthesia
- Depression
- Mydriasis
- Nystagmus (particularly in cats)

CAUSES

Ingestion of metaldehyde



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Strychnine - intermittent seizures that can often be evoked by external stimuli.
- Tremorgenic mycotoxins – tremors and seizures.
- Lead - seizures, behavior changes, blindness, vomiting, diarrhea.
- Zinc phosphide rodenticide—seizures and hyperesthesia.
- Bromethalin rodenticide—ataxia, tremors, seizures.
- Organophosphate and carbamate insecticides - seizures; often accompanied by excessive salivation, lacrimation, urination, defecation, GI upset, emesis.

CBC/BIOCHEMISTRY/URINALYSIS

- No specific diagnostic features
- Metabolic acidosis
- Increased serum muscle enzyme activity
- Changes in hepatic or renal values, likely secondary to uncontrolled hyperthermia

OTHER LABORATORY TESTS

Metaldehyde testing—gastric contents, serum, urine, brain, or liver. Testing capabilities vary widely among labs - contact your lab of choice to see what samples are recommended.

PATHOLOGIC FINDINGS

- Lesions neither consistent nor pathognomonic on gross and histologic examination.
- Gastric contents may have a formaldehyde-like odor.



TREATMENT

APPROPRIATE HEALTH CARE

Emergency evaluation, followed by inpatient intensive care management until convulsions, tremors, and hyperthermia are controlled.

NURSING CARE

- Control hyperthermia with cool intravenous crystalloids, ice packs, fans, enemas, etc.
- Monitor to prevent aspiration of vomitus.
- Crystalloids to correct dehydration or acidosis.
- Monitor CNS status.

DIET

Do not feed patients that are vomiting, convulsing, or heavily sedated.



MEDICATIONS

DRUG(S) OF CHOICE

- No specific antidote available.
- Removal of toxicant via gastric lavage (preferred with large toxicant ingestions and patients that are symptomatic) or emetics.
- Reduce absorption via single dose of activated charcoal with cathartic, if patient is not at risk for aspiration.
- Control convulsions with benzodiazepines (first choice), barbiturates, propofol, or inhalant general anesthetics.
- Methocarbamol or 5% guaifenesin for control of tremors.
- Consider hepatoprotectants in dogs ingesting large doses of metaldehyde.

CONTRAINdicATIONS

Do not induce vomiting or give activated charcoal to a patient that is convulsing or heavily sedated.

PRECAUTIONS

Use depressant drugs very cautiously in an already depressed patient, and only if other options are unavailable or ineffective. Use anticonvulsants at lowest effective doses.



FOLLOW-UP

PATIENT MONITORING

- Periodically allow anticonvulsants to wear off to reevaluate seizure condition.
- Recheck liver enzymes 72 hours post-discharge in dogs that have ingested large amounts of metaldehyde.

PREVENTION/AVOIDANCE

- Do not apply metaldehyde in areas accessible to pets.
- Some manufacturers dye these products green or blue to assist with identification.
- Bittering agents are sometimes added to metaldehyde products but do not reliably discourage ingestion.

POSSIBLE COMPLICATIONS

- Liver or renal dysfunction possible several days after recovery from the initial signs, probably as sequelae to convulsions and hyperthermia.
- Aspiration pneumonia is a concern with any convulsing patient.
- Hyperthermia may lead to DIC or multiple organ failure.
- Temporary blindness has been reported in rare cases.

EXPECTED COURSE AND PROGNOSIS

- Prognosis usually good to excellent if treated early and aggressively.
- Guarded to poor prognosis with delayed or inadequate treatment, especially with large ingestions.
- Fatalities most often occur within 24 hours of ingestion. Survival beyond the first 24 hours is a positive prognostic indicator.



MISCELLANEOUS

ABBREVIATION

DIC = disseminated intravascular coagulation

Suggested Reading

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Client Education Handout
available online

METFORMIN TOXICOSIS



BASICS

OVERVIEW

- Metformin (Glucophage) is a biguanide antihyperglycemic prescription medication labeled for the treatment of non-insulin-dependent (type 2) diabetes mellitus in humans.
- Available as single or extended release formulation (Glucophage XR).
- Formulated as a single ingredient and in combination with other antidiabetic medications.
- The agent potentially could be useful in the adjunctive treatment of non-insulin-dependent diabetes mellitus in cats; use is controversial.
- Toxicity causes gastrointestinal signs and lethargy.
- 243 exposures to metformin were reported to the ASPCA Animal Poison Control Center (APCC) during 2008–2009. Of these, 231 were dogs with 27 showing clinical signs and 12 cases were cats with 2 showing clinical signs. Common findings in dogs recorded in decreasing frequency included vomiting and diarrhea.

SIGNALMENT

- Dogs and cats
- No breed, age, or sex predilections

SIGNS

Dogs

- Common sign: vomiting
- Possible signs: lethargy, depression, anorexia, and hypothermia

Cats

- Frequent sign: vomiting
- Possible signs: lethargy, diarrhea, and vocalization

CAUSES & RISK FACTORS

Ingestion of metformin in single ingredient preparations as well as in combination with other antidiabetic agents.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other gastrointestinal tract irritants

CBC/BIOCHEMISTRY/URINALYSIS

- Azotemia reported in humans due to acute renal failure in cases of biguanide lactic acidosis; not reported in animal toxicities.
- Hypoglycemia not reported.

OTHER LABORATORY TESTS

- Blood gases—lactic acidosis rare but possible with large ingestions (a Shih Tzu ingesting 167.2 mg/kg of metformin developed lactic acidosis, vomiting, and hypothermia. No hypoglycemia developed and the dog fully recovered with treatment).
- High performance liquid chromatography may identify presence of metformin in plasma; drug levels are not clinically useful.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

N/A



TREATMENT

- Induce emesis within the first 2–3 hours of exposure.
- Activated charcoal should only be considered with very large exposure.
- Treat gastrointestinal signs supportively.
- Treat lactic acidosis if present.



MEDICATIONS

DRUG(S)

- Metoclopramide 0.1–0.4 mg/kg PO, SC, or IM q6h.
- Sucralfate 0.5–1 g PO q8–12h for dogs and 0.25–0.5 g PO q8–12h for cats.
- Famotidine 0.5 mg/kg orally, subcutaneously, or intramuscularly q12–24h for dogs and cats.
- Ranitidine 0.5–2 mg/kg PO, SC, or IM q8–12h for dogs and 2.5 mg/kg IV q12h or 3.5 mg/kg PO q12h for cats.
- Omeprazole 0.5–1 mg/kg PO q24h for dogs and 0.7 mg/kg PO q24h for cats.
- Bicarbonate: if serum bicarbonate or total CO₂ is unavailable: 2–3 mEq/kg IV over 30 minutes if patient has decreased tissue perfusion or renal failure and does not have diabetic ketoacidosis. Must be used judiciously.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Concurrent administration of cimetidine may reduce the urinary excretion of metformin by competing for renal tubular organic cationic transport systems.

- The manufacturer states that other cationic drugs that undergo substantial tubular secretion (e.g., amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim, and vancomycin) may possibly decrease the urinary excretion of metformin.



FOLLOW-UP

PATIENT MONITORING

N/A

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

Good prognosis assuming lactic acidosis does not occur



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

PREGNANCY/FERTILITY/BREEDING

- No evidence of harm to the fetus or impaired fertility during reproduction studies in rats and rabbits given metformin hydrochloride dosages of 600 mg/kg daily.
- No adequate and controlled studies to date using metformin hydrochloride in pregnant women.
- Excreted in milk in levels similar to plasma. Caution advised in lactating queens.

SEE ALSO

Poisoning (Intoxication) Therapy

INTERNET RESOURCES

- <http://chem.sis.nlm.nih.gov/chemidplus/rn/657-24-9>
- <http://www.aspapro.org/search/index/METFORMIN>

Suggested Reading

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METHEMOGLOBINEMIA



BASICS

DEFINITION

- Methemoglobin content in blood > 1.5% of total hemoglobin.
- Methemoglobin differs from hemoglobin in that the iron moiety of heme groups has been oxidized from the ferrous (+2) to the ferric (+3) state.

PATHOPHYSIOLOGY

- About 3% of hemoglobin is oxidized to methemoglobin each day in normal animals as a result of autoxidation of hemoglobin or secondary to oxidants produced in normal metabolic reactions.
- Methemoglobin usually accounts for < 1% of total hemoglobin, because it is constantly reduced back to hemoglobin by an NADH-dependent cytochrome b_5 reductase (methemoglobin reductase) enzyme reaction within RBCs.
- Caused by either increased production of methemoglobin by oxidants or decreased reduction of methemoglobin associated with a deficiency of the RBC cytochrome b_5 reductase enzyme.

SYSTEMS AFFECTED

- Hemic/Lymphatic/Immune—reduced oxygen-carrying capacity of blood, because methemoglobin cannot bind oxygen; if methemoglobin content reaches high values (e.g., > 50% of total hemoglobin), various organs may suffer hypoxic injury.
- Hepatobiliary—in addition to hypoxic injury, the liver may be damaged directly by oxidant drugs that it metabolizes.
- Renal/Urologic—in addition to hypoxic injury, the kidneys may be damaged if intravascular hemolysis occurs.

SIGNALMENT

- Dogs and cats.
- Deficiency in RBC cytochrome b_5 reductase has been recognized in Chihuahuas, borzois, English setters, terrier mixes, cockapoos, coonhounds, poodles, corgis, Pomeranians, pit bull mixes, and toy Eskimo dogs and in domestic shorthair cats.

SIGNS

Caused Directly

- Possibly none in animals with mild to moderate methemoglobinemia.
- Cyanotic-appearing mucous membranes—may be difficult to recognize in heavily pigmented animals.
- Lethargy, tachycardia, tachypnea, ataxia, and stupor caused by hypoxia when methemoglobin content exceeds 50%.
- Coma-like state and death when methemoglobin content reaches 80%.

Caused by Associated Diseases

- Vomiting, anorexia, and diarrhea possible in patients with drug toxicity.

- Hemoglobinuria secondary to severe intravascular hemolysis in some patients with concomitant Heinz body hemolytic anemia.
- Subcutaneous edema, especially involving the face, and salivation in cats with acetaminophen toxicity.

CAUSES

- Toxicity—acetaminophen, benzocaine, phenazopyridine, and skunk musk also cause Heinz body hemolytic anemia; excess nitrite in pet food and hydroxycarbamide toxicity are reported to cause methemoglobinemia without Heinz body hemolytic anemia.
- Deficiency in RBC cytochrome b_5 reductase.

RISK FACTORS

- Application of benzocaine to traumatized skin or mucous membranes increases the likelihood of systemic absorption and methemoglobinemia.
- Cats are much more likely to develop clinically significant methemoglobinemia than are dogs after acetaminophen administration; this drug is not recommended for use in cats.
- Methemoglobinemia secondary to cytochrome b_5 reductase deficiency is an inherited disorder.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Both low blood oxygen tension and methemoglobinemia can cause cyanotic-appearing mucous membranes and dark-colored blood samples.
- Hypoxemia is documented by measuring low Po_2 in an arterial blood sample.
- Methemoglobinemia is suspected when arterial blood with normal or high Po_2 is dark-colored.

LABORATORY FINDINGS

Drugs That Alter Laboratory Results

None

Disorders That May Alter Laboratory Results

Hemolysis in the sample may raise the methemoglobin value, especially if the methemoglobin assay is not conducted soon after sample collection.

Valid if Run in Human Laboratory?

- Valid, as long as the method to lyse RBCs does not cause methemoglobin formation in the animal being tested.
- Saponin should not be used to lyse RBCs, because it raises the methemoglobin value in some species.

CBC/BIOCHEMISTRY/URINALYSIS

- Chronic methemoglobinemia secondary to cytochrome b_5 reductase deficiency can result in a slightly high HCT; in contrast, anemia

may accompany methemoglobinemia caused by oxidant drugs.

- If severe or induced by oxidant drugs, evidence of injury to various organs (e.g., high BUN and ALT) may be seen.

OTHER LABORATORY TESTS

- Spot test—determine if the patient's methemoglobin content is clinically important: one drop of blood from the patient is placed on a piece of absorbent white paper and a drop of normal control blood is placed next to it. If the methemoglobin content is ≥ 10%, the patient's blood will be noticeably browner than the bright red of the control blood.
- Co-oximetry is the method of choice for accurate measurement of methemoglobin content in whole blood samples.
- Methemoglobin content in dogs with cytochrome b_5 reductase deficiency varies from 13 to 51%; the methemoglobin content in six deficient cats was 44–52%.
- A definitive diagnosis of cytochrome b_5 reductase deficiency is made by measuring enzyme activity in RBCs; this assay is done in a few research laboratories and requires that arrangements be made before blood samples are submitted.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Blood should be stained for Heinz bodies if evidence of toxicity is present.
- The presence of Heinz bodies indicates exposure to an oxidant drug that may also cause hemolytic anemia.



TREATMENT

- Mild to moderate—does not require specific treatment to reduce the methemoglobin content.
- Drug induced—the use of the drug should be discontinued; RBCs can convert much of the methemoglobin back to hemoglobin within 24 hours after elimination of drug exposure.
- Inherited cytochrome b_5 reductase deficiency—animals have normal life expectancy and generally do not require treatment, although veterinarians may wish to give a single IV injection of methylene blue (see below) 1 hour before a deficient animal is anesthetized for surgery to maximize the amount of hemoglobin that is capable of binding oxygen.
- Whole blood transfusions should be given to patients with severe anemia and those with rapidly decreasing HCT and clinical signs suggesting a deteriorating condition.
- Severe intravascular hemolysis—IV fluid administration recommended.

(CONTINUED)

- Treatment of electrolyte or acid-base imbalances may also be indicated in patients with severe vomiting or diarrhea, concomitant renal injury, or impending shock.
- Administration of oxygen is of limited value because methemoglobin cannot bind oxygen, and an increase in dissolved oxygen results in only a small increase in blood oxygen content.



MEDICATIONS

DRUG(S) OF CHOICE

- Methylene blue—given slowly over several minutes as a 1% solution (1 mg/kg IV), may be administered in patients with severe methemoglobinemia; a dramatic response should occur during the first 30 minutes of treatment; caution: although this dose can be repeated if necessary, methylene blue can cause Heinz body hemolytic anemia in cats and dogs.
- N*-acetylcysteine is efficacious in the treatment of acetaminophen toxicity in cats if given within a few hours after exposure; recommended dosage is 140 mg/kg PO followed by 70 mg/kg q6h for seven treatments.

CONTRAINDICATIONS

None

PRECAUTIONS

In patients that have been given drugs that cause substantial Heinz body formation and methemoglobinemia, methylene blue treatment can potentiate the formation of Heinz bodies and anemia; consequently, it is prudent to measure the HCT for 3 days after methylene blue treatment to ensure that clinically important anemia does not develop.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

- The cyanotic appearance of skin and mucous membranes should disappear after reduction of methemoglobin to an amount that does not produce clinical signs.
- Blood on the spot test should appear bright red after reduction of methemoglobin to values < 10% of total hemoglobin.
- If methylene blue treatment is given or Heinz bodies are present within RBCs, the HCT should be monitored closely, because it usually does not reach its lowest point until approximately 3 days after initial oxidant exposure.

METHEMOGLOBINEMIA

POSSIBLE COMPLICATIONS

Coma and death can occur if methemoglobin content reaches 80% of total hemoglobin.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Heinz body anemia

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Acetaminophen (APAP) Toxicosis
- Anemia, Heinz Body

ABBREVIATIONS

- ALT = alanine aminotransferase
- HCT = hematocrit
- RBC = red blood cell

Suggested Reading

Harvey JW. The erythrocyte: Physiology, metabolism, and biochemical disorders. In: Kaneko JJ, Harvey JW, Bruss ML. Clinical Biochemistry of Domestic Animals, 6th ed. San Diego: Academic Press, 2008, pp. 173–240.

Author John W. Harvey

Consulting Editor Alan H. Rebar

M

METRITIS



BASICS

OVERVIEW

- Bacterial uterine infection that develops in the immediate postpartum period (usually within the first week); occasionally develops after an abortion or non-sterile artificial insemination—rarely after natural breeding.
- Bacteria—ascend through the open cervix to the uterus; a large, flaccid, postpartum uterus provides an ideal environment for growth; gram-negative bacteria (e.g., *Escherichia coli*) commonly isolated.
- Potentially life-threatening infection; may lead to septic shock.
- Directly affects uterus; systemic involvement as sepsis develops.
- Can become chronic and lead to infertility.

SIGNALMENT

- Postpartum bitch and queen
- No age or breed predilection

SIGNS

Historical Findings

- Malodorous, purulent, sanguinopurulent, or dark green vulvar discharge
- Depression
- Anorexia
- Neglect of puppies and kittens
- Reduced milk production
- Polyuria/polydipsia due to endotoxin effect on renal tubules.

Physical Examination Findings

- Fever
- Large uterus on abdominal palpation
- Dehydration
- Injected mucous membranes
- Tachycardia—with sepsis

CAUSES & RISK FACTORS

- Dystocia
- Obstetric manipulation
- Retained fetuses or placentas
- Prolonged delivery (large litter)
- Post-abortion, and post-natural or artificial insemination (rare)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Subinvolution of placental sites—no sign of infection on cytologic examination of vagina.
- Eclampsia—differentiated by serum calcium concentration.
- Mastitis—differentiated by physical examination findings.

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilia with left shift.
- Leukopenia—occasionally with endotoxic shock.
- High PCV, total protein, creatinine, BUN, and urine specific gravity—secondary to dehydration. Normocytic, normochromic nonregenerative anemia may also occur.
- High liver enzyme—with endoxemias.
- Low urine specific gravity—may see with endoxemias.
- Hypoalbuminemia, elevation of C-reactive protein, and acute phase proteins may occur.
- Urinalysis may reveal isosthenuria, bacteruria (obtain via U/S guided cystocentesis).

OTHER LABORATORY TESTS

N/A

IMAGING

- Radiography—reveals a large uterus and possibly retained fetus(es).
- Ultrasonography—reveals intrauterine fluid accumulation and increased horn width, retained placenta(s), and retained fetus(es); shows abdominal effusion secondary to uterine rupture.

DIAGNOSTIC PROCEDURES

- Vaginal cytologic examination—detect degenerative neutrophils with intracellular and extracellular bacteria.
- Guarded anterior vaginal or transcervical culture—aerobes and anaerobes; identify organism and its antibiotic sensitivity pattern.



TREATMENT

- Inpatient until systemic signs resolve.
- Dehydration—intravenous balanced electrolyte solution.
- Treat shock.
- Electrolyte imbalances and hypoglycemia—correct; identified by serum chemistry profile.
- Ovariohysterectomy—treatment of choice for retained fetus(es) or placenta(s), uterine rupture, or severe infection, and if future breeding is not desired.
- Chronically affected patient that does not respond to medical treatment—may perform hysterotomy and lavage as long as the uterus has no friable areas.
- Friable uterus—pack off and handle gently at surgery.



MEDICATIONS

DRUG(S)

- Antibiotics—start with broad-spectrum agents (oral if patient is stable; intravenous if patient is in shock); choice confirmed by bacterial culture and sensitivity; continued at least 14 days. Give at separate time from PGF_{2α} administration due to risk of vomiting.
- Nursing planned—amoxicillin-clavulanic acid (dogs, 12.5–25 mg/kg PO q12h; cats, 62.5 mg/cat PO q12h); can administer q8h with Gram-negative infections; or oxacillin (22–40 mg/kg PO q8h) to start.
- Nursing not planned—enrofloxacin (2.5–10 mg/kg PO q12h) to start.
- Oxytocin 0.5–1 U/kg IM (do not exceed 20 IU total); then repeat in 1–2 hours; may note inadequate response if > 48 hours since parturition.
- PGF_{2α} 10–50 µg/kg SC q3–5h for 3–5 days or 100 µg/kg SC q12h for 3–5 days; to evacuate uterus, ultrasound prior to cessation of treatment to ensure resolution of fluid accumulation in uterine lumen.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Prostaglandin—may induce uterine rupture if the tissue is devitalized.
- Oxytocin—not effective beyond 48 hours postpartum.
- Uterine flushing—may cause rupture of devitalized wall.



FOLLOW-UP

PATIENT MONITORING

- CBC, temperature, vaginal cytologic examination, and clinical signs.
- Ultrasonography—monitor evacuation of uterine fluid.

POSSIBLE COMPLICATIONS

- Ovariohysterectomy—necessary when medical treatment is ineffective.
- Uterine rupture and peritonitis—may occur with medical treatment.
- Owners may need to foster or hand-raise puppies and kittens, monitor daily weight gain to ensure adequate nutrition: pups should gain 10% of birth weight per day; kittens should gain a minimum of 7–10 g/day.

EXPECTED COURSE AND PROGNOSIS

- Ovariohysterectomy—prognosis for recovery good; recommended for older patients.
- Medical treatment—prognosis for recovery dependent on early recognition of problem by owner—good if early, may adversely affect future reproduction.



MISCELLANEOUS

ABBREVIATIONS

- PCV = packed cell volume
- PGF_{2α} = prostaglandin F_{2α}

Suggested Reading

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MICROSPORIDIOSIS (ENCEPHALITOZOONOSIS)



BASICS

OVERVIEW

- Encephalitozoonosis is now called microsporidiosis.
- Obligate intracellular spore forming parasite found in a wide array of domestic mammals.
- Infection with the parasites *Encephalitozoon cuniculi* and other species.
- *Encephalitozoon cuniculi* has been divided into three strains—I rabbit type, also detected in man, II mouse type, and III dog type.
- Affects brain, kidney, liver, intestine, eye, lungs.
- Uncommon in the United States but may be more prevalent in other countries.
- Organ systems affected:
 - Neurologic ◦ Renal/Urologic
 - Hepatobiliary ◦ Gastointestinal ◦ Ocular
 - Hemic/lymphatic/immune

SIGNALMENT

- Dogs and cats
- No sex or breed predilection
- Young animals

SIGNS

- Appears a few weeks postpartum
- Stunted growth
- Ill-thrift
- Depression
- Inappetance and weight loss
- Nephritis progressing to renal failure
- Neurologic abnormalities—convulsions, viciousness, biting, vocalization, ataxia, circling, hypermetria
- Ocular abnormalities—including cataracts, uveitis, and blindness

CAUSES & RISK FACTORS

- Transmitted through ingestion, inhalation, transplacentally or rarely through epithelium after trauma.
- Infectious spores are excreted in urine, feces, and mucus.
- Can be ingested from tissues of infected rabbits or mice.
- Kennel housing is a risk factor.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Rabies
- Canine distemper
- Canine herpesvirus
- Neosporosis
- Toxoplasmosis
- Hydrocephalus
- Feline panleukopenia
- Septicemia

CBC/BIOCHEMISTRY/URINALYSIS

- Normochromic, normocytic anemia
- Lymphocytosis and monocytosis

- High serum ALT and ALP expected
- Azotemia—variable
- Hyperproteinemia
- Urinalysis—haematuria and proteinuria

OTHER LABORATORY TESTS

- Serology (immunofluorescent antibody staining, complement fixation, ELISA, and Western immunoblot assays)—blood and CSF (IFA > 100 or ELISA > 800).
- PCR—highly specific and sensitive but not routinely available in veterinary diagnostic labs.
- Histopathology—brain, lung, kidney, placenta, eye. Difficult to identify parasites by light microscopy with H&E stains. Trichrome stain, Calcofluor white fluorescent stain or Fungi-Fluor stain can be used to identify organisms.
- Cytology—aqueous humor and lens material (low sensitivity).
- Urine sediment—special stains may identify parasite spores.

IMAGING

May be contributory but not diagnostic.

DIAGNOSTIC PROCEDURES

CSF—pleocytosis, increased protein. May see organisms with special stains.

PATHOLOGIC FINDINGS

- Urogenital—lymphocytic-plasmacytic interstitial nephritis, hemorrhagic cystitis, renal cortical cysts, or infarcts.
- Neurologic—lymphocytic-plasmacytic meningoencephalitis, thrombosis and encephalomalacia, perivascular cuffing with occasional intracellular parasitic cysts containing Gram-positive spores.
- Hepatic—multifocal microgranulomatous hepatitis.
- Respiratory—interstitial pneumonia.
- Cardiac—fibrous pericarditis.
- Gastrointestinal—regional enteritis.
- Other—reticuloendothelial hyperplasia of the spleen and hyperplasia of the bone marrow. Necrotic, tortuous medium-sized to small arteries (polyarteritis nodosa).



TREATMENT

- Inpatient with supportive therapy.
- Poor understanding of the disease progression exists. Most diagnosed post-mortem. Asymptomatic infections likely occur.
- Euthanasia—when severe neurologic signs occur.



MEDICATIONS

DRUG(S)

- No treatment has been reported. Try benzimidazoles, particularly albendazole

(400 mg q12h for > 3 weeks), because they work in mice and humans.

- Trimethoprim or pyrimethamine and sulphonamides, alone or in combination, with albendazole have been effective in humans with disseminated infections.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PREVENTION/AVOIDANCE

- Sanitation—important; accomplish with 70% ethanol, hydrogen peroxide, 10% formalin and 10% bleach.
- Spores survive in humid environments at ambient temperatures.

EXPECTED COURSE AND PROGNOSIS

A number of patients recover without further signs if neither the renal nor the cerebral manifestation becomes severe.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Potential risks to humans, especially the immunosuppressed and children.
- Single report of possible direct transmission between dog and child.

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- CSF = cerebrospinal fluid
- PCR = Polymerase chain reaction

Suggested Reading

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M

MOVEMENT DISORDERS



BASICS

OVERVIEW

• Movement disorders—CNS disorders characterized by the occurrence of continuous or episodic involuntary movements with dystonia, ballism, chorea or athetosis in a fully conscious animal; unrelated to epileptic activity. Movements restricted to one body part, e.g. one, two limbs or the whole body. Hyperkinetic movement disorders often occur as paroxysmal dyskinesias with episodes of abnormal movements or increased muscle tone alternating with normal neurologic function. • Abnormal CNS neural transmission, ion channelopathy, neurotransmitter dysfunction.

SIGNALMENT

• Dog; less common in cat. • Breed-related syndromes. • Age of onset variable. Often < 3 years.

SIGNS

• Physical examination—unremarkable. • *Paroxysmal dyskinesia*—in Bichon frises, Bolonkas, border terriers (*canine epileptoid cramping*), Chinooks, soft-coated Wheaten terriers: repeated flexion or kicking of one hind limb, difficulty walking, extensor rigidity with resulting ataxia, kyphosis or scoliosis, some with backward gait; no autonomic signs; normal mentation; some border terriers prone to vomiting and diarrhea; minutes to hours; triggered by excitement, stress. • *Episodic falling*—in CKCS, Scotty cramp in Scottish terriers: muscle hypertonicity with temporary inability to relax trunk and limb muscles, stiffness, kyphosis, lateral or forward collapse. Triggered by excitement, stress. • *Neuromyotonic collapse* in JRTs—with hereditary ataxia, myokymia, facial rubbing; lateral recumbency, rigidity; conscious, severe hyperthermia, lasts hours; triggered by hot weather; also in a dachshund. • *Startle disease*—in Irish wolfhound puppies: extensor rigidity when handled, relaxed when sleeping, cyanotic; suspected in Labrador retriever puppies with *reflex myoclonus*. • *Episodic head tremor or head bobbing*—Doberman, English bulldogs, boxer, others: rapid yes or no head excursions, triggered by stress, interruptible, variable duration, non-predictable occurrence.

CAUSES & RISK FACTORS

• Genetic defects in neural transmission—CKCS (brevican), Irish wolfhounds (glycine receptor), Russell terrier (KCNJ10), soft-coated Wheaten terrier. • Metabolic. • Drugs—phenobarbital-induced dyskinesia, propofol. • Toxins—herbicides, mycotoxins, chlorinated hydrocarbons, bromethalin. • Triggered by excitement, stress, exercise; heat in JRT.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- *Epilepsy*—impaired mentation during the episode unless simple focal seizure limited to one limb; short duration < 5 minutes, autonomous signs (urination, salivation, mydriasis). • *Obsessive compulsive behavior*—complex behavior, normal mentation and muscle tone, interruptible. • *Pain episodes*—spinal pain. • *Myoclonic epilepsy*—stimulus-induced repetitive shock-like contractions; miniature wire-haired dachshund, beagle, basset. • *Myotonic myopathy*—muscle stiffness or collapse, worse after rest and myotonic dimpling: Chow-chows, miniature schnauzer. Hyperadrenocorticism: myotonic discharges on EMG. • *Potassium-aggravated muscle stiffness*—cats. • *Exercise-induced collapse*—Labrador and other dog breeds. • *Constant repetitive myoclonus*—following encephalomyelitis (distemper), lead, persists in sleep.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

- Genetic testing. • Electrolytes, CK, liver function tests, fasting glucose, T4/TSH, ACTH test. • Neurometabolic screen—lactate/pyruvate, urinary organic acids/amino acids.

IMAGING

MRI brain, spinal cord—exclude structural disease.

DIAGNOSTIC PROCEDURES

- Video documentation. • Scotty cramp—methysergide 0.3 mg/kg IV provokes episodes. • Video electroencephalography. • Electromyography. • CSF—exclude inflammatory CNS disease.

PATHOLOGIC FINDINGS

Unremarkable. Stiff Labradors—astrogliosis.



TREATMENT

- Control environment—many episodes triggered by stress, excitement, exercise; heat in JRT. • Dietary change in Border terriers.



MEDICATIONS

DRUG(S)

- No evidence-based treatments. • Stiff Labradors—positive response to NSAIDs. • Diazepam 0.5 mg/kg q8h; clonazepam 0.5 mg/kg q8–12h; acetazolamide 4–8 mg/kg q8–12h (side effects: abdominal pain,

lethargy, weakness); 4-aminopyridine 0.25–0.5 mg/kg q12h; fluoxetine 1–2 mg/kg q24h.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Clinical signs do not usually respond to antiepileptic drugs.



FOLLOW-UP

PATIENT MONITORING

Acetazolamide—hypokalemia, acidosis

PREVENTION/AVOIDANCE

Avoid potential triggers. Avoid heat in JRTs.

POSSIBLE COMPLICATIONS

Hyperthermia (death) in JRT neuromyotonia

EXPECTED COURSE AND PROGNOSIS

Unpredictable frequency



MISCELLANEOUS

AGE-RELATED FACTORS

Often appears in dogs < 3 years old

PREGNANCY/FERTILITY/BREEDING

Breeding not recommended. Genetic testing recommended.

SEE ALSO

- Exercise-Induced Weakness/Collapse in Labradors • Head Tremors (Bobbing), Idiopathic—Dogs • Myoclonus • Shaker/Tremor Syndrome, Corticosteroid Responsive

ABBREVIATIONS

- CKCS = Cavalier King Charles spaniel
- CNS = central nervous system • CSF = cerebrospinal fluid • JRT = Jack Russell terrier • MRI = magnetic resonance imaging
- NSAID = non-steroidal anti-inflammatory drug

INTERNET RESOURCES

- www.offa.org/breed_tests.html
- www.caninegeneticdiseases.net/CGD_main.htm
- www.aht.org/cms-display/genetics_canine.html

Suggested Reading

Urkasemsin G, Olby NJ. Canine paroxysmal movement disorders. Vet Clin North Am Small Anim Pract 2014, 44:1091–1102.

Author Andrea Fischer

Consulting Editor Joane M. Parent



Client Education Handout
available online

MUCOPOLYSACCHARIDOSES



BASICS

OVERVIEW

Mucopolysaccharidosis should be considered as a differential diagnosis for young dogs and cats with stunted growth, progressive skeletal malformations, and neutrophil and lymphocyte inclusions. The mucopolysaccharidoses are characterized by the accumulation of GAG and result from the impaired function of 1 of 11 enzymes required for normal GAG degradation. Almost all of these disorders have been described in animals. Undegraded GAGs are stored in lysosomes, resulting in progressive tissue and organ dysfunction, including CNS (usually clinically insignificant), skeleton, eye, cardiovascular system and liver.

Types of MPS Reported in Dogs and Cats

- MPS I— α -l-iduronidase deficiency; dermatan and heparan sulfate stored.
- MPS II—iduronate sulfatase deficiency; dermatan and heparan sulfate stored; first MPS recognized in humans.
- MPS IIIA—heparan N-sulfatase deficiency; heparan sulfate stored.
- MPS IIIB— α N acetyl glucosaminidase deficiency; heparan sulfate stored.
- MPS VI—arylsulfatase B deficiency; dermatan sulfate stored; first MPS recognized in an animal.
- MPS VII— β -glucuronidase deficiency; dermatan, heparan, and chondroitin sulfate stored.

SIGNALMENT

- Cats—MPS I and VII, domestic shorthair; MPS VI, Siamese and domestic shorthair.
- Dogs—MPS I, Plott hounds; MPS II, Labrador retrievers; MPS IIIA, wire-haired dachshunds and Huntaway dogs, Rotweiler dog, Boston terrier dog; MPS IIIB, skipper dog; MPS VI, miniature pinschers, miniature schnauzers, Welsh corgis, and a Chesapeake Bay retriever dog; MPS VII, mixed breeds and German shepherds.
- Both sexes equally affected by MPS I, III, VI, and VII; primarily males affected by MPS II.

SIGNS

- Dwarfism (except cats with MPS I), small ears, wide-spaced eyes, flattened face with possible protuberant tongue.
- Severe bone disease (dysostosis multiplex).
- Degenerative joint disease, including hip subluxation.
- Facial dysmorphia—more evident in Siamese cats, which normally have an elongated face, than in other cats.
- Hepatomegaly (except cats with MPS VI).
- Corneal clouding—a result of fine granular opacities in the corneal stroma, first apparent at approximately 8 weeks of age.

- Large tongue.
- Thickening of the heart valves.
- Excess urinary excretion of GAG.
- Metachromatic granules (Alder-Reilly bodies) in blood leukocytes.
- Disease progresses; clinical signs apparent at 2–4 months of age.
- Affected animals may live several years, but locomotor difficulty is progressive.
- Skeletal abnormalities more severe in cats with MPS VI than in those with MPS I; some MPS VI cats develop posterior paresis owing to spinal cord compression.
- Manipulation of the head or neck usually painful.

CAUSES & RISK FACTORS

- MPS transmission is autosomal recessive, except MPS II, which is X-linked recessive.
- In-breeding increases risk if the defective gene is present in the family.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Metachromatic granules within neutrophils and lymphocytes—suggest MPS; also observed with GM₂ gangliosidosis, a lysosomal storage disease that, unlike MPS, is characterized by progressive neurologic disease and early death; granules may also be observed in neutrophils of some Burmese cats that have normal lymphocytes and have no clinical abnormalities; very rarely, toxic granulation of neutrophils can have a similar appearance.
- Corneal clouding—also observed with numerous other lysosomal storage diseases, including acid lipase deficiency, GM₁ and GM₂ gangliosidosis, and mannosidosis; lysosomal enzyme panels can be performed to definitively diagnose the type of storage disorder; corneal edema and corneal dystrophy may have a similar appearance.
- Whereas the radiographic appearance of MPS is characteristic, other disorders with similarities include congenital hypothyroidism, epiphyseal dysplasia, and hypervitaminosis A.

CBC/BIOCHEMISTRY/URINALYSIS

- Examination of Wright's-stained blood films reveals neutrophils and monocytes containing numerous distinctive metachromatic granules.
- Granules quite indistinct in animals with MPS I.
- Granules usually not apparent when stained with Diff-Quik.
- Occasional lymphocytes have vacuoles that contain metachromatic granules.

OTHER LABORATORY TESTS

- Wright's-stained cytologic preparations of lymph node, liver, bone marrow, and joint fluid specimens reveal characteristic metachromatic granules within cells.

- Presence of excess GAG in urine usually indicates MPS. Screening tests (Berry spot test) and quantitative analysis are available.
- Definitive diagnosis made by measuring lysosomal enzyme activity in serum, leukocyte pellets, or frozen liver.
- DNA testing on blood samples or cheek swabs is now available for most of the MPS disorders in dogs and cats.

IMAGING

- Radiography—low bone density with thin cortices.
- Epiphyseal abnormalities—vary from slight irregularities to large scalloped defects in subchondral bone.
- Joint changes—acetabular flattening and periaricular osteophyte formation.
- In some cats, proliferative bone is present around all articular facets of vertebrae, causing fusion of cervical vertebrae.

DIAGNOSTIC PROCEDURES

- Specialized laboratories can measure lysosomal enzyme activity in leukocyte pellets and detect specific gene mutations in some disorders.
- DNA testing for most of the mucopolysaccharidosis disorders is available through Penngen (research.vet.upenn.edu) or email penngen@vet.penn.edu.

PATHOLOGIC FINDINGS

Distended lysosomes seen in cells of many tissues examined by light and electron microscopy.



TREATMENT

DEFINITIVE TREATMENT

- BMT—after successful engraftment, donor-derived normal leukocytes provide missing enzyme to various tissues; when performed at a very early age, affected animals lead near-normal lives; not as helpful when performed after skeletal maturity; expensive, life-threatening, and a normal sibling is needed as a donor.
- Enzyme-replacement therapy (ERT), using recombinant enzyme, has been quite effective in animal models of MPS. The major limitations are inability of intravenously injected enzyme to reach the CNS (and synovial joints in some diseases), the cost, an immune response in some patients and the need for frequent, life-long injections.
- Both BMT and enzyme replacement are expensive and have been employed primarily in animal models to determine the potential success in children; very few privately owned animals have been treated.
- Gene therapy has been very effective in some animal models and is the primary treatment modality that is currently being evaluated. The basic premise is to provide some autologous cells with the relevant

MUCOPOLYSACCHARIDOSES

(CONTINUED)

normal cDNA to produce and secrete normal enzyme for uptake by abnormal cells. The major difficulties are obtaining adequate levels of gene product in the specific cell types in which they are needed (e.g., in the CNS), maintaining expression over long periods of time *in vivo*, and regulating the levels of gene expression.

**MEDICATIONS****DRUG(S)**

Affected animals are susceptible to viral and bacterial respiratory infection; antibiotics may be indicated.

**FOLLOW-UP****PREVENTION/AVOIDANCE**

- Avoid in-breeding in family with history of disease.
- Enzyme assays should be performed to diagnose heterozygotes.

EXPECTED COURSE AND PROGNOSIS

- Prognosis reasonably good in animals treated at a young age. However, treatment is very expensive, possibly life-threatening, and usually only performed experimentally.
- Untreated animals usually develop severe skeletal and joint disease and may become non-ambulatory at 3–5 years of age.

**MISCELLANEOUS****ABBREVIATIONS**

- BMT = bone marrow transplant
- CNS = central nervous system
- GAG = glycosaminoglycan
- MPS = mucopolysaccharidoses

INTERNET RESOURCES

Penngen: research.vet.upenn.edu

Suggested Reading

Haskins M. Animal models for mucopolysaccharidosis disorders and their clinical relevance. *Acta Paediatr Suppl* 2007, 96:56–62.

Ponder KP, O'Malley TM, Wang P, et al. Neonatal gene therapy with a gamma retroviral vector in mucopolysaccharidosis VI cats. *Mol Ther* 2012, 20:898–907.

Author Mary Anna Thrall

Consulting Editor Alan H. Rebar

MULTIPLE MYELOMA



BASICS

DEFINITION

- Malignant plasma cells in the bone marrow.
- Diagnosis requires constellation of pathologies including bone marrow plasmacytosis, osteolytic bone lesions, and serum or urine myeloma proteins (M-component).

PATHOPHYSIOLOGY

- Proliferation of malignant plasma cells that produce immunoglobulins or subunits.
- Immunoglobulins may polymerize and increase serum viscosity. • Bleeding disorders due to paraprotein coating of platelets, thrombocytopenia, hyperviscosity, or interference with coagulation factors.
- Nephrotoxicity due to protein deposition of amyloid or direct effect of the protein on renal tubular epithelial cells. • Hypercalcemia due to osteoclast activation and bone lysis.

SYSTEMS AFFECTED

- Musculoskeletal: multiple punctate areas of bone lysis in the absence of bony proliferation.
- Nervous, cardiovascular, and respiratory: abnormalities secondary to hyperviscosity.
- Soft tissues—neoplastic infiltration.

INCIDENCE/PREVALENCE

- Dogs: 1% of all malignancies; < 8% of hematopoietic malignancies; 3.6% of all bone tumors. • Cats: < 1% of hematopoietic tumors.

SIGNALMENT

Dog and cat, 6–13 years

SIGNS

Due to bone infiltration and lysis, immunoglobulins produced, and infiltration of organ(s).

Physical Examination Findings

Dogs

- Lethargy, weakness (62%) • Lameness (47%) • Bleeding diathesis (37%): gingiva and epistaxis • Funduscopic abnormalities including retinal hemorrhage or detachment and tortuous vessels (35%)

Cats

Anorexia, weight loss, malaise, polydipsia, polyuria



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Ehrlichiosis, leishmaniasis • Metastatic bone lesions • Rheumatoid arthritis

CBC/BIOCHEMISTRY/URINALYSIS

Dogs

- Hemogram: nonregenerative anemia (66%); neutropenia (25%); thrombocytopenia (33%)
- Chemistry: hyperglobulinemia, hypercalcemia (10–25%), azotemia (33%)

- Urinalysis: proteinuria, isosthenuria, cylindruria, pyuria, hematuria, or bacteriuria

OTHER LABORATORY TESTS

- Serum protein electrophoresis: monoclonal gammopathy in the beta or gamma region, and occasionally a biclonal gammopathy will be present. • Urine protein electrophoresis: Bence-Jones proteins in 25–40%
- Coagulation profile: ~50% will have abnormal coagulation values.

IMAGING

- Radiography (dogs): 25–66% have multifocal, lytic lesions or diffuse osteoporosis.
- Radiography (cats): bony lesions rare, more common for visceral organ infiltration (myeloma-related disorder). • Ultrasonography: detect changes in visceral organs.

DIAGNOSTIC PROCEDURES

- Diagnosis depends on identifying at least 3 of 4 pathologies:
 - Monoclonal gammopathy
 - Lytic bone lesions
 - Bence-Jones proteinuria
 - Bone marrow cytology: > 20% plasma cells or > 5% malignant plasma cells. • For cats—bone marrow involvement is rare, and hence diagnosis is based upon the identification of malignant plasma cells within the visceral organs (myeloma-related disorder).



TREATMENT

APPROPRIATE HEALTH CARE

- Hospitalization if azotemia, hypercalcemia, bleeding disorder, or bacterial infection
- Plasmapheresis lowers protein burden: for symptomatic patient, withdraw a volume of venous blood, centrifuge, discard plasma, and return RBCs to patient in IV crystalloid fluids
- Phlebotomy for hyperviscosity, replace with an equal volume of isotonic fluids IV
- Always consult a veterinary oncologist for latest information regarding treatment.

CLIENT EDUCATION

- Inform client that chemotherapy is palliative but long remissions are possible. • Warn client that relapse will occur. • Discuss side effects, which depend on the drugs used.

SURGICAL CONSIDERATIONS

Areas non-responsive to chemotherapy or solitary lesions can be removed surgically.

RADIATION THERAPY

Radiation therapy can be palliative and highly effective for managing osteolytic bone cancer pain. Indications include painful bone lesions, spinal cord compression, pathologic fractures (after fracture stabilization), or a large soft tissue mass. Consult with a radiation oncologist.



MEDICATIONS

DRUG(S) OF CHOICE

- Dogs—melphalan and prednisone;

cyclophosphamide can be used in addition to or in place of melphalan. • Cats—melphalan and prednisone • Intravenous aminobisphosphonate drugs for management of hypercalcemia and palliation of bone pain. • Consult a veterinary oncologist or reliable drug resource for dosages.

PRECAUTIONS

- Melphalan—delayed thrombocytopenia
- Cyclophosphamide—sterile hemorrhagic cystitis



FOLLOW-UP

PATIENT MONITORING

- CBC and chemistry every 2 weeks for 2 months, then monthly. • Serum electrophoresis and/or Bence-Jones proteinuria monthly until at least 50% decrease in baseline values, then once every 2–3 months.

POSSIBLE COMPLICATIONS

Chemotherapy may cause leukopenia or thrombocytopenia, anorexia, alopecia, hemorrhagic cystitis, and/or pancreatitis.

EXPECTED COURSE AND PROGNOSIS

- Improvement in clinical signs and laboratory abnormalities expected within 3–6 weeks. • Radiographic abnormalities could take longer and be partial.

Dogs

- Median survival with alkylating agents and prednisone: 18 months Overall response rate > 90% • Hypercalcemia, extensive bone lysis, or Bence-Jones proteinuria may have shorter survival • Death typically due to kidney failure, secondary infections, or bone/spinal pain.

Cats

Survival with alkylating agents and prednisone—2–9 months.



MISCELLANEOUS

SEE ALSO

- Hypercalcemia • Renal Failure, Chronic

Suggested Reading

Vail D. Myeloma-Related Disorders. In: Withrow SJ, Vail DM, Page RL, eds., Small Animal Clinical Oncology, 5th ed. St Louis, MO: Elsevier Saunders, 2013, pp. 665–678.

Author Shawna L. Klahn

Consulting Editor Timothy M. Fan

Acknowledgment The author and editors acknowledge the prior contribution of Wallace B. Morrison.



Client Education Handout
available online

MUMPS



BASICS

OVERVIEW

- Common illness in humans (primary natural hosts)
- Dogs contract the disease from infected children
- Incidence (dogs)—low

SIGNALMENT

- Dogs of all ages
- No sex or breed predilections

SIGNS

- Enlarged parotid salivary glands
- Fever
- Anorexia

CAUSES & RISK FACTORS

Mumps virus—family Paramyxoviridae; genus *Paramyxovirus*



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Benign parotid salivary gland enlargement
- Neoplasia

M

CBC/BIOCHEMISTRY/URINALYSIS

No specific findings

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Serologic—mumps viral antibodies



TREATMENT

Usually not required



MEDICATIONS

DRUG(S)

None

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

None



FOLLOW-UP

PATIENT MONITORING

Monitor hydration, electrolytes, acid-base balance, and body temperature.

EXPECTED COURSE AND PROGNOSIS

Patients usually recover within 5–10 days of infection.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Mumps virus spreads only from acutely infected humans to susceptible dogs.

Suggested Reading

Greene CE. Mumps. In: Greene CE, ed., Infectious Diseases of the Dog and Cat, 4th ed. St. Louis, MO: Saunders Elsevier, 2012, pp. 66–67.

Author Stephen C. Barr

Consulting Editor Stephen C. Barr

Acknowledgment The author and editors acknowledge the prior contribution of Johnny D. Hoskins.



BASICS

DEFINITION

Vibrations caused by disturbed blood flow

Timing of Murmurs

- Systolic murmurs occur between S1 and S2 (systole).
- Diastolic murmurs occur between S2 and S1 (diastole).
- Continuous and to-and-fro murmurs occur throughout all or most of the cardiac cycle.
- Continuous murmurs are usually accentuated near S2 and to-and-fro murmurs are usually absent near S2.

Grading Scale for Murmurs

- Grade I—barely audible.
- Grade II—soft, but easily auscultated. Doesn't radiate far from point of maximal intensity.
- Grade III—intermediate loudness; heard easily some distance from PMI, but not to opposite side of chest; most hemodynamically important murmurs are at least grade III.
- Grade IV—loud murmur radiating widely, often including opposite side of chest.
- Grade V—very loud, audible with stethoscope barely touching the chest; palpable thrill.
- Grade VI—very loud, audible without the stethoscope touching the chest; palpable thrill.

Configuration

- Plateau murmurs have uniform loudness and are typical of regurgitant murmurs such as mitral and tricuspid insufficiency and ventricular septal defect.
- Crescendo-decrescendo murmurs get louder and then softer and are typical of ejection murmurs such as pulmonic and aortic stenosis and atrial septal defect.
- Decrescendo murmurs start loud and then get softer and are typical of diastolic murmurs such as aortic or pulmonic insufficiency and mitral or tricuspid stenosis.

Location

Dogs

- Mitral area—left fifth intercostal space at costochondral junction.
- Aortic area—left fourth intercostal space above costochondral junction.
- Pulmonic area—left second to fourth intercostal space at sternal border.
- Tricuspid area—right third to fifth intercostal space near costochondral junction.

Cats

- Mitral area—left fifth to sixth intercostal space one-fourth ventrodorsal distance from sternum.
- Aortic area—left second to third intercostal space just above the pulmonic area.
- Pulmonic area—left second to third intercostal space one-third to one-half ventrodorsal distance from sternum.

- Tricuspid area—right fourth to fifth intercostal space one-fourth ventrodorsal distance from sternum.

PATHOPHYSIOLOGY

- Disturbed blood flow associated with high flow through normal or abnormal valves or with structures vibrating in the blood flow.
- Flow disturbances associated with outflow obstruction or forward flow through stenosed valves or into a dilated great vessel.
- Flow disturbances associated with regurgitant flow through an incompetent valve, septal defect, or patent ductus arteriosus.

SYSTEMS AFFECTED

Cardiovascular

SIGNALMENT

Dog and cat

SIGNS

Relate to cause of the murmur

CAUSES

Systolic Murmurs

- Mitral and tricuspid valve endocardiosis
- Cardiomyopathy and AV valve insufficiency
- Physiologic flow murmurs
- Anemia
- Mitral and tricuspid valve dysplasia
- Systolic anterior mitral motion
- Dynamic right ventricular outflow obstruction
- Dynamic subaortic stenosis
- Atrial septal defect
- Ventricular septal defect
- Pulmonic stenosis
- Aortic stenosis
- Tetralogy of Fallot
- Mitral and tricuspid valve endocarditis
- Hyperthyroidism
- Heartworm disease

Continuous or To-and-Fro Murmurs

- Patent ductus arteriosus
- Ventricular septal defect with aortic regurgitation
- Aortic stenosis with aortic regurgitation

Diastolic Murmurs

- Mitral and tricuspid valve stenosis
- Aortic and pulmonic valve endocarditis

RISK FACTORS

Cardiac disease



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differential Signs

- Must differentiate from other abnormal heart sounds—split sounds, ejection sounds, gallop rhythms, and clicks.
- Must differentiate from abnormal lung sounds and pleural rubs; listen to see if timing of abnormal sound is correlated with respiration or heartbeat.

Differential Causes

- Pale mucous membranes support diagnosis of anemic murmur.
- Location and radiation of murmur and timing during cardiac cycle can help determine cause; see algorithm.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia in animals with anemic murmurs
- Polycythemia in animals with right-to-left shunting congenital defects
- Leukocytosis with left-shift in animals with endocarditis

OTHER LABORATORY TESTS

N/A

IMAGING

- Thoracic radiography—useful for evaluating heart size and pulmonary vasculature in hopes of determining cause and significance of murmur.
- Echocardiography—recommended when a cardiac cause is suspected and the nature of the defect is unknown.
- Doppler studies sometimes required to confirm cause of murmur.

DIAGNOSTIC PROCEDURES

- Electrocardiography may be useful in assessing heart enlargement patterns in animals with murmurs.
- Blood cultures and serology for *Bartonella* if suspect endocarditis.

M



TREATMENT

- Outpatient unless heart failure is evident.
- Base decisions on the cause of the murmur and associated clinical signs.
- None indicated for murmur alone.



MEDICATIONS

DRUG(S)

N/A

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

Low-grade systolic ejection murmurs in puppies may be physiologic; most resolve by 6 months of age. If murmur still present after 6 months, include diagnostic imaging.

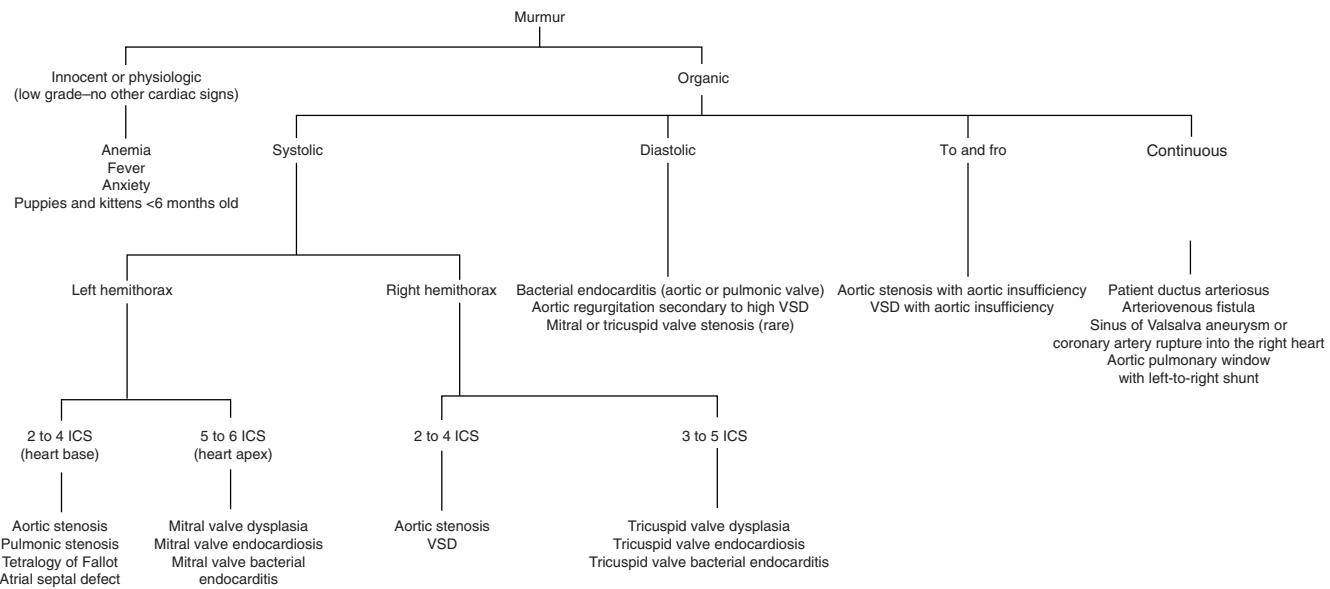


Figure 1.

POSSIBLE COMPLICATIONS

If murmur is associated with structural heart disease, may see signs of congestive heart failure (e.g., coughing, dyspnea, and ascites) or exercise intolerance.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

- Murmurs present since birth generally associated with a congenital defect or physiologic flow murmur.
 - Acquired murmurs in geriatric, small-breed dogs usually associated with degenerative valve disease.

- Acquired murmurs in large-breed dogs usually associated with dilated cardiomyopathy.
 - Acquired murmurs in geriatric cats usually associated with cardiomyopathy or hyperthyroidism.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Murmurs in puppies and kittens may reflect a congenital defect and thereby influence decisions on breeding that animal or repeating the mating.

SEE ALSO

See “Causes”

ABBREVIATIONS

- AV = atrioventricular
 - PMI = point of maximal intensity

- S1 = first heart sound
 - S2 = second heart sound
 - VSD = ventricular septal defect

Suggested Reading

Gompf RE. The history and physical examination. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., Manual of Canine and Feline Cardiology, 5th ed. St. Louis, MO: Saunders Elsevier, 2015 (in press).

(in press).
Keene B, Smith FWK, Tilley LP, Hansen B. Rapid Interpretation of Heart Sounds, Murmurs, Arrhythmias, and Lung Sounds: A Guide to Cardiac Auscultation in Dogs and Cats, 3rd ed. CD-ROM and Manual. Philadelphia: Elsevier, 2015.

Author Francis W.K. Smith, Jr.

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MUSCLE RUPTURE (MUSCLE TEAR)



BASICS

OVERVIEW

A normal muscle may be stretched, pinched, or injured directly, resulting in fiber disruption, weakening, and immediate or delayed separation of the uninjured portions. Alternatively, the muscle structure may be compromised by systemic or iatrogenic conditions, and normal activity may cause muscle disruption. The rupture may be complete or incomplete, and it may be mid-substance or at the muscle-tendon junction. The acute stage is characterized by a typical inflammatory reaction that becomes chronic with collagen maturation, cross-linking, fibrosis, and adhesion development over time. Frequently the acute phase is overlooked, as the signs may be temporary and respond well to rest. The chronic effects are often progressive and unresponsive to support therapies.

SIGNALMENT

- Limb and masticatory muscles are the primary structures affected.
- Traumatic injury is indiscriminate, although certain activities may predispose because of exposure.
- The ruptures that are apparently unrelated to trauma seem to affect middle-aged to older working dogs, with no reported sex predilection.
- Cats are affected less frequently than dogs.

SIGNS

Acute Injury

- Immediate lameness that is characterized by the specific muscle affected.
- Localized swelling, heat, and pain.
- Generally present for a few days to a week.
- Animals may experience re-injury.

Chronic Phase (If It Develops)

- Progressive.
- Painless.
- Usually associated with scar tissue that impedes normal function of an extremity.

CAUSES & RISK FACTORS

- Trauma
- Repeated overuse
- Overextension
- Myositis
- Degenerative (unknown etiology)
- Myopathy secondary to medical conditions such as Cushing disease
- Apparent risk factor for dogs is involvement in hunting, tracking, or similar activities in the outdoors.

Gait Analysis and Physical Examination Findings

- Various disorders will result in characteristic gait abnormalities and pain elicited on specific limb manipulation—a few of which are listed below.

- Psoas muscle injury:
 - Pain on internal rotation with extension or abduction of the pelvic limb.
 - Pain on palpation of the lesser trochanter of the affected femur.
 - Short, choppy gait.
- Gracilis, semimembranosus, and semitendinosus muscle contractures:
 - These animals are typically not painful on palpation of the gracilis, semitendinosus or semimembranosus muscles.
 - Palpation of a fibrous band in the area of the affected muscle is also apparent.
 - Shortened stride with medial rotation of the paw, internal rotation of the hock, and external rotation of the calcaneus, with internal rotation of the stifle in late phase of the forward stride.
- Infraspinatus muscle contracture:
 - Significant forelimb lameness with circumduction of the affected limb.
 - Marked elbow adduction/foot abduction; upon flexion of the elbow, the distal antebrachium will deviate laterally.
 - Fibrous band will be apparent on palpation of the infraspinatus muscle.
- Quadriceps contracture:
 - Typically occurs with limb disuse/immobilization after femur fracture fixation in young dogs without appropriate physical therapy.
 - Patient will be unable to flex stifle.
- Achilles mechanism injuries:
 - Non-weight-bearing lameness with soft tissue swelling proximal to the calcaneous.
 - Hyperflexion of the tarsus.
 - Hyperflexion of the digits, if superficial digital flexor is unaffected (crab claw).
- Sartorius muscle injury/fibrosis:
 - Scant reports in the veterinary literature.
 - Non-painful, non-weight-bearing pelvic limb.
 - Palpable fibrous band in the area of the sartorius muscle.
 - Short choppy gait, characterized by an inability to extend the hip.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Neurologic dysfunction—recognized by neurologic abnormalities.
- Tendon rupture—visible or palpable disruption in the tendon.
- Origin/insertion avulsion fracture—radiographic evidence of bone fragment defect and translocation.

- Luxation/subluxation—palpable or radiographic evidence of joint instability or malalignment.

CBC/BIOCHEMISTRY/URINALYSIS

No injury-specific findings

OTHER LABORATORY TESTS

- CPK may be elevated in acute cases.
- No known specific tests available.

IMAGING

Radiographic Findings

- Soft tissue swelling may be evident in the early stages.
- Calcification of muscle can occur in the traumatized area in chronic situations.
- Avulsion fractures and calcification of the tendon of insertion or origin may be noted on radiographs.

Ultrasonographic Findings

- Local swelling and disorientation of the normal muscle fiber orientation may be seen at the site of injury in acute cases.
- Scar tissue and contracted areas of fibrous tissue can be seen in the muscle in chronic cases—noted as hyperechoic foci in the muscle belly of concern.
- Measurable differences between normal and abnormal sides may be useful in documenting the affected muscle site.

Cross-Sectional Imaging Studies

- CT findings—produces better tissue contrast than the above but still constrained to an axial plane of view.
- MRI findings—edema and hemorrhage cause a change in the signal that can be differentiated from changes due to fibrous tissue replacement of muscle. This allows localization of the problem and helps to identify the type of problem.

DIAGNOSTIC PROCEDURES

Muscle Biopsy

The presence of fibrous tissue and the loss of muscle cells may be documented. Differentiating disuse atrophy from neurologic atrophy and from injury-induced fibrosis may be impossible without corroborating evidence.



TREATMENT

- There is no documented evidence to support a single “best” way to treat acute muscle injuries, preventing fibrous contracture and adhesions. It is generally believed that immediate post-injury care should involve rest, local cold application followed within hours (24–48 hours) by heat, and passive physical therapy (movement). Severe, strict immobilization (via cast or cage) is potentially contraindicated as it may encourage muscle contracture and muscle fibrosis, leading to irreversible long-term debilitation. Light or non-weight-bearing activity is appropriate for

MUSCLE RUPTURE (MUSCLE TEAR)

(CONTINUED)

an extended period of time (4–6 weeks). Analgesics and anti-inflammatory drugs should be recommended for several days to weeks. Surgery may be performed within a few days of the injury to repair obvious, acute muscle rupture that results in a separation of the uninjured muscle segments. An essential part of muscle repair is effective tension relief for the injured muscle so that healing can occur without disruption as function returns. Internal or external orthopedic devices may be necessary to provide effective tension relief. Owners should be made aware of the possibility of scar-related problems affecting the patient's gait in the long-term.

- Once the muscle injury becomes chronic and associated with contracture or adhesions, treatment is aimed at function salvage. Surgical release of the adhesions or fibrous tissue bands is often accompanied by instantaneous symptomatic relief. The prevention of readhesion and progressive contracture is much less rewarding.
- Specific muscle injuries have widely disparate prognoses. Infraspinatus and psoas muscle contractures respond well to surgical excision of the tendon of insertion. Gracilis, semimembranosus, and semitendinosus contractures have a 100% recurrence rate after surgical resection. Quadriceps contracture has a similarly dismal failure rate after surgery.
- Muscle injuries that have healed in an elongated state have a better prognosis for surgical improvement of function than contracted muscles. The most common

elongation injury affects the muscles of the calcaneus (Achilles) group. Hock hyperflexion can be surgically reconstructed to return these animals to relatively normal function. This is usually accomplished by shortening the Achilles tendon rather than the injured muscle or musculotendinous junction.



MEDICATIONS

DRUG(S)

None are specific. Anti-inflammatory drugs may be indicated in acute situations.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Immobilization of the injured muscle in a position that allows adhesions to develop to nearby bone will often result in "tie down" contractures.



FOLLOW-UP

PATIENT MONITORING

Repetitive range-of-motion monitoring and recheck examination.

PREVENTION/AVOIDANCE

Early inflammation control and non-weight-bearing passive physical therapy accompanied by strict cage rest may be beneficial.

POSSIBLE COMPLICATIONS

Contracture of the muscle and fibrous replacement of muscle tissue.

EXPECTED COURSE AND PROGNOSIS

Specific to the muscle and the type of injury.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Joint hypermobility, angular limb deformities, flexion/extension joint abnormalities.

AGE-RELATED FACTORS

Growth plate fractures in young dogs, particularly distal femoral Salter-Harris fractures, are associated with quadriceps contracture.

ABBREVIATIONS

- CPK = creatine phosphokinase
- CT = computed tomography
- MRI = magnetic resonance imaging

Suggested Reading

Vaughan LC. Muscle and tendon injuries in dogs. J Small Anim Pract 1979, 20:711–736.

Authors Mathieu M. Glassman and Michael Weh

Consulting Editor Walter C. Renberg

MUSHROOM TOXICOSES

**BASICS****DEFINITION**

- Eight categories on basis of toxin and toxicodrome (Table 1).
- Mixed toxicodromes can occur if mixture of species consumed.

PATHOPHYSIOLOGY

See Table 2

SYSTEMS AFFECTED

See Table 3

INCIDENCE/PREVALENCE

- Cyclopeptide and gastrointestinal groups—common
- Others—occasional

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT**Species**

Dogs; others rarely

Mean Age and Range

All ages

SIGNS**General Comments**

- Psychoactive species often dried for transportation and sale; dried product remains toxic for at least 6 months.
- Psychoactive species often prepared as aqueous extracts.
- Psychoactive species often coated with chocolate to facilitate ingestion (counters the astringent taste) and smuggling; combined mushroom and chocolate toxicity may occur.
- Psychoactive species often given as holiday presents.
- In many parts of the world psychoactive species are sold openly.

Historical Findings

- Many cases involve substance abuse.

Physical Examination Findings

See Table 4

Cyclopeptide

- Three sequential disease phases—GI, latent, and hepatorenal.
- Delayed onset of GI phase and the recrudescence of hepatorenal disease following a latent period are key diagnostic features. With the exception of MMH, all other types of mushroom poisoning occur relatively rapidly and usually resolve relatively

quickly. Recrudescence characterized by hepatorenal disease does not occur in MMH poisoning.

- Gastroenteritis phase (onset > 6 hours; lasts about 24 hours)—severe vomiting, bloody diarrhea, abdominal pain, fever, dehydration, electrolyte disturbance, hypoglycemia.
- Latent phase (lasts 12–24 hours)—apparent remission.
- Hepatorenal phase (starts 3–4 days post-ingestion)—liver and kidney failure, icterus, depression, signs of hepatic encephalopathy and cerebral edema, hypoglycemia, seizures, coagulopathies, metabolic acidosis, renal insufficiency, severe ileus, cardiac conduction abnormalities, coma.
- High morbidity and mortality; death during the hepatorenal phase (3–7 days post-ingestion).

MMH (Gyrometrin)

- Gastroenteritis (onset > 6 h)—vomiting, bloody diarrhea, abdominal pain, fever, dehydration, electrolyte disturbance, hypoglycemia.
- Ataxia
- Anxiety, hyperactivity, tremor, seizure
- Typically self-limiting; resolving over several days
- In rare severe cases, hepatic failure may develop

Table 1

<i>Group</i>	<i>Key Species</i>
Cyclopeptide	<i>Amanita phalloides</i> , many <i>Amanita</i> sp., <i>Galerina</i> sp.
Monomethyl hydrazine (MMH)	<i>A. muscaria</i> (fly agaric), <i>A. pantherina</i> (panther cap), <i>Gyromitra</i> sp., <i>Lycoperdon</i> sp.
Muscarine	<i>Clitocybe</i> sp., <i>Inocybe</i> sp., <i>A. pantherina</i>
Ibotenic acid/muscimol	<i>Coprinus atramentarius</i> , <i>A. pantherina</i> , <i>A. muscaria</i>
Hallucinogens	<i>Psilocybe</i> sp., <i>Panaeolus</i> sp., <i>Gymnopilus</i> sp., <i>Stropharia</i> sp., <i>Conocybe</i> sp.
GI irritants	<i>Chlorophyllum</i> sp., many others
Acute renal failure	<i>Cortinarius</i> sp.

Table 2

<i>Group</i>	<i>Mechanism</i>
Cyclopeptide	Amatoxins inhibit RNA polymerase II blocking RNA and DNA transcription. Targets are exposed rapidly, dividing cells (intestinal crypt epithelium, hepatocytes, and renal tubular epithelia)
MMH	Phallotoxin irreversibly polymerizes actin filaments in the hepatobiliary tree, resulting in cholestasis
Muscarine	Gyromitrin hydrolyses to MMH, which causes ↓ CNS GABA
Ibotenic acid/muscimol	Post-ganglionic M ₁ and M ₂ cholinergic agonist
Hallucinogens	Ibotenic acid, a glutamate agonist, is rapidly metabolized to muscimol, a GABA-B agonist
GI irritants	Psilocybin metabolized to psilocin, a 5-HT _{1A} and 5-HT _{2A/2C} serotonin agonist
Acute renal failure (orellanine)	Irritants, allergens
	Toxins are 2,2-bipyridine and compounds resembling paraquat and diquat—redox cycling is likely mechanism

MUSHROOM TOXICOSES

(CONTINUED)

Table 3

<i>Group</i>	<i>Target</i>
Cyclopeptide	Gastrointestinal—severe gastroenteritis 6–24 h post-ingestion Hepatobiliary—delayed-onset (3–4 d) centrilobular hepatic necrosis Renal—delayed onset (3–4 d) acute renal tubular nephrosis Metabolic—hypoglycemia Hemic—coagulopathy Immune—prone to sepsis
MMH	Nervous—cerebral edema, hepatorenal encephalopathy, coma Gastrointestinal—vomiting/diarrhea 6–8 hrs post-ingestion Nervous—CNS excitation, seizure Neuromuscular—ataxia, tremor
Muscarine	Hepatobiliary—hepatitis and failure (rare) Gastrointestinal—diarrhea, emesis, excessive lacrimation Urinary—frequent urination Ophthalmic—miosis, cycloplegia Respiratory—bronchospasm, bronchoconstriction Cardiovascular—bradycardia, hypotension
Ibotenic acid/muscimol	Nervous—cycles of CNS stimulation followed by depression, visual hallucinations, confusion, agitation, aggression, pointless motor activity, seizure, coma, sympathomimetic signs Ophthalmic—mydriasis Metabolic—hyperthermia
Hallucinogens	Nervous—dysphoria, anxiety, confusion, agitation, aggression, pointless motor activity, seizure, coma, sympathomimetic signs Neuromuscular—ataxia, hyperreflexia
GI irritants	Gastrointestinal—emesis, diarrhea
Acute renal failure (orellanine)	Renal—delayed-onset (up to 20 d) tubulointerstitial nephrosis

M**Table 4**

<i>Group</i>	<i>Common DDx</i>
Cyclopeptide	GI phase— <i>infectious gastroenteritis, GI irritants and corrosives</i> Hepatorenal phase—white phosphorus, hepatotoxic mycotoxins and hepatotoxic algal toxins, hepatotoxic plants
MMH/Gyrometrin	GABA antagonists, CNS stimulants, seizure agents, isoniazid
Muscarine	Anticholinesterase pesticides, cholinergic medications and toxins
Ibotenic acid/muscimol	Other hallucinogens, stimulants, head injury, CNS infection
Hallucinogens	LSD and other hallucinogens, head injury, CNS infection
GI irritants	<i>Infectious gastroenteritis, GI irritants and corrosives</i>
Acute renal failure (orellanine)	Ethylene glycol, diquat, plants affecting the kidneys

Muscarine

- Rapid onset (15–60 minutes) • Generally resolves in 2–6 hours (max 24 hours)
- DUMBELS—diarrhea, urination, miosis, bronchospasm, bronchoconstriction, emesis, lacrimation, salivation • Rarely, liver damage

Ibotenic Acid/Muscimol

- Rapid onset (30–60 minutes) • Initial CNS stimulation, ataxia, hyperactivity, pointless running, manic excitement, seizure, visual hallucinations (“biting at imaginary flies”)

- Subsequent CNS depression—drowsiness, stupor, sleep coma • Periods of CNS excitement alternating with CNS depression
- Death is rare • GI disturbance NOT a feature

Hallucinogens

- Onset within 4 hours • Sympathomimetic signs • Dysphoria, agitation, anxiety, aggression • Hyperthermia • Rarely—convulsions, coma, death • GI disturbance NOT a feature

GI Irritants

- Onset within 2 hours • Malaise, weakness, emesis, diarrhea • Fluid and electrolyte disturbances • Usually self-limiting; resolves in 24 hours

CAUSES

See Tables 2 and 3

RISK FACTORS

- Inexperience in harvesting wild mushrooms
- Owner substance abuse
- Cultivation/trafficking of hallucinogenic species • Mushroom picking season

(CONTINUED)

MUSHROOM TOXICOSES**Table 5**

<i>Group</i>	<i>Effects</i>
Cyclopeptide	GI phase—hemococoncentration, electrolyte disturbances, GI blood loss Hepatorenal failure—enzymatic evidence of hepatocellular necrosis and cholestasis, elevated serum and urine bilirubin, elevated serum bile acids, uremia, electrolyte disturbances, initial polyuria followed by isosthenuria or anuria, hypoglycemia, coagulopathies, urinary casts, evidence of sepsis
MMH	Nonspecific; evidence of oxidative injury to erythrocytes (methemoglobinemia, ↑ free hemoglobin, ↑ sulfhemoglobin) may be present in early stages
Muscarine	Nonspecific; rarely enzymatic evidence of hepatocellular injury
Ibotenic acid/muscimol	Nonspecific
Hallucinogens	Nonspecific
GI irritants	Hemococoncentration, electrolyte disturbances
Acute renal failure (orellanine)	Initial polyuria followed by isosthenuria or anuria, electrolyte disturbance (notably hyperkalemia), uremia

Table 6

<i>Group</i>	<i>Other Tests</i>
Cyclopeptide	Expert identification of mushroom species; Meixner test for amatoxins (false negatives may occur); amanitin measurement in body fluids
MMH	Expert identification of mushroom species; blood level not well correlated with severity; detection in stomach contents, mushrooms
Muscarine	Expert identification of mushroom species; detection in body fluids, stomach contents, mushrooms
Ibotenic acid/muscimol	Expert identification of mushroom species; detection in body fluids, stomach contents, mushrooms
Hallucinogens	Expert identification of mushroom species; detection in body fluids, stomach contents, mushrooms
GI irritants	Expert identification of mushroom species
Acute renal failure	Expert identification of mushroom species; detection of orallanine in body fluids, feces, stomach contents, mushrooms

M

Table 7

<i>Group</i>	<i>Target</i>
Cyclopeptide	None proven effective Thioctic acid (1–2 mg/kg q6h) credited with xyxy↓ human mortality Silibinin (50 mg/kg/day q6h); combine with n-acetylcysteine Penicillin theoretically beneficial, but limited practical effectiveness
MMH	Pyridoxine 25 mg/kg
Muscarine	Atropine to effect (endpoint is drying of secretions)
Ibotenic acid/muscimol	N/A
Hallucinogens	N/A
GI irritants	N/A
Acute renal failure (orellanine)	N/A

MUSHROOM TOXICOSES

(CONTINUED)

Table 8

<i>Group</i>	<i>Target</i>
Cyclopeptide	IV glucose or dextrose if required Fresh frozen plasma Blood transfusion Vitamin K (Vitamin K ₁)—0.5–1.5 mg/kg IM or SC q12h up to 3 doses in 24-hour interval 1 time; oral vitamin K ₁ —1 mg/kg PO q24h if enteric bile acids and their uptake are adequate Potassium if hypokalemia of hepatic failure present Furosemide 2–4 mg/kg IV q8–12h; for oliguric or anuric renal failure in patients with normal hydration status; combine with dopamine Dopamine 0.5–3 microgram/kg for oliguric or anuric renal failure; combine with furosemide Parenteral silymarin derivatives reputedly beneficial
MMH	Diazepam 0.25–0.5 mg/kg IV or IM; for seizures
Muscarine	Atropine to effect (drying of secretions; 0.02–0.04 mg/kg half-dose IV, half-dose IM; titrate to effect)
Ibotenic acid/muscimol	Diazepam 0.25–0.5 mg/kg IV or IM; for seizures
Hallucinogens	Diazepam 0.25–0.5 mg/kg IV or IM; for seizures
GI irritants	N/A
Acute renal failure (orellanine)	Furosemide 2–4 mg/kg IV q8–12h; for oliguric or anuric renal failure in patients with normal hydration status; combine with dopamine Dopamine 0.5–3 microgram/kg for oliguric or anuric renal failure; combine with furosemide

M**DIAGNOSIS**

- DIFFERENTIAL DIAGNOSIS
 - CBC/BIOCHEMISTRY/URINALYSIS
 - OTHER LABORATORY TESTS
 - DIAGNOSTIC PROCEDURES
- See Tables 5 and 6

**TREATMENT****APPROPRIATE HEALTH CARE**

- Inpatient medical management.
- Intensive care for cyclopeptides.
- No early discharge until cyclopeptide poisoning has been disproved.

NURSING CARE

- Upper GI decontamination (preferably induction of emesis using apomorphine 0.04 mg/kg IV or into the conjunctival sac; or gastric lavage) is warranted in the case of confirmed cyclopeptide poisoning provided:

 - (1) patient presents within 2 hours of ingestion;
 - (2) emesis has not already occurred;
 - (3) contraindications (CNS excitation, preexisting cardiovascular disease) are not present. Benefits of the technique are at best unproven and at worst, useless.

- Repeat-dose activated charcoal administration (1–4 g/kg q3–6h for 24–36h; mix in water (1 g/5–10 mL water) aimed at decreasing toxin enterohepatic cycling is of potential, but unproven, benefit in cyclopeptide poisoning.
- Single-dose activated charcoal administration within 2 hours of ingestion is possible, but unproven, benefit in other types

of mushroom poisoning in the absence of contraindications.

- Fluid resuscitation (IV crystalloids) as required.

ACTIVITY

Prevent misadventure

DIET

NPO if GI distress

CLIENT EDUCATION

"There are old mushroom hunters, there are bold mushroom hunters, but there are no old and bold mushroom hunters."

**MEDICATIONS****DRUG(S) OF CHOICE**

- Antidotes: See Table 7
- Supportive: See Table 8

CONTRAINDICATIONS

- MMH poisoning—short-acting hypnotics
- Ibotenic acid/muscimol—atropine, propofol

ALTERNATIVE DRUG(S)

Methocarbamol 55–220 mg/kg IV, do not exceed 330 mg/kg/day; administer half dose quickly and then remainder to effect; for control of seizures.

**FOLLOW-UP****PATIENT MONITORING**

- Cyclopeptides—serum hepatic enzymes, serum bilirubin, serum bile acids
- Serum electrolyte status
- CNS state

- Orellanine—serum BUN and creatinine, serum electrolytes.

EXPECTED COURSE AND PROGNOSIS

- Cyclopeptides and orellanine—very poor
- Others—generally good unless organ damage present

**MISCELLANEOUS****SEE ALSO**

- Hepatic Failure, Acute
- Renal Failure, Acute
- Seizures (Convulsions, Status Epilepticus)—Cats
- Seizures (Convulsions, Status Epilepticus)—Dogs

ABBREVIATIONS

- CNS = central nervous system
- GABA = gamma-aminobutyric acid
- GI = gastrointestinal
- MMH = monomethylhydrazine

Suggested Reading

Judge BS, Ammirati JF, Lincoff GH, et al. Ingestion of a newly described North American mushroom species from Michigan resulting in chronic renal failure: *Cortinarius orellanos*. Clin Toxicol 2010, 48(6):545–549.

Rumack BH, Spoerke DG. Handbook of Mushroom Poisoning: Diagnosis and Treatment. New York: CRC Press, 1994.

Schonwald S. Mycotoxins and toxicogenic fungi. In: Dart RC, ed., Medical Toxicology, 3rd ed. Baltimore, MD: Lippincott, Williams & Wilkins, 2004, pp. 1719–1735.

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MYASTHENIA GRAVIS



BASICS

DEFINITION

A disorder of neuromuscular transmission characterized by muscular weakness and excessive fatigability.

PATOPHYSIOLOGY

Transmission failure at the neuromuscular junction—results from structural or functional abnormalities of the nicotinic AChRs or other end-plate proteins and enzymes (congenital form) and from autoantibody-mediated destruction of AChRs and postsynaptic membranes (acquired form).

SYSTEMS AFFECTED

- Neuromuscular—result of abnormalities or destruction of AChRs, choline acetyltransferase or end-plate cholinesterase.
- Respiratory—may find aspiration pneumonia secondary to megaesophagus.

GENETICS

- Congenital familial forms—Jack Russell terrier, springer spaniel, smooth fox terrier; smooth-haired miniature dachshund, Gammel Dansk Hønsehund, Labrador retriever; autosomal recessive mode of inheritance.
- Acquired—as with other autoimmune diseases, requires appropriate genetic background for disease to occur; multifactorial, involving environmental, infectious, and hormonal influences.
- Familial forms of acquired MG occur in the Newfoundland and Great Dane breeds.

INCIDENCE/PREVALENCE

- Congenital—rare
- Acquired—not uncommon in dogs; uncommon in cats

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Congenital—Jack Russell terriers; springer spaniels; smooth fox terriers; smooth-haired miniature dachshunds, Gammel Dansk Hønsehund. Labrador retriever.
- Acquired—several breeds: golden retrievers; German shepherds; Labrador retrievers; dachshunds; Scottish terriers; Akitas; and Abyssinian and Somali cats.

Mean Age and Range

- Congenital—6–8 weeks of age.
- Acquired—bimodal age of onset; dogs: 1–4 years of age and 9–13 years of age.

Predominant Sex

- Congenital—none.
- Acquired—may be a slight predilection for females in the young age group; none in the old age group.

SIGNS

General Comments

- Acquired—may have several clinical presentations ranging from focal involvement of the esophageal, pharyngeal, and extraocular muscles to acute generalized collapse.
- Should be on the differential diagnosis of any dog with acquired megaesophagus, lower motor neuron weakness, or a cranial mediastinal mass.

Historical Findings

- Regurgitation—common; important to differentiate between vomiting and regurgitation.
- Voice change.
- Exercise-related weakness.
- Acute collapse.
- Progressive weakness.
- Sleep with eyes open.

Physical Examination Findings

- Patient may look normal at rest.
- Excessive drooling, regurgitation, and repeated attempts at swallowing.
- Muscle atrophy—usually not found.
- Dyspnea—with aspiration pneumonia.
- Fatigue or cramping—with mild exercise.
- Careful neurologic examination—subtle findings: decreased or absent palpebral reflex (may be fatigable); may note a poor or absent gag reflex; spinal reflexes usually normal but fatigable (rarely absent and dog unable to support its weight).
- Ventroflexion of the neck (cats, uncommon in dogs).

CAUSES

- Congenital
- Immune-mediated
- Paraneoplastic

RISK FACTORS

- Appropriate genetic background
- Neoplasia—particularly thymoma
- Methimazole treatment (cats)—may result in reversible disease
- Vaccination can exacerbate active MG
- Intact female



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other disorders of neuromuscular transmission—tick paralysis; botulism; cholinesterase toxicity.
- Acute or chronic polyneuropathies.
- Polymyopathies—including polymyositis.
- Diagnosis depends upon a careful history, thorough physical and neurologic examinations, and specialized laboratory testing.

CBC/BIOCHEMISTRY/URINALYSIS

- Normal.
- Serum creatine kinase activity—usually normal; may be elevated if MG is associated with polymyositis and concurrent thymoma.

OTHER LABORATORY TESTS

- Serum AChR antibody titer—diagnostic for acquired form.
- Thyroid and adrenal function—may see abnormalities associated with acquired form.

IMAGING

Thoracic radiographs—megaesophagus; cranial mediastinal mass, aspiration pneumonia.

DIAGNOSTIC PROCEDURES

- Ultrasound-guided biopsy of cranial mediastinal mass—may support diagnosis of thymoma.
- Dramatic increase in muscle strength after administration of edrophonium chloride (0.1 mg/kg IV)—may see false-negative and false-positive responses.
- Decreased or absent palpebral reflex—may return after edrophonium chloride administration.
- Electrophysiologic evaluation—necessity questionable with increased availability of AChR antibody testing; many patients with acquired form are poor anesthetic risks.
- Electrocardiogram—with bradycardia; third-degree heart block has been documented in some patients with acquired disease.

PATHOLOGIC FINDINGS

Biopsy of a cranial mediastinal mass may reveal thymoma, thymic hyperplasia, or thymic atrophy.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—until adequate dosages of anticholinesterase drugs are achieved.
- Aspiration pneumonia—may require intensive care
- Gastrostomy tube—may be required if patient is unable to eat or drink without significant regurgitation.

NURSING CARE

- Oxygen therapy, intensive antibiotic therapy, intravenous fluid therapy, and supportive care—generally required for aspiration pneumonia.
- Nutritional maintenance with a gastrostomy tube—multiple feedings of a high-caloric diet; good hygiene care.
- Elevation of food and water.

ACTIVITY

Self-limited owing to the severity of muscle weakness and extent of aspiration pneumonia.

DIET

May try different consistencies of food—gruel; hard food; soft food; evaluate what is best tolerated.

CLIENT EDUCATION

- Warn client that, although the acquired disease is treatable, most patients require months of special feeding and medication.

MYASTHENIA GRAVIS

(CONTINUED)

- Inform client that a dedicated owner is important to a favorable outcome for acquired myasthenia.
- Prognosis is poor for congenital myasthenic syndrome.

SURGICAL CONSIDERATIONS

- Cranial mediastinal mass—thymoma.
- Before attempting surgical removal, stabilize patient with anticholinesterase drugs and treat aspiration pneumonia.
- Weakness may not be clinically evident initially.
- Suspected thymoma—test all patients for acquired MG before surgery.



MEDICATIONS

DRUG(S) OF CHOICE

- Anticholinesterase drugs—prolong the action of acetylcholine at the neuromuscular junction; pyridostigmine bromide tablets or syrup (Mestinon syrup, diluted half and half in water) at 1–3 mg/kg PO q8–12h.
- Corticosteroids 0.5 mg/kg q24h; initiated if there is a poor response to pyridostigmine or if there is no response to the edrophonium chloride challenge.

M

CONTRAINDICATIONS

Avoid drugs that may reduce the safety margin of neuromuscular transmission—aminoglycoside antibiotics; antiarrhythmic agents; phenothiazines; anesthetics; narcotics; muscle relaxants; magnesium.

PRECAUTIONS

- Avoid large volumes of barium for evaluating megaesophagus.
- Large air-filled esophagus seen on survey radiographs—barium study not indicated.
- Avoid immunosuppressive dosages of prednisone—may worsen muscle weakness.
- Avoid unnecessary vaccinations.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

- Azathioprine 2 mg/kg PO through gastrostomy tube q24h. Taper to q48h when clinical remission of the disease.

- Mycophenolate 20 mg/kg PO q12h. Reduce dosage by 50% once significant improvement or resolution of clinical signs is noted.



FOLLOW-UP

PATIENT MONITORING

- Return of muscle strength should be evident.
- Thoracic radiographs—evaluated every 4–6 weeks for resolution of megaesophagus.
- AChR antibody titers—evaluated every 8–12 weeks; decrease to the normal range with immune remission.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Aspiration pneumonia
- Respiratory arrest

EXPECTED COURSE AND PROGNOSIS

- No severe aspiration pneumonia or pharyngeal weakness—good prognosis for complete recovery; resolution usually within 6–8 months.
- Thymoma present—guarded prognosis unless complete surgical removal and control of myasthenic signs are achieved.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Other autoimmune disorders—thyroiditis; skin disorders; hypoadrenocorticism, thrombocytopenia, hemolytic anemia, inflammatory bowel disease.
- Disorders of the thymus—thymoma; thymic hyperplasia.
- Other neoplasias.

AGE-RELATED FACTORS

Bimodal age of onset—1–4 years of age and 9–13 years of age.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

- Humans—weakness may improve during pregnancy but worsens after delivery; some neonates of affected mothers have a temporary myasthenia gravis-like weakness that lasts several days to weeks that is due to *in utero* transfer of autoantibodies from the mother.
- Documented in dogs after whelping.

SEE ALSO

- Chapters covering autoimmune diseases
- Megaesophagus

ABBREVIATIONS

- AChR = acetylcholine receptor
- MG = myasthenia gravis

INTERNET RESOURCES

Comparative Neuromuscular Laboratory:
<http://vetneuromuscular.ucsd.edu>.

Suggested Reading

Khorzad R, Whelan M, Sisson A, Shelton GD. Myasthenia gravis in dogs with an emphasis on treatment and critical care management. *Vet Emerg Crit Care* 2011, 21:193–208.

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Client Education Handout
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MYCOBACTERIAL INFECTIONS



BASICS

OVERVIEW

- Mycobacteria—gram-positive, acid-fast higher bacteria (genus *Mycobacterium*); obligate or sporadic pathogens in humans and animals.
- Tuberculosis—caused by *Mycobacterium tuberculosis* (humans), *M. bovis* (cattle, wild mammals), *M. microti* and *M. microtii*-like (voles); dogs and cats exposed to infected primary hosts sporadically infected; disseminated or multi-organ disease caused by obligate parasitic organism; rare in dogs and cats.
- Leprosy—*M. lepraeumurium* (from rodents) and two unnamed leprosy organisms (*M. visibilis* [provisional]).
- Cats—two syndromes: *M. lepraeumurium* (syndrome 1) affects young cats with localized nodular disease, especially limbs, with sparse to moderate numbers of acid-fast bacilli present in lesions; unnamed species with affinity to *M. malmoense* (syndrome 2) affects older cats with generalized skin lesions and large numbers of acid-fast bacilli in lesions.
- Dogs—canine leproid granuloma syndrome caused by unnamed and uncultured *Mycobacterium* spp. identified by DNA sequencing.
- Systemic or non-cutaneous infection with non-tuberculous mycobacteria—*M. chelonae-abscessus* group, *M. avium* complex, *M. fortuitum*, *M. genavense*, *M. kansasi*, *M. massiliense*, *M. simiae*, *M. smegmatis*, *M. thermoresistable*, *M. xenopi*; sporadic infections in dogs and cats; some patients with concurrent infections or immunosuppression or the result of traumatic tissue introduction of saprophytic organism; syndromes include pleuritis, granulomas, disseminated disease, neuritis, or bronchopneumonia.
- Cutaneous/subcutaneous infections due to rapidly growing mycobacteria (mycobacterial panniculitis). • Dogs and cats—caused by saprophytic mycobacteria *M. fortuitum* group, *M. chelonae-abscessus* group, *M. smegmatis* groups, *M. phlei*, *M. terrae* complex, *M. thermoresistable*, *M. ulcerans*.

SYSTEMS AFFECTED

- Respiratory
- Skin/Exocrine
- Determined by cause

SIGNALMENT

Tuberculosis

- Cats and dogs of any age.
- Basset hound and Siamese cat reported as most susceptible; evidence unclear (possible statistical aberration).

Feline Leprosy

Free-roaming cats and kittens; kittens and young adult cats in syndrome 1; older cats (average 9 years) in syndrome 2.

Canine Leproid Granuloma

Reported cases; mostly shorthaired outdoor-housed large-breed dogs, especially boxers and German shepherd dogs.

Systemic Non-tuberculous Mycobacteriosis

A sporadic disease that can affect dogs and cats of any age

Mycobacterial Panniculitis

Adult dogs and cats

SIGNS

Tuberculosis

- Correlated with the route of exposure.
- Major sites of involvement—opharyngeal lymph nodes, cutaneous and subcutaneous tissues of the head and extremities; pulmonary system; gastrointestinal system.
- Dogs—respiratory, especially coughing.
- Cats—from contaminated milk: weight loss, chronic diarrhea, and thickened intestines; from predation: cutaneous nodules, ulcers, and draining tracts.
- Most dogs and many cats—pharyngeal and cervical lymphadenopathy; unproductive vomiting, ptalism, or tonsillar abscess; lymph nodes are visible or firm, fixed, tender; may ulcerate and drain.
- Pyrexia.
- Depression.
- Anorexia and weight loss.
- Hypertrophic osteopathy or hypercalcemia.
- Disseminated disease—body cavity effusion; visceral masses; bone or joint lesions; dermal and subcutaneous masses and ulcers; lymphadenopathy and/or abscesses; CNS signs; sudden death.

Feline Leprosy

- Syndrome 1—initially nodules on limbs; progress rapidly, may ulcerate; aggressive clinical course; recurrence after surgical excision; widespread lesions develop in several weeks.
- Syndrome 2—initially skin nodules that do not ulcerate, progressive over months to years.
- Feline multisystemic granulomatous mycobacteriosis—diffuse cutaneous thickening and multiple organ involvement.

Canine Leproid Granuloma

- Well-circumscribed painless nodules (2 mm–5 cm) in dermis or subcutis; especially dorsal fold of pinnae and head, but may be anywhere on the body; large lesions ulcerate.
- No systemic signs of illness.

Systemic Non-tuberculous Mycobacteriosis

- Pulmonary and systemic infections with AM are rare in dogs, in which case the signs are as for TB.
- With *M. avium* infection, disease most often disseminated.

Mycobacterial Panniculitis

- Cutaneous—traumatic lesion that fails to heal with therapy; spreads locally in the subcutaneous tissue (panniculitis); original lesion enlarges, forming a deep ulcer that drains hemorrhagic exudate; surrounding tissue becomes firm; satellite pinpoint ulcerations open and drain.
- Wound dehiscence at surgery sites.

CAUSES & RISK FACTORS

Tuberculosis

- Source of exposure—always an infected typical host.
- Dogs—usually from an

infected person in the household

(*M. tuberculosis*); route is ingestion of expectorated infectious material; aerosol exposure; patients often found in urban areas with immigrants.

- Cats—classically exposed by drinking unpasteurized milk of infected cattle (*M. bovis*); much less common now; may be exposed by predation on infected small mammals (*M. bovis*, undefined tuberculosis species).

Feline Leprosy

- Syndrome 1: cases have been reported from temperate coastal areas and port cities; cool climate may facilitate growth of the organism in extremities.
- Syndrome 2: cases are from rural environments; old age or immune-incompetence may be risk factors but remain undefined; exposure to rodents postulated.

Canine Leproid Granuloma

- Associated with fly bites and may fluctuate seasonally; short coats may predispose
- Disease likely to be worldwide; most cases reported from Australia, Asia and Brazil
- In the US reported in California, Hawaii, and Florida.

Systemic Non-tuberculous Mycobacteriosis

- Patients are immunosuppressed or have concurrent systemic disease
- Exposure—routes of exposure in pulmonary and systemic disease are unknown.

Mycobacterial Panniculitis

- Infections usually have antecedent trauma or surgical wound; most patients are immunocompetent.
- Trauma and accidental inoculation of the subcutaneous fat results in infection; history of bite wound possible (subcutaneous disease).
- Fat animals are more at risk than lean ones.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Mycobacterial infections have different prognoses, treatments, and public health consequences but may initially have similar signs, especially cutaneous lesions.
- All manifestations: fungal and other actinomycotic infections should be considered.
- Panniculitis: nocardiosis can be clinically identical.

OTHER LABORATORY TESTS

Tuberculosis

Tuberculosis (dogs)—intradermal skin testing with PPD or BCG on inner pinna; may produce false-positive results owing to cross-reactions with non-tuberculous mycobacteria.

IMAGING

Radiography

- Thoracic, abdominal, or skeletal lesions—suggest granulomatous infectious disease

MYCOBACTERIAL INFECTIONS

(CONTINUED)

- No specific lesions for the mycobacterioses
- Pulmonary tuberculosis lesions—may become calcified or cavitated.

DIAGNOSTIC PROCEDURES

- Based on biopsy material from affected tissue. • Aspiration of purulent material from any site after disinfection of overlying skin may be used for microbiologic identification; ultrasound-guided aspiration techniques may be warranted. • Biopsy specimens—should be uncontaminated by surface bacteria; must incorporate the center of a granulomatous focus. • Smears from infected tissues—for detection with acid-fast carbolfuchsin or auramine-rhodanine fluorochromes; on routine staining, organisms are negatively stained, showing “ghosts” of bacilli within macrophages; swabs or aspirates of draining cutaneous lesions or lymph nodes, trans-tracheal wash; endoscopic brushings; rectal cytology; impressions taken at surgical biopsy; heat-fixed smears should be submitted with tissue for culture. • Culture—special media and techniques required; referral to specialized laboratories may be required for non-tuberculous organisms (*Mycobacterium Mycology Referral*, University of Texas Health Center at Tyler, Microbiology Section).
- PCR methodologies—useful for any of the mycobacterial infections using tissue specimens or fluids; for canine leproid granuloma and the two feline leprosy syndromes, primers are not commercially available, but can be used to identify the suspect organisms.

M



TREATMENT

TUBERCULOSIS

- Permission of health authorities should be obtained in cases of *Mycobacterium tuberculosis* infection and zoonotic potential should be considered. • Multiple agent chemotherapy with drugs used to treat human tuberculosis has been successful; *M. avium* complex infections are difficult to treat.

FELINE LEPROSY

- Before widespread dissemination, individual lesions may be excised with aggressive margins—possibly curative. • Surgical treatment should be preceded by systemic therapy.

CANINE LEPROID GRANULOMA

- Excision is curative; lesions often self-cure; antimicrobial therapy may assist healing.

SUBCUTANEOUS AND SYSTEMIC NON-TUBERCULOUS INFECTIONS

- Treatment should be based on organism identification and antibiotic sensitivity testing. • Multiple drug therapy is often warranted. • Aggressive surgical debulking may aid resolution; antimicrobial therapy pre- and intra-operatively is recommended.



MEDICATIONS

DRUG(S)

Tuberculosis

- Always use multi-drug oral therapy; never attempt single-drug therapy for any organism.
- Current recommendation—fluoroquinolones, clarithromycin, and rifampin for 6–9 months. • Enrofloxacin, orbifloxacin, marbofloxacin, moxifloxacin, and ciprofloxacin 5–15 mg/kg PO q24h.
- Rifampin 10–20 mg/kg PO q24h or divided q12h (maximum, 600 mg/day).
- Clarithromycin 5–10 mg/kg PO q24h.
- Isoniazid and rifampin—combinations have been used; little is known about use in cats; one report of treatment (cat) with isoniazid, rifampin, and dihydrostreptomycin for 3 months noted weight loss but successful outcome. • Isoniazid 10–20 mg/kg (up to 300 mg total) PO q24h. • Ethambutol 15 mg/kg PO q24h. • Pyrazinamide—instead of ethambutol; 15–40 mg/kg PO q24h.
- Dihydrostreptomycin 15 mg/kg IM q24h.

Feline Leprosy

- Rifampin 10–20 mg/kg q24h or divided q12h. • Clarithromycin as above.

Subcutaneous and Systemic Non-tuberculous Infections

- In vitro sensitivity testing may be used to choose chemotherapy. • Antibiotics reported to be effective against AM isolates are macrolide, trimethoprim-potentiated sulfonamide, tetracycline, aminoglycoside, and fluoroquinolone antibiotics. • Anti-TB drugs are not generally effective.
- Single-agent therapy not recommended due to poor long-term response; double-agent therapy recommended. • Fluoroquinolones, trimethoprim-potentiated sulfonamides, aminoglycosides, tetracyclines, and clarithromycin are useful for some isolates.
- Response may be predicted by which species is isolated, but long-term therapy should be based on sensitivity testing. • Treatment should be continued for 2–6 months.
- Relapses are common.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Traditional antituberculosis drugs—watch for adverse reactions; experience is limited, especially in cats.



FOLLOW-UP

PATIENT MONITORING

- Antituberculosis and antileprosy drugs—examine monthly; monitor for anorexia and weight loss. • Liver profile monthly. • Instruct owners to report cutaneous lesions immediately.

PREVENTION/AVOIDANCE

Counsel owners about the risk of reverse zoonosis when a human tuberculosis case is in a household with dogs or cats.

EXPECTED COURSE AND PROGNOSIS

Tuberculosis

- Guarded; but undefined as experience with modern drugs is limited.

Feline Leprosy

- Guarded to poor—syndrome 1.
- Fair—syndrome 2, especially if lesions are amenable to surgical excision.

Canine Leprorid Granuloma

Good

Subcutaneous and Systemic Non-tuberculous Infections

- Relapses are common; aggressive surgical approaches and multiple drug therapy may improve outlook.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Tuberculosis—affected domestic pets are potential serious zoonotic threats to owners; public health authorities should be notified of any antemortem or post-mortem diagnosis; do not attempt treatment without agreement of public health authorities.
- *M. tuberculosis*—greatest potential for zoonosis, especially with draining cutaneous lesions. • Disease transmission from dogs and cats to humans—rarely recorded.

ABBREVIATIONS

- AM = atypical mycobacteriosis • CNS = central nervous system • PCR = polymerase chain reaction • TB = tuberculosis

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BASICS

DEFINITION

- Class Mollicutes (Latin, *mollis*, "soft"; *cutis*, "skin"). • Divided into hemotrophic (formerly Haemobartonella and Eperythrozoon), which are discussed elsewhere, and non-hemotrophic types, which are discussed here.
- More than 80 genera; three families: Mycoplasmas, Ureaplasmas, and Acholeplasmas.
- Smallest (0.2–0.3 μm) and simplest prokaryotic cells capable of self-replication.
- Fastidious, facultative anaerobic, gram-negative rods.
- Lack a cell wall; thus plastic, highly pleomorphic, fragile and sensitive to lysis by osmotic shock, detergents, alcohols, and specific antibody plus complement; enclosed by a trilayered cell membrane built of amphiphatic lipids (phospholipids, glycolipids, lipoglycans, sterols) and proteins; therefore resistant to lysozyme and cell wall-inhibiting antibacterials; most require sterols for growth.
- Different from wall-defective or wall-less L-form bacteria, which can revert to the normal cell wall strain.
- Reproduce by binary fission; genome replication not necessarily synchronized with cell division, resulting in budding forms and chains of beads.
- Small genome, typically 0.6–1.6 Mb.
- Low genomic G + C content (23–40 mol%).
- Small genome believed to be result of reductive evolution from a common gram-positive ancestor adapting to obligate parasitic life.
- Ubiquitous in nature as parasites, commensals, or saprophytes in animals, plants, and insects; many are pathogens of humans, animals, plants, and insects.

PATOPHYSIOLOGY

- Often part of the resident flora as commensals on mucous membranes of the upper respiratory, digestive, and genital tracts; pathogenicity and role in disease often controversial.
- Species show considerable host specificity.
- Mechanisms by which disease is caused are poorly understood.
- Some species attach to cells by specific receptors; small size and plastic nature enable them to adapt to the shape and contours of host cell surfaces.
- Intimate contact with host cells—necessary for assimilation of vital nutrients and growth factors (e.g., nucleic acid precursors), which organism cannot synthesize; along with the tendency of exogenous proteins to bind to mycoplasmal membrane may allow organism to evade the host's immune response; may incorporate host cell antigen onto mycoplasma membrane (capping) because lack of cell wall; conversely, mycoplasmal protein antigen may become incorporated onto surface of host cell, thereby involving host cell in deleterious immunologic reactions intended against the

organism.

- Products produced during growth—capsular carbohydrate, hemolysins, proteolytic enzymes, ammonia, and endonucleases; accumulation of Mycoplasma metabolites (i.e., H_2O_2 , NH_3) may contribute to cytopathic effects and tissue damage; cytotoxic glycoproteins and proteins have been isolated from the membranes of several species.
- Immune response—predominantly humoral; as with bacterial infections, IgM and IgA are first antibodies to appear, followed by IgG.
- Fibrinous exudate accompanying infections—protects organism from antibodies and antimicrobial drugs; contributes to chronicity.
- Secondary bacterial invaders—common (e.g., attachment to respiratory tract cells results in destruction of cilia, which predisposes patient to secondary bacterial infection).
- Sialidase, a virulence factor that promotes colonization, tissue invasion, and damage to host cells, varies in expression among strains of canine mycoplasma species.

SYSTEMS AFFECTED

Dogs

- Gastrointestinal—associated with colitis.
- Musculoskeletal—arthritis; from *M. spumans*.
- Renal/Urologic—urinary and genital tract infections (e.g., balanoposthitis, urethritis, prostatitis, cystitis, nephritis, vaginitis, endometritis); caused by *M. canis* and *M. spumans*.
- Reproductive—Mycoplasma and Ureaplasma; associated with infertility, early embryonic death, abortion, stillbirths or weak newborns, and neonatal mortality.
- Respiratory—pneumonia and upper respiratory infections; caused by *M. cynos*; associated with *M. canis*, *M. spumans*, *M. edwardii*, *M. feliminutum*, *M. gateae*, and *M. bovigenitalium*.

Cats

- Musculoskeletal—chronic fibrinopurulent polyarthritis and tenosynovitis; associated with *M. gateae* and unspecified mycoplasmal organisms.
- Ophthalmic—conjunctivitis; associated with *M. felis* (5–25%).
- Renal/Urologic—urinary tract infections.
- Reproductive—abortions and fetal deaths; associated with *M. gateae* and Ureaplasmas.
- Respiratory—pneumonia, associated with *M. gateae*, *M. feliminutum*, and *M. felis*; upper respiratory infections, associated with *M. felis*.
- Skin/Exocrine—chronic cutaneous abscesses.

INCIDENCE/PREVALENCE

- Frequent inhabitants of mucosal membranes; *M. gateae* and/or *M. felis* found in oral cavity or urogenital tract of 70–80% of healthy cats.
- Rate of isolation in diseased dogs much higher than in normal dogs (e.g., lung, uterus, prepuce).

GEOGRAPHIC DISTRIBUTION

Ubiquitous

SIGNALMENT

Species

Dog and cat

Mean Age and Range

All ages

SIGNS

General Comments

- Pathogenic role controversial.

Historical Findings

- Polyarthritis—chronic intermittent lameness; reluctance to move; joint pain.
- Fever.
- Malaise.
- Conjunctivitis—unilateral or bilateral.

Physical Examination Findings

- Polyarthritis—diffuse limb edema; joint swelling; pain.
- Conjunctivitis—blepharospasm; chemosis; conjunctival hyperemia; epiphora; and serous or purulent ocular discharge.
- Mild rhinitis—sneezing.

CAUSES

- *Mycoplasma* flora of dogs—*M. canis*, *M. spumans*, *M. maculosum*, *M. edwardii*, *M. cynos*, *M. molare*, *M. opalescens*, *M. feliminutum*, *M. gateae*, *M. arginini*, *M. bovigenitalium*, *M. mucosicanis*, *Acholeplasma laidlawii*, and Ureaplasmas.
- *Mycoplasma* flora of cats—*M. felis*, *M. gateae*, *M. feliminutum*, *M. arginini*, *M. pulmonis*, *M. arthritidis*, *M. gallisepticum*, *Acholeplasma laidlawii*, and Ureaplasmas.

RISK FACTORS

- Commensals—occasionally cause systemic infection associated with immunodeficiency, immunosuppression, or cancer.
- Impaired resistance of the host—may allow organism to cross the mucosal barrier and disseminate (e.g., primary ciliary dyskinesia).
- Organism may be opportunistic—one factor in a multifactorial causal complex (e.g., impaired pulmonary clearance from viral infection may allow organism to establish infection in lungs as secondary opportunistic pathogen).
- Predisposing factors—stresses (e.g., reproductive problems associated with overcrowded operations) and other factors (e.g., urinary tumors and urinary calculi).
- Rate of isolation of organism in diseased dogs much higher than in normal dogs.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Upper respiratory infection (dogs and cats)—viruses (parainfluenza virus, canine distemper, herpesvirus, feline calcivirus, reovirus); *Chlamydia psittaci*; bacteria (*Bordetella bronchiseptica*, staphylococci, streptococci, coliforms).
- Urinary tract infection (dogs and cats)—bacteria (staphylococci, streptococci, coliforms); fungus (*Candida*); parasites.
- Infertility, early

MYCOPLASMOSIS

(CONTINUED)

embryonic death, abortion, stillbirths or weak newborns, and neonatal mortality (dogs)—bacteria (*Brucella*, *Salmonella*, *Campylobacter*, *E. coli*, *streptococcus*); viruses (canine herpesvirus, canine distemper, canine adenovirus); *Toxoplasma gondii*; endocrinopathies (progesterone deficiency, hypothyroidism). • Prostatitis (dogs)—bacteria (*E. coli*, *Brucella canis*); fungi (*Blastomyces*, *Cryptococcus*). • Arthritis (dogs and cats)—immune-mediated; bacteria (staphylococci, streptococci, coliforms, anaerobes); L-form bacteria; *Rickettsia* (*Ehrlichia*); *Borrelia burgdorferi*; fungi (*Coccidioides*, *Cryptococcus*, *Blastomyces*); protozoa (*Leishmania*); viruses (feline calicivirus). • Conjunctivitis (cats)—feline herpesvirus; feline calicivirus; feline reovirus; *Chlamydia psittaci*; bacteria.

CBC/BIOCHEMISTRY/URINALYSIS

With Polyarthritis

- Mild anemia
- Neutrophilic leukocytosis
- Hypoalbuminemia
- Hypoglobulinemia
- Proteinuria, resulting from immune-complex glomerulonephritis

OTHER LABORATORY TESTS

- Serologic tests—complement fixation, agar gel immunodiffusion, ELISA; detect organism. • Difficult to demonstrate in and from tissues. • Extremely pleomorphic—in smears (e.g., conjunctival scrapings) seen as coccobacilli, coccal forms, ring forms, spirals, and filaments. • Stains—stain poorly (gram-negative); preferred: Giemsa or other Romanowsky stain. • Fluorescent antibody test—definitive diagnosis; isolate and identify or detect the organism in tissues; can submit cotton swabs placed in Hayflick broth medium or commercially available swabs; organisms fragile; refrigerate specimens and deliver to the laboratory within 48 hours; freeze to preserve longer. • Culture urine sediment after centrifugation; fastidious, require complex growth media; form microcolonies having characteristic “fried egg” appearance. • PCR of 16S rRNA.
- PCR-DGGE—used to identify difficult-to-culture or difficult-to-differentiate mycoplasma.

IMAGING

Polyarthritis—no radiographic changes.

DIAGNOSTIC PROCEDURES

- Polyarthritis—high numbers of non-degenerative neutrophils in synovial fluid.
- Prostatic fluid—inflammatory cells with negative bacterial culture.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient



MEDICATIONS

DRUG(S) OF CHOICE

- Sensitive to antibiotics that specifically inhibit synthesis in prokaryotes.
- Tetracyclines 22 mg/kg PO q8h.
- Doxycycline 5 mg/kg PO q12h.
- Pradofloxacin 5 mg/kg PO q12h.
- Chloramphenicol 40–50 mg/kg IV, IM, SC, PO q8–12h. • No standardized procedure for in vitro antimicrobial susceptibility tests.
- Topical antibiotic—conjunctivitis.

CONTRAINDICATIONS

- Topical steroid ointments—improper use for conjunctivitis may prolong infection and predispose patient to corneal ulceration.
- Tetracyclines—avoid use in animals < 6 months of age. • Tetracycline and chloramphenicol—avoid use in pregnant animals.

PRECAUTIONS

Sulfonamides and β -lactams—Inhibit peptidoglycan synthesis; organism resistant because of lack of cell walls.

ALTERNATIVE DRUG(S)

- Gentamicin
- Kanamycin
- Spectinomycin
- Spiramycin
- Tylosin
- Erythromycin
- Nitrofurans
- Fluoroquinolones



FOLLOW-UP

PATIENT MONITORING

Treat for an extended period of time

PREVENTION/AVOIDANCE

- No vaccines are available.
- Organism readily killed by drying, sunshine, and chemical disinfection.

EXPECTED COURSE AND PROGNOSIS

Prognosis good in animals with competent immune systems and given appropriate antibiotic therapy.



MISCELLANEOUS

ASSOCIATED CONDITIONS

M. pneumoniae—infects respiratory tracts in humans worldwide; causes mycoplasmal pneumonia, bronchitis, or upper respiratory infection; usually self-limited; rarely fatal.

AGE-RELATED FACTORS

Tetracyclines—avoid in animals < 6 months of age.

ZOONOTIC POTENTIAL

- Not generally considered zoonotic unless person is immunosuppressed.
- Reported development of suppurative mycoplasmal tenosynovitis in a veterinarian who was scratched by a cat being treated for colitis.
- Host specificity of mycoplasmas has been questioned by some; particularly between closely related species of mammals.

PREGNANCY/FERTILITY/BREEDING

Tetracycline and chloramphenicol—do not use in pregnant animals.

SYNONYMS

Pleuropneumonia-like organisms

ABBREVIATIONS

- ELISA = enzyme-linked immunosorbent assay
- PCR = polymerase chain reaction
- PCR-DGGE = polymerase chain reaction denaturing gradient gel electrophoresis

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Client Education Handout
available online

MYCOTOXICOSIS—AFLATOXIN



BASICS

OVERVIEW

Aflatoxins are hepatotoxic mycotoxins (mold toxins) and are the most common cause of mycotoxicosis associated with pet food. The four major forms of aflatoxin in feedstuffs are aflatoxin B1, B2, G1, and G2. Aflatoxin B1 is the most common and most toxic.

SIGNALMENT

- Rarely reported in dogs, but occurs periodically in large outbreaks associated with pet foods.
- Only reported experimentally in cats.
- Young males and pregnant females might be more susceptible.

SIGNS

Acute Onset

- Most common form in small animals
- Refusal of contaminated feeds
- Rapid onset of signs may develop up to 3 weeks post-exposure
- Vomiting and diarrhea
- Icterus
- Coagulopathy and gastrointestinal hemorrhage

Chronic

- Anorexia or feed refusal
- Vomiting
- Diarrhea
- Liver failure
- Ascites

CAUSES & RISK FACTORS

- Common in various cereal grains; peanuts, other nuts, and potatoes.
- Post-production contamination of improperly stored pet foods; foods with obvious mold spoilage; garbage ingestion.
- Mycotoxin-producing molds grow at temperatures of 24–35°C, moisture of 18–20%.
- Acute signs have been seen in dogs ingesting food containing 60 ppb aflatoxin.
- Activated to toxic epoxide by liver cytochrome P450 enzymes.
- Depletes glutathione.
- Binds with nucleic acids, proteins, and subcellular organelle.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Leptospirosis
 - Serology
- Parvovirus
 - ELISA
 - Serology
 - Viral isolation
- Anticoagulant rodenticide toxicosis
 - Anticoagulant rodenticide screen

- Other causes of subacute to chronic liver disease and associated DIC

CBC/BIOCHEMISTRY/URINALYSIS

- Decreased serum protein C, antithrombin III, and cholesterol
- Hyperbilirubinemia
- Hypoalbuminemia
- Elevated ALT
- Variable elevations in GGT, AST, and ALP

OTHER LABORATORY TESTS

Prolonged APTT and PT

DIAGNOSTIC PROCEDURES

- Liver biopsy
- Histopathology
- Assay suspect food samples for aflatoxin.
 - Contaminated food is often gone due to delayed clinical signs.

PATHOLOGIC FINDINGS

- Hepatomegaly with fatty change
- Icterus
- Ascites
- Multifocal hemorrhage, especially gastrointestinal
- Microvesicular fatty change in hepatocytes
- Centrilobular hepatocellular necrosis
- Canalicular cholestasis
- Bridging portal fibrosis, proliferation of bile ducts



TREATMENT

- Transfusion of whole blood or plasma
- Correct fluid and electrolyte imbalances
- Activated charcoal for recent, high-dose exposure
- B vitamins, vitamin K₁, vitamin E, and other antioxidants
- Gastroprotectants
- Clean, uncontaminated diet
 - High-quality protein source



MEDICATIONS

DRUG(S)

- No specific antidotal therapy.
- Limited success with hepatoprotectants.
- Parenteral N-acetylcysteine in severely affected dogs.
 - 20% solution diluted 1:4 in sterile saline slow IV at a loading dose of 140 mg/kg, follow with maintenance dose of 70 mg/kg IV q8h × 7 doses.
- S-Adenosylmethionine
 - 20 mg/kg PO daily as enteric-coated tablets given on empty stomach × 1–2 weeks.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Avoid drugs metabolized by the liver.



FOLLOW-UP

PATIENT MONITORING

- Daily serum enzymes and chemistry, including cholesterol
- PT and APTT
- Protein C

PREVENTION/AVOIDANCE

- Avoid using moldy feedstuff.
- Store food in cool, clean, dry area.
- Clean food containers and feed bowls regularly.

POSSIBLE COMPLICATIONS

Chronic liver disease possible.

EXPECTED COURSE AND PROGNOSIS

Prognosis—poor, even with treatment. Improved prognosis if treatment initiated before onset of signs.



MISCELLANEOUS

AGE-RELATED FACTORS

Young animals more susceptible to aflatoxin

PREGNANCY/FERTILITY/BREEDING

- Indirect effects on uterus
- Potentially teratogenic
- Pregnant animals may be more susceptible

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- APTT = activated partial thromboplastin time
- AST = aspartate aminotransferase
- DIC = disseminated intravascular coagulation
- ELISA = enzyme-linked immunosorbent assay
- GGT = gamma-glutamyltransferase
- PT = prothrombin time

Suggested Reading

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MYCOTOXICOSIS—DEOXYNIVALENOL



BASICS

OVERVIEW

- Deoxynivalenol (DON [vomitoxin]) is a toxin that can be produced by *Fusarium* fungi in grains such as wheat, oats, barley, and corn.
- The main source of exposure for dogs and cats is through the ingestion of pet food made with DON-contaminated grain.
- Although the exact mechanism is not well defined, DON can inhibit cellular protein synthesis and activate intracellular kinases involved in signal transduction. In addition, ingestion of DON can cause feed refusal possibly related to upregulation of proinflammatory cytokines such as IL-6, and it may have a central emetic effect that results in vomiting.

SIGNALMENT

- Dogs and cats.
- No breed or sex predisposition.
- Signs may be more common in young animals.

SIGNS

- Sudden onset of anorexia and vomiting, which may result in weight loss.
- Onset of clinical signs can occur within minutes of exposure.
- Abnormal clinical signs may also resolve rapidly following removal of contaminated food.

CAUSES & RISK FACTORS

- Animals are exposed to DON when grain containing DON is mixed into their complete feed.
- There are marked species differences in toxicity: pig (most sensitive) > rodent > dog > cat > poultry > human > ruminant (least sensitive).
- Experimentally, food intake of beagles and Brittany dogs is reduced when DON concentrations in their food are $> 4.5 \pm 1.7$ mg DON/kg of food.
- Food intake in cats is reduced with DON concentrations $> 7.7 \pm 1.1$ mg/kg.
- Vomiting in dogs and cats is common when DON concentration in their food is > 8 mg.

M



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of inappetence and vomiting.
- Viral, bacterial, or parasitic infections.
- Other toxicoses (e.g., exposure to organophosphates/carbamates or ethylene glycol).
- Ingestion of poisonous plants causing irritation to the gastrointestinal tract.
- Ingestion of lilies by cats, resulting in severe kidney failure.
- Other medical conditions, such as pancreatitis, neoplasia, and inflammation of the gastrointestinal tract.

CBC/BIOCHEMISTRY/URINALYSIS

Nonspecific, but may be used to rule out other causes of inappetence and vomiting.

OTHER LABORATORY TESTS

Analysis of pet food for DON by thin-layer chromatography or high-pressure liquid chromatography.

IMAGING

May be used to rule out other causes of inappetence and vomiting.

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

There are no pathognomonic gross or microscopic lesions.



TREATMENT

Removal of contaminated pet food should result in rapid cessation of vomiting and return to normal food intake.



MEDICATIONS

DRUG(S)

N/A

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Monitor hydration and electrolytes if vomiting has been severe.
- Ensure animal returns to normal weight following removal of pet food containing DON.

PREVENTION/AVOIDANCE

Provide high-quality pet food free of DON.

EXPECTED COURSE AND PROGNOSIS

The prognosis is excellent following removal of feed containing DON.



MISCELLANEOUS

AGE-RELATED FACTORS

In other, more well-studied species (e.g., swine), young animals are more severely affected and at lower concentrations of DON in the feed than are adults.

ABBREVIATION

DON = deoxynivalenol

Suggested Reading

Hughes DM, Gahl MJ, Graham CH, et al. Overt signs of toxicity to dogs and cats of dietary deoxynivalenol. *J Anim Sci* 1999; 77:693–700.

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Author Stephen B. Hooser

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MYCOTOXICOSIS—TREMORGENIC TOXINS



BASICS

OVERVIEW

- Penitrem A—produced by the fungus *Penicillium crustosum* (and perhaps other *Penicillium* spp.); poisoning by this toxin has been reported in dogs ingesting moldy bread, cheese, and English walnuts.
- Roquefortine—produced by *Penicillium roquefortii* (and perhaps other *Penicillium* spp.); has been reported to cause poisoning in dogs through ingestion of moldy cheese or decaying organic material (compost).

SIGNALMENT

- Dogs and rarely cats.
- Poisoning by penitrem A and roquefortine has been reported in dogs of various ages and breeds soon after the ingestion of moldy foods or compost.

SIGNS

- Moderate to severe muscle tremors and seizures—begin minutes to hours (2–4 hours in case reports) after ingestion of moldy food or compost.
- Affected dogs may be hyperresponsive to external stimuli.
- Early signs—may include panting, hyperactivity, vomiting, ataxia, incoordination, weakness, tachycardia, and/or rigidity.
- Prolonged muscle tremors or seizures—may lead to hyperthermia, hypoglycemia, dehydration, and anorexia.
- Severe cases—may result in death.
- Liver necrosis—has been reported experimentally.

CAUSES & RISK FACTORS

- Dogs (and potentially cats) are exposed to penitrem A and roquefortine when they ingest moldy food or decomposing organic matter (compost).
- Experimentally, doses of 0.125 mg/kg penitrem A produced tremors within 30 minutes. Doses of 0.5 mg/kg of penitrem A resulted in acute onset of tremors, severe liver necrosis, and death.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Toxic causes of seizures—strychnine; insecticides (e.g., organophosphate, carbamate, organochlorine, nicotine, pyrethroid); metaldehyde; zinc phosphide; bromethalin; methylxanthines (theobromine and caffeine); amphetamines; cocaine; sago palm; xylitol.

- Non-toxic causes of seizures—
inflammation; congenital abnormal myelin formation; metabolic conditions (e.g., hepatic or uremic encephalopathy).

CBC/BIOCHEMISTRY/URINALYSIS

CBC, biochemistry, and urinalysis to assess the patient's status and to help rule out other causes of tremors and seizures.

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Thin-layer chromatography or high-pressure liquid chromatography—analysis of vomitus, stomach contents, and gastric lavage washings for penitrem A or roquefortine.
- The presence of roquefortine C in vomitus or stomach contents can serve as a sensitive biomarker for penitrem A intoxication.
- Bile analysis—reported to be of value.

PATHOLOGIC FINDINGS

- There are no pathognomonic lesions associated with penitrem A or roquefortine toxicosis.
- High doses of penitrem A have been reported to cause severe liver damage experimentally.



TREATMENT

- Remove contaminated food or organic material.
- Induce vomiting (if patient is not at risk of aspirating vomitus) or institute gastric lavage followed by administration of activated charcoal.
- Thermoregulation as indicated.



MEDICATIONS

DRUG(S)

- Diazepam (0.25–1 mg/kg IV prn)—to control seizures.
- Barbiturates (phenobarbital 2–5 mg/kg IV prn)—if tremors and seizures cannot be controlled with diazepam.
- Methocarbamol to control tremors (50–220 mg/kg IV, do not exceed 330 mg/kg/day). Give 1/2 rapidly and administer rest to effect.
- Sodium bicarbonate—may be required if an acid-base imbalance exists.
- Other symptomatic and supportive therapy—as indicated.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

Patients should be monitored for occurrence of tremors or seizures, hyperthermia, dehydration, acid-base imbalances, liver damage, rhabdomyolysis, and respiratory difficulties.

PREVENTION/AVOIDANCE

Prevent animals from eating moldy food items, garbage, or compost.

POSSIBLE COMPLICATIONS

- Seizures—may not be controlled with diazepam.
- Acid-base imbalances—may develop.
- Hepatic damage and rhabdomyolysis—may occur.
- Aspiration pneumonia has been reported as a sequelae to vomiting and/or gastric lavage.
- Exposure can be fatal if lethal doses are consumed and are absorbed before gastrointestinal decontamination and therapy are instituted.

EXPECTED COURSE AND PROGNOSIS

- Very good if appropriate therapy is promptly instituted, the toxin is removed from the gastrointestinal tract, and the seizures are controlled with diazepam or barbiturates.
- Recovery in most clinical cases is reported to be complete within 24–48 hours.
- In a few reported cases, signs of weakness, muscle rigidity, and incoordination were persistent and slowly resolved over 1–2 weeks.
- A few severe cases have been reported to be fatal.



MISCELLANEOUS

Suggested Reading

Barker AK, Stahl C, Ensley SM, et al.

Tremorgenic mycotoxicosis in dogs. Comp Cont Ed Vet 2013, 35(2):E1–E6.

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M

MYELODYSPLASTIC SYNDROMES



BASICS

OVERVIEW

- Category of diseases characterized by nonregenerative anemias or cytopenias and dysplastic features in the blood or bone marrow.
- Primary myelodysplastic syndromes result from a clonal expansion of a genetically altered pluripotent stem cell resulting in a hypercellular bone marrow with maturation arrest as a consequence of apoptosis.
- Subcategorized as MDS with excessive blasts, which may progress to acute myeloid leukemia, MDS with refractory cytopenia, and MDS with erythroid predominance.
- Secondary MDS in dogs is associated with neoplasia (lymphoma, multiple myeloma), drug or toxin exposure, immune-mediated disease, infections, or ionizing radiation exposure.
- Secondary MDS in cats is typically associated with FeLV infection.

SIGNALMENT

- Dog and less commonly cat
- Primary MDS typically older dogs

SIGNS

- Lethargy
- Exercise intolerance
- Depression
- Anorexia
- Fever
- Pale mucous membranes
- Petechiation
- Heart murmur due to anemia

CAUSES & RISK FACTORS

- Viral—FeLV, FIV, parvovirus
- Neoplasia—lymphoma, multiple myeloma
- Autoimmune—immune-mediated hemolytic anemia, immune-mediated thrombocytopenia
- Drug—chemotherapeutics, estrogen, chloramphenicol, cephalosporins, phenylbutazone, trimethoprim-sulfadiazine, quinidine, thiacetarsamide, griseofulvin, albendazole
- Iron deficiency, folic acid deficiency
- Lead toxicity
- Infectious—ehrlichiosis, bacterial septicemia, and endotoxemia



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Need to differentiate between primary and secondary MDS.
- Other causes of nonregenerative anemias—anemia of chronic disease, chronic renal failure, myeloproliferative diseases, lymphoproliferative diseases, myelofibrosis.

CBC/BIOCHEMISTRY/URINALYSIS

Nonregenerative anemia, cytopenias

OTHER LABORATORY TESTS

To diagnose underlying causes of secondary MDS—viral antigen/antibody titers, iron levels, tick titers, Coombs' test.

IMAGING

- As needed to rule out secondary causes of MDS.
- Abdominal radiography—evaluate for lead foreign bodies.
- Abdominal ultrasonography—evaluate for abdominal masses consistent with retained testes and Sertoli cell tumors associated with estrogen secretion.

DIAGNOSTIC PROCEDURES

Bone marrow aspirate or biopsy



TREATMENT

- Inpatient or outpatient.
- If secondary MDS—treat underlying disease (e.g., discontinue drug, treat underlying infection).
- If neutropenic—limit exposure to other sick animals.
- Blood transfusions for anemic patients.



MEDICATIONS

DRUG(S)

- For neutropenia—broad-spectrum antibiotics and filgrastim (3–5 µg/kg SC q24h in dogs and cats).

- For anemia—erythropoietin (35–50 U/kg SC 3 times a week) or darbepoetin (0.45 µg/kg once a week).
- Chemotherapy for primary MDS has been reported—hydroxyurea, cytosine arabinoside, prednisone, cyclosporine A, vincristine.
- Interferon α (cats with FeLV).



FOLLOW-UP

- Serial monitoring of CBC for resolution of cytopenias.
- Prognosis dependent on primary versus secondary.
- Increasing blast percentage, multiple cytopenias, marked cellular atypia are poor prognostic factors for patients with primary MDS.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

- Do not use chemotherapy in pregnant or nursing animals.
- It is not recommended to breed animals with cancer.

SEE ALSO

- Feline Immunodeficiency Virus Infection
- Feline Leukemia Virus Infection
- Myeloproliferative Disorders

ABBREVIATIONS

- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- MDS = myelodysplastic syndromes

Suggested Reading

Juopperi TA, Bienzle D, Bernreuter DC, Vernau W, Thrall MA, McManus PM. Prognostic markers for myeloid neoplasms: a comparative review of the literature and goals for future investigation. *Vet Pathol* 2011, 48(1):182–197.

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MYELOMALACIA, SPINAL CORD (ASCENDING, DESCENDING)



BASICS

OVERVIEW

- Acute, progressive, ischemic, or hemorrhagic necrosis of the spinal cord after acute spinal cord injury (SCI).
- First appears at the site of injury; then progresses both cranially and caudally.
- Death is caused by respiratory paralysis once the intercostal and phrenic nerves become affected.
- Prevalence is about 10% in dogs with acute paraplegia and loss of pain perception following acute intervertebral disc herniation (IVDH).

SIGNALMENT

- Any age or breed.
- Because of the close association between acute (type I) IVDH and myelomalacia, chondrodystrophic breeds (such as dachshunds Cocker Spaniel, French bulldog) most commonly affected because of their predisposition to the former.

SIGNS

- **Not clinically recognizable in acute phase of SCI.**
- Acute onset of paraplegia with loss of pain sensation following spinal injury—initial clinical sign.
- Thoracolumbar injury—pelvic limbs paralysis (absent motor function) with normal to exaggerated spinal reflexes in the pelvic limbs; some dogs might present with absent spinal reflexes.
- Pain perception—usually absent caudal to the lesion.
- Spinal cord malacia—progresses to involve the lumbosacral spinal segments within 12–72 hours causing pelvic limb areflexia and atonia, absent deep pain perception in pelvic limbs and tail, dilated anus, decreased abdominal tone and flaccid, easily expressed urinary bladder; thoracic and cervical spinal cord segments may be involved within 24 hours to 10 days after the initial insult causing loss of the cutaneous trunci reflex, progression to tetraplegia, bilateral Horner syndrome, hypoventilation and death.
- Subarachnoid hemorrhage secondary to necrosis of the microvasculature in the spinal cord—may cause hyperthermia and extreme diffuse meningeal pain.

CAUSES & RISK FACTORS

- Acute intervertebral disc herniation (type I disc)
- Acute vertebral or spinal cord trauma
- Fibrocartilaginous embolisms



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cannot be differentiated from spinal shock following acute SCI (acute paralysis with

initial areflexia that improves after a few hours to days post injury).

- Diagnosis based on hind limb upper motor neuron paralysis with absent nociception that progresses to a lower motor neuron paralysis and a rostrally advancing line of analgesia and cutaneous trunci reflex.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal, initially.
- Road accident—nonspecific abnormalities related to other organ injury.
- After condition has developed, degenerative left-shift caused by massive spinal cord necrosis may occur.

OTHER LABORATORY TESTS

Serum glial fibrillary acidic protein (GFAP)—elevated; experimental test not widely available and requiring spectrophotometry.

IMAGING

- Spinal survey radiography—evidence of calcified, herniated disc, narrowed intervertebral disc space; vertebral fracture or luxation.
- Myelography—cord compression; edema; contrast medium infiltration into the spinal parenchyma.
- MRI—parenchymal T1 hypointensity, T2 hyperintensity (suggestive if length of the hyperintense region is more than 6 times the length of L2 vertebrae on T2W sagittal view), extensive spinal cord swelling; associated with other evidence of spinal injury.

DIAGNOSTIC PROCEDURES

Cerebellomedullary cistern CSF—unspecific results related to stage of development of clinical ascending/descending myelomalacia; neutrophilic pleocytosis, hemorrhagic xanthochromia (yellow discoloration) and high protein concentration can be present.

PATHOLOGIC FINDINGS

Extensive necrosis with ischemic changes, neutrophils and macrophages infiltration, multifocal hemorrhages with necrotic blood vessels, swollen axons and neuronal degeneration.



TREATMENT

- None to reverse spinal cord damage and stop disease progression.
- Rapid spinal cord decompression—indicated for IVDH but myelomalacia cannot be reliably diagnosed in the acute phase of SCI; delaying surgical treatment on a dog with complete sensorimotor loss can significantly alter its chances of recovery; owners should be informed of the risk of development of myelomalacia postoperatively despite rapid decompression.
- Strong suspicion of

myelomalacia—poor outcome, consider euthanasia.



MEDICATIONS

DRUG(S)

- Therapy is controversial.
- Pain medications; gabapentin (10 mg/kg q8h), opioids (fentanyl, hydromorphone) to relieve pain associated with SCI.

CONTRAINdications/POSSIBLE INTERACTIONS

- Gabapentin may cause sedation.
- Common opioids side effects include sedation, nausea, constipation, dysphoria.



FOLLOW-UP

- In rare cases, condition progresses only caudally; paralysis is permanent, but respiratory compromise does not occur.
- Reported after decompressive hemilaminectomy or laminectomy, suggesting that surgery does not prevent its occurrence.



MISCELLANEOUS

SEE ALSO

Intervertebral Disc Disease, Thoracolumbar

ABBREVIATIONS

- CSF = cerebrospinal fluid
- IVDH = intervertebral disc disease
- MRI = magnetic resonance imaging
- SCI = spinal cord injury

Suggested Reading

Brisson BA. Intervertebral disc disease in dogs. *Vet Clin North Am Small Anim Pract* 2010; 40:829–858.

Olby NJ. The pathogenesis and treatment of acute spinal cord injuries in dogs. *Vet Clin North Am Small Anim Pract* 2010; 40:791–807.

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MYELOPATHY—PARESIS/PARALYSIS—CATS



BASICS

DEFINITION

- Myelopathy—any disease affecting the spinal cord; can cause paralysis (complete loss of voluntary movements) or paresis (weakness) that may affect all four limbs (tetraparesis/plegia), the pelvic limbs (para-only, the ipsilateral front and pelvic limbs (hemi-), or one limb (mono-). • Paresis/paralysis can also be caused by neuromuscular disorders.

PATHOPHYSIOLOGY

- Myelopathy—can affect gray or white matter of the spinal cord or, most often, both.
- Lesions of the ascending white matter tracts—affect sensory modalities such as touch, pressure, proprioception, pain, and temperature sensation below the level of the lesion.
- Lesions of the descending white matter tracts—affect the motor pathways producing signs of upper motor neuron disorder. The upper motor neurons cell bodies are located in the brain; they control voluntary activity and have inhibitory function on the lower motor neurons. Signs of upper motor neuron disease include paresis/paralysis, normal to increased muscle tone (hypertonia), and normal to exaggerated spinal reflexes (hyperreflexia) below the level of the lesion.
- Lesions in the gray matter of the spinal cord—affect sensory and motor functions of the region innervated by the nerves whose cell bodies are located in the gray matter. The motor nerves in the gray matter of the spinal cord are also called lower motor neurons. Signs of lower motor neuron disease include paresis/paralysis, decreased or absent muscle tone (hypo- or atonia), atrophy of the muscles innervated by that segment, and, reduced or absent spinal reflexes (hypo- or areflexia).

SYSTEMS AFFECTED

Nervous

GENETICS

- Lysosomal storage diseases—gangliosidosis GM1/GM2, sphingomyelinosis (Niemann-Pick disease), mucopolysaccharidosis VI (MPS VI), and glycogenosis type IV cause paresis or paralysis in cats; autosomal recessive pattern of inheritance.
- Neuroaxonal dystrophy and spinal muscular atrophy—degenerative diseases of the spinal cord reported as autosomal recessive conditions.
- Syringohydromyelia/myelodysplasia may be associated with sacrocaudal (sacrococcygeal) dysgenesis—autosomal dominant condition in Manx cats.

SIGNALMENT

Breed Predilections

- Gangliosidosis GM1/GM2—Siamese, Burmese, Korat cats, and DSH. • Glycogen

storage disease type IV—Norwegian forest cats. • Spinal muscular atrophy—Maine Coon. • Syringohydromyelia/myelodysplasia—Manx and Manx crosses with sacrocaudal dysgenesis.

- Sphingomyelinosis (Niemann-Pick disease)—Siamese, Balinese, and DSH.
- Mucopolysaccharidosis type VI—Siamese and DSH. • Mucopolysaccharidosis type VII—DSH. • Idiopathic complex polysaccharide storage disease—Abyssinians.
- Neuroaxonal dystrophy—Siamese and DSH.

SIGNS

- Signs vary with location and severity of lesion.
- Cervical lesion—all limbs or ipsilateral limbs affected with proprioceptive ataxia and tetraparesis/plegia, hemiparesis/plegia; normal to increased reflexes and tone; ± neck pain; ± ipsi-/bilateral Horner's syndrome; ± urinary incontinence with bladder difficult to express; increased urethral sphincter tone and tense bladder.
- Cervicothoracic lesion—all limbs or ipsilateral limbs affected with proprioceptive ataxia and tetraparesis/plegia, hemiparesis/plegia; hypo-/areflexia, hypo-/ataxia and muscle atrophy in front limbs with normal to increased reflexes and tone in pelvic limbs; ± neck pain; ± ipsi-/bilateral Horner's syndrome; ipsi-/bilateral decreased/absent cutaneous trunci reflex; ± urinary incontinence with bladder difficult to express; increased urethral sphincter tone and tense bladder.
- Thoracolumbar lesion—normal front limbs; both hind limbs or ipsilateral hind limb affected with proprioceptive ataxia and paraparesis/plegia; normal to increased reflexes and tone; ± thoracolumbar pain; ± decreased/absent cutaneous trunci reflex below the lesion; ± decreased/absent sensation below lesion; ± Schiff-Sherrington posture; ± urinary incontinence with bladder difficult to express, increased urethral sphincter tone and tense bladder.
- Lumbosacral lesion—normal front limbs; hind limbs or ipsilateral hind limb affected with proprioceptive ataxia and paraparesis/plegia or monoparesis/plegia; hypo-/areflexia; hypo-/ataxia; muscle atrophy; ± regional pain; ± urinary and fecal incontinence, large and flaccid bladder easy to express, decreased urethral sphincter tone; ± decreased or absent tail and anal tone; ± decreased or absent sensation below lesion.

CAUSES

- Degenerative and/or inherited—neuroaxonal or neuronal dystrophy, spinal muscular atrophy, storage diseases (gangliosidosis GM1/GM2, sphingomyelinosis, glycogenosis type IV, idiopathic complex polysaccharide storage disease, and mucopolysaccharidosis type VI) and spinal dural ossification.
- Anomalous—syringohydromyelia, myelodysplasia, meningocele or meningomyelocele, and

tethered spinal cord often associated with sacrocaudal dysgenesis, spinal arachnoid cyst, spinal intradural epithelial cyst, spinal dermoid cyst/sinus. • Metabolic—hypervitaminosis A, nutritional secondary hyperparathyroidism, cobalamin deficiency-associated myelopathy.

- Neoplastic—lymphoma, vertebral column neoplasia (osteosarcoma, fibrosarcoma, plasma cell tumor, and chondrosarcoma), meningiomas, sarcomas, histiocytic tumors, glial tumors (astrocytoma, oligodendrogioma, gliomatosis cerebri), primitive neuroectodermal tumors, peripheral nerve sheath tumors, and metastatic tumors.

• Inflammatory or infectious—FIP, Borna virus (Europe), bacterial meningomyelitis, fungal meningomyelitis (*Cryptococcus neoformans*, *Coccidioides immitis*, *Histoplasma capsulatum*), *Toxoplasma gondii* meningomyelitis, eosinophilic meningomyelitis, idiopathic poliomyelitis, and FeLV-associated myelopathy.

- Traumatic—vertebral fractures/luxations and penetrating wounds (bite wounds, BB pellets, microchips); intervertebral disc disease.
- Vascular—ischemia or infarct of unknown etiology, fibro-cartilaginous embolisms, ischemic myelopathy secondary to hyaline arteriopathy, intraosseous vascular malformations, and myelopathy secondary to aortocaval fistula.

RISK FACTORS

- Outdoor cats—at risk for traumatic and infectious myelitis.
- FeLV-positive cats—at risk for lymphoma and FeLV-associated myelopathy.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiate from other disease processes that can cause paresis/paralysis—ischemic neuromyopathy caused by arterial thromboembolism, and peripheral neuromuscular diseases such as diabetic neuropathy, polyradiculoneuritis, hypokalemic myopathy, muscular dystrophy, polymyositis, and myasthenia gravis.

CBC/BIOCHEMISTRY/URINALYSIS

- Often normal. • Various nonspecific abnormalities can be found associated with infectious myelitis and lymphoma.
- Lysosomal storage diseases—abnormal accumulation of products of cell metabolism can be seen within the cytoplasm of peripheral leukocytes.

OTHER LABORATORY TESTS

- Serology—FeLV/FIV, *Cryptococcus neoformans*, *Coccidioides immitis*, *Histoplasma capsulatum*, and *Toxoplasma gondii*. • Latex agglutination test—*Cryptococcus neoformans* (serum or cerebrospinal fluid).
- α-Acid

(CONTINUED)

glycoprotein (AGP) can be used as a discriminating marker for FIP when coupled with other high-risk factors. • Urine metabolic screening for lysosomal storage diseases. • Genetic test for glycogen storage disease type IV in Norwegian forest cats, mucopolysaccharidoses type VI and VII, GM2 in Burmese and related breeds, GM1 and GM2 in Korat cats, spinal muscular atrophy in Maine Coon.

IMAGING

- Spinal radiography—may reveal congenital or acquired (MPS VI) vertebral malformations, discospondylitis, vertebral fractures and luxations, bony tumors, and radiographic signs suggestive of intervertebral disc disease.
- Myelography—may reveal extradural compression consistent with intervertebral disc disease or tumor, or intradural-extramedullary tumors.
- CT—more sensitive than radiography for diagnosis of discospondylitis, vertebral fractures, and bony tumors; may reveal syringomyelia and intramedullary tumors.
- MRI—more sensitive than CT for diagnosis of intramedullary tumors, inflammatory/infectious and vascular diseases, and anomalies, such as syringomyelia, myelodysplasia, meningocele or meningomyelocele, tethered spinal cord, spinal arachnoid cyst, spinal intradural epithelial cyst, and spinal dermoid cyst/sinus.

DIAGNOSTIC PROCEDURES

Cerebrospinal Fluid

- To confirm an inflammatory process affecting meninges and/or spinal cord.
- Elevated total nucleated cell count and proteins suggest an inflammatory process affecting meninges and/or spinal cord; should be examined for fungal and bacterial organisms.
- Other laboratory tests performed on CSF—latex agglutination test for *Cryptococcus neoformans*; ELISA for *Cryptococcus neoformans* and *Histoplasma capsulatum*; PCR for feline coronavirus and *Toxoplasma gondii*; bacterial and fungal culture.

Electrodiagnostics

Electromyography, nerve conduction velocity, repetitive stimulations—help differentiating paresis/paralysis caused by a myelopathy from peripheral neuromuscular disorders.



TREATMENT

APPROPRIATE HEALTH CARE

- Emergency evaluation and possible surgery—when a traumatic cause of paresis/paralysis is suspected.
- Inpatient medical management—for severe neurologic deficits such as paralysis and urinary incontinence.

NURSING CARE

- Non-ambulatory cats should be confined to a soft padded crate or enclosed area, kept dry and clean, and turned every 6 hours if they are not able to assume a sternal position.
- If there is urinary incontinence, the bladder should be expressed every 6–8 hours.
- Prevent/treat decubital ulcers and urine scalding.
- Treat constipation.
- Physical therapy is useful to prevent muscle atrophy and contractures and to keep the joints flexible, especially for postoperative rehabilitation in vertebral trauma or intervertebral disc disease.

ACTIVITY

Restricted—especially when a traumatic cause of paresis/paralysis is suspected, but also to prevent trauma secondary to paresis/paralysis.

CLIENT EDUCATION

If the cat is treated as an outpatient, discuss all aspects of nursing care and possible complications with the client.

SURGICAL CONSIDERATIONS

Surgical management—for vertebral fractures and luxations, intervertebral disc disease, and some neoplasms.



MEDICATIONS

DRUG(S) OF CHOICE

- Not recommended until a diagnosis has been established.
- Spinal trauma—methylprednisolone sodium succinate administered within 8 hours from injury, 30 mg/kg as slow IV bolus followed by 15 mg/kg IV, 2 and 6 hours later, followed by CRI at 2.5 mg/kg/h for 42 hours.

CONTRAINdicATIONS

Corticosteroids—contraindicated when an infectious disease is suspected; may also alter CSF, MRI, or CT results, precluding reaching a diagnosis.



FOLLOW-UP

PATIENT MONITORING

Repeat neurologic examination—frequency determined by the severity and progression of the neurologic status.

POSSIBLE COMPLICATIONS

- Urinary infection
- Urine scalding
- Constipation or fecal incontinence
- Muscle atrophy and contractures
- Decubital ulcers



MISCELLANEOUS

SEE ALSO

Schiff-Sherrington Phenomenon

AGE-RELATED FACTORS

- Cats < 2 years—myelopathies often caused by anomalous or inherited, inflammatory, or infectious, metabolic, and traumatic diseases.
- FIP is the most important cause of myelopathy in this age group.
- Cats 2–8 years—LSA, FIP, and trauma important causes of myelopathy.
- Cats > 8 years—vascular and neoplastic diseases more common, especially LSA and vertebral tumors.

ZOONOTIC POTENTIAL

Toxoplasma gondii infections represent a zoonotic potential.

ABBREVIATIONS

- CSF = cerebrospinal fluid
- CT = computed tomography
- ELISA = enzyme-linked immunosorbent assay
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- LSA = lymphoma
- MPS = mucopolysaccharidosis
- MRI = magnetic resonance imaging

INTERNET RESOURCES

- UC Davis genetic laboratories: <https://www.vgl.ucdavis.edu/services/cat/>
- Other genetic laboratories in US, Europe, Asia and Australia: <http://felinegenetics.missouri.edu/cat-dna-testing-laboratories>

Suggested Reading

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- Author** Katia Marioni-Henry
Consulting Editor Joane M. Parent



Client Education Handout
available online

M

MYELOPROLIFERATIVE DISORDERS



BASICS

OVERVIEW

- Unregulated neoplastic proliferation of nonlymphoid cells originating in the bone marrow (granulocytic, monocytic, erythrocytic, and megakaryocytic cells) resulting in accumulations of differentiated cells.
- Includes polycythemia vera, chronic myelogenous leukemia, essential thrombocythemia, and possibly primary myelofibrosis.
- Believed to represent a spectrum of disorders in which the stem cell involved is a hematopoietic precursor capable of differentiating into all blood cell types except lymphocytes.

SIGNALMENT

- Cat and dog—more common in cat
- May be more common in large-breed dogs than small-breed dogs

SIGNS

- Pale mucous membranes
- Petechiation
- Lethargy
- Inappetance
- Weight loss
- Hepatosplenomegaly
- Peripheral lymphadenomegaly—occasionally
- Neurologic signs—disorientation, ataxia, seizure

CAUSES & RISK FACTORS

- Cats—most commonly associated with FeLV infection; when recovering from panleukopenia or hemobartonellosis, may be a relatively higher risk of developing a mutant cell line induced by FeLV.
- Dogs—has been experimentally induced with chronic low-dose radiation exposure.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute lymphocytic leukemia—usually differentiated by special staining techniques (immunohistochemistry or immunocytochemistry for lymphoid markers) or PARR.
- Leukemoid response secondary to inflammation.

- Other causes of eosinophilia—parasitism; allergic disease; eosinophilic gastroenteritis; mast cell neoplasia; differentiate from eosinophilic leukemia.

- Relative and secondary absolute polycythemia.
- Reactive thrombocytosis—secondary to inflammation, hemolytic or iron deficiency anemia, splenectomy, rebound from immune-mediated thrombocytopenia, and drug-induced (e.g., vincristine).

CBC/BIOCHEMISTRY/URINALYSIS

- Severe, nonregenerative anemia
- Severe elevated hematocrit in cases of primary polycythemia vera
- Circulating nucleated red blood cells
- Megaloblastic erythrocytes
- Leukocytosis or leukopenia
- Thrombocytopenia with abnormal platelet morphology
- Thrombocytosis in cases of essential thrombocythemia
- Circulation of immature myeloid cells

OTHER LABORATORY TESTS

- Examination of bone marrow aspirate or core biopsy—reveals hypercellular bone marrow with abnormal morphology in all cell lines; neoplastic proliferation or absence of one cell line.
- Immunohistochemical or other special stains—may be necessary to determine cell lineage.

IMAGING

Abdominal radiography and ultrasonography—hepatomegaly and splenomegaly common.

DIAGNOSTIC PROCEDURES

Examination of bone marrow aspirates or core biopsy



TREATMENT

- Outpatient or inpatient.
- Supportive care—blood transfusions and fluid administration to correct dehydration.
- Therapeutic phlebotomies.
- Radiophosphorus (^{32}P) has been effective in cases of polycythemia vera and essential thrombocythemia but there are limited facilities that can offer this therapy.
- Seek consultation from a veterinary oncologist regarding treatment.



MEDICATIONS

DRUG(S)

- Little information available in the literature regarding treatment.
- Cytosine arabinoside—may be used; $100 \text{ mg/m}^2 \text{ SC}$ divided q12h 4 days per week, or as a constant rate infusion over 6–8 hours at a dose of 400 mg/m^2 .
- Hydroxyurea $30\text{--}45 \text{ mg/kg q24h}$ for 7–10 days; then $30\text{--}45 \text{ mg/kg q48h}$ or 15 mg/kg q24h ; essentially, titrate dosage to patient response.
- Antibiotics—may be indicated to combat secondary infection.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Chemotherapy can be toxic; seek advice before treatment if unfamiliar with cytotoxic drugs.



FOLLOW-UP

- Complete blood count and examination of bone marrow aspirate—determine response to treatment and progression of disease.
- Prognosis—guarded.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

- Chemotherapy drugs are contraindicated in pregnant animals.
- It is not recommended to breed animals with neoplasia.

ABBREVIATIONS

- FeLV = feline leukemia virus
- PARR = polymerase chain reaction for antigen receptor rearrangement

Suggested Reading

Young KM, Vail DM. Canine Acute Myeloid Leukemia, Myeloproliferative Neoplasms, and Myelodysplasia. In: Withrow SJ, Vail DM, Page RL, eds. Small Animal Clinical Oncology, 5th ed. Philadelphia: Saunders, 2013, pp. 653–665.

Author Rebecca G. Newman

Consulting Editor Timothy M. Fan

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MYOCARDIAL INFARCTION



BASICS

OVERVIEW

- Rapid development of myocardial necrosis resulting from sustained, complete reduction of blood flow to a portion of the myocardium, caused by thrombus formation.
- Uncommon as a naturally occurring disease in dogs. • Microscopic intramural myocardial infarctions and focal areas of myocardial fibrosis are common in dogs with acquired cardiovascular disease. • Consistent ECG characteristics of spontaneous myocardial infarction are not well characterized in dogs and cats.

SIGNALMENT

Rare in dog and cat

SIGNS

Historical Findings

- Lethargy • Anorexia • Weakness • Dyspnea
- Collapse • Vomiting • Obesity • Unexpected death

Physical Examination Findings

- Lameness • Tachycardia • Heart murmur
- Cardiac rhythm disturbances • Low-grade fever

CAUSES & RISK FACTORS

- Atherosclerosis and coronary artery disease
- Nephrotic syndrome • Vasculitis
- Hypothyroidism • Bacterial endocarditis
- Neoplasia • Septicemia • Intramural coronary arteriosclerosis in old dogs
- Subvalvular aortic stenosis

Cats

- Cardiomyopathy • Thromboembolism



DIAGNOSIS

Generally presumptive, based on acute onset of signs in a patient with predisposing factors

and consistent ECG changes (ST segment changes).

DIFFERENTIAL DIAGNOSIS

Other Causes of ST Segment Changes

- Normal variation • Myocardial ischemia/hypoxia • Hyperkalemia or hypokalemia
- Digitalis toxicity • Trauma to the heart
- Pericarditis • Artifact—wandering baseline

Other Causes of Weakness and Collapse

- Trauma • Neurologic disease • Thromboembolism • Pericardial effusion • Arrhythmia

CBC/BIOCHEMISTRY/URINALYSIS

- Mild leukocytosis • High liver enzymes
- Hyperlipidemia—if animal is hypothyroid
- High amylase • High creatine kinase and cardiac isoenzymes

OTHER LABORATORY TESTS

Low T_4 and T_3

IMAGING

- Echocardiography—2-D and M-mode echocardiography useful in evaluating wall motion abnormalities and overall left ventricular function.

DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

- Sudden deviation of the ST segment • Tall peaked T waves—first few hours • Sudden development of Q waves or a change in direction of the T wave • Axis shift of the frontal plane • Low-voltage QRS complexes
- Sudden development of bundle branch block or heart block • Sudden onset of ventricular arrhythmias because of myocardial ischemia • Sloppy “R” wave descent may be associated with intramural myocardial infarction



TREATMENT

- Treat the underlying disorder; likewise the symptomatic therapy (e.g., congestive heart failure). • Must identify and immediately treat life-threatening arrhythmias.



Figure 1.

Transmural infarction of the left ventricle in a dog with arteriosclerosis and hypothyroidism. The first three rapid successive complexes represent ventricular tachycardia. The sinus rhythm that follows illustrates small complexes, marked elevation of the S-T segment, and first-degree AV block (prolonged P-R interval). (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)



MEDICATIONS

DRUG(S)

- Thrombolytic agents, IV—(e.g., streptokinase); cost prohibitive and lack of experience with myocardial infarction in veterinary medicine with dosage and use.
- Lidocaine for ventricular arrhythmias.
- Beta-blockers—use cautiously with dilated cardiomyopathy because of possible development of low-output CHF. • Antithrombotic agents (e.g., dalteparin; low molecular weight heparin, heparin and aspirin).



FOLLOW-UP

- Determined by clinical status and diagnosis of underlying disorder. • Monitor anticoagulated patient; CBC and bleeding profiles, including fibrinogen.



MISCELLANEOUS

ABBREVIATIONS

- CHF = congestive heart failure • ECG = electrocardiogram • T_3 = triiodothyronine
- T_4 = thyroxine

Suggested Reading

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MYOCARDIAL TUMORS



BASICS

OVERVIEW

- Primary and metastatic myocardial tumors are rare tumors in dogs and cats.
- Incidence 0.19% in dogs and 0.03% in cats.
- Reported primary tumors include hemangiosarcoma, ectopic thyroid carcinoma, lymphoma, rhabdomyoma, rhabdomyosarcoma, thymoma, mesothelioma, chondrosarcoma, osteosarcoma, fibrosarcoma, myxoma, myxosarcoma, lipoma, peripheral nerve sheath tumor, granular cell tumor.

SIGNALMENT

- Dog and cat—but less common in cat.
- In dog—any age but more common between 7 and 15 years.
- Possible increased incidence in neutered animals.
- Increased incidence in saluki, French bulldog, Irish water spaniel, flat-coated retriever, golden retriever, boxer, Afghan hound, English setter, Scottish terrier, Boston terrier, bulldog, German shepherd dog.

SIGNS

- Sudden collapse
- Abdominal distention
- Exercise intolerance
- Dyspnea
- Anorexia
- Vomiting
- Diarrhea
- Acute death

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Idiopathic pericardial effusion
- Pericarditis
- Cardiomyopathy
- Heart failure
- Valvular disease
- Heart base tumors

CBC/BIOCHEMISTRY/URINALYSIS

Anemia in some patients

OTHER LABORATORY TESTS

Serum/plasma cardiac troponin I levels are increased in patients with cardiac hemangiosarcoma and might have utility for the detection of other myocardial neoplasms.

IMAGING

- Thoracic radiography—may reveal a globoid heart suggestive of pericardial effusion, masses in the area of the atria, or metastatic lesions in the lungs.
- Echocardiography—helpful in finding primary masses—positive predictive value of 92%, negative predictive values 64%.

DIAGNOSTIC PROCEDURES

- Pericardiocentesis and fluid evaluation—helpful in diagnosis of lymphoma.
- Cytology of pericardial effusion limited in usefulness in differentiating neoplastic from non-neoplastic effusions.
- ECG—may be normal or display a variety of arrhythmias, may see electrical alternans and small complexes with pericardial effusion.
- Surgical biopsy of mass—if possible.



TREATMENT

- Surgical removal of mass—if possible
- Pericardectomy—may offer relief of pericardial effusion
- Address concern for sudden death with owner



MEDICATIONS

DRUG(S)

- Management of arrhythmias—lidocaine (dogs) 2–4 mg/kg IV (to a maximum 8 mg/kg over 10-minute period), CRI—25–75 µg/kg/minute IV, mexiletine (dogs) 5–8 mg/kg PO q8–12h, sotalol 1–2 mg/kg PO q12h.
- Chemotherapy dependent on tumor type (see Lymphoma and Hemangiosarcoma chapters).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Chemotherapy can cause gastrointestinal, bone marrow, cardiac, and other

toxicities—seek advice if unfamiliar with cytotoxic drugs.



FOLLOW-UP

- Serial echocardiograms—to monitor tumor response to chemotherapy.
- Thoracic radiography and abdominal ultrasonography—to monitor for metastatic disease progression.
- ECG—to monitor response to anti-arrhythmogenic medications.
- Blood tests—especially CBC to monitor for bone marrow suppression secondary to chemotherapy.
- Prognosis—guarded to poor.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

- It is not recommended to breed animals with cancer.
- Chemotherapy is teratogenic—do not give to pregnant animals.

SEE ALSO

- Chemodectoma
- Hemangiosarcoma, Heart
- Lymphoma—Cats
- Lymphoma—Dogs

ABBREVIATION

ECG = electrocardiogram

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MYOCARDITIS



BASICS

DEFINITION

- Inflammation of the heart muscle, often caused by infectious agents affecting the myocytes, interstitium, vascular elements, or pericardium.
- Viral, bacterial, rickettsial, fungal, and protozoal diseases are all associated with myocardial inflammation (i.e., myocarditis).
- Pharmacologic agents (e.g., doxorubicin) can also be causative.

PATHOPHYSIOLOGY

- Mechanisms—toxin production, direct invasion of myocardial tissue, and immune-mediated myocardial damage; vasculitis associated with systemic disease; allergic reactions and direct myocyte damage caused by pharmacologic agents. Protozoa (e.g., *Trypanosoma cruzi*) lead to granulomatous myocarditis; viral myocarditis is associated with cell-mediated immunologic reactions.
- Myocardial involvement may be focal or diffuse. Clinical manifestations depend on the extent of the lesions. Diffuse, severe involvement may lead to global myocardial damage and CHF; discrete lesions involving the conduction system may cause profound arrhythmias.

SYSTEMS AFFECTED

- Systemic organ involvement depends on the causative agent
- Cardiovascular—myocardial failure or arrhythmias
- Respiratory—if pulmonary edema develops

INCIDENCE/PREVALENCE

- Viral myocarditis (e.g., parvovirus, distemper virus, and herpesvirus)—rare; very young puppies in their first months of life may be profoundly affected; in a second form (parvoviral), dilated cardiomyopathy develops in dogs 5–6 months of age that were infected during their first weeks of life.
- Protozoal myocarditis associated with *T. cruzi* (i.e., Chagas disease) reported in dogs < 2 years old from the southeastern United States. Males are more commonly affected than females.
- Toxoplasma gondii* occasionally causes myocarditis. Immunosuppressed animals (e.g., cats with feline leukemia virus) are at high risk.
- Hepatozoon canis* reported in dogs living in the Texas Gulf region.
- Fungal myocarditis—primarily seen in association with systemic fungal infection; myocardial involvement varies with regional prevalence and prevalence of the systemic manifestation.
- Bacterial myocarditis—can be caused by generalized sepsis and bacteremia.
- Doxorubicin cardiotoxicity—reported in dogs receiving cumulative doses = 150–240 mg/m².
- Spirochetal myocarditis associated with *Borrelia burgdorferi*—documented in 10% of humans with Lyme disease; incidence and prevalence in dogs not well documented.

GEOGRAPHIC DISTRIBUTION

Suspect myocarditis associated with infectious agents wherever these diseases are endemic (see above).

SIGNALMENT

Species

Dog and cat

Mean Age and Range

Viral myocarditis—seen primarily in animals < 1 year of age

SIGNS

General Comments

- Related to the degree and location of myocardial involvement.
- Range from those of arrhythmias to those of CHF.
- Onset of cardiac dysfunction in association with systemic illness or the use of specific pharmacologic agents is often the hallmark of myocarditis.

Historical Findings

- Coughing, exercise intolerance, dyspnea—associated with CHF.
- Syncope and weakness—associated with arrhythmias.
- Concurrent systemic manifestations—often seen with infective myocarditis.
- Use of antineoplastic or other pharmacologic agents—associated with the onset of cardiac dysfunction.

Physical Examination Findings

- Gallop rhythm or murmur may be found—depends on the nature of the myocardial damage.
- Arrhythmias—may be auscultated.
- Fever—common in patients with active infection associated with myocarditis.

CAUSES

- Virus (e.g., parvovirus, distemper virus, herpesvirus, West Nile virus).
- Protozoa (e.g., *Trypanosoma cruzi*, *Toxoplasma gondii*, *Neospora caninum*, *Hepatozoon Canis*, *Babesia* spp., and *Leishmania* spp.).
- Bacteria (e.g., *Bartonella vinsonii* subsp. *Berkhoffii*).
- Fungus (e.g., *Cryptococcus neoformans*, *Coccidioides immitis*, *Blastomycetes dermatitidis*, and *Aspergillus terreus*).
- Algae (e.g., *Prototricha* spp.).
- Doxorubicin.

RISK FACTORS

- Exposure to infectious agents
- Use of myocardiotoxic compounds
- Immunosuppression
- Debilitating diseases



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Always consider preexisting heart disease, including congenital defects, cardiomyopathy, and acquired valvular disease.
- History of a heart murmur or the presence of arrhythmias before onset of systemic illness helps differentiate from other diseases.
- Extracardiac organ involvement and identification of infectious agents may aid in the diagnosis.

CBC/BIOCHEMISTRY/URINALYSIS

Abnormalities—vary, depending on organ involvement.

OTHER LABORATORY TESTS

- Serologic tests to help identify an infectious agent.
- Cytologic examination of pericardial, pleural, and peritoneal effusions to identify the infectious organism.
- Blood culture to diagnose bacteremia.
- Troponin—levels may be high.

IMAGING

Thoracic Radiographic Findings

- Cardiac silhouette may appear large or normal depending on the extent of involvement.
- Pulmonary edema, congestion, or pleural effusion in patients with CHF.
- Globoid heart in some animals with pericardial effusion.
- Pulmonary granuloma may be found in animals with granulomatous myocardial infection.

Echocardiographic Findings

- Reflect the extent of myocardial damage; may be normal if lesions are small or primarily affect the conduction system.
- Pericardial effusion in some patients; pericardium may appear thickened and hyperechoic, depending on the extent of pericardial involvement.
- Myocardium may appear mottled with patchy areas of hyperechogenicity caused by myocardial inflammation, fibrosis, or granulomas.
- Regional dyskinesis caused by focal involvement may be appreciated on 2-D echocardiography.

Angiography

- Because of the quality and non-invasive nature of echocardiography, cardiac catheterization is rarely indicated for the diagnosis.
- May use angiography to detect specific chamber involvement or pericardial effusion, if echocardiography is not available.

DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

- Heart enlargement patterns in some patients—depending on the extent of chamber involvement.
- Arrhythmias—include both atrial and ventricular tachyarrhythmias.
- Differentiate right and left bundle branch blocks and hemiblocks from ventricular enlargement patterns.
- Atrioventricular nodal conduction disturbances in some patients.

Endomyocardial Biopsy

- Useful for detection of infectious agents (e.g., protozoa, fungal elements) or inflammatory cell infiltrates.

Pericardiocentesis

- Alleviates pericardial effusion.
- Submit fluid for cytologic examination and possible bacterial culture.

Holter Monitor Study

- To detect arrhythmias, frequency, and severity.
- To monitor antiarrhythmic therapy.

M

MYOCARDITIS

(CONTINUED)

PATHOLOGIC FINDINGS

- Dilated cardiac chambers with patchy areas of hyperemia, necrosis, or fibrosis.
- Granulomas seen grossly in some patients.
- Microscopic examination of the myocardium or pericardium may reveal inflammatory cells (e.g., lymphocytes, plasma cells, and macrophages), patchy fibrosis, or the infectious agents themselves.
- Myofiber dropout—seen in patients with doxorubicin toxicity.



TREATMENT

APPROPRIATE HEALTH CARE

- Hospitalize patients with CHF for initial medical management.
- Hospitalize patients with severe ventricular arrhythmias for initial antiarrhythmic therapy.
- Hospitalize patients with severe systemic manifestations for aggressive medical therapy.

ACTIVITY

Restricted

DIET

Sodium restriction if CHF

CLIENT EDUCATION

- Cardiac manifestations may persist even with resolution of systemic illness.
- Certain arrhythmias (i.e., ventricular tachyarrhythmias) may predispose to sudden death.
- Antemortem diagnosis may be difficult.
- Some infectious agents may pose a public health risk.

SURGICAL CONSIDERATIONS

Complete atrioventricular block may require pacemaker implantation.



MEDICATIONS

DRUG(S) OF CHOICE

- If a specific etiologic agent is identified, direct treatment against it.
- Tailor antiarrhythmic therapy to the predominant arrhythmia.
- Treat CHF with furosemide (1–2 mg/kg PO q6–12h), enalapril (0.25–0.5 mg/kg PO q12–24h), and digoxin (0.22 mg/m² PO q12h) or pimobendan (0.25 mg/kg PO q12h).

CONTRAINDICATIONS

Public health considerations may preclude treatment of some infectious diseases (i.e., *T. cruzi*).

PRECAUTIONS

- All antiarrhythmic drugs have proarrhythmic properties and should be monitored closely.
- Systemic organ involvement (e.g., renal involvement) may necessitate modifying drug dosages or use of various cardiac drugs; monitor systemic function carefully.



FOLLOW-UP

PATIENT MONITORING

- Antiarrhythmic therapy—frequent auscultation and ECG
- Serologic titers when appropriate
- Auscultation and follow-up radiographs—treatment of CHF
- Hemograms and serum biochemical analysis—systemic effects

PREVENTION/AVOIDANCE

- Avoid breeding animals with a poor vaccination history.
- Avoid endemic areas if possible.
- Monitor ECG and echocardiogram when using doxorubicin.

EXPECTED COURSE AND PROGNOSIS

- Depend on the extent and severity of myocardial involvement.
- Many systemic fungal and protozoal diseases do not respond well to medical management.
- Patients with extensive myocardial inflammation, degeneration, and signs of CHF—very poor prognosis.
- Patients with isolated, controllable arrhythmias—good prognosis if the underlying cause can be treated successfully.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Often accompanies systemic illness

AGE-RELATED FACTORS

Viral myocarditis—most often seen in animals < 1 year old

ZOONOTIC POTENTIAL

- Varies with infectious agent involved
- May be high with protozoal and mycotic infections

PREGNANCY/FERTILITY/BREEDING

Some viral diseases (e.g., canine herpesvirus and parvovirus) have been passed to the fetus during pregnancy.

SEE ALSO

- Aspergillosis—Disseminated
- Babesiosis
- Bartonellosis
- Blastomycosis
- Canine Distemper
- Canine Parvovirus Infection
- Chagas Disease (American Trypanosomiasis)
- Coccidioidomycosis
- Cryptococcosis
- Hepatozoonosis
- Herpesvirus Infection—Dogs
- Leishmaniasis
- Neosporosis
- Protothecosis
- Toxoplasmosis
- Ventricular Premature Complexes
- Ventricular Tachycardia

ABBREVIATIONS

- CHF = congestive heart failure
- ECG = electrocardiogram

Suggested Reading

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BASICS

OVERVIEW

- Involuntary, rhythmic or irregular muscle jerks. Can involve only a few adjacent muscles (focal), many or most muscles of the body (generalized), or many muscles in different jerks (multifocal) synchronously or asynchronously. • The myoclonic movements are spontaneous or activated by sensory stimulation (reflex myoclonus). • May persist during sleep. • CNS dysfunction involving segmental lower motor neurons and interneurons of the spinal cord or the brainstem. • Canine distemper virus infection—most frequent cause of myoclonus in dogs; thought to be secondary to some pacemaker activity in neurons damaged by the virus. May be caused by other encephalitides and degenerative processes affecting motor neurons.

SIGNALMENT

Acquired

- Dog and rarely cat. • No breed, sex, or age predispositions.

Congenital

- Familial reflex myoclonus—Labrador retriever and Dalmatian; develops in the first 3 weeks of life. • Spongy degeneration of either gray and/or white matter—dogs: myoclonus of the paravertebral muscles in neonate silky terrier; Samoyed at 2 weeks; Saluki at 3 months; Labrador retriever at 4–6 months. Cats—Egyptian mau at 7 weeks. Rare syndromes.

SIGNS

Historical Findings

- Canine distemper—after a bout of gastrointestinal signs, cough, and/or ocular or nasal purulent discharge; persists at rest and even during sleep or light anesthesia; consistent frequency in a given patient; distemper diagnosis may precede the myoclonus by months to years; occurs more frequently in chronic phase of distemper.
- Familial reflex myoclonus—observed when the patient starts walking; intermittent muscle contractions induced by auditory or tactile stimulus and by exercise; involves all limbs, neck, and head (e.g., the facial and masticatory muscles); patient unable to rise without assistance. • With spongy degeneration—variety of signs observed such as tremor, spasticity, opisthotonus, and myoclonus. • Chlorambucil-induced myoclonus reported in a cat with lymphoma.

Physical Examination Findings

- The patient may be otherwise healthy.
- Masticatory and appendicular muscles—most frequent affected muscles in distemper virus-induced myoclonus; may be paresis of the affected limb. • May see other signs

suggesting distemper (e.g., hard pads, ocular and nasal purulent discharge, and chorioretinitis). • Neurologic deficits suggest multifocal lesions in some patients.

CAUSES & RISK FACTORS

Congenital

- Familial in Labrador retrievers. • Spongy degeneration of unknown cause but likely inherited. • Treatment with chlorambucil in cats.

Acquired

- Canine distemper virus—the only CNS disease repeatedly associated with myoclonus in dogs; unvaccinated dogs at risk.
- Encephalitis of any cause—dogs and cats.
- Degenerative disease—especially spongy degeneration. • Described in a dog with lead poisoning. • Total intravenous anesthesia with propofol. • Intrathecal administration of morphine.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- The quickness of the jerks and the absence of voluntary influence help differentiating myoclonus from other movement disorders.
- Congenital myoclonus—in neonates or during the first months of life in otherwise healthy dogs. Excitement, voluntary activity, and tactile/auditory stimuli often increase the myoclonus. • Canine distemper virus—unvaccinated dog; observed before, during, or after the acute CNS disease; more frequently observed later when the animal is otherwise healthy. Myoclonus involves one limb, more than one limb, the facial or the masticatory muscles. • Lafora disease (progressive myoclonic epilepsy)—neurodegenerative disease that can cause myoclonic jerks. Differentiated on presence of other seizure types (generalized tonic-clonic seizures) and altered mentation. • Myoclonic epilepsy—jerks usually generalized, proximal more than distal, and flexor more than extensor; exacerbated by sensory stimulus (light, noise) and voluntary movements. Other types of seizures may be present concomitantly.

CBC/BIOCHEMISTRY/URINALYSIS

- Congenital or post canine distemper virus infection—normal. • Other acquired forms—may suggest a specific cause if the patient has infectious encephalomyelitis; otherwise, normal.

IMAGING

MRI—may help determine diagnosis in acute acquired disease.

DIAGNOSTIC PROCEDURES

Acute onset—CSF analysis, serologic testing, imaging to determine the cause if other physical or neurologic signs present. Electroencephalography and

electromyography—may help differentiate myoclonic epilepsy and peripheral nervous system disease from myoclonus.



TREATMENT

- Active encephalomyelitis—inpatient; establish a diagnosis and initiate treatment.
- Exercise—as tolerated. • Diet—ensure proper nutrition with active CNS disease; modify, if necessary, with vomiting or diarrhea. • Familial reflex myoclonus—clinical signs in Labrador retriever and Dalmatian are severe and usually not compatible with quality of life.



MEDICATIONS

DRUG(S)

- With chronic, inactive canine distemper—treatment often unnecessary; alleviation may be obtained with procainamide (125–250 mg/dog PO q6–12h).
- Gabapentin reported beneficial in tremor syndrome (10–20 mg/kg q8h). • Clorazepate (0.6–2 mg/kg PO q8h)—familial reflex myoclonus; may see improvement. • Active encephalomyelitis—treat accordingly.



FOLLOW-UP

- Monitor CNS disease. • Myoclonus usually persists indefinitely; spontaneous remission may occur. • Active distemper virus infection—poor-to-grave prognosis.
- Chronic distemper—myoclonus persists but patient otherwise healthy.



MISCELLANEOUS

ABBREVIATIONS

- CNS = central nervous system • CSF = cerebrospinal fluid • MRI = magnetic resonance imaging

Suggested Reading

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MYOPATHY, FOCAL INFLAMMATORY



BASICS

DEFINITION

- Masticatory—focal inflammatory myopathy affecting the muscles of mastication (temporalis, masseter, and pterygoid muscles) and sparing the limb muscles.
- Extraocular—selectively affects the extraocular muscles, sparing limb and masticatory muscles.

PATOPHYSIOLOGY

- Masticatory—suspected immune-mediated cause owing to auto-antibodies against type 2M fibers and a positive clinical response to immunosuppressive doses of corticosteroids.
- Extraocular—suspected immune-mediated cause owing to positive clinical response to corticosteroids.

SYSTEMS AFFECTED

Neuromuscular—muscles of mastication; extraocular muscles

GENETICS

- Unknown.
- As with auto-immune diseases in general, the appropriate genetic background must exist.
- Masticatory—Cavalier King Charles spaniels have a familial form and may be affected at less than 6 months of age.
- Extraocular—golden retrievers may have a genetic predisposition.

INCIDENCE/PREVALENCE

- Unknown
- Masticatory—relatively common

GEOGRAPHIC DISTRIBUTION

Probably worldwide

SIGNALMENT

Species

- Dog (common)
- Cat (rare)

Breed Predilections

- Various.
- Masticatory—rottweiler, Doberman, Samoyed, and Cavalier King Charles spaniel develop severe forms.
- Extraocular—golden retriever.

Mean Age and Range

No obvious age predisposition

Predominant Sex

None obvious

SIGNS

General Comments

Masticatory—usually related to abnormalities of jaw movement, jaw pain, and masticatory muscle atrophy; not a “tabletop” diagnosis; usually requires laboratory testing to confirm diagnosis.

Historical Findings

- Masticatory—acute or chronic pain when opening the jaw; inability to pick up a ball or

get food into the mouth; acutely swollen muscles; progressive muscle atrophy.

- Extraocular—bilateral exophthalmos.

Physical Examination Findings

- Masticatory—marked jaw pain with manipulation and/or trismus; acute muscle swelling with exophthalmos; muscle atrophy with enophthalmos; inability to open the jaw under anesthesia.
- Extraocular—bilateral exophthalmos; impaired vision.

CAUSES

Immune-mediated

RISK FACTORS

- Appropriate genetic background.
- Possible previous bacterial or viral infection.
- Vaccination may exacerbate active disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Retro-orbital abscess—probe behind last upper molar.
- Temporomandibular joint disease—radiographically abnormal joint.
- Polymyositis—high serum creatine kinase activity; generalized EMG abnormalities; diagnostic muscle biopsies.
- Neurogenic atrophy of temporalis muscles—determined by EMG and muscle biopsy.
- Atrophy of masticatory muscles from corticosteroids—history of corticosteroid use; characteristic changes on muscle biopsy.
- Atrophy of masticatory muscles from endocrine disorders—test for thyroid and adrenal disorders.

CBC/BIOCHEMISTRY/URINALYSIS

Serum creatine kinase activity—normal or mildly elevated

OTHER LABORATORY TESTS

- Muscle biopsy—diagnostic test of choice for masticatory muscle disease.
- Immunohistochemical assay—demonstrate auto-antibodies against masticatory muscle type 2M fibers in frozen muscle biopsy sections; negative in polymyositis and extraocular disease.
- ELISA—demonstrate auto-antibodies against masticatory muscle type 2M fiber proteins.

IMAGING

- Radiography of the temporomandibular joints.
- Orbital sonogram—for extraorbital disease; demonstrate swollen extraocular muscles.
- MRI—for demonstration of inflammation/myonecrosis in muscles.

DIAGNOSTIC PROCEDURES

EMG—differentiate between extraocular disease and polymyositis; abnormal masticatory muscles in masticatory myositis

only; generalized abnormalities including masticatory muscles in polymyositis.

PATHOLOGIC FINDINGS

Masticatory

- Swelling or atrophy of the masticatory muscles.
- Biopsy specimen—may see myofiber necrosis, phagocytosis, mononuclear cell infiltration with a multifocal and perivascular distribution; may see myofiber atrophy and fibrosis with chronic condition; eosinophils rare.

Extraocular

Mononuclear cell infiltration—restricted to extraocular muscles



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient

NURSING CARE

Gastrostomy tube—may be required with severe restrictions in jaw mobility; requires good hygiene and supportive care.

ACTIVITY

N/A

DIET

Masticatory—may require liquid food or gruel until jaw mobility is regained; may need a gastric feeding tube to facilitate fluid and caloric intake.

CLIENT EDUCATION

- Warn client that long-term corticosteroid therapy may be required.
- Inform client that residual muscle atrophy and restricted jaw movement may occur with chronic masticatory muscle disease.

SURGICAL CONSIDERATIONS

Not indicated



MEDICATIONS

DRUG(S) OF CHOICE

Corticosteroids—immunosuppressive dosages, tapered as jaw mobility, swelling, and serum creatine kinase activity return to normal; maintained at lowest alternate-day dosage that prevents restricted jaw mobility; treated for a minimum of 6 months.

CONTRAINdicATIONS

N/A

PRECAUTIONS

- Corticosteroids—watch for infection and undesirable side effects.
- Clinical signs may recur if treatment is stopped too soon.

POSSIBLE INTERACTIONS

N/A

(CONTINUED)

MYOPATHY, FOCAL INFLAMMATORY**ALTERNATIVE DRUG(S)**

Intolerable side effects of corticosteroids—
institute a lower dose of corticosteroids and
combine with another drug (e.g.,
azathioprine).

**FOLLOW-UP****PATIENT MONITORING**

- Masticatory—return of jaw mobility and decreased serum creatine kinase activity.
- Extraocular—decreased swelling of extraocular muscles.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Corticosteroids—undesirable side effects.
- Recurrence of clinical signs—treatment stopped too early.
- Poor clinical response—inadequate dosages of corticosteroids.
- Restrictive strabismus (extraocular myositis).
- Note position of tongue—venous congestion and tongue protrusion may occur under anesthesia.

EXPECTED COURSE AND PROGNOSIS

- Masticatory—jaw mobility should return to normal unless the condition is chronic and severe fibrosis develops; good prognosis if treated early with adequate dosages of corticosteroids.
- Extraocular—good response to corticosteroids; good prognosis unless chronic with restrictive strabismus.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Other concurrent auto-immune disorders

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Unknown

SYNONYMS

- Atrophic myositis
- Eosinophilic myositis

SEE ALSO

- Myopathy Inflammatory—Polymyositis and Dermatomyositis
- Myopathy, Noninflammatory—Endocrine

ABBREVIATIONS

- ELISA = enzyme-linked immunosorbent assay
- EMG = electromyogram
- MRI = magnetic resonance imaging

INTERNET RESOURCES

Comparative Neuromuscular Laboratory:
<http://vetneuromuscular.ucsd.edu>.

Suggested Reading

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Author G. Diane Shelton

Consulting Editor Walter C. Renberg



**Client Education Handout
available online**

M

MYOPATHY, GENERALIZED INFLAMMATORY



BASICS

DEFINITION

- Polymyositis—a condition in which skeletal muscles are damaged by a non-suppurative inflammatory process dominated by lymphocytic infiltration. Terminology restricted to the immune-mediated form.
- Dermatomyositis—polymyositis is associated with characteristic skin lesions.

PATOPHYSIOLOGY

- Inflammation of skeletal muscles—results in muscle weakness, stiffness, myalgia, and atrophy.
- Muscle inflammation—may be a result of immune-mediated, infectious, or paraneoplastic disorders; may be a sequela to certain drug therapies.

SYSTEMS AFFECTED

- Gastrointestinal—particularly the pharyngeal and esophageal muscles, because they are composed predominantly of skeletal muscle in dogs.
- Neuromuscular—generalized muscle involvement including masticatory and limb muscles.
- Skin/Exocrine—particularly if related to a generalized immune-mediated connective tissue disorder. Skin lesions predominate over neuromuscular signs in canine dermatomyositis.

GENETICS

- Unknown.
- As for autoimmune diseases in general, the appropriate genetic background must exist.
- Familial form of autoimmune polymyositis in Newfoundland and Vizsla.
- Dermatomyositis—reported to have an autosomal dominant inheritance pattern in rough-coated collie and Shetland sheepdog.

INCIDENCE/PREVALENCE

- Unknown.
- Generalized inflammatory myopathies—not common but recognition may be increasing.

GEOGRAPHIC DISTRIBUTION

Probably worldwide

SIGNALMENT

Species

Dog and rarely cat

Breed Predilections

- Polymyositis—various breeds of dogs and cats may be affected; breed-associated in Newfoundland, boxer, and Vizsla.
- Dermatomyositis—reported in rough-coated collie, Shetland sheepdog, and Australian cattle dog.

Mean Age and Range

- Polymyositis—none obvious
- Dermatomyositis—3–5 months of age

Predominant Sex

None obvious

SIGNS

General Comments

- Polymyositis—usually associated with a stiff-stilted gait, variable myalgia, and/or muscle weakness. May see regurgitation and megaesophagus.
- Elevated serum creatine kinase activity—supports but does not make the diagnosis of myositis. Do not rule out polymyositis if creatine kinase activity normal.
- Muscle biopsy—needed to confirm the diagnosis.

Historical Findings

- Stiff-stilted gait—acute or chronic
- Muscle swelling and/or atrophy
- Variable muscle pain
- Generalized muscle weakness and exercise intolerance
- Regurgitation of food or difficulty swallowing

Physical Examination Findings

- Variable pain upon palpation of muscle groups
- Generalized muscle atrophy, including the muscles of mastication
- Gait abnormalities, including a stiff-stilted gait
- Neurologic examination—not abnormal; may be a decreased gag reflex if the pharyngeal muscles are affected
- Dermatomyositis (dogs)—typical skin lesions

CAUSES

- Immune-mediated
- Infectious—*Toxoplasma gondii*; *Neospora canis*; *Sarcocystis spp*; tick-related diseases, bacterial infection uncommon
- Drug-induced
- Paraneoplastic or pre-neoplastic syndrome

RISK FACTORS

- Appropriate genetic background
- Possibly previous bacterial or viral infection
- Neoplasia, possibly occult
- Exposure to ticks



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Polyarthritis—differentiated by physical examination and evaluation of joint fluid.
- Noninflammatory muscle disorders—differentiated by muscle biopsy.
- Polyneuropathy—differentiated by neurologic examination, electrophysiology, and muscle and peripheral nerve biopsies.
- Chronic intervertebral disc disease—differentiated by neurologic examination and serum creatine kinase activity.
- Myasthenia gravis—differentiated by positive AChR antibody titer.

CBC/BIOCHEMISTRY/URINALYSIS

Serum creatine kinase activity—variably elevated

OTHER LABORATORY TESTS

- Serum antinuclear antibody titer—may be positive in connective tissue disorders.
- May see concurrent hypothyroidism.
- Cardiac troponin I—may have concurrent myocarditis.

IMAGING

- Regurgitation—evaluate thoracic radiography for esophageal dilatation, neoplasia.
- Cardiac silhouette—evaluate myocardial size and shape.
- Pharyngeal weakness—perform a dynamic study for the evaluation of the swallowing process.

DIAGNOSTIC PROCEDURES

- Muscle biopsy—single most important test for diagnosing polymyositis; sample multiple muscles, because condition may be missed if distribution is patchy.
- Echocardiograph—evaluate myocardial function.
- Electrodiagnostic evaluation (EMG, measurement of nerve conduction velocity)—performed to determine the distribution of muscle involvement and the muscles to be biopsied; should help differentiate myopathic from neuropathic causes of muscle weakness.

PATHOLOGIC FINDINGS

- Muscle swelling or atrophy.
- Biopsy specimens—usually contain mononuclear cell infiltrates.
- Rare neutrophils or eosinophils—may be noted.
- Regenerating myofibers—may be observed.
- Intramyofiber parasite cyst—rare.
- Chronic condition—may see extensive myofiber atrophy and fibrosis.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient

NURSING CARE

Supportive care—may be required to prevent skin wounds and decubital ulcers in non-ambulatory severely affected patients.

ACTIVITY

Should increase, along with muscle strength, as muscle inflammation decreases.

DIET

- Megaeosophagus—may require feeding from an elevation; try foods of different consistencies.
- Severe regurgitation—may need to place a gastric feeding tube to maintain hydration and nutrition.

CLIENT EDUCATION

- Warn client that long-term immunosuppressive therapy may be required for an immune-mediated condition.

(CONTINUED)

- Inform client that residual muscle atrophy and contractures may occur with chronic disease and extensive fibrosis.
- Suggest genetic counseling for familial disorders.

SURGICAL CONSIDERATIONS

Only for concurrent neoplasia



MEDICATIONS

DRUG(S) OF CHOICE

- Corticosteroids—immunosuppressive dosages usually result in clinical improvement of immune-mediated condition; decrease to the lowest alternate-day dosage that maintains normal creatine kinase activity and improved muscle strength and mobility; may require long-term therapy.
- Identified infectious agent—initiate specific therapy.
- Identified myocardial failure—initiate specific therapy.

CONTRAINdications

N/A

PRECAUTIONS

Corticosteroids—observe for infection and undesirable side effects; remember that chronic therapy may lead to muscle atrophy (steroid myopathy).

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Intolerable side effects of corticosteroids— institute a lower dose of corticosteroids combined with another drug (e.g., azathioprine, cyclosporine).

MYOPATHY, GENERALIZED INFLAMMATORY



FOLLOW-UP

PATIENT MONITORING

- Serum creatine kinase activity—periodic evaluation; if elevated, should decrease into the normal range.
- Corticosteroids—side effects.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Corticosteroids—undesirable side effects.
- Recurrence of clinical signs—treatment stopped too early.
- Poor clinical response—inadequate dosages of corticosteroids. May need additional or alternative immunosuppressant.

EXPECTED COURSE AND PROGNOSIS

- Immune-mediated condition—good to fair prognosis.
- Paraneoplastic disorder associated with occult neoplasia—guarded prognosis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Other concurrent autoimmune disorders
- Neoplasia

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Unknown

SEE ALSO

Myopathy, Noninflammatory—Endocrine

ABBREVIATIONS

- AChR = acetylcholine receptor
- EMG = electromyogram

INTERNET RESOURCES

Comparative Neuromuscular Laboratory:
<http://vetneuromuscular.ucsd.edu>

Suggested Reading

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Client Education Handout
available online

M

MYOPATHY, NONINFLAMMATORY—ENDOCRINE



BASICS

DEFINITION

Myopathies associated with various endocrinopathies (including hypothyroidism, hyperthyroidism, hypoadrenocorticism, hyperadrenocorticism) and associated with exogenous corticosteroid use (steroid myopathy).

PATHOPHYSIOLOGY

With Adrenal Dysfunction

- Glucocorticoid excess—impaired muscle protein metabolism; may accelerate degradation of myofibrillar and soluble protein in skeletal muscle; impairment of carbohydrate metabolism owing to induction of an insulin-resistant state; may note elevated ACTH levels.
- Adrenal insufficiency—circulatory insufficiency; fluid and electrolyte imbalance; impaired carbohydrate metabolism.

With Thyroid Disease

- Hyperthyroidism—increased mitochondrial respiration; accelerated protein degradation and lipid oxidation; glycogen depletion; impaired glucose uptake.
- Hypothyroidism—impaired muscle energy metabolism by reduced glycogen breakdown, gluconeogenesis, and oxidative and glycolytic capacity; impaired insulin-stimulated carbohydrate metabolism.

SYSTEMS AFFECTED

- Neuromuscular—impaired energy metabolism.
- Cardiovascular—impaired energy metabolism; circulatory disorders.

GENETICS

N/A

INCIDENCE/PREVALENCE

- Exact incidence unknown.
- Myopathies related to exogenous corticosteroids—common.
- Myopathies associated with Cushing syndrome and hypothyroidism—not uncommon.

GEOGRAPHIC DISTRIBUTION

Probably worldwide

SIGNALMENT

Species

- Dog—steroid myopathy; weakness associated with hyperadrenocorticism and hypoadrenocorticism; hypothyroidism.
- Cat—weakness associated with hyperthyroidism.

Breed Predilections

Affects several breeds

Mean Age and Range

- Steroid myopathy—dogs of any age
- Other disorders—see specific disease

Predominant Sex

None found

SIGNS

General Comments

Corticosteroid use in dogs—muscles very susceptible; muscle atrophy (particularly the masticatory muscles) is not uncommon with prolonged corticosteroid use.

Historical Findings

- Muscle weakness, atrophy, and stiffness
- Regurgitation
- Dysphagia
- Dysphonia

Physical Examination Findings

- Muscle weakness, stiffness, cramping, and myalgia
- Muscle hypertrophy or atrophy
- May not note other clinical signs of an endocrine disorder

CAUSES

- Endocrine dysfunction
- Auto-immune
- Neoplastic

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Inflammatory myopathies—distinguished by muscle biopsy.
- Noninflammatory myopathies—distinguished by muscle biopsy.

CBC/BIOCHEMISTRY/URINALYSIS

- Baseline testing—abnormalities consistent with endocrine disorder.
- Serum creatine kinase activity—usually normal, but may be mildly elevated if necrotic muscle fibers.

OTHER LABORATORY TESTS

Thyroid and adrenal function tests—should be diagnostic

IMAGING

- Dynamic studies—evaluate pharyngeal and esophageal function; with regurgitation and dysphagia.
- Cardiac evaluation—for cats with hyperthyroidism.

DIAGNOSTIC PROCEDURES

- Muscle biopsy—fiber typing in fresh frozen muscle biopsy sections important; paraffin sections will not be diagnostic.
- Electromyography.

PATHOLOGIC FINDINGS

- Hyperadrenocorticism and steroid myopathies—selective atrophy of type 2 muscle fibers; may see lobulated or ragged-red fibers with associated myotonia.
- Hypoadrenocorticism—muscle biopsies normal.

- Hyperthyroidism (cats)—muscle biopsies normal.

- Hypothyroidism—atrophy of type 2 fibers; may see an increase in type 1 fibers; may see PAS-positive deposits and nemaline rod bodies.



TREATMENT

APPROPRIATE HEALTH CARE

Depends on specific endocrine disorder

NURSING CARE

Physical therapy—with musculoskeletal manifestations

ACTIVITY

- Clinical corticosteroid myopathy (humans)—inactivity worsens condition; increased muscle activity may partially prevent atrophy.
- Physical therapy—may help prevent and treat muscle weakness and wasting in dogs receiving glucocorticoids.

DIET

- Regurgitation and megaesophagus—feed from an elevation.
- Dysphagia and esophageal dilation—give food with the best-tolerated consistency.
- Gastric feeding tube—if oral feeding is not tolerated.

CLIENT EDUCATION

Depends on specific endocrine disorder

SURGICAL CONSIDERATIONS

Removal of neoplasia



MEDICATIONS

DRUG(S) OF CHOICE

- Depends on specific endocrine disorder.
- Corticosteroid myopathy—decrease corticosteroid dosage to the lowest possible level; use a non-fluorinated corticosteroid and alternate-day dosing.
- Intramyofiber lipid storage with steroid myopathy—L-carnitine (50 mg/kg PO q12h) may improve muscle strength.

CONTRAINdications

N/A

PRECAUTIONS

Depend on specific endocrine disorder

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Fluorinated corticosteroids, triamcinolone, betamethasone, and dexamethasone—most likely to produce muscle weakness; use an equivalent dose of another corticosteroid.

(CONTINUED)

MYOPATHY, NONINFLAMMATORY—ENDOCRINE**FOLLOW-UP****PATIENT MONITORING**

- Depends on specific endocrine disorder.
- Steroid myopathy—should note return of muscle strength and mass with decreased steroid use.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Depend on specific endocrine disorders

EXPECTED COURSE AND PROGNOSIS

- Myotonia associated with hyperadrenocorticism—poor prognosis for resolution.
- Steroid myopathy—good prognosis for return of muscle strength and mass; recovery may take weeks.
- Hypothyroid myopathy—improvement in muscle pain and stiffness common.

- Hyperthyroidism (cats)—good prognosis for return of muscle strength following reversion to euthyroid state.
- Hypoadrenocorticism—good prognosis for return of muscle strength.
- Dysphagia and regurgitation—may resolve with adequate treatment.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- May note multiple endocrinopathies
- Hypothyroidism (dogs)—concurrent myasthenia gravis

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Unknown

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- PAS = periodic acid-Schiff

INTERNET RESOURCESComparative Neuromuscular Laboratory:
<http://vetneuromuscular.ucsd.edu>.*Suggested Reading*

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Consulting Editor Walter C. Renberg

M

MYOPATHY, NONINFLAMMATORY—HEREDITARY LABRADOR RETRIEVER



BASICS

OVERVIEW

- An inherited myopathy of Labrador retrievers.
- Recognized worldwide.
- Autosomal recessive mode of inheritance.
- More recently named centronuclear myopathy (CNM).
- Pathophysiologic mechanism(s) are still unclear; however, the causative genetic mutation has been identified (*PTPLA* gene mutation).
- Loss of tendon reflexes and histologic examination of muscle—may be more typical of a neurogenic than a myopathic cause.
- No immunohistochemical abnormalities to suggest a disorder of muscle protein.
- No morphologic changes in the CNS or peripheral nerves identified.

SIGNALMENT

- Occurs in black and yellow Labrador retrievers.
- Age of onset—variable (6 weeks–7 months); most commonly recognized at 3–4 months.
- Affects males and females.
- A similar inherited CNM has been identified in young male and female Great Danes.

M

SIGNS

- Severity ranges from stilted gait and exercise intolerance to severe muscle weakness, bunny-hopping pelvic limb gait, ventroflexion of the head and neck, arched back, and abnormal joint posture (cow-hocked stance, hyperextended carpi).
- Worsens with exercise, excitement, and cold weather.
- Patient may collapse with forced exercise.
- Some improvement with rest.
- Generalized muscle atrophy—mild to severe.
- Atrophy of proximal limb and masticatory muscles often most prominent.
- Tendon reflexes—normal, hypoactive, or absent.
- Occasionally, patients become recumbent or develop megaesophagus.

CAUSES & RISK FACTORS

Autosomal recessive mode of inheritance



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- With little muscle atrophy—exercise intolerance may mimic signs of myasthenia gravis, cardiac or orthopedic disease.
- Exercise-induced collapse syndrome also recognized in this breed; however, not associated with muscle atrophy and collapse seen only after strenuous exercise.

- With marked muscle atrophy—consider other myopathies (infectious, immune-mediated, metabolic, congenital) and generalized lower motor neuron disorders.
- Infectious myopathy due to congenital neospora caninum infection has a higher incidence in Labrador retrievers.
- Congenital muscular dystrophy in a male due to dystrophin deficiency and in a female due to sarcolemmal collagen deficiency myopathy have also been reported in Labrador retrievers.
- An X linked myotubular myopathy (XLMTM), which is an unrelated centronuclear myopathy, due to a mutation in *MTM1* gene, has also been identified in young male Labrador retrievers. Affected dogs show progressive weakness and muscle atrophy in the first 2 months of life resulting in euthanasia before 6 months of age.

CBC/BIOCHEMISTRY/URINALYSIS

Creatine kinase—normal or mildly or moderately elevated

OTHER LABORATORY TESTS

A DNA test is available for the causative genetic mutation.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- EMG—spontaneous activity, including complex repetitive discharges, especially in proximal limb and masticatory muscles; may reveal no abnormalities with mild disease.
- Muscle histology—reveals variation in fiber size, angular atrophy of both type 1 and 2 myofibers, grouped atrophy, increase in central nuclei, muscle degeneration and regeneration, and fibrosis; may note deficiency in type 2 myofibers or predominance of type 1 myofibers.
- DNA test for causative genetic mutation.



TREATMENT

- None specific.
- Avoid cold, because it exacerbates clinical signs.
- Discourage breeding of affected animals and parents and littermates of affected dogs.
- Do not repeat dam-sire matings that result in affected offspring.



MEDICATIONS

DRUG(S)

Supplementation with L-carnitine (50 mg/kg PO q12h) may be of benefit in improving muscle strength.

CONTRAINdications/POSSible INTERACTIONS

None known



FOLLOW-UP

- Clinical signs generally stabilize at approximately 1 year of age.
- Mild disease—may be an acceptable pet; may show some improvement in exercise tolerance.
- Aspiration pneumonia—a risk in dogs with megaesophagus.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

ABBREVIATIONS

- CNM=centronuclear myopathy
- CNS = central nervous system
- EMG = electromyogram

INTERNET RESOURCES

<http://www.ivis.org>, Labrador Retriever Hereditary Myopathy

Suggested Reading

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Author Georgina Child

Consulting Editor Walter C. Renberg

MYOPATHY, NONINFLAMMATORY—HEREDITARY MUSCULAR DYSTROPHY



BASICS

OVERVIEW

- Muscular dystrophy is an inherited, progressive and degenerative, generalized myopathy. Most muscular dystrophies are due to mutations in genes that code for muscle membrane associated proteins in the dystrophin-glycoprotein (DAG) complex
- Most common form in dogs occurs as a result of a deficiency of the protein dystrophin.
- Muscular dystrophy due to dystrophin deficiency has an X-linked mode of inheritance and affected animals are predominantly male.
- Dystrophin deficiency—identified first in golden retrievers. Subsequently cases have been reported in Irish terriers, Samoyeds, rottweilers, Belgian shepherds, Pembroke Welsh corgis, Brittany spaniels, German shorthaired pointers, rat terriers, miniature schnauzers, Labrador retrievers, Alaskan malamutes, wirehaired fox terriers, Japanese spitz, Cavalier King Charles spaniels. Sporadic cases in other breeds are likely.
- The dystrophin gene is large and new mutations are likely to occur.
- Hypertrophic muscular dystrophy associated with dystrophin deficiency also occurs in domestic shorthair cats.
- Deficiency of other muscle-associated proteins, e.g., alpha2 laminin (merosin) and sarcoglycan, has been identified more recently in dogs and cats and is not necessarily X-linked (females affected).
- A muscular dystrophy associated with loss of alpha-dystroglycan with an autosomal recessive mode of inheritance occurs in young Devon Rex and Sphynx cats.
- Unclassified muscular dystrophies have also been reported in other dogs (males and females).

SIGNALMENT

- Seen primarily in neonate and young dogs (< 1 year).
- Described in cats.
- Muscular dystrophy due to dystrophin deficiency primarily affects males.
- Several dog breeds known to be affected. Best described in golden retrievers.
- Females—usually carriers of dystrophin gene defect, but dystrophin-deficient females may exhibit muscle weakness, tremors, limb deformities, and exercise intolerance.
- Muscular dystrophy due to other muscle protein or unclassified defects may be seen in young male or female dogs and cats of any breed.

SIGNS

Dogs

- Golden retrievers—exercise intolerance; stilted gait; bunny-hopping pelvic limb gait; plantigrade stance; partial trismus; muscle atrophy (especially the trunci and temporalis

muscles); hypertrophy of some muscles (especially the tongue); kyphosis; lordosis; drooling; dysphagia; aspiration pneumonia (due to pharyngeal and/or esophageal involvement).

- Other breeds—similar; include vomiting and megaesophagus.
- Abnormalities vary in severity, onset, and progression; may be seen as early as 6 weeks; tend to stabilize by 6 months.
- Stunting and ineffective suckling—may be evident in younger pups.
- Cardiac failure—may occur owing to cardiomyopathy.
- Severe muscle contractures may develop.
- Spinal reflexes—normal initially; may become hypoactive.

Cats

- Dystrophin deficient—muscle hypertrophy; stiff gait; cervical rigidity; exercise intolerance; vomiting; may see calcified nodules on the tongue.
- Usually young animals but not apparent in one cat until 21 months of age.
- Other hereditary myopathies in cats may cause muscle atrophy; weakness; ventroflexion of the head and neck; dorsal protrusion of the scapulae with triceps brachii and dorsal cervical muscles most severely affected.

CAUSES & RISK FACTORS

- Dystrophin deficiency—inherited defect of the X chromosome.
- Other muscular dystrophies may not be X-linked.
- Devon Rex myopathy—autosomal recessive.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other inherited myopathies including centronuclear myopathies, X-linked myotubular myopathy, infectious (especially protozoal), immune-mediated, or metabolic myopathies; distinguished by muscle histology and demonstration of dystrophin deficiency or other muscle membrane protein associated deficiency.

CBC/BIOCHEMISTRY/URINALYSIS

- Dystrophin deficiency—normal except for marked elevation in serum creatine kinase (may be > 10,000 U/L; further increased after exercise). AST also likely to be elevated.
- Other muscular dystrophy—CK may be normal.

OTHER LABORATORY TESTS

- Muscle biopsy—dystrophin deficiency demonstrated by immunohistochemical evaluation of fresh frozen muscle; diagnostic.
- Immunohistochemistry and immunoblotting analysis of muscle biopsy specimens can also assess abnormalities of other muscle proteins including dystrophin associated proteins, laminin, sarcoglycan.

- DNA tests available for specific genetic abnormalities in some breeds.
- Serologic testing—may be warranted to rule out infectious and immune-mediated causes.

DIAGNOSTIC PROCEDURES

Electromyography—shows complex repetitive discharges.

PATHOLOGIC FINDINGS

Histologic examination of muscle—muscle fiber necrosis and regeneration; myofiber mineralization (may be dramatic); myofiber hypertrophy (may be variation in myofiber size); fibrosis.



TREATMENT

None proven effective



MEDICATIONS

DRUG(S)

Glucocorticosteroids—may provide some improvement; reason unknown. However, myofiber calcification increases, which may be deleterious.



FOLLOW-UP

PATIENT MONITORING

Monitor periodically for aspiration pneumonia or cardiomyopathy.

PREVENTION/AVOIDANCE

- Discourage breeding of affected animals.
- Do not repeat dam-sire matings that result in affected offspring.

EXPECTED COURSE AND PROGNOSIS

- Overall prognosis—guarded to poor as no effective palliative treatment.
- Golden retrievers—signs tend to stabilize at 6 months.
- Other dog breeds and cats—progression variable.



MISCELLANEOUS

ABBREVIATION

AST = aspartate aminotransferase

Suggested Reading

- Dickinson PJ, LeCouteur RA. Feline neuromuscular disorders. Vet Clin North Am Small Anim Pract 2004, 34(6):1307–1359.
Shelton GD, Engvall E. Muscular dystrophies and other inherited myopathies. Vet Clin North Am Small Anim Pract 2002, 32(1):103–124.

Author Georgina Child

Consulting Editor Walter C. Renberg

MYOPATHY, NONINFLAMMATORY—HEREDITARY MYOTONIA



BASICS

OVERVIEW

- Characterized by persistent contraction or delayed relaxation of muscle fibers on initiation of movement or when stimulated to contract. • May affect all skeletal muscles.
- Myotonia may be congenital or acquired.
- A genetic basis has been determined in some breeds • Acquired myotonia may be associated with non-inflammatory or inflammatory myopathy. • Neuromyotonia and myokymia, characterized by continuous muscle fiber activity, are believed to be due to hyperexcitability of terminal nerve branches (neuromyotonia) or hyperexcitability of the motor nerve axon at any level (myokymia) rather than a primary muscle disorder.
- Neuromyotonia is characterized by muscle stiffness and delayed relaxation. • Myokymia describes rhythmic undulating muscle movements that produce a rippling movement of the skin. • The cause of neuromyotonia and myokymia (CMFA) in all reported cases remains unclear. • CMFA and spinocerebellar ataxia may occur concurrently in Jack Russell Terriers (and related breeds) and both are associated with a genetic mutation causing neuronal ion channel dysfunction.

M

SIGNALMENT

- Congenital myotonia—chow chows, miniature schnauzers and Australian cattledogs; rarely seen in other dog breeds.
- Clinical signs seen when affected puppies begin to walk. • Acquired myotonia—all breeds of any age potentially susceptible.
- Myotonia reported in young domestic cats.
- Neuromyotonia and myokymia (CMFA)—described in predominantly young JRTs worldwide, rarely in other breeds and a cat.

SIGNS

- Difficulty rising. • Stiffness after rest or initiation of activity. • May note dyspnea, voice change, dysphagia, and/or regurgitation, especially after eating. • May improve with exercise. • May be exacerbated by cold.
- Muscle stiffness and myokymia observed in young JRTs may result in life threatening hyperthermia. In this breed clinical signs are episodic but dogs may have continuous ataxia.

Physical Examination Findings

- Hypertrophy of proximal limb muscles, neck muscles, and tongue. • Tongue may protrude from the mouth. • Abduction of thoracic limbs. • Stiff, stilted, pelvic limb gait.
- Patient may fall and remain rigid in lateral recumbency for short periods. May become cyanotic. • Affected miniature schnauzers may have craniofacial abnormalities such as mandibular shortening.

CAUSES & RISK FACTORS

- Chow chows—suspected autosomal recessive mode of inheritance. • Miniature schnauzers, Australian cattledogs—autosomal recessive mode of inheritance (*CLCN1* gene).
- Jack Russell terrier group CMFA and spinocerebellar ataxia—autosomal recessive mode of inheritance (*KCNJ10* gene).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other myopathies—distinguished by signalment and clinical, electromyographic, and histologic findings. • Hypertonicity disorders or other movement disorders—recognized breed association.

CBC/BIOCHEMISTRY/URINALYSIS

Creatine kinase—may be normal or slightly elevated.

OTHER LABORATORY TESTS

DNA testing for known genetic mutations

DIAGNOSTIC PROCEDURES

- Percussion of muscles and tongue—causes sustained dimpling. • Electromyography—myotonia characterized by multifocal or generalized high-frequency discharges that wax and wane in amplitude and frequency (dive bomber—sounding potentials) and are increased after muscle percussion. Myokymic discharges—rhythmic high-frequency bursts of single motor unit potentials are characteristic findings in myokymia.

PATHOLOGIC FINDINGS

- Muscle histology—congenital myotonia : normal or mild changes. • Degenerative and/or inflammatory changes on muscle histology may be seen in cases of acquired myotonia. • No abnormalities found on muscle biopsy in JRTs with neuromyotonia and myokymia (CMFA).



TREATMENT

- None specific. • Discourage activities that result in hyperventilation. • Avoid strenuous exercise and excitement. • Avoid cold.
- Anesthesia (induction and recovery)—possible risk of respiratory obstruction owing to adduction of vocal cords or regurgitation.



MEDICATIONS

DRUG(S)

- Membrane-stabilizing drugs—procainamide, quinidine, phenytoin, and

mexiletine; may decrease severity of clinical signs.

- Procainamide reported to be most effective in chow chows. Treatment may decrease stiffness, stridor, and regurgitation, but gait remains abnormal.
- Extended release procainamide 40–50 mg/kg q8–12h or mexiletine 8.3 mg/kg q8h reported to be effective in miniature schnauzers.
- Procainamide 10 mg/kg q8h or mexiletine 4 mg/kg q12h or sustained-release phenytoin at an increasing dose 50–100 mg/kg for 6 weeks then on serum concentration monitoring 2–8 mg/L reported to reduce frequency of episodes of CMFA in approximately half of affected JRTs, but response is generally temporary.
- Anaesthesia and cooling to treat hyperthermia may be required to treat episodes of CMFA in JRTs.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Myotonia in humans is worsened with treatment with dantrolene, beta-adrenergic blocking agents, diuretics, and neuromuscular blocking agents. Bromide-containing agents such as potassium bromide may be contraindicated.



FOLLOW-UP

PREVENTION/AVOIDANCE

- Chow chows, miniature schnauzers, Australian cattledogs—inherited condition; advise owner regarding breeding. • DNA testing for carrier dogs prior to breeding.
- Discourage breeding of affected animals.
- Do not repeat dam-sire matings that resulted in affected offspring.

POSSIBLE COMPLICATIONS

- Respiratory obstruction and/or aspiration of regurgitated food—may be life-threatening; advise owners of the clinical symptoms and treatment. • Hyperthermia associated with CMFA in JRTs is life-threatening.

EXPECTED COURSE AND PROGNOSIS

Prognosis guarded

ABBREVIATIONS

- CMFA = continuous muscle fiber activity
- JRT = Jack Russell terrier

Suggested Reading

Vite CH. Myotonia and disorders of altered muscle cell membrane excitability. Vet Clin North Am Small Anim Pract 2002, 32(1):169–187.

Author Georgina Child

Consulting Editor Walter C. Renberg

MYOPATHY, NONINFLAMMATORY—HEREDITARY SCOTTY CRAMP



BASICS

OVERVIEW

- Inherited disorder in Scottish terriers characterized by episodic muscle hypertonicity or cramping.
- Not associated with any morphologic changes in muscle, peripheral nerve, or the CNS.
- Is better characterized as a hypertonicity disorder than a myopathy.
- Thought to be the result of a disorder in serotonin metabolism within the CNS.
- Similar condition (reflex myoclonus) reported in young Dalmatians and Labrador retrievers—may be result of low numbers of neurotransmitter glycine receptors in the CNS.
- Episodic muscle hypertonicity syndromes also occur in Cavalier King Charles spaniels (episodic falling syndrome), Norwich terriers, Bichon frises, border terriers (Spike's disease or canine epileptoid cramping syndrome), Wheaten terriers, springer spaniels, and sporadically in other breeds.

SIGNALMENT

- Young Scottish terriers, typically < 1 year of age. Clinical signs may be seen in puppies as early as 6–8 weeks of age.
- No known sex predilection.

SIGNS

- Normal at rest and on initial exercise.
- Further exercise or excitement—abduction of the thoracic limbs; arching (kyphosis) of the thoracolumbar vertebral column; stiffening or overflexion of the pelvic limbs (goose-stepping gait).
- Patient may fall, with tail and pelvic limbs flexed tightly against the body.
- Respiration—may cease for a short time.
- Facial muscles—may be contracted.
- No loss of consciousness.
- Severity varies.
- Episodes—may last up to 30 minutes.

CAUSES & RISK FACTORS

Inherited condition with probable autosomal recessive mode of transmission



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Seizure disorder—distinguished on basis of family history, typical clinical signs with no

loss of consciousness, and induction of signs with serotonin antagonists.

- Cerebellar cortical degeneration described in Scottish terriers—clinical signs are not episodic and neurologic abnormalities are slowly progressive.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

DNA test available for episodic falling syndrome in Cavalier King Charles spaniels. Genetic abnormality associated with other hypertonicity disorders not yet determined.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Clinical signs may be induced by giving the serotonin antagonist methysergide (0.3 mg/kg PO). Cramping is evident in 2 hours and may last for 8 hours.



TREATMENT

Behavioral modification and/or environmental changes—eliminate triggering situations (excitement, stress); may be adequate in controlling episodes.



MEDICATIONS

DRUG(S)

- Acepromazine maleate (0.1–0.75 mg/kg IM or PO), diazepam (0.5–1.5 mg/kg PO q8h), or vitamin E (> 125 U/kg q24h)—may reduce the incidence and severity of Scottie cramp.
- Fluoxetine, a selective serotonin reuptake inhibitor, resulted in a marked reduction in the clinical signs in one Scottish terrier at a dose of 1.2 mg/kg q12h initially followed by 0.8 mg/kg q12h. Clinical improvement has been maintained for > 1 year.
- Clonazepam 0.5 mg/kg q8h may result in improvement in Cavalier King Charles spaniels with hypertonicity syndrome (episodic falling syndrome).

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Serotonin antagonists—increase severity of clinical signs.
- Aspirin, indomethacin, phenylbutazone, Banamine (flunixin meglumine), and penicillin—may exacerbate clinical signs.



FOLLOW-UP

PATIENT MONITORING

Nonprogressive

PREVENTION/AVOIDANCE

- Discourage breeding of affected and related animals.
- Do not repeat dam-sire matings that result in affected offspring.

EXPECTED COURSE AND PROGNOSIS

- Mild to moderate—fair to good long-term prognosis; usually manageable disability by owners; nonprogressive.
- Severe—guarded prognosis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

M

ABBREVIATION

CNS = central nervous system

Suggested Reading

Geiger KM, Klopp LS. Use of a selective serotonin reuptake inhibitor for treatment of episodes of hypertonia and kyphosis in a young adult Scottish Terrier. J Am Vet Med Assoc 2009, 235:168–171.

Meyers KM, Clemons RM. Scotty cramp. In: Kirk RW, ed., Current Veterinary Therapy VIII. Philadelphia: Saunders, 1983, pp. 702–704.

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Author Georgina Child

Consulting Editor Walter C. Renberg

MYOPATHY, NONINFLAMMATORY—METABOLIC



BASICS

DEFINITION

- Myopathy associated with disorders of glycogen metabolism, lipid metabolism, or oxidative phosphorylation and mitochondrial metabolism.
- Currently poorly characterized in veterinary medicine.

PATOPHYSIOLOGY

- Usually associated with inherited or acquired enzyme defects involving major metabolic pathways.
- May result in storage of the abnormal metabolic byproduct or morphologic abnormalities of mitochondria.

SYSTEMS AFFECTED

- Cardiovascular—dependent on oxidative metabolism for energy.
- Hemic/Lymphatic/Immune—RBCs depend on glycolytic metabolism.
- Nervous—dependent on glycolytic and oxidative metabolism for energy.
- Neuromuscular—dependent on oxidative metabolism for energy.
- Storage products in other organs—liver, spleen.

M

GENETICS

Undetermined

INCIDENCE/PREVALENCE

Rare, except lipid-storage myopathies

GEOGRAPHIC DISTRIBUTION

Unknown; probably worldwide

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Muscle phosphofructokinase deficiency—English springer spaniel, American cocker spaniel, whippet.
- Acid maltase deficiency—Lapland dog.
- Branching enzyme deficiency—Norwegian forest cat.
- Debranching enzyme deficiency—German shepherd, Akita, curly-coated retrievers.
- Pyruvate dehydrogenase phosphatase 1 deficiency—Clumber spaniel, Sussex spaniel.
- Mitochondrial myopathy—Old English sheepdog, Yorkshire terrier, possibly Jack Russell terrier.

Mean Age and Range

- Inherited metabolic defects—2–3 months
- Acquired metabolic defects—adults

Predominant Sex

None found

SIGNS

General Comments

Very few of these conditions have been adequately described.

Historical Findings

- Muscular weakness
- Exercise intolerance
- Cramping
- Collapse
- Regurgitation and/or dysphagia
- Esophageal and/or pharyngeal abnormalities
- Dark urine; myoglobinuria, hemoglobinuria
- Encephalopathy.
- Vomiting

Physical Examination Findings

- Exercise-related weakness, stiffness, and/or cramping
- Abnormal neurologic examination—disorientation; stupor; coma
- Abdominal distention—storage product accumulation in liver
- May appear normal, with fluctuating clinical signs

CAUSES

- Inborn error of metabolism
- Acquired metabolic defect
- Viral infections
- Drug-induced
- Environmental factors

RISK FACTORS

- Inherited disorders
- Appropriate genetic background
- Others unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Inflammatory myopathies—differentiated by muscle biopsy.
- Other non-inflammatory myopathies—differentiated by muscle biopsy.
- Other metabolic encephalopathies—differentiated by laboratory evaluation.

CBC/BIOCHEMISTRY/URINALYSIS

- Plasma lactate and pyruvate levels—elevated resting or post-exercise with disorders of fatty acid oxidation or oxidative phosphorylation; no elevation with glycolytic disorders.
- Serum creatine kinase activity—may be elevated with exercise and normal at rest; may be persistently elevated.
- Hypoglycemia—may occur with some glycolytic and oxidative disorders.
- Hyperammonemia—may occur with urea cycle defects.

OTHER LABORATORY TESTS

- Quantitation of plasma amino acids—abnormal accumulations.
- Quantitation of urine organic acids—demonstrate abnormal organic acid production.
- Quantitation of plasma, urine, and muscle carnitine—may be low with primary or secondary disorders of carnitine; low with primary organic acidurias.
- Specific enzyme assays—depend on suspected metabolic defect.

- Fibroblast cultures—study metabolic defect.
- DNA-based tests to identify affected dogs and carriers when available.

IMAGING

MRI—evaluate the CNS; reveals abnormalities in humans.

DIAGNOSTIC PROCEDURES

- Light microscopy—fresh frozen muscle sections; demonstrates storage products (glycogen, lipid) or abnormal mitochondria.
- Electron microscopy of muscle reveals abnormal mitochondria, paracrystalline inclusions, and glycogen or lipid accumulation.
- Cardiovascular system evaluation—may have concurrent cardiomyopathy.
- Other organ biopsies—with organomegaly.

PATHOLOGIC FINDINGS

- Triglyceride droplets in muscle—lipid storage myopathy
- Ragged-red fibers in muscle—mitochondrial myopathy
- Glycogen deposition in muscle—glycogen storage disorder



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—may require intensive care for severe encephalopathy, seizures, lactic acidemia, hypoglycemia, or hyperammonemia.
- Outpatient—clinical signs related only to neuromuscular system.

NURSING CARE

Depends on type and severity of disorder

ACTIVITY

Exercise restriction—with muscle weakness, stiffness, or exercise-induced collapse.

DIET

- Avoid prolonged periods of fasting.
- Restrictions—depend on underlying defect.
- Vitamin and co-factor therapy—determined by underlying defect.

CLIENT EDUCATION

- Warn client that most inherited metabolic defects cannot be cured, although some can be treated.
- Advise against breeding affected individuals.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

- Depend on the abnormality and clinical signs.
- Lipid storage myopathies—L-carnitine (50 mg/kg PO q12h); riboflavin (50–100 mg

(CONTINUED)

PO q24h); coenzyme Q10 (1 mg/kg PO q24h).

- Mitochondrial myopathies—may benefit from therapy similar to that listed for lipid storage myopathies.

CONTRAINDICATIONS

None known

PRECAUTIONS

Avoid fasting and strenuous exercise if they precipitate clinical signs.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Lipid storage myopathies—return of muscle strength; elimination of muscle pain.
- Elevated serum creatine kinase—should return to normal.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Severe neurologic impairment

EXPECTED COURSE AND PROGNOSIS

- Untreatable disorder—poor prognosis.
- Lipid storage myopathies—good prognosis if no underlying organic academia.

MYOPATHY, NONINFLAMMATORY—METABOLIC



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Iatrogenic and naturally occurring Cushing syndrome
- Lipid storage myopathies—found in some dogs
- Hemolytic anemia—due to underlying metabolic defect

AGE-RELATED FACTORS

- Inborn errors—usually found in young dogs
- Acquired defects—found in adult dogs

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Unknown

SYNONYMS

- Acid maltase deficiency—glycogenosis type II
- Cori disease—glycogenosis type III
- Glycogen storage disorders
- Lipid storage myopathies
- Mitochondrial myopathies
- Phosphofructokinase deficiency—glycogenosis type VII

ABBREVIATIONS

- CNS = central nervous system
- MRI = magnetic resonance imaging
- RBC = red blood cell

INTERNET RESOURCES

- Comparative Neuromuscular Laboratory: <http://vetneuromuscular.ucsd.edu>.

- PennGen: <http://vet.upenn.edu/researchcenters/penngen>.
- VetGenLLC: <http://www.vetgen.com/>

Suggested Reading

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M

MYXEDEMA AND MYXEDEMA COMA



BASICS

OVERVIEW

• Myxedema coma is a rare, life-threatening, manifestation of severe hypothyroidism and is considered an endocrine emergency. • The development of myxedema coma requires a precipitating event that overwhelms normal homeostatic mechanisms. No single event has been identified in animals. • The greatest challenge with myxedema coma is recognizing the syndrome. Once it is recognized, immediate and intensive supportive care is necessary. Successful treatment has been reported; however, mortality rates can be high.

SIGNALMENT

- Dogs, the majority of which have been Doberman pinschers • Age range: 5–7 years
- No sex predilection • Myxedema coma is not reported in cats

SIGNS

Historical Findings

• The common findings in patients with myxedema coma are changes in mental status, altered thermoregulation, and non-pitting skin edema. • Mentation changes, due to brain edema, can range from altered alertness to coma. Mental depression is the most common assessment of mental status. Coma is not consistently reported. • Other signs consistent with hypothyroidism may be reported. • Patients may have been previously diagnosed with hypothyroidism.

Physical Examination Findings

• Hypothermia without shivering is a consistent finding with myxedema coma. Thyroxine amplifies catecholamine function, helping to stimulate muscular activity associated with shivering. Reduced T_4 level blunts the ability to shiver. • Cold extremities due to peripheral vasoconstriction and central shunting of blood secondary to hypothermia. • Non-pitting edema of the skin is due to cutaneous deposition of glycosaminoglycans in the interstitial space. • Decreases in lung and heart sounds may be noted due to pleural effusion (present in up to 50% of cases).

CAUSES & RISK FACTORS

• Myxedema coma results from chronic untreated severe primary hypothyroidism. • Both forms of primary hypothyroidism (lymphocytic thyroiditis and idiopathic thyroid atrophy) have reportedly been associated with the development of myxedema coma. • A secondary precipitating event is usually associated with the onset of a myxedema crisis. Precipitating events can include, but are not limited to, infections, respiratory disease, heart failure, and hypovolemia. • Sporadic reports exist suggesting that exposure to cold temperatures may act as a precipitating event, though this has not been consistently reported.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Weakness may be associated with cardiovascular disease, neurologic disease, and other endocrinopathies. • Dilated cardiomyopathy if patient is a Doberman pinscher. • Hypothermia may be associated with shock and other cardiovascular and endocrine diseases. Hypothermia associated with factors other than myxedema coma will usually be accompanied by shivering.

CBC/BIOCHEMISTRY/URINALYSIS

- Mild nonregenerative anemia is most commonly noted • Hypercholesterolemia
- Hypertriglyceridemia • Hypoglycemia
- Hyponatremia • Hypoxemia • Hypercarbia
- Urinalysis is normal

OTHER LABORATORY TESTS

- Thyroid function tests indicate severe hypothyroidism with low total T_4 , low free T_4 , and elevated TSH levels. • Buccal mucosal bleeding time is prolonged (hypothermia reduces platelet function).
- Fluid analysis of pleural effusion—modified transudate.

IMAGING

Thoracic radiographs—pleural effusion in up to 50% of cases. Pulmonary edema localized in the perihilar region is rarely noted.

PATHOLOGIC FINDINGS

Skin biopsies may demonstrate dermal thickening, myxedema, and vacuolation of arrector pili muscles.



TREATMENT

- Myxedema coma is a medical emergency.
- Once a presumptive diagnosis of myxedema coma is made, immediate inpatient treatment is necessary. • Due to the critical and life-threatening nature of myxedema coma, treatment must be initiated before thyroid function test results confirm a clinical suspicion of myxedema. • Immediate provision of a patent airway and resuscitation of hypotension are necessary. • Mechanical ventilation may be necessary. • IV fluid therapy is administered to support blood pressure and to address decreased sodium levels. Patients with myxedema coma have a decreased ability to clear free water.
- Administer intravenous fluids: 0.9% sodium chloride (20 mL/kg—initial bolus). Reassess and continue intravenous fluids (2.5–7 mL/kg/h). Rate selected based on blood pressure, heart rhythm, heart rate, and respiratory rate. • The hallmark of therapy is intravenous administration of synthetic thyroid hormone. • Rapid rewarming must be avoided as this may cause peripheral

vasodilatation, hypotension, and potential cardiovascular collapse. Correction of hypothermia should be passive and occur over a number of hours.



MEDICATIONS

DRUG(S)

- Definitive immediate treatment: levothyroxine, 5 $\mu\text{g}/\text{kg}$ (0.005 mg/kg) IV q12h. • A more conservative replacement dose should be used when there is concern about cardiac function, especially the heart's ability to deal with a sudden and rapid increase in metabolic rate. Decrease levothyroxine dose by 50–75% in these cases.
- Once the patient's condition has stabilized and the patient is able to swallow, oral levothyroxine therapy should be initiated at 0.02 mg/kg PO q12h.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Lower IV levothyroxine dose should be considered in patients with cardiac disease.
- Rapid rewarming must be avoided.



FOLLOW-UP

- Prognosis is grave. • If patient survives initial treatment, treatment and monitoring as recommended for hypothyroidism must be initiated. • Evaluation for potential underlying precipitating event.



MISCELLANEOUS

SEE ALSO

Hypothyroidism

ABBREVIATIONS

- T_4 = thyroxine, tetraiodothyronine
- TSH = thyroid stimulating hormone

Suggested Reading

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NAIL (CLAW) AND NAILBED (CLAWFOLD) DISORDERS



BASICS

DEFINITION

- Ungual fold—crescent-shaped tissue that surrounds the proximal nail • Coronary band and dorsal ridge—produces most of the nail
- Paronychia—inflammation of soft tissue around the nail • Onychomycosis—fungal infection of the nail • Onychorrhexis—brittle nails that tend to split or break
- Onychomadesis—sloughing of the nail
- Nail dystrophy—deformity caused by abnormal growth; often a sequela of a disorder
- Onychomalacia—softening of the nails

PATOPHYSIOLOGY

Nails and unguial folds—subject to trauma, infection, vascular insufficiency, immune-mediated disease, neoplasia, defects in keratinization, and congenital abnormalities.

SIGNALMENT

- Dog and cat • Mean age range—SLO 3–8 years • No predominant sex reported
- Dachshunds—onychorrhexis • German shepherd dogs, rottweilers, possibly giant schnauzers and Doberman pinschers—SLO
- Siberian huskies, dachshunds, Rhodesian ridgebacks, rottweilers, cocker spaniels—idiopathic onychodystrophy • German shepherd dogs, whippets, English springer spaniels—idiopathic onychomadesis

SIGNS

- Licking at the feet and/or unguial folds
- Lameness • Pain • Swelling, erythema, and exudate of unguial fold • Deformity or sloughing of nail • Discoloration of the nail
- Hemorrhage from the nail or at loss of a nail
- Previous description of being “tender-footed”

CAUSES

Paronychia

- Infection—bacteria, dermatophyte, yeast (*Candida*, *Malassezia*), leishmaniasis
- Demodicosis • Immune-mediated—pemphigus, bullous pemphigoid, SLE, drug eruption, SLO • Neoplasia—subungual squamous cell carcinoma, melanoma, eccrine carcinoma, osteosarcoma, subungual keratoacanthoma, inverted squamous papilloma • Arteriovenous fistula

Onychomycosis

- Dogs—*Trichophyton mentagrophytes*—usually generalized • Cats—*Microsporum canis*

Onychorrhexis

- Idiopathic—especially in dachshunds; multiple nails • Trauma • Infection—dermatophytosis, leishmaniasis

Onychomadesis

- Trauma • Infection • Immune-mediated—pemphigus, bullous pemphigoid, SLE, drug eruption, SLO • Vascular insufficiency—vasculitis, cold agglutinin disease
- Neoplasia—see above • Idiopathic

Nail Dystrophy

- Acromegaly • Feline hyperthyroidism
- Zinc-responsive dermatosis • Congenital malformations



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Trauma or neoplasia often affects a single nail. • Involvement of multiple nails suggests a systemic disease. • Immune-mediated diseases (except SLO) usually have other skin lesions in addition to nail or unguial fold lesions.

CBC/BIOCHEMISTRY/URINALYSIS

May show evidence of SLE, diabetes mellitus, hyperthyroidism, or other systemic illness.

OTHER LABORATORY TESTS

- FeLV • Serum thyroxine • ANA titer

IMAGING

Radiographs—osteomyelitis of third phalanx, neoplastic change

OTHER DIAGNOSTIC PROCEDURES

- Biopsy—often involves a third phalanx amputation; inclusion of the coronary band required for diagnosis of most diseases
- Cytology of exudate from the nail and/or fold • Skin scraping • Bacterial and fungal culture



TREATMENT

PARONYCHIA

- Surgical removal of nail plate (shell)
- Antimicrobial soaks • Identify underlying condition and treat specifically.

ONYCHOMYCOSIS

- Antifungal soaks—chlorhexidine, povidone iodine, lime sulfur • Surgical removal of nail plate—may improve response to systemic medication • Amputation of third phalanx

ONYCHORRHEXIS

- Repair with fingernail glue (type used to attach false nails in humans). • Remove splintered pieces and maintain with rotary sander (Dremel). • Treat underlying cause. • Amputate third phalanx, last resort.

ONYCHOMADESIS

- Antimicrobial soaks • Treat underlying cause

NEOPLASIA

- Determined by biologic behavior of specific tumor • Surgical excision • Amputation of digit or leg • Chemotherapy and/or radiation therapy

NAIL DYSTROPHY

Treat underlying cause



MEDICATIONS

DRUG(S) OF CHOICE

- Bacterial paronychia—systemic antibiotics based on culture and sensitivity. • Yeast paronychia—*Candida* or *Malassezia* paronychia—ketoconazole (5–10 mg/kg PO q12–24h); topical nystatin or miconazole. • Onychomycosis—griseofulvin (50–150 mg/kg PO/day) or ketoconazole (5–10 mg/kg PO q12h) for 6–12 months until negative cultures; itraconazole (10 mg/kg PO q24h) for 3 weeks and then pulse therapy until resolved.

- Onychomadesis—determined by cause; immunomodulation therapy for immune-mediated diseases; medications include cyclosporine, doxycycline with niacinamide, pentoxifylline, vitamin E, essential fatty acid supplementations, and chemotherapeutic agents (e.g., azathioprine, chlorambucil).

CONTRAINdications

Griseofulvin—do not use in pregnant animals.

PRECAUTIONS

- Griseofulvin—may cause bone marrow suppression, anorexia, vomiting, and diarrhea; absorption enhanced if given with a high-fat meal. • Ketoconazole—may cause anorexia, gastric irritation, hepatic toxicity, and lightening of the hair coat.

N



FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS

- Bacterial or yeast paronychia and onychomycosis—treatment may be prolonged and response may be influenced by underlying factors. • Onychorrhexis—may require amputation of the third phalanx for resolution. • Onychomadesis—prognosis determined by underlying cause; immune-mediated diseases and vascular problems carry a more guarded prognosis than do trauma or infectious causes. • Neoplasia—excised by amputation of the digit; malignant tumors metastasize by the time of diagnosis.



MISCELLANEOUS

ABBREVIATIONS

- ANA = antinuclear antibody • FeLV = feline leukemia virus • SLE = systemic lupus erythematosus • SLO = symmetrical lupoid onychodystrophy

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Client Education Handout
available online

NARCOLEPSY AND CATAPLEXY



BASICS

OVERVIEW

Narcolepsy/cataplexy refer to the same disorder, cataplexy being the clinical sign easiest to recognize in domestic animals.

Narcolepsy

- Sleep disorders.
- Syndrome characterized by excessive sleepiness, cataplexy, sleep paralysis, and hypnagogic hallucinations (humans). Sudden episodes of paradoxical sleep without a preceding period of slow-wave sleep.

Cataplexy

- Sudden, episodic, and spontaneous collapse secondary to complete atonia of skeletal muscles (flaccid paralysis) caused by inhibition of spinal cord lower motor neurons.
- Patient stays alert and will follow with its eyes.
- Most common clinical sign of narcolepsy in small animals.

SIGNALMENT

- Dog and rarely cat.
- Proven hereditary—Labrador retriever, dachshund, and Doberman pinscher.
- Autosomal recessive gene mutation—*canarc-1* gene found on chromosome 12, which codes for a hypocretin (orexin) receptor. Mutations of *OxR2* (type II orexin receptor gene). Increased microglial expression of MHC II in Doberman pinscher.
- Assumed genetic basis for miniature poodle—mode of inheritance unknown.
- For inherited disease, clinical signs appear between 2 and 4 months of age with escalation of signs around 1 year of age. Possible disappearance of clinical signs later in life.

- Acquired form may develop in older animals (possible depletion of hypocretin production by hypothalamus) and can occur in any dog breed or mixed breed, at any age.
- Clinical signs in acquired form will usually remain for life.

SIGNS

- Physical and neurologic examinations—normal except during an episode.
- Onset—peracute.
- Excessive daytime sleepiness and fragmented sleep patterns reported in domestic animals, but cataplexy is usually the clinical sign recognized by owners.
- Cataplexy episodes—acute onset of flaccid paralysis without loss of consciousness lasting a few seconds to minutes (up to 20 minutes) with sudden return to normal; multiple episodes in 1 day.
- Narcolepsy—eye movements, muscular twitching, and whining (as in REM sleep) frequently observed during episodes.

- Patients are usually aroused by loud noises, petting, or other external stimuli.

CAUSES & RISK FACTORS

- Hereditary in some breeds.
- Possible immune system involvement in acquired disease.
- Neurotransmitter abnormalities—serotonin, dopamine, norepinephrine, neuropeptide hypocretin (orexin).
- Rarely reported with pontomedullary (brainstem) lesions.
- Excitement, emotions, feeding, and general anesthesia may induce narcoleptic episodes.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Syncope.
- Seizure activity—urinary or fecal incontinence, excessive salivation and muscle rigidity are not characteristic of narcolepsy in which atonia predominates. Recovery after a narcoleptic event is immediate.
- Non-convulsive seizure (drop attack).
- Neuromuscular disorders—onset of clinical signs usually not as sudden and recovery not immediate as in narcolepsy.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

- DNA test for specific breeds (Labrador retriever, dachshund, and Doberman pinscher).
- CSF—normal. Low levels of orexin A in CSF.
- Standardized food-elicited cataplexy test; play-elicited cataplexy.

IMAGING

Brain MRI—normal

DIAGNOSTIC PROCEDURES

- Observe an episode—if a consistent activity (feeding, excitement, etc.) elicits attacks, attempt to simulate the activity.
- Food-elicited cataplexy test—place 10 pieces of food in a row 12–24 inches apart; record the time required for the patient to eat all the pieces and the number, type, and duration of any attacks that occur; normal dogs eat all food in < 45 seconds and have no attacks; affected dogs take > 2 minutes to eat the food and can have 2–20 attacks.
- Play-elicited cataplexy: 2 dogs are left in a room and allowed to interact together and with toys.
- Physostigmine (cholinesterase inhibitor) challenge to induce cataplexy in an affected dog—administer 0.025–0.1 mg/kg IV; repeat the food-elicited test 5–15 minutes after the injection; increase dosage if necessary (0.05 mg/kg; 0.075 mg/kg; 0.10 mg/kg); effects of each dose last 15–45 minutes.



TREATMENT

- Primary goal—reduce the severity and frequency of cataplectic episodes.
- Inform client that cataplexy is not a fatal disease, choking on food and airway obstruction do not occur, and the pet is not suffering.
- Inform client that activities such as hunting, swimming, and unleashed exercise put the patient at risk.
- If episodes are infrequent and quality of life is preserved, treatment should be postponed and environment adapted to avoid specific stimulations.



MEDICATIONS

DRUG(S)

- Imipramine 0.5 mg/kg PO q8h
- Methylphenidate 0.25 mg/kg PO q12–24h
- Selegiline 2 mg/kg q24h
- Yohimbine 50–100 µg/kg SC or PO q8–12h
- Combination also possible—imipramine and methylphenidate

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Many patients develop drug tolerance; change of drug may become necessary.
- Increased heart and respiratory rates, anorexia, tremors, exercise-induced hyperthermia.



FOLLOW-UP

- Avoiding inciting activities may reduce episodes so that medication is not needed.
- Patients with the inherited form may improve with age.
- Prognosis varies even with treatment; some patients remain symptomatic.



MISCELLANEOUS

ABBREVIATIONS

- CSF = cerebrospinal fluid
- MRI = magnetic resonance imaging

INTERNET RESOURCES

<http://med.stanford.edu/school/Psychiatry/narcolepsy/>

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NASAL AND NASOPHARYNGEAL POLYPS



BASICS

OVERVIEW

- Non-neoplastic, inflammatory growths arising from epithelium, usually originate from a stalk.
- Nasal—uncommon; originate from the mucosa of the nasal turbinates and are inflammatory in dogs and cats.
- Nasopharyngeal—relatively common; originate from the base of the epithelial lining of the tympanic bulla or eustachian tube; when polyps extend into the nasopharynx referred to as nasopharyngeal polyps; when extending into the ear, known as middle ear polyps, aural or auricular polyps, or benign, inflammatory polyps.

SIGNALMENT

- Nasal polyps—middle-aged to older dogs and cats.
- Nasopharyngeal polyps—typically kittens and young adult cats, but can be seen in older cats (months—15 years), rarely seen in dogs.

SIGNS

Nasal Polyps

- Chronic mucopurulent nasal discharge
- Noisy breathing—stertor
- Nasal congestion and/or discharge
- Sneezing or epistaxis
- Decreased nasal airflow, generally unilateral
- Generally non-responsive to antibiotics

Nasopharyngeal or Aural Polyps

- Inspiratory stridor
- Gagging
- Cyanosis
- Voice change
- Dysphagia
- Chronic, non-responsive otitis
- Head tilt
- Nystagmus
- Ataxia
- Horner's syndrome

CAUSES & RISK FACTORS

Unknown—suspect congenital or response to chronic inflammatory processes.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Feline upper respiratory disease complex
- Nasopharyngeal stenosis
- Chronic otitis externa or media
- Nasal or nasopharyngeal foreign body
- Laryngeal paralysis
- Nasal neoplasia—lymphoma, nasal adenocarcinoma

- Laryngeal neoplasia—squamous cell carcinoma, lymphoma, adenocarcinoma
- Aural neoplasia—ceruminous adenocarcinoma

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

FeLV/FIV—general retroviral screening

IMAGING

- Skull radiographs—soft tissue density within nasal cavity, nasopharynx, tympanic bulla, external ear canal; 25% false negative rate.
- Computerized tomography and MRI—better sensitivity for nasal, nasopharyngeal, and aural masses.

DIAGNOSTIC PROCEDURES

- Digital palpation of soft palate, visual examination of the nasopharynx and larynx under general anesthesia utilizing spay hook, dental mirror, and laryngoscope.
- Flexible fiber-optic caudal rhinoscopy to examine the dorsal nasopharynx, choanae, and caudal nasal cavity.
- Rigid rostral rhinoscopy to examine the nasal cavity.
- Deep otoscopic examination.
- Fine-needle aspirate and/or biopsy.
- Cytology and histopathology.



TREATMENT

- Excisional biopsy for nasal polyps.
- Traction removal of nasopharyngeal polyps via oral cavity.
- Ventral bulla osteotomy for nasopharyngeal polyps to release stalk and remove epithelial lining.
- Surgery—treatment of choice: excision via the oral cavity for nasopharyngeal polyps, or rhinotomy for nasal polyps; complete excision of root and base of polyp is mandatory to prevent recurrence.
- Concurrent bulla osteotomy—may prevent recurrence of nasopharyngeal polyps. Recommended if bullous involvement is obvious.



MEDICATIONS

DRUG(S)

- Appropriate antimicrobial medications if secondary nasal or otic infection present.
- Consider anti-inflammatory course of corticosteroids following traction removal of nasopharyngeal polyps; decreased recurrence rate reported.



FOLLOW-UP

- Incomplete removal of polyp and stalk may result in recurrence.
- Horner's syndrome can occur following removal by traction or ventral bulla osteotomy, usually transient but can be permanent.
- Facial paresis or paralysis or vestibular syndrome may develop after bulla osteotomy but is generally transient.
- Prognosis excellent with complete removal.



MISCELLANEOUS

ABBREVIATIONS

- FeLV = feline leukemia
- FIV = feline immunodeficiency virus
- MRI = magnetic resonance imaging

Suggested Reading

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NASAL DERMATOSES—CANINE



BASICS

DEFINITION

Pathologic condition of the nasal skin involving either the haired portion (bridge of the nose/dorsal muzzle) or non-haired portion (nasal planum).

PATHOPHYSIOLOGY

Dependent on cause

SYSTEMS AFFECTED

Skin/Exocrine

SIGNALMENT

- Dogs < 1 year of age—dermatophytosis, zinc-responsive dermatosis, dermatomyositis, demodicosis, eosinophilic nasal furunculosis (often insect trigger; also seen in adult patients).
- Zinc-responsive dermatosis—Siberian husky, Alaskan malamute.
- Dermatomyositis—collie, Shetland sheepdog.
- Uveodermatologic syndrome—Akita, Samoyed, Siberian husky.
- Systemic lupus erythematosus and discoid lupus erythematosus—collie, Shetland sheepdog, German shepherd dog.
- DLE may occur more often in females.
- Epitheliotropic lymphoma—old dogs.
- Nasal arteritis—St Bernard.
- Nasal solar dermatosis—lightly pigmented breeds.
- Nasal parakeratosis—Labrador retriever.
- Senile idiopathic nasal hyperkeratosis—older cocker spaniel.
- Seasonal nasal hypopigmentation—Labrador retriever, golden retriever, Siberian husky, Bernese mountain dog.
- Idiopathic leukoderma/leukotrichia (vitiligo)—Doberman pinscher, rottweiler, dachshund.
- Reactive histiocytosis (“clown nose”)—Bernese mountain dog, golden retriever.

SIGNS

- Depigmentation
- Hyperpigmentation
- Erythema
- Erosion/ulceration
- Hemorrhage
- Vesicles/pustules
- Crusts
- Scarring
- Alopecia
- Nodules/plaques

CAUSES

- Nasal pyoderma/furunculosis
- Demodicosis
- Dermatophytosis
- Other fungal infections—cryptoccosis, sporotrichosis, aspergillosis
- DLE and SLE
- Eosinophilic nasal furunculosis

- Mosquito-bite dermatitis
- Pemphigus foliaceus
- Pemphigus erythematosus
- Pemphigus vulgaris
- Arteritis
- Nasal solar dermatitis
- Dermatomyositis
- Zinc-responsive dermatosis
- Uveodermatologic syndrome
- Superficial necrolytic dermatitis
- Vitiligo
- Idiopathic nasal depigmentation
- Contact hypersensitivity—plastic dish dermatitis, topical drug hypersensitivity (neomycin)
- Neoplasia—squamous cell carcinoma, basal cell carcinoma, epitheliotropic lymphoma, fibrosarcoma, cutaneous histiocytosis
- Trauma
- Idiopathic sterile granuloma
- Idiopathic nasal hyperkeratosis
- Distemper virus dermatitis
- Insect trigger

RISK FACTORS

- Adult cats—may be inapparent carriers of dermatophytes.
- Rooting behavior—pyoderma, dermatophytosis.
- Sun exposure—nasal solar dermatitis, DLE, SLE, PE.
- Poorly pigmented nose—nasal solar dermatitis, squamous cell carcinoma.
- Large, rapidly growing breeds—zinc-responsive dermatosis.
- Immunosuppression—demodicosis, pyoderma, dermatophytosis.
- Insect exposure—mosquito-bite dermatitis and possibly eosinophilic nasal furunculosis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Nasal Solar Dermatitis

- Lesions—confined to nose; precipitated by heavy sunlight exposure.
- Begins in poorly pigmented skin at junction of nasal planum and dorsal muzzle.
- Lightly pigmented eyelid margins may also be affected.
- Negative direct immunofluorescence.

DLE

- Primarily affects nasal area.
- May affect mucocutaneous margins of the lips and eyelids.
- Exacerbated by sunlight.
- Dermatitis often preceded by depigmentation.
- Positive DIF at basement membrane zone.
- Biopsy—interface dermatitis with pigmentary incontinence.

SLE

- Multisystemic disease.

- Skin lesions—often involve nose, face, mucocutaneous junctions; multifocal or generalized.
- ANA positive.
- Positive DIF at basement membrane zone.

Pemphigus Foliaceus

- Lesions—usually start on face and ears; commonly involve footpads; eventually generalize.
- Progressive development, often first noted at junction of nasal planum and dorsal muzzle.
- Biopsy—subcorneal pustules with acantholysis.
- Positive DIF in intercellular spaces of epidermis.

Pemphigus Erythematosus

- Lesions—primarily confined to face and ears; typically more severe than lesions of DLE.
- Dermatitis often preceded by depigmentation.
- Biopsy—intradermal pustules with acantholysis and pigmentary incontinence.
- Positive DIF at basement membrane zone and intercellular spaces.

Demodicosis

- Often starts on face or forelimbs; affects only haired skin of the dorsal muzzle.
- Juvenile-onset frequently facial at first.
- May generalize.
- Diagnosis by skin scrapings.

Plastic (or Rubber) Dish Dermatitis

- Depigmentation and erythema of anterior nasal planum and anterior lips.
- No ulceration or crusting.
- History of exposure.
- Similar to contact dermatitis.
- Uncommon; overly suspected—lesions more often due to trauma from roughened bowl edges. Similar symptoms seen with trauma from Kong and other rubber toys.

Dermatomyositis

- Breeds at increased risk.
- Young age of onset.
- Nasal, facial, and extremity lesions—characterized by erosion, alopecia, scarring, and hyperpigmentation.
- Lesions especially noted at points of trauma or pressure.
- Polymyositis and megaesophagus may be seen.
- Biopsy—interface dermatitis with follicular atrophy.
- Negative DIF.

Uveodermatologic Syndrome

- Breeds at increased risk.
- Dermatitis often preceded by ocular symptoms.
- Uveitis and cutaneous macular depigmentation without inflammation—nose, lips, and eyelids.
- Striking leukotrichia and leukoderma.
- Biopsy of early lesions—interface dermatitis, pigmentary incontinence.

(CONTINUED)

NASAL DERMATOSES—CANINE**Zinc-Responsive Dermatoses**

- Breeds at increased risk.
- Typical signalment or diet (i.e., high-fiber or calcium supplementation).
- Crusted lesions—face, mucocutaneous junctions, pressure points, footpads.
- Biopsy—parakeratotic hyperkeratosis.

Other

- Nasal pyoderma/furunculosis—acute onset of folliculitis on haired portion of nose.
- Dermatophytosis—haired portion of the nose; diagnose by culture or biopsy.
- Eosinophilic nasal furunculosis—haired portion of dorsal muzzle; diagnose by biopsy.
- Vitiligo—cutaneous macular depigmentation without inflammation on nose, lips, eyelids, footpads, and nails; leukotrichia with leukoderma may be seen; diagnose by biopsy.
- Nasal hypopigmentation—normal black coloration of nasal planum fades to light brown or whitish color; may be seasonal or wax and wane; considered cosmetic not pathologic.
- Idiopathic nasal hyperkeratosis—dry, horny growths of keratin localized to nasal planum; may or may not be associated with digital hyperkeratosis.
- Other diseases—differentiate by history or biopsy (i.e., neoplastic cell infiltrate).

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal.
- SLE—may see hemolytic anemia, thrombocytopenia, evidence of glomerulonephritis (high BUN, proteinuria), joint disease, or other symptoms based on body system(s) affected.

DIAGNOSTIC PROCEDURES

- Skin scrapings—*Demodex*.
- Cytology—fungal organisms, bacteria, eosinophils, or acantholytic keratinocytes (pemphigus).
- Dermatophyte test medium—dermatophytosis.
- Culture on Sabouraud agar—other fungal infections.
- Bacterial culture and sensitivity or cytologic evaluation—pyoderma.
- Joint tap—evidence of polyarthritis in SLE.
- ANA—positive in cases of SLE.
- Ocular examination—uveitis in uveodermatologic syndrome.
- ECG—evidence of myocarditis in SLE.
- EMG—evidence of polymyositis in SLE and dermatomyositis.
- DIF—deposition of immunoglobulin at the basement membrane zone in DLE, SLE, and PE, and intercellular spaces of epidermis in PF, PE, and PV.
- Neoplasia—cytology or biopsy.
- Skin biopsy.

PATHOLOGIC FINDINGS

- Folliculitis/furunculosis (\pm mites, bacteria, fungal elements)—demodicosis, dermatophytosis, nasal pyoderma/furunculosis.

- Eosinophilic predominance—mosquito-bite dermatitis, eosinophilic nasal furunculosis.
- Follicular atrophy and perifollicular fibrosis—dermatomyositis.
- Interface dermatitis—DLE, SLE, dermatomyositis, uveodermatologic syndrome.
- Intraepidermal pustules with acantholysis—PF and PE.
- Suprabasilar acantholysis—PV.
- Parakeratotic hyperkeratosis—zinc-responsive dermatosis.
- Hypomelanosis—vitiligo, uveodermatologic syndrome.
- Granulomatous/pyogranulomatous dermatitis—pyoderma, fungal, foreign body, idiopathic sterile granuloma.
- Neoplastic cell infiltrate—cutaneous histiocytosis, other neoplasia.

**TREATMENT**

- Outpatient, except SLE with multi-organ dysfunction or tumors requiring surgical excision or radiation therapy.
- Reduce exposure to sunlight—DLE, SLE, PE, nasal solar dermatitis, squamous cell carcinoma.
- Discourage rooting behavior—pyoderma, dermatophytosis.
- Protection from insects.
- Warm soaks—aid removal of exudate and crusts.
- Replace plastic or rubber dish and avoid contact with topical drug or other agent causing hypersensitivity reaction.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Fungal infections—systemic antifungals: griseofulvin, ketoconazole, itraconazole; topical enilconazole for aspergillosis; surgical excision of early discrete lesions.
- Nasal solar dermatitis—topical corticosteroids; antibiotics for secondary infection; sunscreens.
- Idiopathic sterile granuloma—surgical excision when feasible; immunosuppressive therapy with glucocorticoids \pm azathioprine, cyclosporine, tetracycline and niacinamide.
- DLE and PE—topical corticosteroids or tacrolimus; tetracycline and niacinamide; oral therapy (as for PF) if temporarily needed in severe cases.
- PF, PV, SLE—immunosuppressive therapy with prednisolone \pm azathioprine (dogs), chlorambucil, chrysotherapy.
- Vitiligo/nasal depigmentation—no treatment.
- Neoplasia—surgical excision; chemotherapy; radiation therapy.

- Idiopathic nasal hyperkeratosis—topical antibiotic-corticosteroid cream, topical keratolytic and humectant topical tacrolimus (Protopic).
- Other diseases—see specific cause.

CONTRAINDICATIONS

Avoid chrysotherapy in patients with renal disease.

PRECAUTIONS

- Griseofulvin—can cause anorexia, vomiting, diarrhea, and bone marrow suppression; feed with high-fat diet.
- Ketoconazole—may cause anorexia, gastric irritation, hepatotoxicity, and lightening of hair coat.

**FOLLOW-UP****PATIENT MONITORING**

Varies with specific disease and treatment prescribed.

POSSIBLE COMPLICATIONS

Scarring with deep infections or overly vigorous cleaning.

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

Dermatophytosis

PREGNANCY/FERTILITY/BREEDING

Griseofulvin is teratogenic

SYNONYMS

- Superficial necrolytic dermatitis = superficial necrolytic migratory erythema and hepatocutaneous syndrome
- Uveodermatologic = Vogt-Koyanagi-Harada-like syndrome

ABBREVIATIONS

- ANA = antinuclear antibody
- DIF = direct immunofluorescence
- DLE = discoid lupus erythematosus
- ECG = electrocardiogram
- EMG = electromyography
- PE = pemphigus erythematosus
- PF = pemphigus foliaceus
- PV = pemphigus vulgaris
- SLE = systemic lupus erythematosus

Suggested Reading

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Client Education Handout
available online

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NASAL DISCHARGE



BASICS

DEFINITION

Can be serous, mucoid, mucopurulent, purulent, blood tinged, or frank blood (epistaxis); may contain food debris.

PATHOPHYSIOLOGY

- Secretions—produced by mucous cells of the epithelium and submucosal glands; increased production from glandular hypertrophy and hyperplasia owing to irritation of the nasal mucosa by infectious, mechanical, chemical, or inflammatory stimuli.
- Xeromycteria—“dry nose”; facial nerve damage secondary to middle ear disease can decrease serous secretions from the lateral nasal glands leading to compensatory mucoid secretion; usually unilateral with unilateral nasal planum hyperkeratosis, ± keratoconjunctivitis sicca.

SYSTEMS AFFECTED

- Respiratory—mucosa of the upper tract, including the nasal cavities, sinuses, and nasopharynx; lower tract disease can also result in secretions from the upper airways.
- Gastrointestinal—signs may be observed with swallowing disorders or esophageal or gastrointestinal diseases when secretions are forced into the nasopharynx.
- Hemic/Lymphatic/Immune—blood-tinged discharge or epistaxis owing to platelet or hemostatic defects.
- Ophthalmic—may have KCS ipsilaterally if there is nerve damage due to middle ear disease.

SIGNALMENT

- Dog and cat.
- Young animals—cleft palate; nasal polyp, ciliary dyskinesia; immunoglobulin deficiency.
- Older animals—nasal tumors; primary dental disease (tooth root abscess).
- Hunting dogs—foreign body.
- Dolichocephalic dogs—aspergillosis, nasal neoplasia.

SIGNS

Historical Findings

- Sneezing—often found concurrently.
- Reverse sneezing—can be found concurrently, if nasopharyngeal involvement or passage of nasal secretions through the choanae towards the nasopharynx.
- Important to know both the initial and current character of the discharge as well as whether it originally started unilaterally or bilaterally.
- Stertor—owners frequently report noisy breathing, especially when animal is sleeping.
- Response to previous antibiotic therapy common due to secondary bacterial infection.

Physical Examination Findings

- Secretions or dried discharge on the hair of the muzzle or forelimbs.
- May note reduction in nasal air flow, particularly with nasal neoplasia or fungal infection in the cat.
- Concurrent dental, nasopharyngeal, or lower airway disease.
- Bony involvement—with a tumor or fourth premolar abscess; may be detected as facial or hard palate swelling or as pain secondary to fungal or bacterial osteomyelitis or neoplasia.
- Mucosal depigmentation of the nasal alar cartilage—observed with canine nasal aspergillosis.
- Mandibular lymphadenomegaly—neoplasia, fungal infection, dental disease.
- Polyp—may be visible on otoscopic exam, or pushing the soft palate down on oral exam.
- Chorioretinitis—may be seen with canine distemper or cryptococcosis.
- Deviation of the globe (abscess, sinoorbital aspergillosis in cats, tumors).

CAUSES

- Unilateral—often associated with non-systemic processes; foreign body; dental-related disease; fungal infections; nasal tumor; facial nerve damage leading to xeromycteria.
- Bilateral—infectious agents (e.g., feline viral rhinotracheitis or calicivirus, canine herpesvirus, canine distemper, secondary bacterial infection); IgA deficiency; airborne irritant; allergy; ciliary dyskinesia; lymphoplasmacytic or hyperplastic rhinitis, nasopharyngeal stenosis or atresia.
- Unilateral progressing to bilateral—*Aspergillus*; nasal tumor.
- Either unilateral or bilateral—epistaxis; foreign body; extranasal disease; nasal parasites, inflammatory rhinitis.
- Extranasal diseases—chronic pneumonia, chronic vomiting, nasopharyngeal diseases.

RISK FACTORS

- Dental disease
- Foreign bodies
- Infectious—poorly vaccinated animal; kennel situations, exposure to other animals
- Nasal aspergillosis
- Thrombocyte disorder—thrombocytopenia or thrombocytopathy: primary immune or secondary to infectious (i.e., rickettsial) disease or neoplasia
- Coagulation defect due to rodenticide intoxication
- Nasal mites—kennel-raised dogs
- Immunosuppression, chronic corticosteroid use, FeLV or FIV infection
- Chronic, low-grade pneumonia
- Chronic vomiting
- Chronic otitis (facial nerve damage)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Important to differentiate nasal discharge, secretions, or crusting from diseases that occur at mucocutaneous junctions, such as pemphigus, vasculitis, or leishmaniasis.

Differential Diagnosis Causes

- Serous—mild irritation; viral and parasitic (e.g., nasal mites) disorders.
- Mucoid—allergy; nonspecific airborne irritants; early neoplasia.
- Purulent (or mucopurulent)—secondary bacterial or fungal infection, neoplasia.
- Serosanguinous to epistaxis—nasal tumor and aspergillosis; secondary to violent or paroxysmal sneezing episodes; coagulopathy, platelet disorder, and systemic hypertension.

CBC/BIOCHEMISTRY/URINALYSIS

Results not specific for any particular cause but can detect concurrent problems; part of a thorough evaluation before general anesthesia for diagnostic procedures.

OTHER LABORATORY TESTS

- Serologic tests—help to diagnose fungal or rickettsial disease.
- Coagulation studies—determine platelet numbers and function, coagulation panel.
- Immunoglobulin quantification—investigates IgA deficiency.

IMAGING

Skull Imaging

- Anesthetize and carefully position patient.
- Perform before rhinoscopy and periodontal probing, which can cause nasal bleeding and alter radiographic density.
- Radiography (rarely performed when CT is available):
 - Lateral view—detect any periosteal reaction; note gross changes in the maxillary teeth, nasal cavity, and frontal sinuses; evaluate air column outlining the nasopharynx for filling defects.
 - Open-mouth ventrodorsal and intraoral views (using sheet film)—excellent for evaluating nasal cavities and turbinates.
 - Rostro-caudal view—evaluate each frontal sinus (periosteal reaction and filling).
- CT and MRI—CT superior to radiography in making diagnosis; CT and MRI help detect the extent of bony changes or CNS involvement associated with nasal tumors, fungal rhinitis, or chronic otitis.

Thoracic Radiography

Can reveal alveolar infiltrates in patient with chronic pneumonia; situs inversus or bronchiectasis in some dogs with primary ciliary dyskinesia.

(CONTINUED)

DIAGNOSTIC PROCEDURES

- Blood pressure, platelets, and coagulation profile for epistaxis.
- Rhinoscopy—indicated with chronic or recurrent nasal discharge; acute epistaxis; evaluate both anterior and posterior; may be contraindicated with bleeding disorders.
- Nasal cytologic examination—nonspecific inflammation most commonly found.
- Fungal culture—difficult to interpret; need visualized sampling of a plaque lesion; false-negatives common.
- Bacterial culture could be useful when resistant organisms are suspected, but requires deep nasal sampling under anesthesia.
- Biopsy of the nasal cavity—indicated with chronic nasal discharge or visualized abnormalities; multiple samples required to ensure adequate representation; may perform electron microscopy for suspected ciliary dyskinesia.
- Bronchoscopy—indicated if there has been a history of coughing with nasal discharge.
- Periodontal probing of all upper teeth—perform after rhinoscopy; the normal gingival sulcus: dogs, \leq 4 mm; cats, \leq 1 mm.
- Schirmer tear test, otoscopic exam or CT—to evaluate for possible facial nerve damage from chronic otitis.
- Tracheal scintigraphy and electron transmission microscopy—to confirm primary ciliary dyskinesia.

**TREATMENT**

- Outpatient—adequate hydration, nutrition, warmth, and hygiene (keeping nares clean)—important with chronic sneezing and nasal discharge. Prioritize local therapy (nasal drops, nasal nebulization).
- Inpatient—any surgical treatment, topical therapy for aspergillosis.

**MEDICATIONS****DRUG(S)**

- Secondary bacterial infection—antibiotics; choose a good gram-positive spectrum of activity (e.g., amoxicillin, clavamox, clindamycin, azithromycin, cephalosporins).
- Attempt to dry up serous nasal secretions—decongestants (ephedrine: dogs, 10–50 mg total PO q8–12h, to a maximum of 4 mg/kg; cats, 2–4 mg/kg q8–12h); topical vasoconstrictors (neosynephrine at 0.25–0.5% q8–24h or oxymetazoline at 0.25% q24h) but for a limited period of

time—less than 1 week—these drugs do not treat a specific cause and could induce damage to the nasal mucosa.

- Dental-associated rhinitis—antibiotics; dental surgery as indicated.
- Foreign body—removal, antibiotics.
- Nasal parasites—ivermectin (300 μ g/kg PO or SC weekly for 3 weeks) or milbemycin (in collie and similar breeds at 1 mg/kg PO weekly for 3 weeks) to treat *Pneumonyssoides*; fenbendazole (50 mg/kg PO q24h for 10 days) to treat *Eucoleus* (nasal nematode).
- Nonspecific inflammation—prednisolone (1–2 mg/kg PO q12–24h) or piroxicam (0.3 mg/kg PO q24–48h).
- Canine nasal aspergillosis—topical treatment with enilconazole or clotrimazole.
- Feline cryptococcosis or sporothricosis—itraconazole (5–10 mg/kg PO q24h) or fluconazole (50 mg/cat q12h).
- Feline aspergillosis—topical therapy, itraconazole.
- Neoplasia—radiotherapy and chemotherapy.
- Xeromycteria—oral administration of ophthalmic pilocarpine in an attempt to stimulate nasal secretions.

CONTRAINdications

- Ephedrine—in cardiac patients
- Ivermectin—in collies and similar breeds

PRECAUTIONS

- Itraconazole—anorexia, nausea, vomiting, and high liver enzymes
- Rebound phenomenon—reported with overuse of topical nasal vasoconstrictors

**FOLLOW-UP****PATIENT MONITORING**

- Nasal discharge and sneezing—note changes in frequency, volume, and character.
- Repeat rhinoscopy—indicated to ensure adequate response to treatment of fungal rhinitis.
- Recheck thoracic radiographs or bronchoscopy—monitor response to treatment for chronic pneumonia.

POSSIBLE COMPLICATIONS

- Loss of appetite—especially in cats.
- Extension of primary disease (e.g., fungal infection, tumor) into the mouth, eye, or brain.
- Respiratory distress—with nasal obstruction.
- Involvement of the cribriform plate in dogs with aspergillosis—CNS damage during topical drug therapy is a risk.

NASAL DISCHARGE**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Sinusitis
- Dental disease
- Secondary causes—coagulopathy, pneumonia, cricopharyngeal disease, megaesophagus

AGE-RELATED FACTORS

Middle-aged to old patients—often associated with dental or neoplastic conditions.

PREGNANCY/FERTILITY/BREEDING

The safety of most recommended drugs has not been established in pregnant animals.

SEE ALSO

- Aspergillosis, Nasal
- Cryptococcosis
- Epistaxis
- Nasal and Nasopharyngeal Polyps
- Nasal tumor chapters
- Nasopharyngeal Stenosis
- Primary Ciliary Dyskinesia
- Rhinitis and Sinusitis

ABBREVIATIONS

- CNS = central nervous system
- CT = computed tomography
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- KCS = keratoconjunctivitis sicca
- MRI = magnetic resonance imaging

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NASOPHARYNGEAL STENOSIS



BASICS

OVERVIEW

- Formation of a thin but tough membrane at the choanae or anywhere above the soft palate, resulting in the occlusion of the caudal nasopharyngeal openings or narrowing of the orifice from a 1+ cm oval opening to a 1- to 2-mm opening or less.
- Inflammation secondary to chronic rhinitis, or from chronic regurgitation or vomiting of material into the nasopharynx should be considered as possible causes.
- Congenital narrowing or dysgenesis of the region is also suspected; thickened palatopharyngeal muscles have been reported as a cause of nasopharyngeal stenosis in the dachshund.

SIGNALMENT

- Cats of any breed or sex.
- Less commonly seen in dogs.
- Age—any age as long as ample time has passed since exposure to the inciting cause; congenital cases may present early or late in life.

SIGNS

- Evidence of upper respiratory obstruction
- Whistling or snoring sounds during respiration
- Open-mouth breathing
- Minimal nasal discharge in many cases
- Duration of signs for at least several months
- Aggravation of signs during eating or drinking
- Failure to respond to antibiotics or corticosteroids
- Absence of nasal airflow from one or both nares

CAUSES & RISK FACTORS

- Chronic upper respiratory disease.
- Foreign body or irritant contacting the affected area (perianesthetic regurgitation, reflux of gastric contents secondary to esophageal or gastric disease).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Nasopharyngeal polyps—seen during oral examination or by radiography or endoscopy.
- Chronic rhinitis or sinusitis—moderate to severe nasal discharge and sneezing; obvious radiographic changes commonly seen.
- Foreign body—unilateral mucopurulent nasal discharge; radiographic abnormalities.
- Intranasal neoplasia—unilateral obstruction; nasal discharge often bloody; radiographic changes.
- Mycotic rhinitis—moderate-to-severe nasal discharge, often hemorrhagic; radiographic changes.
- Laryngeal disease—no improvement with open-mouth breathing; lack of snorting and nasal discharge; abnormalities on oral examination.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

IMAGING

- Near-normal radiographic findings.
- Nasopharyngeal stenosis sometimes can be visualized on computed tomography. Sagittal reconstruction of the images can be required.

DIAGNOSTIC PROCEDURES

- Inability to pass a 3.5 French catheter through the ventral nasal meatus into the pharynx in a cat.
- Visualization of the stenosis by use of a retroflexed pediatric bronchoscope into the nasopharynx or use of an illuminated dental mirror.



TREATMENT

- Balloon dilatation—non-invasive; fluoroscopy simplifies procedure; repeat episodes can be required (more in the dog than cat).

- Stent placement may be needed for cases with recurrent stenosis.



MEDICATIONS

DRUG(S)

Antibiotics and steroids sometimes used post balloon dilation.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

Have owners evaluate nasal airflow at home and warn that recurrence is possible.



MISCELLANEOUS

Suggested Reading

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BASICS

DEFINITION

Discomfort along the vertebral column

PATHOPHYSIOLOGY

Caused by multiple neurologic or non-neurologic diseases (e.g., polyarthritis). Secondary to stimulation of nociceptors located in meninges, nerve roots, spinal nerves, vertebrae and associated structures (e.g., periosteum, joint capsules), and epaxial musculature. An intracranial disease can develop referred neck pain when intracranial pressure is elevated.

SYSTEMS AFFECTED

- Nervous • Musculoskeletal
- Neuromuscular

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Intervertebral disc herniation—dogs; extrusion chondrodystrophic breeds, protrusion large breeds. Less common in cats.
- Cervical spondylomyopathy—Doberman, Great Dane, Bernese mountain dog, Rottweiler, Dalmatian. • Atlantoaxial instability—small and miniature canine breeds (e.g., Yorkshire terrier, Chihuahua).
- Steroid-responsive meningitis-arteritis—Bernese mountain dog, Boxer, Beagle.
- Caudal occipital malformation syndrome and syringomyelia—Cavalier King Charles spaniel. • Immune-mediated polymyositis—Newfoundland, Boxer.

Mean Age and Range

- IVDD extrusion—unusual < 2 years, peak 3–8 years. • IVDD protrusion—> 5 years.
- CSM—middle-aged to older Dobermanns (mean: 6 years), young Great Danes (< 3 years). • AA instability—young to middle-aged. • SRMA—< 2 years (8–18 months). • Lumbosacral syndrome—middle-aged large dogs; German shepherd.

SIGNS

Historical Findings

Primary complaint—relates to perceived discomfort; e.g., vocalization, decreased activity, reluctance to get up or lie down, reluctance to go up or down stairs, inability to drink or eat from bowls on the floor (neck), neck muscle spasms. Neck pain may be intermittent.

Physical Examination Findings

- Abnormal neck carriage, reluctance to move the head, stiff neck posture. • Arched back (kyphosis). • Pain on spinal palpation and/or neck manipulation. • Abdominal rigidity (referred from back pain). • Increased epaxial muscle tone. • Intermittent neck muscle spasms. • Reluctance to walk, stilted gait,

limb stiffness, guarded short stride.

- Non-weight-bearing lameness (nerve root signature). • Autonomic signs (e.g., tachycardia, pupillary dilation). • Neurologic deficits possible (e.g., paresis, ataxia).
- Pyrexia (SRMA, infectious diseases).

CAUSES

Degenerative

- IVDD—most common cause of spinal pain in dogs • CSM. • Spinal synovial cysts
- Vertebral facet hypertrophy • Calcification circumscripta

Anomalous/Developmental

- AA instability • COMS and syringomyelia
- Vertebral malformations: e.g., hemivertebra (usually asymptomatic)
- Osteochondromatosis • Dermoid sinus

Neoplastic

- Spinal (primary or secondary), nerve root-peripheral nerve (e.g., peripheral nerve sheath tumor), muscle. • Intracranial tumors with secondary increased ICP (referred neck pain).

Nutritional

Feline hypervitaminosis A

Inflammatory

- Discospondylitis, vertebral osteomyelitis, vertebral physisis. • Infectious meningitis-meningomyelitis—viral (e.g., FIP), bacterial, rickettsial, fungal, protozoal, parasitic, algae.
- Non-infectious meningitis-meningomyelitis—SRMA, MUO/GME.
- Spinal epidural empyema. • Paraspinal abscess. • Polyarthritis—immune-mediated, infectious. • Polymyositis—immune-mediated polymyositis, infectious, exertional rhabdomyolysis.

Idiopathic

Subarachnoid diverticulum (rarely painful)

Traumatic

- Spinal fracture, luxation • Traumatic disc herniation

Vascular

Spinal hemorrhage

RISK FACTORS

- Breed—chondrodystrophic (IVDD), miniature dog (AA instability) • Trauma
- Previous surgical procedure (discospondylitis, subluxation) • Malignant neoplasm • Bite wound, foreign body, UTI, endocarditis • Coagulopathy • Liver diet (hypervitaminosis A) • FeLV infection (spinal lymphoma)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Orthopedic disease • Abdominal pain (back) • Behavioral or abnormal mentation (delirium) • Increased ICP (referred neck pain) • Non-painful myelopathy—e.g., degenerative myelopathy, fibrocartilaginous

NECK AND BACK PAIN

embolic myelopathy • Paroxysmal disorders

- Feline hyperesthesia syndrome

CBC/BIOCHEMISTRY/URINALYSIS

- CBC usually normal. May see neutrophilia (SRMA, dyskostyndylitis), thrombocytopenia (rickettsial disease, malignant neoplasm). • Elevated CK, AST—myositis, recumbence, trauma, anorexia (cat).
- Hyperproteinemia—neoplastic, infectious.
- UTI—focus for discospondylitis, with urinary retention. • Myoglobinuria—myositis.

OTHER LABORATORY TESTS

- Serologic titers, PCR (blood, CSF) for infectious diseases • Blood/urine cultures—discospondylitis • IgA and acute phase proteins levels (blood, CSF) in SRMA
- Serum protein electrophoresis
- Coagulation panel

IMAGING

Survey Spinal Radiography

- Not able to identify spinal cord compression. • IVDD—may detect narrowed intervertebral space, calcified disc. • Detects discospondylitis (normal first 2–3 weeks).
- Spinal neoplasms—osteolysis, bony proliferation, wider vertebral canal. • Detects fractures, luxations, AA instability, facet hypertrophy, malformations, calcification circumscripta, osteochondromatosis.

Thoracic Radiography and Ultrasonography

Detect neoplasms (primary or metastatic), disseminated infections, endocarditis, trauma-related lesions.

Myelography

Detects and delineates spinal cord lesions as extradural, intradural-extramedullary and intramedullary. Low sensitivity in detecting parenchymal lesions.

CT

- More sensitive than radiographs for discospondylitis, vertebral fractures, bone tumors. Clearly defines bony lesions but less soft tissue contrast than MRI. Can be useful to diagnose IVDD extrusion if calcified material. • CT-myelogram—more sensitive to assess spinal cord compressive lesions.

MRI

More sensitive than CT for soft tissue. Most rewarding imaging technique for identifying location and extent of spinal cord parenchymal lesion, nerve roots, nerves, and muscle.

DIAGNOSTIC PROCEDURES

CSF

- Useful in meningitis/meningomyelitis, but normal or nonspecific in many other situations. Rarely, neoplastic cells can be detected (spinal lymphoma). • Consider measuring IgA levels, acute phase proteins, serologic titers, PCRs, culture.

NECK AND BACK PAIN

(CONTINUED)

Arthrocentesis and Synovial Fluid Analysis

Polyarthritis

Electrodiagnostics

EMG, nerve conduction studies—detect and localize neuromuscular disease (e.g., polymyositis).

Fluoroscopy or CT-Guided Percutaneous FNA

Discospondylitis, neoplasms

Biopsy

Bone (e.g., neoplasia, osteomyelitis), muscle (e.g., polymyositis).



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—when severe clinical signs; emergency intensive care due to severe pain or neurologic deficit.
- Outpatient—when medical treatment is pursued (restricted exercise can be done).
- Emergency surgery—if traumatic spinal instability or severe neurologic deficit (non-ambulatory paraparesis, tetraplegia) due to an acute spinal cord compression.

NURSING CARE

- Non-ambulatory patients—soft bedding, alternate recumbence site.
- Vertebral instability—extreme care on manipulation to avoid exacerbating injury.

ACTIVITY

Restrict exercise at least 3–4 weeks in medically treated patients.

DIET

Change diet in case of hypervitaminosis A

CLIENT EDUCATION

- Monitor pain, response to treatment and possible gait abnormalities. Relapses common in many diseases.
- Most common cause of spinal pain in dogs is IVDD. Inform that restricted activity and cage confinement for 3–4 weeks are necessary when medical treatment is pursued; recurrence frequent. If pain persists or neurologic status deteriorates, surgical treatment is recommended, even as an emergency procedure.

SURGICAL CONSIDERATIONS

Vary according to disease. Generally, deep pain perception is considered the most important prognostic indicator for functional recovery in neurologic disease. AA instability correction is associated with high perioperative morbidity and mortality.



MEDICATIONS

DRUG(S) OF CHOICE

- Opioids—tramadol (1–5 mg/kg q6–12h PO, dog), morphine (0.1–1.0 mg/kg q4h,

dog), hydromorphone (0.05–0.2 mg/kg q4h, dog), fentanyl (transdermal patch).

- Glucocorticoids—prednisone 0.5–1 mg/kg q24h (dog) in decreasing dosage. Use of glucocorticoids in acute spinal cord trauma is controversial. Medical management of acute IVDD should focus on cage confinement. Higher doses required in immune-mediated disease (2–4 mg/kg q24h). • NSAIDs—potentially more effective in acute cervical IVDD, Meloxicam (0.1 mg/kg q24h, dog), carprofen (2.2 mg/kg q12h, dog).
- Gabapentin 10–15 mg/kg q8h PO, dog; chronic neuropathic pain (syringomyelia, nerve root disease).
- According to disease—antimicrobials (e.g., discospondylitis), immunosuppressive drugs, chemotherapy (neoplasms).

CONTRAINDICATIONS

- Glucocorticoids, immunosuppressive agents—*infections*.
- Opioids—diarrhea caused by a toxic ingestion, gastrointestinal obstruction.

PRECAUTIONS

- Concurrent administration of NSAIDs and glucocorticoids is strongly contraindicated.
- Glucocorticoids, NSAIDs—may cause gastrointestinal ulceration/hemorrhage.
- Glucocorticoids—may cause UTI.
- Vertebral instability or IVDD—strict cage rest mandatory while on anti-inflammatory and analgesic drugs; increased activity can exacerbate the problem.
- Opioids—caution if respiratory dysfunction, increased ICP, CNS depression, bradycardia, arrhythmias.
- Gabapentin—caution if renal insufficiency.

POSSIBLE INTERACTIONS

- Opioids—increased CNS and respiratory depression when combined with other CNS depressants.
- Gabapentin—oral antacids may decrease oral bioavailability 20%.

ALTERNATIVE DRUG(S)

- NMDA antagonists (e.g., ketamine)—analgesics
- Pregabalin—chronic neuropathic pain
- Furosemide, omeprazol—COMS/syringomyelia
- Azathioprine, cyclosporine, cytosine arabinoside—immune-mediated diseases



FOLLOW-UP

PATIENT MONITORING

- Primarily based on clinical signs and response to treatment. Initially, monitor at least once a week. If acute severe pain and/or neurologic deficit present, inpatient or daily monitoring recommended. Make adjustments or consider surgery when medical treatment is not effective.
- CSF analysis (e.g., SRMA), spinal radiographs (e.g., discospondylitis), acute phase proteins levels, bloodwork/thoracic radiographs/ultrasound (e.g., neoplasms, infectious diseases).

PREVENTION/AVOIDANCE

Avoid excessive activity, jumping, going upstairs/downstairs, and excess weight. Avoid collars.

POSSIBLE COMPLICATIONS

- Recurrences or deterioration. Surgical treatment can be recommended on an emergency basis according to disease.
- Chronic unresponsive pain.
- Permanent neurologic dysfunction.
- Spread to other locations, pathologic vertebral fracture/luxation (discospondylitis, neoplasms).
- Degenerative joint disease (polyarthritis).

EXPECTED COURSE AND PROGNOSIS

- Varies with disease, severity of clinical signs, and neurologic deficit.
- IVDD extrusion—success with medical treatment in dogs with only pain or mild deficits is about 50% at the most.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Immune-mediated non-erosive polyarthritis and SRMA.
- Discospondylitis and UTI.
- FeLV and feline spinal lymphoma.
- Polymyositis and lymphoma.
- Polymyopathies/myositis—megAESOPHAGUS/dysphagia and aspiration pneumonia.

ABBREVIATIONS

- AA = atlantoaxial
- AST = aspartate aminotransferase
- CK = creatine kinase
- CNS = central nervous system
- COMS = caudal occipital malformation syndrome
- CSF = cerebrospinal fluid
- CSM = cervical spondylomyopathy (wobbler)
- CT = computed tomography
- EMG = electromyography
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FNA = fine-needle aspiration
- GME = granulomatous meningoencephalomyelitis
- ICP = intracranial pressure
- IVDD = intervertebral disc disease
- MRI = magnetic resonance imaging
- MUO = meningoencephalomyelitis of unknown origin
- NSAID = nonsteroidal anti-inflammatory drug
- PCR = polymerase chain reaction
- SRMA = steroid-responsive meningitis-arteritis
- UTI = urinary tract infection

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NECROTIZING ENCEPHALITIS



BASICS

DEFINITION

Necrotizing encephalitis historically restricted to a few breeds such as the pug, Yorkshire terrier, and Maltese dog is described nowadays also in other breeds such as the Chihuahua, the Shih Tzu, and others. It includes necrotizing meningoencephalitis (NME) and necrotizing leukoencephalitis (NLE), since an overlap of clinical signs and histopathologic findings occurs.

SYSTEMS AFFECTED

Nervous

GENETICS

A genetic basis probable; in pug dogs familial inheritance pattern; multifactorial disorder suspected

INCIDENCE/PREVALENCE

Not determined but disease occurring regularly

GEOGRAPHIC DISTRIBUTION

Occurs worldwide, mostly seen in toy breeds

SIGNALMENT

Breed Predilections

Maltese, Pugs, Yorkshire terriers, French bulldogs, Chihuahuas, Shih Tzus, Pekingese, and other toy breeds.

Mean Age and Range

Mostly young adult dogs (range 4 months–10 years)

Predominant Sex

No sex predilection

SIGNS

Progressive signs related to a forebrain lesion (abnormal behavior, seizures, circling, blindness), brainstem lesions with central vestibular signs, or a multifocal lesion.

CAUSES & RISK FACTORS

- Genetic risk factors.
- An infectious agent might be suspected.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other CNS inflammatory/infectious diseases—differentiated on serology, CSF, and MRI results.
- Neoplasia—differentiated on MRI findings.

CBC/BIOCHEMISTRY/URINALYSIS

Results are usually normal

OTHER LABORATORY TESTS

Genetic test for predisposition in pug dogs.

IMAGING

CT/MRI—results help support the clinical diagnosis considering breed, age, clinical signs, and course of the disease. Lesions may be asymmetric, multifocal prosencephalic with varying contrast enhancement, and can include multiple cystic areas of necrosis.

DIAGNOSTIC PROCEDURES

- CSF—pleocytosis with predominantly mononuclear cells; mild to marked protein elevation.
- Brain biopsy—to confirm diagnosis.

PATHOLOGIC FINDINGS

- Necrosis and non-suppurative inflammation of the cerebral gray and white matter; multifocal lesions; active lesions consist of a large malacic gliotic center surrounded by a wall of severe mononuclear inflammation.
- Old lesions consist of rarefied or cystic areas surrounded by intense astroglial sclerosis.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient or outpatient based on the neurologic status
- Symptomatic treatment recommended

NURSING CARE

N/A

CLIENT EDUCATION

- Disease cannot be treated specifically; there may be an improvement with anti-inflammatory or immunosuppressive drugs.
- Seizures may be the only sign at onset of the disease in pug dogs—diagnostic workup of pug dogs presented with seizures is recommended.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

- Symptomatic treatment.
- To control seizures, phenobarbital (2–6 mg/kg PO q12h).
- Corticosteroids can reduce the inflammatory response and improve clinical signs (e.g., prednisolone or prednisone 1–2 mg/kg PO q24h for the first 1–2 weeks; then the dosage can be tapered slowly); other immunosuppressive drugs are used successfully.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Cytosine arabinoside, procarbazine, azathioprine, cyclosporine, leflunomide, lomustine, mycophenolate mofetil.



FOLLOW-UP

PATIENT MONITORING

- Regular clinical and neurologic examinations to monitor response to symptomatic treatment.
- Monitoring of phenobarbital serum levels.

PREVENTION/AVOIDANCE

N/A

EXPECTED COURSE AND PROGNOSIS

- The course of the disease is chronic for months or even years; in every confirmed case, the neurologic signs have been progressive.
- Prognosis is guarded.



MISCELLANEOUS

ASSOCIATED CONDITIONS

In one pug dog, myocardial necrosis was seen in addition to the encephalitic lesions.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Three pugs described in Japan had a history of pregnancy before onset of clinical signs.

N

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- MRI = magnetic resonance imaging

Suggested Reading

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NEONATAL MORTALITY (FADING SYNDROME)



BASICS

DEFINITION

- Death occurring between birth and 2–3 weeks of age.
- Fading syndrome describes a clinical presentation rather than a specific etiology.

PATHOPHYSIOLOGY

- Four major factors lead to vulnerability of neonates: poorly developed thermoregulatory mechanisms; increased risk of dehydration (immature kidney function); increased risk of hypoglycemia (small reserve of glycogen); and immunologic immaturity (95% antibodies from colostrum).
- Highly susceptible to environmental, infectious, nutritional, and metabolic factors.

SYSTEMS AFFECTED

- Cardiovascular
- Endocrine
- Metabolic
- Hepatobiliary
- Gastrointestinal
- Nervous
- Renal/Urologic
- Respiratory
- Ocular/Hemic/Lymphatic/immune
- Skin/exocrine

SIGNALMENT

- Dogs and cats.
- Pedigree puppies and kittens—more prone to congenital (and hereditary) defects, higher overall incidence of stillbirth and neonatal mortality.

SIGNS

General Comments

- Preweaning losses—typically 10–30%; about 65% occur during the first week; greater losses in a cattery or kennel should be considered abnormal.
- A thorough history should be taken to identify potential underlying causes. Particular attention should be given to signalment, breeding history, vaccination and worming history, exposure to toxins, problems during parturition, size of the litter and mothering abilities.

Historical Findings

- Low birth weight, loss of weight, and/or failure to gain weight.
- Decreased activity and appetite.
- Weakness.
- Poor suckling response.
- Constantly vocal or restless early, quiet and inactive later.
- Tendency to remain separate from the dam and the rest of the litter.
- Low Apgar scores at birth. (Apgar scores can be used to assess neonatal viability and short-term survival prognosis.)

Physical Examination Findings

- Nonspecific.
- Dark red or bluish ventral abdominal skin indicative of sepsis or cyanosis.
- Red to purple toes, swollen red and/or purulent umbilical stump may indicate sepsis.
- Gross anatomic defects—open fontanelles, cleft palate, imperforate anus, pectus excavatum, or asymmetry of limbs may be noticed. Hair coat abnormalities over the dorsum may indicate spina bifida.
- Weakness, hypothermia (newborn temperature is 34.7–37.2°C [94.5–99°F],

rising to 36.1–37.8°C [99–100°F] during the first week of life), hypoglycemia, and dehydration are common and interrelated.

- Respiratory distress, diarrhea, or hemoglobinuria may be seen.

CAUSES

- Four most common causes: infection, poor maternal management, low birthweight, congenital abnormalities.

Non-infectious

- Dam-related—dystocia or prolonged labor; cannibalism; lactation failure; trauma; inattention or overattention; inadequate nutrition, including taurine deficiency in kittens. Signalment—breed, age (older), size of litter (larger litters) associated with mortality rate.
- Environmental—any factor that discourages nursing and allows hypothermia, including temperature extremes, humidity extremes, inadequate sanitation, overcrowding, and stress.
- Nutritional—inadequate or ineffective nursing; hypoglycemia; hypothermia-induced digestive malfunction.
- Neonatal isoerythrolysis—queen with blood type B; kitten with blood type A.

Birth Defects

- Gross anatomic defects—more frequent in kittens (about 10% of non-surviving neonates) than in puppies. Failure of midline craniofacial closure causing herniation.
- Alimentary—cleft palate; segmental intestinal agenesis or atresia, imperforate anus, congenital megaesophagus, portosystemic shunt, mucopolysaccharide storage disease.
- Cardiac defects—valvular dysplasia; ventricular septal defect; atrioventricular fistula, tetralogy of Fallot, patent ductus arteriosus, congenital rhythm disorders.
- Respiratory defects—thoracic wall abnormalities; pectus excavatum; primary ciliary dyskinesia; surfactant deficiency.
- Renal defects—agenesis, dysplasia, fanconi syndrome, polycystic kidney disease, ureteral abnormalities.
- Endocrine—diabetes mellitus, hypothyroidism, hyposomatotropism, central diabetes insipidus.
- Central nervous system—cerebellar hypoplasia and abiotrophy, hydrocephalus, spinal dysraphism, neuronopathies and lysosomal storage disease.
- Hematologic—coagulopathies, von Willebrand disease, pyruvate kinase deficiency, hemolytic anemia, phosphofructokinase deficiency.
- Immune system—thymus dysfunction and atrophy.
- Miscellaneous—skin defects, ocular defects.

Infectious

- Viral: Kittens—feline calicivirus; FeLV; FIV; feline herpesvirus type 1, feline panleukopenia virus. Puppies—canine adenovirus type 1; canine distemper virus; canine herpesvirus; canine parvovirus type 1 (minute virus) and type 2; canine influenza virus, canine coronavirus.
- Bacterial—acquired mainly

across the placenta or via the umbilicus but can also occur through the gastrointestinal tract, respiratory tract, urinary tract, and skin wounds. *E. coli*, β -hemolytic *Streptococcus*, coagulase-positive *Staphylococcus*, *Salmonella* spp., *Campylobacter* spp., *Bordetella bronchiseptica*, *Pasteurella multocida*, *Brucella canis*, *Leptospirosis*.

- Parasitic (helminths)—*Toxocara* spp., *Ancylostoma* spp.; (protozoal)—*Toxoplasma*, *Neospora*, *Cryptosporidium*, or *Giardia*, (Coccidia) *Isospora*.

RISK FACTORS

- Subnormal birth weight or failure to grow normally—kittens: minimum daily gain of 7–10 g; puppies: should double in weight by 10–12 days; both: 5–10% gain per day generally acceptable.
- Dystocia or prolonged labor.
- Inbreeding—higher incidence of homozygous recessive genotype.
- Sire with blood type A and queen with blood type B.
- Increased litter size, older dam, certain breeds.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Excessive losses often due to a combination of environmental, immunologic, nutritional, infectious, and metabolic factors; detection and correction of problems in each area is necessary to prevent ongoing losses.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Hydration status and age influence results.
- Mild normocytic, normochromic anemia (normal PCV at 1 week 33–52%, at 2 weeks 29–34%).
- White cell counts variable; may note thrombocytopenia and mild to moderate neutrophilia (with left shift) if septic.

Biochemistry

- Hypoglycemia.
- Hypercholesterolemia, hypertriglyceridemia.
- Low alkaline phosphatase and phosphorus (depressed growth).
- Low gamma-glutamyl transferase—indicator of failure to receive colostrum.
- Other changes depend on organ system involved.

Urinalysis

- Hemoglobinuria—with neonatal isoerythrolysis.
- Bacteria—with infection.
- Urine specific gravity > 1.017 suggests inadequate hydration.

OTHER LABORATORY TESTS

- FeLV antigen test.
- FIV antibody test.
- Serology—*Brucella canis*; canine herpesvirus; canine influenza virus; *Toxoplasma*; *Neospora*; *Leptospirosis*.

IMAGING

- Abdominal ultrasound examination may be useful.
- Thoracic and abdominal radiographs can be helpful (e.g., aspiration pneumonia); however, can be difficult to obtain diagnostic

(CONTINUED)

NEONATAL MORTALITY (FADING SYNDROME)

films. May help to radiograph age-matched individual at the same time.

DIAGNOSTIC PROCEDURES

- Histopathologic—examination of multiple tissues collected at necropsy.
- Metabolic screening of urine sample—rule out inborn errors of metabolism.
- Virus isolation.
- Bacterial culture.
- Blood typing in pedigree cats (dam and kitten).
- Fecal examination—parasites.

PATHOLOGIC FINDINGS

- Post-mortem—extremely important; examine as soon after death as possible to minimize autolysis; give special notice to the following items.
 - Stomach—devoid of contents: lack of nursing; consider dam-related causes (e.g., inappropriate behavior or lactation) or neonatal problems (e.g., weakness, trauma, or physiologic abnormality); filled with milk: suggests sudden death (e.g., trauma, peracute illness) or gastrointestinal dysfunction (body temperature $<35^{\circ}\text{C}$ [95°F]).
 - Thymus subnormal size—not pathognomonic for thymic dysfunction; atrophy can be a result of multiple causes (e.g., viral infection, stress, toxins, nutrition, and defective immune system).
 - Petechiation—common; accompanied by hemorrhage in other organ systems suggests coagulopathy or septicemia.
 - Urine in the urinary bladder—implies a degree of renal dysfunction or inadequate care by the dam.
 - Lungs—should appear the same as an adult's; homogeneous dark red color typical of a stillborn animal that has not taken a breath; hemorrhage, edema, congestion, and mottled color abnormal but nonspecific.
- Note malformations.
- Multiple tissue samples—submit to a diagnostic laboratory; virus isolation, bacterial culture and sensitivity, and histopathology; check with laboratory for proper submission.

**TREATMENT**

- Correct any underlying deficiencies in husbandry or breeding selection.
- Warmth—slowly warm neonate to $36\text{--}37.2^{\circ}\text{C}$ ($97\text{--}99^{\circ}\text{ F}$) over several hours (one degree celsius per hour), if necessary; provide ambient temperature of $29\text{--}35^{\circ}\text{C}$ ($85\text{--}95^{\circ}\text{F}$) and relative humidity of 55%–65%.
- Oxygen—supplement at

30%–40%, if necessary. (Difficult to detect hypoxia as puppies and kittens do not always hyperventilate; clinical signs can include increased respiratory effort, bradycardia, hypotension, and a distended abdomen due to aerophagia.)

- Fluid therapy—intravenous via a jugular or cephalic vein or intraosseous in femur or humerus. Fluid requirements: 80–100 mL/kg/day. Care as volume overload can occur.
- Dextrose supplementation 0.5–1.0 g/kg as part of 5–10% solution (D5W or 5% dextrose in Ringer's solution).
- Do not attempt to feed if body temperature $<35^{\circ}\text{C}$ (95°F) and no sucking reflex; once warmed, encourage nursing.
- Neonatal isoerythrolysis—disallow nursing for first 24 hours after birth.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Antibiotics—commonly used are penicillins (penicillin G, ampicillin, amoxicillin, amoxicillin with clavulanic acid) and first-generation cephalosporins; reduce adult dose by one-half and use same dosage interval.
- Supplement—milk replacer formula.
- Vitamin K₁—0.01–0.1 mg SC or IM once.

CONTRAINdicATIONS

Aminoglycosides, tetracyclines, fluoroquinolones, trimethoprim/sulfonamide, and chloramphenicol—avoid during the neonatal period.

PRECAUTIONS

Drug absorption, distribution, metabolism, and excretion for dogs and cats differ significantly during the first 5 weeks of life from those of adults.

POSSIBLE INTERACTIONSN/ALTERNATIVE DRUGS

N/A

**FOLLOW-UP****PATIENT MONITORING**

- Hydration status—monitor regularly (mucous membranes, urine specific gravity).
 - Body weight—monitor daily or every other day in growing neonates.
 - Dam—monitor mothering abilities and milk production.
- Provide supplemental nutrition to neonates if required.

POSSIBLE COMPLICATIONS

N/A

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

Some infectious agents have zoonotic potential (e.g., *Toxoplasma*, *Leptospira*).

PREGNANCY/FERTILITY/BREEDING

Do not breed individuals with congenital defects.

SYNONYMS

- Fading puppy or kitten syndrome
- Wasting syndrome

ABBREVIATIONS

- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus

INTERNET RESOURCES

<http://veterinarymedicine.dvm360.com/vetmed/article/articleDetail.jsp?id=197161>

Suggested Reading:

Hoskins JD. Clinical evaluation of the kitten: From birth to eight weeks of age. Compend Contin Educ Pract Vet 1990, 12:1215–1225.

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Lamm CG. Clinical approach to abortion, stillbirth and neonatal death in dogs and cats. Vet Clin Small Anim 2012, 42:501–513.

Lawler DF. Investigating kitten deaths in catteries. In: August JR, ed., Consultations in Feline Internal Medicine. Philadelphia: Saunders, 1991, pp. 47–54.

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Client Education Handout
available online

NEONICOTINOID TOXICOSIS



BASICS

OVERVIEW

- Neonicotinoids are a class of neuro-active insecticides chemically similar to nicotine.
- Act on insects at three different post-synaptic nicotinic receptors found in CNS.
- Wide safety margin in mammals due to high selectivity for specific subtypes of nicotinic receptors in insects.
- Compounds include imidacloprid and nitenpyram, commonly used veterinary products, as well as acetamiprid, clothianidin, dinotefuran, nithiazine, sulfoxaflor, and thiamethoxam.
- Widespread use in veterinary medicine for flea control (tablets, e.g. Capstar®, collars, topical spot on products, etc.).
- Used in termite and grub control, and crop production against sucking and chewing pests in a variety of formulations.

SIGNALMENT

- Primarily dogs: chewing up ant bait containers, collars, boxes of tablets, bags, liquid products.
- Rarely reported in cats.

SIGNS

- Imidacloprid has shown no adverse effects when used at 5X the maximum dosage in dogs and cats.
- Alopecia and erythema has been reported following dermal application.
- Oral toxicity is possible if the dose or concentration is excessively high.
- Most common complaint following ingestion is hypersalivation.
- Most common adverse effects observed with dosing of neonicotinoids were decreased activity, tremors, mydriasis or miosis and incoordinated gait; hypothermia was observed at higher doses.

CAUSES & RISK FACTORS

- Dogs chewing on containers.
- Wide availability and frequent access to products.



DIAGNOSIS

History of exposure and clinical signs.



TREATMENT

- Dermal exposure—bathe with liquid dishwashing detergent.
- Oral exposure—dilution with cool water, emesis, gastric lavage, activated charcoal, depending on amount ingested and clinical signs.
- Baseline CBC, chemistry profile, and urinalysis to rule out any pre-existing organ dysfunction, which could increase the risk for toxicosis.
- Antihistamines for signs of dermal hypersensitivity.
- Methocarbamol for tremors.
- IV fluids with a balanced crystalloid.



MEDICATIONS

- Dog emesis: apomorphine 0.03 mg/kg IV,
- Cat emesis: xylazine 0.44 mg/kg IM Avoid hydrogen peroxide due to risk for hemorrhagic gastroenteritis.
- Activated charcoal (0.5–1 g/kg PO) and an osmotic cathartic (sodium sulfate, 125 mg/kg PO) × 1 dose.
- Methocarbamol: 50–220 mg/kg IV. Max daily dose 330 mg/kg/day (cats and dogs). Give 1/2 dose rapidly, wait until animal relaxes, and give remainder of dose to effect.



FOLLOW-UP

Patients usually recover with symptomatic and supportive care; no long term organ damage is expected.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

- Puppies /young dogs are less discriminate and more likely to chew up product containers.
- Young and geriatric animals may have lower detoxification capabilities.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Studies confirmed that imidacloprid is not mutagenic, non-embryotoxic, and non-teratogenic.

ABBREVIATION

CNS = central nervous system

INTERNET RESOURCES

National Pesticide Information Center, Imidacloprid fact sheet.

<http://npic.orst.edu/factsheets/imidacloprid.pdf>

Suggested Reading

Ensley SM. Neonicotinoids. In: Gupta RC, ed., Veterinary Toxicology Basic and Clinical Principles, 2nd ed. Waltham, MA: Elsevier, 2012, pp. 596–598.

Author Sharon Lynn Welch

Consulting Editor Lynn R. Hovda

NEOSPOROSIS



BASICS

OVERVIEW

- *Neospora caninum*—recently recognized coccidian protozoan previously confused with *Toxoplasma gondii*; tachyzoites and tissue cysts resemble *T. gondii* under light microscopy.
- Dogs (and coyotes)—definitive host: excrete oocysts in feces, are infective to other dogs and cattle by contaminating feed. Neosporosis is a major cause of abortion in cattle (intermediate host).
- Disease caused by necrosis associated with tissue damage from cyst rupture and tachyzoite invasion.
- Transmission—transplacental, resulting in congenital infection. Ingestion of sporulated oocysts passed in feces of dog, or tissue cysts in tissues from intermediate hosts.

SIGNALMENT

- Dogs—natural infections (mainly puppies); hunting dogs overrepresented.
- Cats—experimentally infected, although antibodies found in domestic and wild cats.

SIGNS

- Similar to those of toxoplasmosis, except neurologic and muscular abnormalities predominate and are often more severe.
- Young dogs (< 6 months)—ascending lower motor neuron rigid paralysis to tetraparesis more common; distinguished from other forms of paralysis by gradual muscle atrophy; stiffness of pelvic limbs more affected than thoracic limbs; progresses to rigid contracture of limbs.
- Cervical weakness and dysphagia, trismus, glossal paralysis—gradually develop, respiratory muscle paralysis eventually leading to death.
- Ataxia secondary to atrophy of the cerebellum.
- Old dogs—usually CNS involvement (seizures, tremors, behavior changes, blindness), polymyositis (lower motor neuron flaccid paralysis), myocarditis, and dermatitis; as in toxoplasmosis, virtually any organ may be affected; head tremor; postural deficits from cerebellar disease; Horner's syndrome.
- Generalized ulcerative and pyogranulomatous dermatitis seen in dogs on immunosuppressive treatment for SLE and lymphoma.

CAUSES & RISK FACTORS

N. caninum: feeding of raw meat to dogs may be a risk factor and should be avoided.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Young dogs—other causes of peripheral multifocal neurologic signs, mainly including

infectious diseases (toxoplasmosis, distemper); progressive polyradiculomyositis; other causes of diffuse lower motor neuron muscular diseases rare.

- Old dogs with CNS disease—other infectious diseases (fungal, rabies, pseudorabies); toxicity (lead, organophosphorus, carbamate, chlorinated hydrocarbon, strychnine); nonsuppurative encephalitis; meningitis; granulomatous meningoencephalitis; metabolic disease (hypoglycemia, hepatic encephalopathy).

CBC/BIOCHEMISTRY/URINALYSIS

- Depending on the organ system involved.
- Muscle involvement—creatinine phosphokinase and AST activities may be high.

OTHER LABORATORY TESTS

- Serologic testing (IFA, ELISA, and immunoprecipitation)—CSF or serum.
- Antibodies do not cross-react with *T. gondii*, but do with *N. hughesi*, a neospora affecting horses.
- Organism detection—oocysts in feces need to be distinguished from *Hammondia* spp.
- Tachyzoites in aspirates, smears, or tissue sections need to be differentiated from those of *Toxoplasma* (immunohistochemistry).
- PCR—used successfully as a diagnostic tool and distinguishes between other parasites.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

CSF—slight increase in protein and nucleated cell number; cells mainly mononuclear; neutrophils may be seen, but some cases have high numbers of eosinophils.

PATHOLOGIC FINDINGS

- Non-suppurative encephalomylitis.
- Severe non-suppurative inflammation of cerebra leptomeninges and cortex.
- Myositis.
- Myofibrosis.
- Polyradiculoneuritis.
- Pneumonia, cerebella atrophy, multifocal necrotizing myocarditis, and nodular dermatitis—described.
- Ulcerative and pyogranulomatous dermatitis.
- *N. caninum* seems to induce more inflammation than does *T. gondii*.
- Histology—differentiation by location in host cell cytoplasm (not within a parasitophorous vacuole as *T. gondii*).
- Tissue cysts—those of *N. caninum* have thicker walls; differentiated from *T. gondii* by immunohistochemical staining.
- Electron microscopy—rhoptries of *N. caninum* tachyzoites electron dense; those of *T. gondii* honeycomb.



TREATMENT

- Once muscle contracture or ascending paralysis has occurred, the prognosis for clinical improvement is poor. Prognosis is grave in young puppies.
- Progression of clinical disease might be arrested by treatment.



MEDICATIONS

DRUG(S)

- See Toxoplasmosis.
- Clindamycin 25–50 mg/kg PO or IM/day, divided into 2 doses; continue for at least 2 weeks after clinical signs cleared.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- Treat for an extended period of time.
- Serologically test dam or other in-contact dogs and cattle.



MISCELLANEOUS

ZOONOTIC POTENTIAL

None identified (unlike *T. gondii*)

SEE ALSO

Toxoplasmosis

ABBREVIATIONS

- AST = aspartate aminotransferase
- CNS = central nervous system
- CSF = cerebrospinal fluid
- ELISA = enzyme linked immunosorbent assay
- IFA = immunofluorescent antibody
- PCR = polymerase chain reaction
- SLE = systemic lupus erythematosus

Suggested Reading

Dubey JP, Schares G. Neosporosis in animals—The last five years. Vet Parasitol 2011; 180:90–108.

Lyon C. Update on the Diagnosis and management of *Neospora caninum* infections in dogs. Top Compan Anim Med 2010; 25:170–175.

Author Stephen C. Barr

Consulting Editor Stephen C. Barr

NEPHROLITHIASIS



BASICS

DEFINITION

- Nephroliths—urooliths located in the renal pelvis or collecting diverticula of the kidney(s).
- Nephroliths or nephrolith fragments may pass into the ureters (ureteroliths).
- Nephroliths that are not infected, not causing obstruction or clinical signs, and not progressively enlarging are termed *inactive*.

PATHOPHYSIOLOGY

Nephroliths can obstruct the renal pelvis or ureter, predispose to pyelonephritis, and result in compressive injury of the renal parenchyma leading to renal failure; see chapters on the different urolith types for pathophysiology of urolithiasis; in cats, nephroliths composed of blood clots that may be mineralized with calcium phosphate or calcium oxalate can form secondarily to chronic renal hematuria.

SYSTEMS AFFECTED

- Renal/urologic—affects the urinary tract, with potential for obstruction, recurrent urinary tract infections, or renal failure.
- Obstruction of the renal pelvis or ureter in an animal with pyelonephritis may result in septicemia and thus affect any body system.

GENETICS

Refer to chapters describing genetics related to different types of uroliths.

INCIDENCE/PREVALENCE

Nephroliths retrieved from dogs and cats compose 1–1.5% of uroliths submitted to the Minnesota Urolith Center for analysis. The true incidence of nephroliths is likely much higher. Many animals with nephroliths are asymptomatic, or are not treated by methods that encompass retrieval of uroliths that can be quantitatively analyzed.

Mineral compositions of canine nephroliths submitted for analysis, in descending frequency—calcium oxalate (38%), struvite (27%), compound (13%), purines (e.g., ammonium urate, sodium urate, uric acid; 12%), mixed (4%), calcium phosphate (3%), cystine (1.5%), and silica (0.6%). Mineral compositions of nephroliths in cats submitted for analysis, in descending frequency—calcium oxalate (76%), struvite (7%), non-crystalline matrix (including dried blood clots) (6%), compound (5.5%), calcium phosphate (2.5%), and purines (< 1%).

SIGNALMENT

Species

Dog and cat

Breed Predilections

Dogs

- Calcium oxalate nephroliths—Shih Tzu, Yorkshire terrier, mixed, miniature schnauzer, and maltese.

- Struvite nephroliths—miniature schnauzer, mixed, Shih Tzu, pug, and miniature poodle.
- Purine nephroliths—English bulldog, Dalmatian, Yorkshire terrier, and Shih Tzu.
- Cystine—mixed, Yorkshire terrier, English bulldog, and French bulldog.

Cats

- Domestic shorthair (42%), European shorthair (7%), American shorthair (4%), domestic longhair (3.5%), Persian (5%), Siamese and Scottish fold both (2.5%), unknown (includes mixed) breed (19%).

Mean Age and Range

- Dogs—mean age of affected animals, 10 years (range, 2 months–21.5 years).
- Cats—mean age of affected animals, 7.7 years (range, 5 months–19.5 years).

Predominant Sex

- Dogs—overall, nephroliths slightly more common in females (59%) than males (39%) (2% unspecified gender); struvite nephroliths, females (82.5%) > males (15.3%); however, calcium oxalate, cystine, and urate nephroliths males > females.
- Cat—overall, nephroliths slightly more common in females (50%) than males (48%) (2% unspecified gender); for calcium oxalate females (55.5%), males (42%); however, non-crystalline matrix (includes dried blood), urate, and struvite nephroliths males > females.

SIGNS

General Comments

Many patients are asymptomatic, and the nephroliths are diagnosed during evaluation of other problems.

Historical Findings

- None or hematuria, vomiting, and recurrent urinary tract infection; dysuria and pollakiuria in animals with urinary tract infection or concomitant urocystoliths.
- Signs attributable to uremia in animals with bilateral obstruction or renal failure.
- Signs referable to lower urinary tract urolithiasis if uroliths are present in the upper and lower urinary tract.
- Renal colic with acute abdominal/lumbar pain and vomiting is uncommon.

Physical Examination Findings

Abdominal or lumbar pain upon palpation or no significant findings.

CAUSES

- For an extensive listing of causes, see chapters on each urolith type. Oversaturation of the urine with calculogenic minerals is a risk factor for urolithiasis.
- Calcium oxalate urolithiasis—hypercalciuria, hypercalcemia, hypocitraturia, hyperoxaluria, primary hyperparathyroidism, excess dietary calcium.
- Calcium phosphate urolithiasis—chronic renal bleeding (cats), hypercalcemia,

hyperparathyroidism, excess dietary calcium and phosphorus, renal tubular acidosis.

- Cystine urolithiasis—cystinuria.

Infection-induced struvite urolithiasis—urinary tract infection with urease-producing microbes. High-protein diets that produce a large quantity of urea that is excreted in urine are also an integral part of the etiopathogenesis of infection-induced struvite uroliths.

- Urate urolithiasis—genetic urate transporter defect in conversion of uric acid to allantoin (Dalmatians, bulldogs, and others), portosystemic shunt.

Xanthine urolithiasis—allopurinol administration and high dietary purine in dogs predisposed to urate urolithiasis. Allopurinol administration in the treatment of leishmaniasis. Apparently an inborn error of purine metabolism in cats.

RISK FACTORS

- Alkaline urine—struvite and calcium phosphate uroliths.
- Acid urine—calcium oxalate, cystine, urate, and xanthine uroliths.
- Urine retention and formation of highly concentrated urine.
- Lower urinary tract infection—ascending infection and pyelonephritis.
- Conditions that predispose to urinary tract infection (e.g., perineal urethrostomy, ectopic ureters, vesicoureteral reflux, and exogenous steroid administration or hyperadrenocorticism [calcium oxalate uroliths]).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Consider nephroliths in any patient with renal failure, recurrent urinary tract infection, acute vomiting (acute pancreatitis, acute gastroenteritis, intestinal or gastric obstruction, etc.), or abdominal or lumbar pain (e.g., intervertebral disc protrusion, peritonitis).
- Nephroliths are usually confirmed by radiographs or ultrasonography; differentiate mineralization of the renal pelvis or collecting diverticula from true nephrolithiasis.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC results—usually normal unless the patient has pyelonephritis; patients with pyelonephritis may have leukocytosis and immature neutrophilia.
- Serum biochemistry analysis—usually normal unless bilateral obstruction, pyelonephritis, or compressive renal injury leads to renal failure (azotemia with an inappropriate urine specific gravity, hyperphosphatemia); hypercalcemia may

(CONTINUED)

contribute to formation of calcium oxalate or calcium phosphate nephroliths.

- Urinalysis—may reveal hematuria and crystalluria; crystal type may indicate mineral composition; pyuria, proteinuria, and bacteriuria may also be seen in animals with urinary tract infection.

OTHER LABORATORY TESTS

- Submit all retrieved nephroliths or nephrolith fragments for quantitative analysis. Although definitive identification of nephrolith type requires quantitative analysis, mineral composition can frequently be predicted on the basis of signalment, radiographic appearance, and urinalysis findings.
- Results of bacterial culture of urine may confirm urinary tract infection in animals with concurrent pyelonephritis.

IMAGING

- Can detect radiopaque nephroliths (e.g., calcium phosphate, calcium oxalate, struvite) by survey radiography; cystine and silica are slightly radiopaque.
- Purines (ammonium urate, sodium urate, uric acid, xanthine etc.) are usually radiolucent unless they contain a mixture of radiodense biogenic minerals.
- Use ultrasonography or excretory urography to confirm, size and number of nephroliths or ureteroliths regardless of radiographic density.

DIAGNOSTIC PROCEDURES

After ESWL, nephrolith fragments can be retrieved for quantitative analysis by voiding, cystoscopy, catheter-assisted retrieval, or voiding urohydropropulsion.



TREATMENT

APPROPRIATE HEALTH CARE

Manage patients with inactive nephroliths as outpatients. When appropriate, medical dissolution protocols can be administered to outpatients. Removal of nephroliths by surgery or ESWL requires hospitalization.

DIET

Medical dissolution of nephroliths requires a diet appropriate for the specific nephrolith type. See "Medications."

CLIENT EDUCATION

- Inactive nephroliths—may not require removal but should be monitored periodically by urinalysis, urine culture, and radiography. Nephroliths can potentially cause obstruction at any time, which can result in hydronephrosis without clinical signs. Conservative management and monitoring carries a slight risk of undetected and potentially irreversible renal damage, which must be weighed against the potential renal damage from nephrotomy.

- Nephroliths (especially metabolic uroliths) tend to recur after removal; monitor the patient every 3–6 months.

SURGICAL CONSIDERATIONS

- Indications for removal of nephroliths—obstruction, recurrent infection, symptomatic nephroliths, progressive nephrolith enlargement, and a non-functional contralateral kidney.
- Treatment options for nephroliths—medical dissolution, surgery, and ESWL. Calcium oxalate is the most common mineral detected in nephroliths retrieved from dogs and cats, and not yet amenable to medical dissolution. Ureteroliths or nephroliths causing complete obstruction are also not amenable to medical dissolution.
- Surgical options—nephrotomy or pyelolithotomy. Because the nephroliths are surrounded by renal tissue, nephrotomy is required in most dogs and cats. Nephrolith removal by percutaneous nephrolithotomy has been reported in dogs.
- ESWL—safe and effective method of treating canine nephroliths and ureteroliths; nephrolith fragments pass down the ureter into the bladder and are voided with urine.
- ESWL—not as effective for treatment of nephroliths and ureteroliths in cats compared with dogs.



MEDICATIONS

DRUG(S) OF CHOICE

- Antibiotics selected on the basis of urine culture and sensitivity testing as needed; perioperative antibiotics are recommended when infected nephroliths are treated by ESWL or surgical removal.
- Medical dissolution protocols are limited to struvite, purine, and cystine uroliths.
- When feasible, consumption of water in high moisture (canned) foods should be incorporated into treatment protocol. Try to increase excretion of urine with a specific gravity < 1.020 (dogs), or < 1.025 (cats).
- Medical dissolution protocols for struvite nephroliths include a calculolytic food (Hill's Prescription Diet s/d) and appropriate antibiotic therapy (i.e., if patient has a urinary tract infection) for the duration of treatment.
- Medical dissolution of canine purine nephroliths can be attempted by a protein and purine restricted, alkalinizing food (Hill's Prescription Diet Canine u/d), allopurinol (15 mg/kg PO q12h), and supplemental potassium citrate as needed to maintain urine pH ~7.0.
- Medical dissolution of canine cystine nephrolithiasis can be attempted using a protein-restricted, alkalinizing diet (Hill's Prescription Diet Canine u/d), 2-MPG or tiopronin (Thiola, 15 mg/kg PO q12h), and

supplemental potassium citrate as needed to maintain urine pH ~7.5.

CONTRAINDICATIONS

- Do not use allopurinol without dietary purine restriction because this combination may cause xanthine nephrolithiasis in dogs predisposed to urate urolithiasis.
- Do not give acidifying diets to azotemic patients unless blood pH and total CO₂ are monitored for development of metabolic acidosis.



FOLLOW-UP

PATIENT MONITORING

Abdominal radiographs (ultrasonography for radiolucent uroliths), urinalysis, and urine culture every 3–6 months to detect nephrolith recurrence. Dogs treated with ESWL—check every 2–4 weeks by radiographs and ultrasonography until nephrolith fragments have passed through the excretory system.

PREVENTION/AVOIDANCE

Eliminate factors predisposing to individual urolith type, augment urine volume, and correct factors contributing to urine retention.

POSSIBLE COMPLICATIONS

Hydronephrosis, renal failure, recurrent urinary tract infection, and pyelonephritis.

EXPECTED COURSE AND PROGNOSIS

- Highly variable; depends on nephrolith type, location, and size, secondary complications (e.g., obstruction, infection, renal failure), and owner compliance with treatment and prevention protocol.
- Inactive nephroliths may remain inactive for years, resulting in an excellent prognosis.
- Excellent results have been reported using ESWL to treat dogs with nephroliths—return to normal health and an excellent prognosis.
- The prognosis for patients with renal failure caused by nephrolithiasis depends on the severity and rate of progression of renal failure.
- Nephroliths causing outflow obstruction or associated with non-functioning kidneys cannot be dissolved medically.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Hyperadrenocorticism and chronic glucocorticoid administration are associated with calcium oxalate uroliths, and urinary tract infection resulting in struvite urolithiasis.

PREGNANCY/FERTILITY/BREEDING

- Contraindication to ESWL
- Acetohydroxamic acid, a urease inhibitor, is teratogenic

N

NEPHROLITHIASIS

(CONTINUED)

SYNOMYMS

Kidney stones, renal calculi, renoliths, kidney calculi

SEE ALSO

- Hydronephrosis
- Pyelonephritis
- Renal Failure, Chronic
- Urinary Tract Obstruction
- Urolithiasis, Calcium Oxalate
- Urolithiasis, Calcium Phosphate
- Urolithiasis, Cystine
- Urolithiasis, Struvite—Cats
- Urolithiasis, Struvite—Dogs

- Urolithiasis, Urate
- Urolithiasis, Xanthine

ABBREVIATIONS

- ESWL = extracorporeal shock wave lithotripsy

INTERNET RESOURCES

www.vet.utk.edu/clinical/sacs/lithotripsy

Suggested Reading

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Consulting Editor Carl A. Osborne



Client Education Handout
available online

NEPHROTIC SYNDROME



BASICS

DEFINITION

Concurrent proteinuria, hypoalbuminemia, hypercholesterolemia, and third-space fluid accumulation (i.e., ascites, subcutaneous edema, etc.).

PATOPHYSIOLOGY

- Glomerular disease may result in marked urinary protein loss. Greater than 3.5 g albumin loss per day in humans often results in nephrotic syndrome. Magnitude of hypoalbuminemia and proteinuria required for development of nephrotic syndrome in dogs and cats is unknown; although affected patients usually have very low serum albumin concentrations, not all dogs with very low serum albumin concentrations will develop nephrotic syndrome.
- Reduced plasma oncotic pressure may result in hyperaldosteronism, which induces sodium and water retention, leading to edema and ascites.
- Alternatively, non-aldosterone mediated sodium retention, or a hypothetical “vascular permeability factor,” have been suggested as mechanisms whereby glomerular protein loss may increase, along with fluid loss from the systemic vasculature.
- Hypercholesterolemia is a consequence of decreased catabolism and increased hepatic synthesis of lipoproteins.
- Other glomerular disease complications frequently diagnosed in dogs with nephrotic syndrome include hypertension, hypercoagulability, muscle wasting, and weight loss.
- Thromboembolism is a consequence of a generalized pro-coagulative state, due in part to increased platelet number and sensitivity, urinary loss of antithrombin, and increased concentrations of some clotting factors.

SYSTEMS AFFECTED

- Renal/Urologic—persistent proteinuria initially without active urine sediment. With progressive disease and nephron loss, azotemia, chronic kidney disease and uremia may occur.
- Cardiovascular—dependent edema, ascites, hypercholesterolemia/hyperlipidemia, hypertension, hypercoagulability, and thromboembolic disease.

GENETICS

Familial glomerular diseases have been reported in several breeds (see Glomerulonephritis and Amyloidosis chapters), but are less likely to result in nephrotic syndrome than non-familial protein-losing nephropathies.

INCIDENCE/PREVALENCE

- Nephrotic syndrome is an uncommon complication of glomerular disease, with a median of 0.5 new cases per year diagnosed at 8 veterinary teaching hospitals in 1 study.

- Nephrotic syndrome has not been associated with histologic subtype of glomerular disease.

SIGNALMENT

Species

Dog and cat

Breed Predilections

No breed appears to be at increased risk of the nephrotic syndrome complication with glomerular disease.

Mean Age and Range

Dogs with nephrotic syndrome are typically younger than those with non-nephrotic glomerular disease (mean, 6.2 years vs. 8.4 years at time of initial diagnosis).

Predominant Sex

None recognized

SIGNS

Historical Findings

- Pitting subcutaneous edema and/or ascites are the most common presenting complaints.
- Clinical signs associated with an underlying infectious, inflammatory, or neoplastic disease may be the primary reason for seeking veterinary care. Subtle edema or ascites may then be detected by physical examination or with diagnostic imaging.
- Rarely, dogs may develop acute dyspnea, severe panting, weakness, or collapse due to pleural or pericardial effusion, pulmonary edema, or pulmonary thromboembolism.

Physical Examination Findings

- Dependent pitting, subcutaneous edema, or ascites.
- Complications of hypertension: retinal hemorrhage or detachment, papilledema, arrhythmias and/or murmurs secondary to left ventricular hypertrophy.
- Dyspnea and/or cyanosis in dogs with pleural effusion or pulmonary thromboembolism.

CAUSES

- Glomerular disease may be a consequence of chronic inflammatory conditions (e.g., infection, neoplasia, or immune-mediated diseases).
- Nephrotic syndrome is unlikely to be solely a consequence of severe proteinuria; additional unidentified factors appear to be necessary.

RISK FACTORS

See “Causes”



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Proteinuria

- Often due to inflammatory post-glomerular urinary tract disease (e.g., bacterial cystitis/pyelonephritis, urolithiasis, tubular renal failure, or lower urinary tract neoplasia). Inflammation of the urinary tract is usually (but not always) associated with active urine

sediment.

- Hyperglobulinemia may be associated with proteinuria, and may be more likely discovered when urinalysis includes the sulfosalicylic acid turbidimetric test (Bumini test).
- Protein-losing nephropathies typically result in inactive urine sediment (although hyaline casts may be present); renal biopsy is the only accurate way to distinguish the various types of glomerular disease.

Hypoalbuminemia

Decreased albumin production (severe liver disease) and gastrointestinal albumin loss (protein-losing enteropathies) must be distinguished from hypoalbuminemia secondary to glomerular disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Persistent, significant proteinuria with inactive urine sediment.
- Hypoalbuminemia and hypercholesterolemia are by definition essential components of the nephrotic syndrome.
- Renal failure may occur with advanced disease. Azotemia may precede loss of urine concentrating ability.

OTHER LABORATORY TESTS

Urine Protein:Creatinine Ratio

- Confirms and quantifies the severity of proteinuria.
- Magnitude of proteinuria can be used to assess response to therapy or progression of disease.

Protein Electrophoresis

Urine and serum protein electrophoresis may identify pre-glomerular proteinuria in patients with monoclonal gammopathies or urinary immunoglobulin light chains (Bence-Jones proteins).

IMAGING

- Radiography—loss of abdominal detail due to ascites is the most common abnormality. Pleural effusion (uncommon), pulmonary edema, or pericardial effusion (very uncommon) may be present.
- Abdominal ultrasonography—usually confirms large volume of peritoneal and retroperitoneal fluid. Mild renomegaly may be observed with glomerular diseases.

DIAGNOSTIC PROCEDURES

Renal biopsy is indicated if significant and persistent proteinuria with inactive urine sediment exists. Microscopic evaluation of renal tissue will establish subtype of glomerular disease and help in formulating a prognosis. Consider renal biopsy only after less-invasive tests (CBC, serum biochemistry profile, urinalysis, quantitation of proteinuria) are completed and blood clotting ability has been assessed.



TREATMENT

APPROPRIATE HEALTH CARE

- Most dogs and cats can be treated as outpatients.
- Severely azotemic or

N

NEPHROTIC SYNDROME

(CONTINUED)

hypertensive patients, or patients with thromboembolic disease, may require hospitalization.

NURSING CARE

- Abdominocentesis—reserve for patients with respiratory distress or abdominal discomfort caused by ascites. Excessive fluid removal will promote further fluid accumulation and contribute to electrolyte abnormalities.
- Plasma transfusion is not indicated for routine treatment of hypoalbuminemia. Very large volumes of plasma are required to significantly increase serum albumin concentration, and transfused proteins have relatively short half-lives.
- Intravenous human albumin can be used in patients with life-threatening complications due to fluid accumulation (e.g., pulmonary edema; pleural effusion).
- Use of low-sodium, "maintenance"-type fluids (e.g., 0.45% NaCl) for all crystalloid needs may minimize extravascular fluid accumulation in hospitalized animals.
- Intravenous synthetic colloids frequently exacerbate fluid extravasation in patients with nephrotic syndrome. There is a faster return to baseline oncotic pressure in nephrotic patients than in healthy animals after colloidal fluid administration, likely due to increased urinary loss and accumulation within interstitial tissues. These fluids should therefore be limited to patients with immediate, life-threatening needs for oncotic pressure support.

ACTIVITY

Activity restriction may decrease likelihood of thromboembolic disease; conversely, increased activity in humans with nephrotic syndrome promotes fluid mobilization and lymphatic uptake.

DIET

- Sodium-reduced, high-quality, low-quantity protein diets are currently recommended. Prescription "renal diets" meet these criteria.
- Normal or high dietary protein may contribute to renal disease progression by exacerbating glomerular hyperfiltration, proteinuria, and glomerulosclerosis.

CLIENT EDUCATION

- If the underlying cause cannot be identified and corrected, glomerular disease usually progresses to azotemic chronic kidney disease.
- Renal biopsy is required to differentiate between the various subtypes of glomerular disease and to optimize treatment protocols.
- Once azotemia and uremia develop, prognosis is poor due to rapid progression of renal failure.
- Nephrotic syndrome is associated with shortened survival time. In one study, median survival time of 61 dogs

with nephrotic syndrome was 12.5 days (range, 0–2,783 days), as compared to 104.5 day (range, 0–3,124 days) median survival time of 99 dogs with non-nephrotic glomerular disease.



MEDICATIONS

DRUG(S)

See Glomerulonephritis chapter for general treatment recommendations.

Edema and Ascites

- Dietary sodium reduction.
- Reserve abdominocentesis and diuretics for patients with respiratory distress or abdominal discomfort. Overzealous diuretic use may result in dehydration and acute renal decompensation.
- Patients who require maintenance diuretic therapy for severe, persistent extravascular fluid accumulation should be treated with an aldosterone antagonist (spironolactone 1–2 mg/kg PO q12h), and supplemented with low doses of loop diuretics (i.e., furosemide 0.5–2 mg/kg PO q8–12h) as needed.
- Plasma or albumin transfusions provide only temporary benefit, and are not recommended when the risk of therapy outweighs any potential benefit.

Proteinuria

- Angiotensin converting enzyme (ACE) inhibitors (e.g., enalapril 0.5 mg/kg PO q12h) decrease severity of proteinuria (see Glomerulonephritis chapter). Because proteinuria is toxic to renal tubules, ACE-inhibitor therapy should be initiated at the time of diagnosis, unless severe azotemia is present.
- Aspirin (0.5 mg/kg PO q12h) decreases thromboembolism risk and should be initiated when serum albumin decreases below 2.0–2.5 g/dL.

PRECAUTIONS

- Dose adjustment of highly protein-bound drugs (e.g., aspirin) may be needed.
- Use ACE inhibitors with caution in patients with serum creatinine > 5.0 mg/dL.
- Diuretics should be used with extreme caution in patients with nephrotic syndrome because of the risk of causing or worsening azotemia.

POSSIBLE INTERACTIONS

See "Precautions"



FOLLOW-UP

PATIENT MONITORING

Urinary protein:creatinine ratio; serum urea nitrogen, creatinine, albumin, and electrolyte

concentrations; blood pressure; and body weight. Ideally, recheck examinations should be scheduled 1, 3, 6, 9, and 12 months after initiation of treatment.

POSSIBLE COMPLICATIONS

- See Glomerulonephritis chapter for discussion of glomerular disease complications unassociated with nephrotic syndrome.
- Complications more likely to develop in nephrotic (vs. non-nephrotic) dogs and cats with glomerular disease include:
- Arterial or venous thrombosis (e.g., pulmonary thromboembolism)
- Electrolyte disturbances, particularly with repeated abdominocenteses or high doses of diuretics
- Faster progression to azotemia and uremia, and decreased median survival time.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Amyloidosis
- Glomerulonephritis
- Glomerulopathy
- Hypercoagulability
- Hypertension

PREGNANCY/FERTILITY/BREEDING

Likely high risk in those patients with severe hypoalbuminemia and/or hypertension.

SEE ALSO

- Amyloidosis
- Glomerulonephritis
- Proteinuria

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- RBC = red blood cell
- WBC = white blood cell

Suggested Reading

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Client Education Handout
available online

NEPHROTOXICITY, DRUG-INDUCED



BASICS

DEFINITION

Renal injury caused by a pharmacologic agent used to diagnose or treat a medical disorder.

PATHOPHYSIOLOGY

- Drugs can cause nephrotoxicosis by interfering with renal blood flow, glomerular function, tubular function, or interstitial inflammation.
- Many drugs are nephrotoxic because they are excreted primarily by the kidneys.
- Most nephrotoxic drugs cause proximal renal tubular necrosis.
- If renal injury is severe, acute kidney failure develops.

SYSTEMS AFFECTED

- Renal/Urologic.
- Gastrointestinal—inappetence, vomiting, diarrhea, or melena due to gastrointestinal irritation or uremic ulceration.
- Endocrine/Metabolic—metabolic acidosis due to decreased elimination of acid by kidneys and inability to reclaim bicarbonate filtered into tubules by glomeruli.
- Hemic/Lymphatic/Immune—anemia due to blood loss or decreased red blood cell survival in patients with uremia; increased susceptibility to infections because of immune dysfunction in patients with uremia.
- Nervous—depression, lethargy associated with effect of uremic toxins on the central nervous system.
- Neuromuscular—weakness due to systemic effects of uremia.
- Respiratory—tachypnea or respiratory distress due to uremic pneumonitis or compensatory response for metabolic acidosis.

SIGNALMENT

Species

Dog and cat

Breed Predilections

N/A

Mean Age and Range

Any age; older patients are more susceptible

Predominant Sex

N/A

SIGNS

Historical Findings

- Polyuria and polydipsia; sometimes oliguria
- Inappetence
- Depression
- Vomiting
- Diarrhea

Physical Examination Findings

- Dehydration
- Oral ulcers
- Uremic halitosis

CAUSES

Antimicrobial Drugs

- Aminoglycosides—all drugs in this class are potentially nephrotoxic, including neomycin, gentamicin, amikacin, kanamycin, and streptomycin. Due to frequent use in the past, nephrotoxicosis associated with aminoglycoside treatment was most often associated with gentamicin.
- Tetracyclines—outdated products can cause acquired Fanconi-like syndrome characterized by glucosuria, proteinuria, and renal tubular acidosis; IV administration to dogs at high dosages ($> 30 \text{ mg/kg}$) can cause acute kidney injury.
- Administration of sulfa drugs (e.g., trimethoprim-sulfadiazine) has been associated with acute kidney injury in dogs, but no causal relationship has been proven.

Antifungal Drugs

Amphotericin B

Antineoplastic Drugs

- Cisplatin—clinically important cause of nephrotoxicosis in dogs.
- Doxorubicin—possible cause of nephrotoxicosis in cats but not well documented.

NSAIDs

- Aspirin, ibuprofen, naproxen, carprofen, piroxicam, meloxicam, flunixin meglumine, and others may cause nephrotoxicosis.
- Most likely to cause renal injury in patients with preexisting kidney disease or patients with concomitant dehydration or other causes of hypovolemia.

ACE Inhibitors

- Enalapril, benazepril, and others.
- Most likely to cause acute kidney injury in patients with hyponatremia, dehydration, or congestive heart failure.

Radiographic Contrast Agents

- Intravenous administration of ionic radiographic contrast agents can cause acute kidney injury, especially in patients with dehydration, hypovolemia, or hypotension associated with inhalational anesthesia.

RISK FACTORS

- Dehydration.
- Advanced age, probably because older patients have preexisting kidney disease.
- Kidney disease, inactive or active.
- Renal hypoperfusion; potential causes include any disorder associated with hypovolemia (e.g., vomiting, hemorrhage, hypoadrenocorticism), low cardiac output (e.g., congestive heart failure, pericardial disease, cardiac arrhythmias, inhalational anesthesia), or renal vasoconstriction (e.g., NSAID administration).
- Electrolyte and acid-base abnormalities including hypokalemia, hyponatremia,

hypocalcemia, hypomagnesemia, and metabolic acidosis.

- Concurrent drug therapy—administration of furosemide increases nephrotoxicosis of aminoglycosides; treatment with cytotoxic drugs (e.g., cyclophosphamide) may increase nephrotoxic potential of drugs.

- Fever.
- Sepsis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Must differentiate from other causes of acute kidney injury (e.g., ethylene glycol toxicosis, raisin/grape ingestion [dogs], lily toxicosis [cats], renal ischemia, leptospirosis).
- Most patients have a history of recent treatment (i.e., within the previous 2 weeks) with a potentially nephrotoxic drug; acute kidney injury may occur several days after discontinuation of an aminoglycoside.
- Accidental ingestion of large doses of medications may occur, especially with palatable chewable formulations (prescribed for this patient or other animals).
- Determine all drugs that have been administered to the patient, including over-the-counter preparations (e.g., aspirin, ibuprofen, and naproxen) and medications prescribed for human use (e.g., NSAID or ACE inhibitor).

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram—usually normal unless concomitant problems exist (e.g., gastrointestinal hemorrhage associated with administration of NSAIDs).
- Biochemistry—normal in early stages of drug-induced nephrotoxicosis or reveals signs consistent with acute kidney injury including azotemia, hyperphosphatemia, and metabolic acidosis.
- Urinalysis—may reveal low urinary specific gravity (often < 1.025), proteinuria, glucosuria, or cylindruria. Casts may be one of the earliest indicators of acute kidney injury.

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Renal biopsy may be indicated to determine cause of acute kidney injury and potential for reversibility, especially in patients that do not favorably respond to treatment as expected. The magnitude of renal morphologic changes may appear mild compared to the magnitude of azotemia.

PATHOLOGIC FINDINGS

Most nephrotoxic drugs cause proximal renal tubular necrosis.

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NEPHROTOXICITY, DRUG-INDUCED

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

- Manage patients with acute kidney injury as inpatients.
- Manage patients without azotemia that can eat, and drink enough to maintain hydration, as outpatients.

NURSING CARE

- Administer balanced polyionic fluid (e.g., lactated Ringer's solution).
- Correct hydration deficits rapidly (i.e., over 6–8 hours) to minimize further renal injury. Calculate volume of fluid to administer as follows: volume (mL) = body weight (kg) ×% dehydration × 1,000 mL.
- In addition to correcting hydration deficits, administer maintenance requirements (~66 mL/kg/day) unless the patient is oliguric or anuric, and replace any ongoing losses caused by vomiting and diarrhea. As a minimum, assume that patients with acute kidney failure are losing 3–5% of their body weight because of ongoing losses.

ACTIVITY

Reduce

DIET

- Outpatients can be fed their regular food.
- Avoid oral feeding until vomiting is controlled, but initiate nutritional support as early as possible with acute kidney injury.
- If oral feeding is not possible initially, consider total or partial parenteral nutrition.
- The appropriate nutritional composition for patients with severe acute kidney injury has not been determined.
- Patients that recover from drug-induced nephrotoxicosis may develop chronic kidney disease, which should be managed by feeding a therapeutic renal diet indefinitely.

CLIENT EDUCATION

- Provide unlimited access to clean, fresh water at all times.
- If any signs of illness such as inappetence, vomiting, or diarrhea develop, return the patient immediately for veterinary care to minimize worsening of renal function.

SURGICAL CONSIDERATIONS

- Avoid elective surgery until kidney disease is resolved.
- If surgery is necessary, administer fluids (5–20 mL/kg/h) during anesthesia to maintain adequate mean arterial blood pressure (> 60 mmHg) and renal perfusion. Monitor urine output and adjust rate of fluid

administration to maintain urine production of 1–2 mL/kg/h.



MEDICATIONS

DRUG(S) OF CHOICE

None

CONTRAINDICATIONS

Do not use furosemide to promote diuresis in patients with aminoglycoside nephrotoxicosis.

PRECAUTIONS

- Avoid drugs that may worsen renal injury in patients with nephrotoxicosis, including NSAIDs, vasodilators, and ACE inhibitors.
- Use less toxic drugs when possible (e.g., carboplatin instead of cisplatin, other effective antimicrobials instead of aminoglycosides).

POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Weigh hospitalized patients several times daily to detect changes in fluid balance and adjust fluid therapy accordingly.
- Perform biochemical analysis, including electrolytes, every 1–2 days to evaluate severity of azotemia and to detect electrolyte and acid/base abnormalities.
- Patients receiving aminoglycosides—perform urinalysis every 1–2 days to detect early signs of nephrotoxicosis such as glucosuria, increased proteinuria, and cylindruria; discontinue aminoglycoside if any of these signs are observed.
- Measure urine output to determine if patient is polyuric or oliguric; adjust fluid therapy on the basis of these findings and determine need for additional treatment to stimulate urine production. Do not overhydrate patient with parenteral fluids.

PREVENTION/AVOIDANCE

- Avoid or correct risk factors that predispose to development of drug-induced nephrotoxicosis.
- Initiate saline diuresis to all dogs receiving cisplatin.
- Avoid using nephrotoxic drugs unless they are necessary (e.g., use aminoglycosides only if patient has overwhelming sepsis and culture results indicate aminoglycosides are the only effective antimicrobial).
- Monitor serum aminoglycoside concentration and perform frequent

urinalyses while administering an aminoglycoside.

- Do not administer furosemide with an aminoglycoside as this combination is likely to enhance nephrotoxicity of the aminoglycoside.

POSSIBLE COMPLICATIONS

- Acute kidney injury
- Chronic kidney disease

EXPECTED COURSE AND PROGNOSIS

- Patients without azotemia may develop acute kidney injury after several days of exposure, especially to aminoglycosides.
- Renal injury caused by nephrotoxic drugs may lead to development of chronic kidney disease months to years after recovery from drug-induced renal injury.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

Renal Failure, Acute

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- NSAID = nonsteroidal anti-inflammatory drug

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Consulting Editor Carl A. Osborne

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NERVE SHEATH TUMORS



BASICS

OVERVIEW

- Tumors of the peripheral nerves, spinal nerves, or nerve roots.
- Malignant peripheral nerve sheath tumor is the recommended denomination for these tumors, instead of schwannoma, neurilemmoma, or neurofibroma, since determination of the cell of origin is often impossible.
- Most tumors (80%) occur in the thoracic limb of dogs.
- Approximately 50% of the tumors are located in the plexus or peripheral nerve region and 50% in the nerve root region.

SIGNALMENT

- Dogs—no breed or gender predisposition.
- Mean age in dogs—7.9 years; uncommon in dogs younger than 3 years.
- Rare in cats.

SIGNS

- Chronic progressive thoracic limb lameness.
- Muscle atrophy (neurogenic atrophy) often present, more severe than that observed with orthopedic disorders.
- Decreased muscle tone and decreased flexor reflex can be observed.
- Axillary palpation detects a mass in less than 30% of cases.
- Axillary pain upon palpation occasionally.
- Horner's syndrome can be seen in tumors involving the T1–T3 nerve roots.
- Ataxia, paresis, and asymmetric proprioceptive deficits can be seen if the tumor compresses the spinal cord.
- Cutaneous trunci reflex may be poor to absent on the affected side.
- In lumbosacral tumors, rectal palpation can be useful for mass detection.
- Self-mutilation is occasionally observed.

CAUSES & RISK FACTORS

Mutation of the *neu* oncogene was identified in some cases.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Orthopedic conditions causing thoracic or pelvic limb lameness. Differentiate by orthopedic examination, radiographs, or scintigraphy, and response to rest and anti-inflammatory drugs. The severity of muscle atrophy also useful.
- Lateralized nerve root compression by intervertebral disc disease, lumbosacral disease, or spinal neoplasia. Intervertebral disc disease and lumbosacral disease are usually associated with spinal pain. Advanced imaging (CT or MRI) is required to distinguish these diseases.
- Secondary nerve neoplasia—lymphoma, histiocytic sarcoma, chondrosarcoma. Fine-needle or core biopsy needed to differentiate these conditions.

OTHER LABORATORY TESTS

- CSF analysis—nonspecific findings.
- Cytology—ultrasound-guided fine-needle biopsy can provide diagnostic sample. Cytologic features of MPNST are characteristics of a soft tissue sarcoma.

IMAGING

- Survey radiographs—well-positioned survey radiographs may allow visualization of an enlarged intervertebral foramen; most often unrewarding.
- US—can identify a mass in cases where axillary palpation is unrewarding. Patient sedation allows better positioning and US-guided fine-needle aspiration biopsy. Tumor echogenicity is variable.
- Myelography—if the neoplasm has invaded the vertebral canal, an intradural-extradural pattern can be seen. Due to the location of neoplasms, myelography is diagnostic in approximately 50% of dogs.
- CT and MRI—to visualize proximal or distal limb tumors. Hyperintensity on T2 weighted images is the most common MRI pattern. MPNSTs usually show contrast enhancement on both CT and MRI. Due to the high soft tissue characterization, MRI is the diagnostic modality of choice.

DIAGNOSTIC PROCEDURES

- EMG—to differentiate neurogenic from disuse muscle atrophy. Fibrillation potentials and positive sharp waves are suggestive of neurogenic muscle atrophy. EMG changes found in 96% of dogs with confirmed or suspected nerve sheath tumors. Epaxial muscle EMG changes predictive of vertebral canal invasion in cases of proximal tumors.
- Nerve conduction velocity—conduction velocities may be prolonged with amplitude reduced.
- F-wave, H-wave, cord dorsum potentials—evaluate the root portion of the nerve and can be useful to differentiate a lesion affecting predominantly the sensory or motor root.



TREATMENT

- Surgical resection following the principles of oncologic surgery is the recommended treatment.
- Amputation is usually required to minimize the chance of local recurrence.
- Hemilaminectomy or dorsal laminectomy may be required to allow resection of the nerve root region.
- Oral corticosteroids may allow clinical improvement by reduction of peritumoral edema.
- Radiation therapy—can be used for nonresectable tumors or in cases where surgery is contraindicated. It can also be used postoperatively to decrease the chance of local recurrence.



MEDICATIONS

DRUG(S)

- Chemotherapy—metronomic therapy (cyclophosphamide 10 mg/m² and piroxicam 0.3 mg/kg) can be used for incompletely resected nerve sheath tumors in dogs.
- Dexamethasone 0.1–0.25 mg/kg q24h or prednisone 0.5–1 mg/kg q12–24h can be used to provide short-term improvement.
- Gabapentin 5–20 mg/kg q8–12h can be used for analgesia in cases of neuropathic pain.
- Pregabalin 2–4 mg/kg q12h can be used in cases refractory to gabapentin.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Corticosteroids should not be used in conjunction with nonsteroidal anti-inflammatory drugs.



FOLLOW-UP

- Nerve sheath tumors are locally invasive and rarely metastasize.
- Postoperative local recurrence is common (up to 72% of cases).



MISCELLANEOUS

ABBREVIATIONS

- CSF = cerebrospinal fluid
- CT = computed tomography
- EMG = electromyography
- MPNST = malignant peripheral nerve sheath tumor
- MRI = magnetic resonance imaging
- US = ultrasonography

Suggested Reading

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NEUROAXONAL DYSTROPHY



BASICS

OVERVIEW

- Inherited degenerative diseases of neurons in diverse regions of the CNS, particularly the cerebellum and associated pathways.
- Primary neuroaxonal dystrophy disorders are sometimes classified as abiotrophies.
- Inheritance—autosomal recessive in breeds where heritability is proven. • The main pathologic feature of NAD, axonal spheroids, also occurs in normal aging, as well as secondary to a number of other diseases, such as acquired or inherited metabolic diseases, and toxicities.

SIGNALMENT

- Dog and cat. • Breeds predisposed—domestic and Siamese cats, rottweilers, collies, Papillons, Chihuahuas, German shepherd dogs, Jack Russell terriers, and boxers. • Age at onset—breed-specific, ranging from under 2 months of age in cats, Chihuahuas, and Papillons, to 1–2 years in rottweilers.

SIGNS

- Cerebellar ataxia—progressive dysmetria and hypermetria of the limbs (rarely hypometria) with patellar hyperreflexia.
- Strength and proprioception normal in most cases. Rottweilers may have extensive involvement of the dorsal columns of the cervical spinal cord and may exhibit proprioceptive deficits.
- Loss of menace responses despite normal vision and facial nerves.
- Progressive signs of brainstem involvement may be a feature, especially in papillons, including loss of swallowing reflex and tongue movement; tetraplegia may develop in the final stages.
- Mild intention tremor or head and neck dysmetria in some patients.
- Primarily cerebellar signs in rottweilers, collies, Chihuahuas, and domestic cats; predominantly spinal cord lesions in German shepherd dogs and boxers; tremor and cerebellar ataxia present in all affected animals.

CAUSES & RISK FACTORS

- Unknown
- Usually classified as neuronal abiotrophy
- Autosomal recessive inheritance proven in some breeds
- Breed predisposition



DIAGNOSIS

- Suspicion is based on clinical signs in a predisposed breed, usually in juvenile animals.
- Definitive diagnosis requires histopathologic examination of CNS tissue, usually post-mortem.

DIFFERENTIAL DIAGNOSIS

- Other congenital cerebellar anomalies, abiotrophies, and degenerative disorders. Reported occasionally in cats, and in a number of breeds of dog including border collie, Brittany, Coton de Tulear, Gordon setter, Jack Russell (Parson Russell) terrier, Labrador retriever, Old English sheepdog, and many others.
- Other structural anomalies of the caudal brainstem, including caudal occipital malformation syndrome and Dandy-Walker syndrome. Differentiated by imaging studies, particularly MRI. Certain breeds are predisposed, e.g., caudal occipital malformation syndrome in the Cavalier King Charles spaniel.
- Cerebellar hypoplasia caused by *in utero* infection of kittens with feline panleukopenia virus—apparent by 3–6 weeks of age; non-progressive.
- Distemper encephalitis—differentiated on the basis of systemic signs preceding or accompanying the neurologic deficits and on results of CSF analysis (normal with neuroaxonal dystrophy).
- Other infectious encephalitides—fungal, rickettsial, and protozoal; differentiated on the basis of multisystemic signs in some patients, serologic testing, and CSF analysis.
- Non-infectious inflammatory encephalitides, particularly granulomatous meningoencephalomyelitis. Breed-specific encephalitides (pug, Maltese terrier, Yorkshire terrier) usually cause forebrain signs (seizures), but cerebellar involvement may occur. Differentiated by the presence of inflammatory changes in CSF and, in some cases, by contrast-enhancing lesions in the brain apparent with MRI.
- Neoplasia affecting the cerebellum—primary, metastatic, or locally invasive. Occurs in older dogs and cats, usually over 5 years of age. Differentiated on the basis of imaging studies (particularly MRI), CSF analysis in some cases, and systemic involvement in the case of metastatic neoplasia.
- Cervical spinal cord disease—proprioceptive deficits and tetraparesis.
- Diagnosis of neuroaxonal dystrophy is by exclusion; it may not be possible to reach an antemortem diagnosis.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

N/A

IMAGING

Atrophy of the cerebellum may be appreciable on MRI in certain patients (e.g., papillons).

DIAGNOSTIC PROCEDURES

All antemortem routine tests are normal.

PATHOLOGIC FINDINGS

- Axonal spheroids—present throughout the CNS gray or white matter, depending on the

breed affected. Spheroids contain abnormal accumulations of intracellular proteins, particularly several associated with axonal transport and synaptic function.



TREATMENT

- None available that alters the course of the disease.
- Activity—restrict activity to areas where a fall can be avoided (avoid stairs, swimming pools, etc.).



MEDICATIONS

DRUG(S)

N/A



FOLLOW-UP

- Rottweilers—worsen over 1–5 years; develop clonic patellar and crossed extensor reflexes.
- Not fatal, but severely incapacitating.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- MRI = magnetic resonance imaging
- NAD = neuroaxonal dystrophy

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NEUTROPENIA



BASICS

DEFINITION

- Neutrophil count < 3,000 neutrophils/ μL in dogs and < 2,500 neutrophils/ μL in cats.
- Can develop alone or as a component of pancytopenia. • Often accompanied by a left shift and toxic changes (e.g., cytoplasmic basophilia, foamy cytoplasmic vacuolation, Döhle bodies, and/or toxic granulation).
- Certain breeds, such as greyhounds or Belgian Tervurens, can normally have a neutrophil count below the reference interval for other dogs.

PATHOPHYSIOLOGY

Results from one of four mechanisms—(1) decreased production or release of neutrophils from the bone marrow, (2) a shift of neutrophils from the circulating pool within the large vessels to the marginating pool, adhered to the endothelium of capillaries, (3) increased migration into the tissues from the blood due to severe inflammation/tissue consumption, and (4) immune-mediated destruction.

SYSTEMS AFFECTED

- Predisposes the patient to systemic infection by a variety of pathogens. • Many body systems can be affected in any combination, depending on the site(s) of infection.

GENETICS

- Canine cyclic hematopoiesis is autosomal recessive, involving the adaptor protein complex 3 (AP3) β -subunit, which redirects neutrophil elastase trafficking from membranes to granules. • A genetic trait with delayed penetrance seems likely to explain the age-related neutropenia in Belgian Tervurens.
- Selective cobalamin malabsorption is autosomal recessive, resulting in neutropenia due to failure to express the receptor for intrinsic factor-cobalamin complex. A *CUBN* frameshift mutation is likely causative for Imerslund-Gräsbeck Syndrome (selective cobalamin malabsorption) in border collies.
- An autosomal recessive neutropenia, known as trapped neutrophil syndrome (TNS), has been seen in Australian and New Zealand border collies with a deficiency of segmented neutrophils in the blood and hyperplasia of myeloid cells in the bone marrow due to an alternately spliced transcript of *VPS13B*, similar to Cohen syndrome in humans.

SIGNALMENT

- Nothing specific for generalized infection.
- Schnauzers, beagles, Australian shepherds, Shar-Peis, and border collies with inherited cobalamin malabsorption. • Gray collies and possibly border collies with canine cyclic hematopoiesis. • Belgian Tervuren dogs.
- Related border collies in Australia and New Zealand with chronic neutropenia. • G-CSF

deficiency has been reported in a rottweiler with chronic idiopathic neutropenia.

SIGNS

- Septic animals usually present with nonspecific signs of illness such as lethargy, weakness, and inappetence. They are often febrile, but normothermia does not rule out infection. Other signs can include tachycardia, injected mucous membranes, prolonged capillary refill time, and weak pulses, some of which are related to septicemia and endotoxic shock. • Gray collies with cyclic hematopoiesis exhibit severe neutropenia every 12–14 days. Episodes of fever, diarrhea, gingivitis, respiratory infection, lymphadenitis, and arthritis occur in association with the neutropenia. These dogs seldom live past 1 year of age.
- No clinical signs in Belgian Tervurens.
- Related border collies in Australia and New Zealand with chronic neutropenia had recurrent bacterial infections manifesting as osteomyelitis and gastroenteritis. A dog with heat stroke demonstrated inappropriate rubricytosis with a high normal PCV, moderate mature neutropenia and lymphopenia, and petechiation despite only mild thrombocytopenia. Numerous leukocytes showed evidence of apoptosis; many neutrophils had botryoid nuclei.

CAUSES

Deficient Neutrophil Production, Stem Cell Death, or Inhibition

- Infectious agents—dogs and cats, parvoviruses, bacteria-induced myelonecrosis, and systemic mycosis; cats, FeLV and FIV; dogs, monocytic and granulocytic ehrlichiosis, Babesia infections. • Drugs, chemicals, and toxins—dogs and cats, chemotherapy agents and cephalosporins; cats, T-2 mycotoxin ingestion, chloramphenicol and benzene-ring compounds, methimazole, and griseofulvin; dogs, estrogen, phenylbutazone, trimethoprim-sulfadiazine, phenobarbital.
- Lack of trophic factors—hereditary malabsorption of cobalamin/vitamin B₁₂.
- Ionizing radiation.

Reduced Hematopoietic Space Secondary to Myelophthisis

- Myelonecrosis • Myelofibrosis
- Disseminated neoplasia, leukemia, and myelodysplastic syndrome • Disseminated granulomatous disease (histoplasmosis and cryptococcosis)

Cyclic Stem Cell Proliferation

- Inherited cyclic hematopoiesis
- Cyclophosphamide treatment • Idiopathic disease • Immune-mediated suppression of granulopoiesis • Poorly documented in dogs and cats

Neutrophil Migration

A shift in neutrophils from the circulating neutrophil pool to the marginating neutrophil pool occurs in patients with endotoxemia. Thought to be the mechanism behind

neutropenia in septicemic animals due to *Bartonella* spp. and other bacteria. During the acute phase, neutropenia suggests intense tissue recruitment in response to endothelial damage caused by *Rangelia vitalii* infection. Anaphylaxis is another, although uncommon, cause.

Reduced Survival

- Severe bacterial infection (most common cause)—sepsis, pneumonia, peritonitis, and pyothorax. • Immune-mediated destruction (uncommon). • Drug-induced destruction.
- Hypersplenism (sequestration).
- Neutropenia likely due to oncotic and apoptotic death of mature neutrophils in heat stroke.

RISK FACTORS

- Inherited disease—cyclic hematopoiesis in Gray collies and possibly border collies.
- Inherited cobalamin malabsorption in giant schnauzers, beagles, Australian shepherds, and border collies. • Drug and chemical exposure—estrogen overdose in dogs (pancytopenia) and chloramphenicol and benzene-ring compounds in cats. • Exposure to various infectious agents—dogs and cats, overwhelming bacterial infection; dogs, acute infection with *Ehrlichia canis*, parvovirus, *Babesia canis rossi* (travel history to/from South Africa), *Rangelia vitalii* (travel history to/from Brazil), and *Anaplasma phagocytophilum* (more likely lymphopenic and eosinopenic than neutropenic); cats, panleukopenia, FIV, and FeLV infection.
- Middle-aged and old animals are less effective at repopulating the bone marrow after a severe toxic insult.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Most neutropenias are due to non-bacterial infectious diseases such as FeLV, FIV, systemic mycoses, and parvoviruses. • Bacterial infection with marked inflammation and/or endotoxemia. • Direct cytotoxic effects of drugs or other toxins on myeloid stem cells and circulating cells. • Primary bone marrow disease. • Immune-mediated destruction.
- Breed of dog may promote suspicion of inherited disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Diagnosis is verified by CBC and leukocyte differential counts. • Multiple CBCs necessary to confirm true neutropenia and/or exclude a diagnosis of cyclic hematopoiesis.
- Urinalysis with bacterial culture and sensitivity to evaluate for urinary tract infection.

Factors That May Erroneously Alter Laboratory Results

- Failure to properly mix the blood specimen before sampling for CBC (laboratory error).

NEUTROPENIA

(CONTINUED)

- Obtaining blood specimen from an IV catheter used for fluid administration (diluted specimen).
- Partial clotting of the blood specimen with neutrophil entrapment or aggregation (poor anticoagulation).
- Leukocytosis/leukocyte agglutination can happen in the tube after sample is collected due to the coating of WBCs with antibody. This will falsely decrease the WBC count as the clumped WBCs are not counted by automated hematology analyzers.

OTHER LABORATORY TESTS

- Serologic test—exclude ehrlichiosis, anaplasmosis, and parvovirus in dogs and panleukopenia, FeLV, and FIV infections in cats.
- Demonstration of anti-neutrophil antibodies by flow cytometry and observation of leukoagglutination—essential for diagnosing immune-mediated neutropenia.
- Consider microbiologic culture of blood or putative sites(s) of bacterial infection or empiric antibiotic administration if occult infection is suspected.

IMAGING

Survey radiography and ultrasonography may help locate occult sites of infection not apparent during physical examination.

DIAGNOSTIC PROCEDURES/PATHOLOGIC FINDINGS

- Examination of a bone marrow aspirate and core biopsy—to evaluate neutrophil production and exclude myelophthisis, myelonecrosis, and myelofibrosis. Animals rebounding from peripheral neutropenia can potentially be misdiagnosed with acute leukemia due to high percentage of myeloblasts in marrows that have extreme left-shifting.
- Cytologic examination of preparations—to document excess tissue demand for neutrophils, verify sequestration of neutrophils in body cavities or between tissue planes, confirm bacterial infection, and identify sites of insensible or occult loss of neutrophils from mucous membranes or skin lesions.
- Culture of infection site or blood culture in febrile animals.
- Provocative exposure to parenteral cobalamin/vitamin B₁₂ should reverse anemia, neutropenia, and neutrophil hypersegmentation in affected breeds.



TREATMENT

APPROPRIATE HEALTH CARE

- Primary concern is the presence or development of infection.
- In the absence of pyrexia, broad-spectrum oral antibiotics that spare normal anaerobic GI flora should be given prophylactically on an outpatient basis

(especially if the count is < 1,000 neutrophils/ μ L). • Pyrexia—indicates current infection; treated more aggressively; inpatient treatment recommended for administration of parenteral crystalloid fluids and antibiotics that target both anaerobic and aerobic bacteria until the infection is contained.



MEDICATIONS

DRUG(S)

- Non-febrile (dogs and cats)—trimethoprim-sulfadiazine (15 mg/kg PO q12h) or cephalaxin (30 mg/kg PO q12h) or enrofloxacin (5–20 mg/kg PO q24h; note potential for retinal toxicity in cats at doses > 5 mg/kg).
- Febrile (dogs and cats)—ampicillin (22 mg/kg IV q6–8h) or ampicillin + sulbactam (15 mg/kg IV q8h) or cefazolin (20–30 mg/kg IV q6–8h) and enrofloxacin (5–10 mg/kg IV q24h; note potential for retinal toxicity in cats).
- If clinically warranted, additional anaerobic coverage is provided by metronidazole (15 mg/kg IV q12h) and/or a later generation cephalosporin.
- rhG-CSF (dogs and cats) 5–10 mg/kg/day SC for 3–6 doses may be effective to stimulate neutrophilic production short term; however, it is a foreign protein and eventually elicits the production of a neutralizing antibody in 14–21 days, which may then cross-react with endogenous G-CSF.
- Neutrophilia subsides within 5 days after G-CSF is discontinued.
- Immune-mediated neutropenia—prednisolone (1–4 mg/kg PO q12h).

PRECAUTIONS

Maintain hydration when administering sulfa drugs to prevent renal crystallization.



FOLLOW-UP

PATIENT MONITORING

- Neutropenia is most likely to occur 7–10 days after the administration of most chemotherapeutic drugs but may develop as late as 2–3 weeks following lomustine and carboplatin administration.
- Periodic CBCs; improvement denoted by a rising leukocyte or neutrophil count, resolution of left shift, and disappearance of toxic changes. Seen after appropriate antimicrobial therapy if bacterial sepsis was the initiating cause of the neutropenia.
- Rebound neutrophilic leukocytosis expected during recovery from neutropenia.
- With the accelerated neutrophil production seen with rhG-CSF therapy, toxicity and left-shifting are expected and cannot be interpreted as sepsis.

POSSIBLE COMPLICATIONS

Secondary infections



MISCELLANEOUS

ASSOCIATED CONDITIONS

Secondary infection, sepsis

AGE-RELATED FACTORS

Repopulation of bone marrow with hematopoietic cells is more difficult in middle-aged and old animals because of age-related reduction in stem cell numbers.

PREGNANCY/FERTILITY/BREEDING

Pregnant Animals

- Drugs listed should be used only if the benefits supersede the inherent risks.
- Sulfa drugs cross the placenta and can cause jaundice, hemolytic anemia, and kernicterus.
- Trimethoprim crosses the placenta; no harm accompanies drug administration in early pregnancy; however, this drug should not be used near term because of folic acid inhibition.
- Adequately controlled safety studies of rhG-CSF have not been performed in dogs and cats (including pregnant animals); high-dose administration (80 μ g/kg/day) of rhG-CSF in pregnant rabbits was associated with fetal resorption, abortion, and increased genitourinary tract hemorrhage.

SEE ALSO

- Canine Parvovirus Infection
- Ehrlichiosis
- Feline Immunodeficiency Virus Infection
- Feline Leukemia Virus Infection
- Feline Panleukopenia
- Hyperestrogenism (Estrogen Toxicity)

ABBREVIATIONS

- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- GI = gastrointestinal
- PCV = packed cell volume
- rhG-CSF = recombinant human granulocyte colony-stimulating factor
- WBC = white blood cell

Suggested Reading

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NOCARDIOSIS



BASICS

OVERVIEW

- An uncommon infection of dogs and cats.
- Organism—soil saprophyte; enters body through contamination of wounds or by respiratory inhalation.
- A compromised immune system enhances the likelihood of infection.

SYSTEMS AFFECTED

- Lymphatic • Musculoskeletal • Nervous
- Respiratory • Skin/Exocrine

SIGNALMENT

Dogs and cats of any breed

SIGNS

- Depends on the site of infection.
- Pleural—pyothorax, resulting in dyspnea, emaciation, and fever.
- Cutaneous—chronic, non-healing wounds; often accompanied by fistulous tracts; if extended, may result in lymphadenopathy, draining lymph nodes, and osteomyelitis.
- Disseminated—most common in young dogs; usually begins in the respiratory tract; lethargy, fever, and weight loss; cyclic fever may be characteristic; CNS may be affected; pleural and/or abdominal effusion may occur.
- May cause pneumonia or pyothorax in cats.

CAUSES & RISK FACTORS

- *Nocardia asteroides* (dogs and cats)
- *N. brasiliensis* (cats only) • *N. nova* (common in Australia; now in United States)
- *Proactinomyces* spp. (rare)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Cutaneous

- Actinomycosis • Atypical mycobacteriosis
- Leprosy • Sporotrichosis • Bite wound abscesses • Draining tracts resulting from foreign bodies

Pleural

- Bacterial pyothorax • Thoracic neoplasia
- Chronic diaphragmatic hernia

Disseminated

- Plague • Systemic fungal infections • Feline infectious peritonitis

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilic leukocytosis.
- Nonregenerative anemia—with long-standing infections (anemia of chronic disease).
- Chemistries—usually normal; hypergammaglobulinemia may be seen with long-standing infections.

OTHER LABORATORY TESTS

N/A

IMAGING

Radiographs—may reveal pleural or peritoneal effusion, pleuropneumonia, or osteomyelitis.

DIAGNOSTIC PROCEDURES

- Cytology—thoracentesis or abdominocentesis for samples; stain these or other exudates with Romanowsky, gram, and modified acid-fast stains for rapid diagnosis; may reveal gram-positive branching filamentous rods and cocci; cannot be distinguished from *Actinomyces* spp.
- Culture—diagnostic; aerobic culturing on Sabouraud medium.

PATHOLOGIC FINDINGS

- *N. asteroides*—more suppurative pyogranulomatous reaction than with *Actinomyces* spp.
- *N. brasiliensis*—granulomatous reaction with extensive fibrosis.
- Although the organism is usually present, it cannot be distinguished histopathologically from *Actinomyces* spp.



TREATMENT

- Pleural or peritoneal effusions and disseminated form—inpatient until clinically stable and effusion removed; fluid therapy for rehydration and maintenance often needed.
- Long-term antibiotic therapy and draining fistulous tracts—outpatient.
- Diet—encourage consumption by offering foods with appealing tastes and smells; forced enteral feeding for anorectic inpatients essential; orogastric tube feeding preferred.
- Surgery—when feasible, surgical drainage should accompany medical therapy; important to place a thoracostomy tube for pleural effusion; attempt surgical drainage and debridement of draining tracts and lymph nodes; take care to identify foreign bodies.



MEDICATIONS

DRUG(S)

- Cultured organism—antibiotic sensitivity testing.
- No culture or results pending—good first-choice drugs: sulfonamides (e.g., sulfadiazine at 100 mg/kg IV, PO as a loading dose followed by 50 mg/kg IV, PO q12h) and sulfonamide-trimethoprim combinations (15–30 mg/kg PO q12h).
- Aminoglycosides—gentamicin (3 mg/kg IV, IM, SC q8h); amikacin (6.5 mg/kg IV, IM, SC q8h).
- Tetracyclines—doxycycline (10 mg/kg PO q24h); tetracycline hydrochloride

(15–20 mg/kg PO q8h); minocycline (5–12.5 mg/kg PO q12h).

- Erythromycin 10–20 mg/kg PO q8h; or combined with ampicillin (20–40 mg/kg PO q8h) or amoxicillin (6–20 mg/kg PO q8–12h).
- Amoxicillin or ampicillin plus an aminoglycoside—synergistic combination; consider in any serious infection when culturing is not possible or is pending.
- Average treatment period is 6 weeks; however, medical treatment should extend several weeks past apparent remission of the disease.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Tetracyclines (cats)—may cause fever up to 41.5°C (107°F); discontinue and replace if fever increases during therapy.
- Long-term sulfonamide-trimethoprim may cause anorexia and irreversible bone marrow suppression in cats. Prevent by supplementing with folate administration (1 mg PO q24h).



FOLLOW-UP

Monitor carefully for fever, weight loss, seizures, dyspnea, and lameness the first year after apparently successful therapy because of the potential for bone and CNS involvement.

N



MISCELLANEOUS

SEE ALSO

Actinomycosis

ABBREVIATION

CNS = central nervous system

Suggested Reading

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Authors Gary D. Norsworthy and Lisa Restine

Consulting Editor Stephen C. Barr

NONSTEROIDAL ANTI-INFLAMMATORY DRUG TOXICOSIS



BASICS

DEFINITION

- Toxicosis secondary to the acute or chronic ingestion of an NSAID.
- NSAIDs—classified as carboxylic acids (aspirin, indomethacin, sulindac, ibuprofen, naproxen, carprofen, meclofenamic acid, etodolac, and flunixin meglumine) or enolic acids (phenylbutazone, dipyrone, meloxicam, tepoxalin, and piroxicam); selective COX-2 inhibitors (deracoxib, firocoxib, mavacoxib (Europe), and robenacoxib).
- Newer selective COX-2 inhibitors and NSAIDs with preferential activity against COX-2 may have fewer adverse reactions than older COX-1 inhibitors.

PATHOPHYSIOLOGY

- Action—analgesic, antipyretic, and anti-inflammatory due to the inhibition of cyclooxygenase; decreases production of prostaglandins that act as mediators of inflammation.
- Well absorbed orally.
- Clearance—varies greatly among species; eliminated slowly in dogs and cats.
- Metabolized in the liver to active or inactive metabolites.
- Excreted in the kidney via glomerular filtration and tubular secretion, and/or biliary excretion.

SYSTEMS AFFECTED

- Gastrointestinal—erosions and ulcers.
- Hemic/Lymphatic/Immune—may note bleeding disorders secondary to decreased platelet aggregation.
- Hepatobiliary—idiosyncratic hepatocellular damage.
- Renal/Urologic—acute renal failure; acute interstitial nephritis.

GENETICS

- Species differences in absorption, excretion, and metabolism of different agents are dramatic; avoid extrapolation of data from other species or dosages.
- Off-label use of NSAIDs can result in significant, potentially life-threatening adverse effects in all species, especially in cats.
- Over-the-counter NSAIDs (especially ibuprofen and naproxen) are common causes of NSAID toxicosis in dogs and cats.

Naproxen has an extremely long half-life in domestic animals and exposures carry a high risk of significant adverse effects.

INCIDENCE/PREVALENCE

Among the ten most common toxicoses reported to both the American Society for the Prevention of Cruelty to Animals Animal Poison Control Center and the Pet Poison Helpline.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

- Dogs and cats
- No breed or gender predilections

SIGNS

General Comments

- Gastrointestinal irritation—usually develops within a few hours.
- Renal involvement or gastrointestinal ulceration—may be delayed several days.

Historical Findings

- Evidence of accidental consumption of owner's medication.
- Lethargy.
- Anorexia.
- Vomiting—with or without blood.
- Diarrhea.
- Icterus.
- Melena.
- Collapse and sudden death—may occur secondary to a perforated gastric ulcer.
- Polyuria, polydipsia, and oliguria.
- Ataxia, seizures, coma—may occur with large ingestions.

Physical Examination Findings

- Depression
- Pale mucous membranes
- Painful abdomen
- Dehydration
- Fever
- Tachycardia
- Icterus

CAUSES

Accidental exposure or inappropriate administration

RISK FACTORS

- Animals predisposed to renal disease—old age; preexisting renal, hepatic, or cardiovascular disease; hypotension; other concurrent illness and/or medications.
- Neonates may be more sensitive.
- Previous history of gastrointestinal ulcer or bleeding.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other conditions (medical or intoxications) that cause gastrointestinal and renal effects; diagnosis based on history of exposure and compatible clinical signs.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia—regenerative or nonregenerative, depending on duration of bleeding.
- Leukocytosis—associated with perforated gastric ulcer and accompanying peritonitis.
- BUN and creatinine—may be elevated secondary to prerenal azotemia or primary renal insult.
- Liver enzymes—occasionally elevated.
- Monitor urine output for evidence of oliguria; monitor for glucosuria, proteinuria, and casts.

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Endoscopy—verify gastrointestinal ulceration.

PATHOLOGIC FINDINGS

- Gastrointestinal irritation, ulceration, or hemorrhage with possible gastric perforation and peritonitis.
- Renal tubular or papillary necrosis or interstitial nephritis.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—mild clinical signs (with low ingested dose); managed at home with appropriate medication and dietary and symptomatic measures.
- Inpatient—high ingested dose; potential for renal toxicosis; relatively serious clinical signs (frequent vomiting, bloody vomitus, melena, anemia, or evidence of renal involvement); aggressive treatment to avoid life-threatening complications.

Recent Ingestion

- Ingestion within a few hours and no vomiting—induce emesis (apomorphine or hydrogen peroxide) unless patient has seizures or marked CNS depression.
- After emesis—activated charcoal (1–2 g/kg PO) and a cathartic (magnesium or sodium sulfate at 0.25 tsp/5 kg or 70% sorbitol at 3 mL/kg) if no diarrhea.
- Repeat activated charcoal (one-half the original dose) for NSAIDs that undergo enterohepatic recirculation.

NURSING CARE

- Fluid therapy—restore hydration when moderate to severe vomiting; administration of at least twice maintenance rates with known or potential renal involvement (see Renal Failure, Acute).
- If severely anemic, a blood transfusion may be indicated.

ACTIVITY

N/A

DIET

- Vomiting—NPO
- Vomiting resolved—begin with a bland, low-protein diet

CLIENT EDUCATION

- Stress the importance of contacting a veterinarian, ASPCA APCC, or PPH whenever an animal is exposed to a non-prescribed NSAID.
- Inform client that dogs and particularly cats have a low tolerance to NSAIDs.

(CONTINUED)

NONSTEROIDAL ANTI-INFLAMMATORY DRUG TOXICOSIS

- With a prescribed NSAID, instruct client to look for adverse or idiosyncratic effects and to stop the drug and contact the clinic if they occur.

SURGICAL CONSIDERATIONS

Surgical intervention may be required for a perforated gastric ulcer.

**MEDICATIONS****DRUG(S) OF CHOICE*****H₂-Receptor Antagonists***

- For gastrointestinal upset or ulceration.
- Primarily effective for treating ulcers from acute overdose or from chronic administration after the drug withdrawn.
- Ranitidine or famotidine may be best choices as cimetidine may inhibit microsomal enzymes that metabolize some NSAIDs.
- Ranitidine—dogs, 2 mg/kg PO, IV q8h; cats, 2.5 mg/kg IV q12h or 3.5 mg/kg PO q12h.
- Famotidine—dogs, 0.5–1.0 mg/kg PO, SC, IV, or IM q12–24h; cats, 0.5 mg/kg PO, SC, IV, or IM q12–24h.

Other

- Sucralfate—dogs, 0.5–1 g PO q8–12h; cats, 0.25 g PO q8h; binds to proteins in the ulcer base; stimulates mucus and bicarbonate secretion.
- Misoprostol 1–3 µg/kg PO q8h; PGE₂ analog; prevents gastrointestinal bleeding and ulceration; promotes healing during chronic use in humans and dogs treated with aspirin.
- Omeprazole—0.5–1 mg/kg PO q24h; potent inhibitor of gastric acid secretion; blocks the final step of hydrochloric acid production.
- Dopamine—may be indicated for acute renal failure.
- Standard anticonvulsant therapy—diazepam, pentobarbital, phenobarbital, if needed.
- A test dose of naloxone may be useful in comatose patients.
- Duration of treatment—depends on the half-life of the particular agent ingested.

CONTRAINDICATIONS

Avoid concomitant use of corticosteroids or multiple NSAIDs together; contraindicated in pregnancy (abortifacient effect).

PRECAUTIONS

Patients using other nephroactive or nephrotoxic drugs (e.g., aminoglycosides and ACE inhibitors)—at higher risk for developing NSAID nephropathy.

POSSIBLE INTERACTIONS

NSAIDs—highly protein-bound; may be affected by concurrent use of other highly protein-bound drugs.

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

- Urine output—monitor carefully for oliguria; examine for casts, protein, and glucose.
- Stool and vomitus—check for gastrointestinal bleeding (may not develop for several days).
- BUN and creatinine—daily for several days (full extent of renal damage may not be immediately evident).

PREVENTION/AVOIDANCE

- Store medications out of the reach of pets.
- Discourage owners from medicating pet without supervision of a veterinarian.
- Pretest high-risk patients with appropriate laboratory tests before beginning therapy.

POSSIBLE COMPLICATIONS

- Perforation of a gastric ulcer and peritonitis
- Irreversible acute and chronic renal failure

EXPECTED COURSE AND PROGNOSIS

- Gastric upset or ulceration—usually complete recovery with appropriate treatment.
- Renal effects—generally reversible with early and aggressive treatment.
- Acute hepatopathies—generally resolve with symptomatic treatment after discontinuation of the drug.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

- Exposure during pregnancy—risk for fetal cardiopulmonary and renal effects.
- May prolong pregnancy, especially if administered during the third trimester and before the onset of labor.

SEE ALSO

- Aspirin Toxicosis
- Poisoning (Intoxication) Therapy
- Renal Failure, Acute

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- ASPCA APCC = American Society for the Prevention of Cruelty to Animals Animal Poison Control Center
- CNS = central nervous system
- COX-2 = cyclooxygenase-2
- NSAID = nonsteroidal anti-inflammatory drug
- PPH = Pet Poison Helpline

INTERNET RESOURCES

<http://www.aspapro.org/animal-poison-control.php>

N

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NOTOEDRIC MANGE



BASICS

OVERVIEW

- A non-seasonal, intensely pruritic, highly contagious parasitic skin disease of cats caused by *Notoedres cati*.
- The mite is closely related to *Sarcoptes scabiei* var. *canis*.
- Mites burrow through the superficial skin between follicles causing intense pruritus.
- Can cause transient pruritus in humans.

SIGNALMENT

- Domestic cats of all ages and both sexes.
- Fairly host-specific, but can also produce symptoms in dogs, cheetahs, raccoons, rabbits, coatis, palm civets, bobcats, ocelots, foxes, and humans.
- All in-contact cats usually develop clinical signs.
- Epizootic in localized areas.
- Endemic in large feral cat populations.
- Transmission by direct contact: the mite is very short-lived when off the host.

SIGNS

- Non-seasonal intense pruritus.
- Following exposure, initial pruritus may be mild, but progresses to severe.
- Change from mild pruritus to onset of severe pruritus (incubation period) of 3–6 weeks may indicate eventual seroconversion and the development of hypersensitivity (IgG as well as humoral response).
- Rare individuals do not seroconvert, and therefore may not develop severe pruritus.
- Papules and crusts develop on pinnae and spread to eyelids, face, and neck (also known as “head mange”).
- Progresses to the legs, feet (due to sleeping position) and perineum.
- Severe self-trauma leads to secondary lesions.
- Skin becomes thickened, lichenified, and covered with gray-yellow crust.
- Large patches of lesions and alopecia develop over the entire body if untreated.
- Unlike canine scabies, large numbers of mites are present on the skin.
- Peripheral lymphadenopathy often develops.
- Causes significant debilitation in severe cases.

CAUSES & RISK FACTORS

Close contact with other cats



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Atopy
- Cutaneous adverse reaction to food
- Bacterial folliculitis

- Dermatophytosis
- Demodicosis
- *Malassezia* dermatitis
- *Cheyletiellosis*
- Trombiculosis (chiggers)
- Otodectic dermatitis
- Pemphigus foliaceus
- Pemphigus erythematosus
- Systemic lupus erythematosus

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Superficial skin scraping—relatively easy to find mites.
- Mite smaller than *S. scabiei*, with dorsal anus, typical dorsal concentric “finger print” striae, and only two pairs of forelegs protruding from the body line.
- Serum testing (ELISA) for mite antibody not available.



TREATMENT

- When scabicidal dips are used, the entire cat must be treated.
- Treatment failures occur if product is not applied to the face and ears.
- All in-contact cats should be treated.
- Response is usually quick if all in-contact animals are treated.
- Thorough cleaning of the cat's environment may be helpful if severely contaminated.
- Systemic antibiotics—may be needed to resolve secondary bacterial folliculitis.



MEDICATIONS

DRUG(S) OF CHOICE

- Lime sulfur rinses 2%–3%; apply to entire body weekly for six to eight applications; clipping might be necessary to permit adequate contact with the skin.
- Ivermectin—effective; 0.2–0.3 mg/kg SC every 2 weeks for two to three treatments.
- Amitraz rinse (125–250 ppm) weekly for a minimum of three treatments.
- Doramectin 0.2–0.3 mg/kg SC once.
- Selamectin—off-label; applied every 2 weeks for three applications.
- Imidacloprid/moxidectin spot-on applied once or twice as directed on the label.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Amitraz rinse may cause sedation.
- Lime sulfur has unpleasant odor and is staining.



FOLLOW-UP

PREVENTION/AVOIDANCE

Reinfestation may occur if contact with infested animals continues; the source of infestation must be determined (if possible) as well as all in-contact cats must be treated.

POSSIBLE COMPLICATIONS

- Topical scabicidal treatments are more prone to failure because of incomplete application of the treatment solution.
- Persistent infection if not all in-contact animals are treated.

EXPECTED COURSE AND PROGNOSIS

- Response to therapy is rapid providing all in-contact animals are treated; symptoms should significantly reduce within 2 weeks of treatment.
- There is no immunity from repeat infestation; clinical signs following a reinfestation are likely to be more rapid due to previous exposure and sensitization.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Humans in close contact with an affected cat may develop a pruritic, papular rash (often on arms, chest, or abdomen).
- Human lesions are usually transient and resolve spontaneously following treatment of affected animals.

ABBREVIATION

ELISA = enzyme-linked immunosorbent assay

Suggested Reading

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Consulting Editor Alexander H. Werner

NYSTAGMUS



BASICS

DEFINITION

- Involuntary, rhythmic oscillation of the eyeballs.
- Jerk nystagmus—most common; slow eye movements in one direction with a rapid recovery phase in the opposite direction.
- Pendular nystagmus—seen less frequently; characterized by small oscillations of the eyes with no fast or slow component.

PATHOPHYSIOLOGY

- Neural projections traverse in the brainstem from the vestibular nuclei to CN III, IV, and VI nuclei, which innervate the extraocular muscles. This system provides coordinated conjugate eye movements in association with changes in head position.
- Physiologic nystagmus (ocular-vestibular reflex)—normal finding, induced by rotating the head from side to side; characterized by a jerk nystagmus with a slow drifting of the eye in the opposite direction of the head rotation followed by a fast compensatory phase in the same direction as the head movement. Decreased to absent physiologic nystagmus is indicative of vestibular disease.
- Pathologic nystagmus—a sign of vestibular dysfunction; characterized by a jerk nystagmus that develops independent of head movement. The nystagmus is described according to the axis of movement of the globe (horizontal, rotary or vertical), and the direction of the fast phase of movement.
- Spontaneous nystagmus—pathologic nystagmus that occurs when the head is in a normal position and not moving; frequently resolves after several days.
- Positional nystagmus—pathologic nystagmus, elicited only when the head is placed in unusual position; can often be seen in more chronic conditions.
- Jerk nystagmus must be differentiated from pendular nystagmus, which is most often observed as an incidental finding in Siamese, Birman, and Himalayan cats.
- Pendular nystagmus—congenital abnormality in which a larger-than-usual portion of the optic nerve fibers crosses in the chiasm; can also be seen with cerebellar disease and with visual deficits.

SYSTEMS AFFECTED

Nervous

GENETICS

N/A

INCIDENCE/PREVALENCE

Nystagmus, as a sign of vestibular disease, is a relatively common clinical presentation in dogs and cats.

SIGNALMENT

Species

Dog and cat

Breed Predilections

None

Mean Age and Range

Varies, depending on underlying cause; neoplastic and vascular conditions and canine geriatric vestibular disease more common in older animals.

Predominant Sex

None

CAUSES

Peripheral Vestibular Disease

- Metabolic—hypothyroidism.
- Neoplastic—nerve sheath tumor or tumor involving surrounding bone or soft tissues.
- Inflammatory—otitis media-interna; nasopharyngeal polyps (cats).
- Idiopathic—canine geriatric vestibular disease; feline idiopathic vestibular disease.
- Toxic—e.g., aminoglycosides, topical iodophors, topical chlorhexidine.
- Trauma.

Central Vestibular Disease

- Degenerative—storage disorders; neuronal degeneration; demyelinating disease.
- Neoplastic—primary or metastatic tumors.
- Nutritional—thiamin deficiency.
- Inflammatory/infectious—viral (canine distemper, feline infectious peritonitis); bacterial; protozoal (toxoplasmosis, neosporosis); fungal (cryptococcosis, blastomycosis, histoplasmosis, coccidioidomycosis, aspergillosis); rickettsial (ehrlichiosis, Rocky Mountain spotted fever); inflammatory, non-infectious (granulomatous meningoencephalomyelitis, necrotizing encephalitis).
- Toxic—lead; hexachlorophene; metronidazole.
- Trauma.
- Vascular—hemorrhage; infarction.

RISK FACTORS

Systemic administration of certain antibiotics (metronidazole, aminoglycoside), otic administration of iodophors and chlorhexidine solutions.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Peripheral Vestibular Disease

- Nystagmus—either rotary or horizontal in character, with the fast phase directed away from the side of the lesion; does not change direction.
- Other signs of vestibular disease—head tilt, ataxia, circling, falling or rolling, and vestibular strabismus often present and occur ipsilateral to the lesion.
- Ipsilateral facial nerve deficits and/or Horner's syndrome—can be seen due to the close association of CN VII and sympathetic

nerve to CN VIII as they course through the petrous temporal bone.

Central Vestibular Disease

- Nystagmus—horizontal, rotary, or vertical; can change direction with different head positions.
- Other signs of vestibular disease—head tilt, ataxia, circling, falling or rolling, and vestibular strabismus often present.
- Involvement of other brainstem structures—alterations in level of consciousness, paresis, postural reaction deficits, and other CN deficits (V and VII most common); deficits are typically ipsilateral to the lesion.
- Paradoxical vestibular disease—with certain lesions of the cerebellum; in these cases, postural reaction deficits occur ipsilateral to the lesion whereas the head tilt and other vestibular signs are contralateral to the lesion.

CBC/BIOCHEMISTRY/URINALYSIS

Results usually normal

OTHER LABORATORY TESTS

- Thyroid profile—if hypothyroidism is suspected.
- Bacterial culture of sample obtained via myringotomy—if otitis media-interna is likely.
- Serologic testing—for potential infectious agents.

IMAGING

- Imaging of the tympanic bullae to assess for otitis media-interna—survey radiographs of limited value; CT and MR are more sensitive.
- Brain imaging (CT or MR)—indicated in animals with central vestibular disease to evaluate for structural brain abnormalities. MR is superior to CT for imaging the brain.

DIAGNOSTIC PROCEDURES

Cerebrospinal fluid—if central disease, to evaluate for inflammation.

PATHOLOGIC FINDINGS

Variable, depending of the underlying cause



TREATMENT

APPROPRIATE HEALTH CARE

- The cause of the disease and the severity of signs determine whether the animal is best treated on an inpatient or an outpatient basis.
- In general, animals with central disease require more intensive care than those with peripheral disease.

NURSING CARE

- Fluid therapy is indicated in the acute stages of disease for animals that experience anorexia and vomiting.
- Animals with severe vestibular dysfunction should be confined to a well-padded area in the acute stage of the disease to minimize self-trauma secondary to disorientation.

N

NYSTAGMUS

(CONTINUED)

ACTIVITY

- Animals should be housed on non-slippery surfaces; stairs should be avoided.
- Exercise should be supervised, with assistance provided until signs of imbalance resolve.

DIET

N/A

CLIENT EDUCATION

- Many animals show improvement over the first several days; the nervous system is able to compensate for vestibular disturbances that remain static or are slowly progressive regardless of cause.
- Compensation involves visual and somatosensory (tactile) cues and is dependent on feedback from vestibular pathways; return to normal activity should be encouraged to enhance compensatory mechanisms.

SURGICAL CONSIDERATIONS

Signs of vestibular dysfunction can transiently worsen after an anesthetic episode; most likely reflects a loss of compensation.



MEDICATIONS

DRUG(S) OF CHOICE

- Meclizine (dogs, 4 mg/kg PO q24h) or maropitant (dogs, 1 mg/kg SC or 2 mg/kg PO q24h; cats, 1 mg/kg SC q24h)—used to treat motion sickness; can alleviate nausea and vomiting associated with acute disease.
- Diazepam (dogs, 0.5 mg/kg PO q8h)—recommended in cases of metronidazole toxicity; can help decrease acute vestibular signs from other causes by decreasing the resting activity of vestibular neurons and alleviating the imbalance in vestibular input to the brain.
- Specific medical therapy is directed at the underlying cause, if one can be identified.

N

CONTRAINDICATIONS

- Avoid potential ototoxic drugs, such as aminoglycosides. Toxicity is more likely in animals with renal impairment.
- Avoid instilling topical medications into the ear of an animal with suspected otitis media-interna, especially if the tympanic membrane cannot be visualized or is not intact. Such agents can exacerbate vestibular signs and cause deafness.

PRECAUTIONS

- Avoid the use of metronidazole at daily doses greater than 60 mg/kg, as this has been associated with vestibular dysfunction in dogs.
- Vestibular dysfunction can develop after administration of metronidazole at lower dosages but is less likely.

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

Repeat neurologic examination—perform 2 weeks after initial diagnosis to monitor for improvement or progression of disease.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Dehydration and electrolyte imbalance associated with anorexia and vomiting.
- Rare extension of otitis media-interna into the adjacent brainstem.

EXPECTED COURSE AND PROGNOSIS

- Prognosis varies, depending on the cause of the vestibular disturbance.
- In general, animals with peripheral vestibular disease have a better prognosis than those with central involvement.

- Residual deficits can remain after resolution of the underlying disease process due to irreversible damage to the neural structures.
- Recurrence is possible with some of the conditions (otitis media/interna, canine geriatric vestibular disease, feline idiopathic vestibular disease).



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Ataxia
- Head Tilt
- Otitis Media and Interna

ABBREVIATIONS

- CN = cranial nerve
- CT = computed tomography
- MR = magnetic resonance

INTERNET RESOURCES

https://www.vetlearn.com/_preview?_cms.fe.previewId=1f98fff0-caa9-11e1-aa85-005056ad4736&cWT.mc_id=newsletter%3BPV071112

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BASICS

DEFINITION

An excess of body fat frequently resulting in adverse health effects. Even a moderate excess in body fat can increase morbidity and reduce lifespan.

PATHOPHYSIOLOGY

Accumulation of adipose tissue due to an imbalance between energy intake and energy expenditure. Contributing factors are lifestyle related, including neutering, limited activity, and abundant access to food. Secondary complications from obesity may be due to increased inflammatory mediators and oxidative stress, along with insulin resistance induced in obese subjects.

SYSTEMS AFFECTED

- Endocrine
- Musculoskeletal
- Adipose tissue from obese subjects is infiltrated with macrophages. Both adipocytes and associated macrophages secrete inflammatory and endocrine mediators such as tumor necrosis factor-alpha, resistin, interleukins, and other mediators. These mediators contribute to insulin resistance or arthritic changes common in obese individuals. Secondary problems more common in obese dogs and cats include diabetes mellitus, orthopedic problems, dermatologic conditions, urinary tract disease, and liver, cardiac, and renal dysfunction.

SIGNALMENT

- Dog and cat.
- All ages, with the greatest prevalence (nearly 50%) in middle-aged dogs and cats.
- Most common in neutered, indoor pets.

SIGNS

Historical Findings

- Weight gain
- Exercise intolerance may be reported

Physical Examination Findings

Excess body fat and body condition score (see "Diagnostic Procedures")

CAUSES & RISK FACTORS

- Obesity is caused by an imbalance between energy intake and energy expenditure, with intake exceeding expenditure.
- Neutering, decreased opportunities for activity, and age can reduce energy expenditure.
- Overfeeding of high-calorie foods, frequently alternating foods, and provision of excess treats contribute to excess energy intake.
- Hypothyroidism, insulinoma, or hyperadrenocorticism are infrequent causes of obesity.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Abdominal distention from pregnancy, ascites, or neoplasia

DIAGNOSTIC PROCEDURES

- Diagnosis of obesity is by body condition scoring and body weight.
- Body condition scoring provides a semiquantitative assessment of composition. It involves visual assessment and palpation, especially over the ribs, lumbar area, and tailhead, and comparison with a standard. Using a nine-point system, each unit above ideal reflects an excess of body weight of about 10–15%. Animals with a BCS ≥ 7 are obese.
- Body weight.



TREATMENT

- Weight loss, induced by reducing calorie intake below calorie expenditure.
- Successful weight loss also requires long-term maintenance of the reduced weight.
- Both of these goals depend on changes in the way the owner feeds and interacts with the pet.

CLIENT EDUCATION

• Obesity management relies on client compliance and changes in feeding and behavioral interactions. Client-focused steps to a successful weight management program include:

- Recognition of the problem—many owners do not recognize their own pet as overweight. Use a BCS system to illustrate how the diagnosis is being made. Show the owner how to assess and monitor the BCS of his or her own pet.
- Importance of the problem—clients that perceive obesity strictly as an aesthetic problem may not be sufficiently motivated to manage it. Educate clients about the increased risk for diseases (e.g., osteoarthritis, diabetes mellitus, feline lower urinary tract diseases, etc.) or shortened lifespan to identify this as a condition that requires appropriate management.
- Client input regarding the weight loss program—determine what clients are willing and able to do. Will they feed a therapeutic diet? Do they provide table foods? Can they feed measured amounts and/or multiple meals? Can they increase the pet's exercise? In multiple-pet households, will clients feed pets separately?
- Compliance with a weight loss program—clients should receive written instructions regarding specific amounts to provide using

the agreed-upon food. Be sure the client understands that "cups" of food refers to an 8-oz. measuring cup. For cats and small dogs, a smaller measure or use of a kitchen or gram scale to measure food allowances can aid accuracy. Treats should be offered as part of the program (see below) since most clients will continue to provide these.

- Ongoing communication—frequent follow-up during the weight loss program aids client compliance.

DIET

- Certain macronutrients can facilitate healthier or easier weight loss:
 - Protein—increased dietary protein facilitates loss of body fat while minimizing loss of lean body mass, which is the metabolically active tissue. Preserving LBM should help with long-term weight control by maintaining a higher resting energy requirement. Protein also stimulates metabolism, increases energy expenditure, and contributes to satiety.
 - Fiber—dietary fiber provides little dietary energy so helps reduce total calories in the diet. Fiber also stimulates intestinal metabolism and contributes to satiety.
 - Decreased fat—fat is energy dense, so low-fat diets are lower in energy.
- Increased moisture—use of high-moisture canned foods can reduce energy density (as fed) so allows the owner to feed a greater volume. Use of high-moisture diets can facilitate short-term weight loss in cats.
- Other dietary factors that may aid in weight management:
 - Carnitine—produced endogenously from lysine and methionine, this compound is necessary for fat oxidation. Supplementation may be beneficial when dietary protein intake is limited.
 - Isoflavones—metabolically active phytonutrients that stimulate energy metabolism: may reduce weight rebound and support maintenance of lean body mass.

Main Meal

- Calories should be restricted without excessive restriction of essential nutrients. A low-calorie therapeutic diet with an increased nutrient:calorie ratio is recommended for weight loss.
- The amount fed should target a 1–2% loss in body weight/week. Faster weight loss may increase loss of lean body mass and stimulate weight rebound once weight loss is achieved.
- Initial feeding is based on 60–75% of calculated MER using target body weight. Target body weight can be estimated using the current weight and BCS; or an intermediate target, e.g., 20% below current weight, can be selected.

OBESITY

(CONTINUED)

- Average MER = 55 kcal/kg for cats; 110 kcal/kg^{0.75} for dogs.
- Adjust feeding amounts monthly to compensate for decreases in MER due to calorie restriction and weight loss, as well as individual differences in MER.
- High-moisture diets can be used to reduce calories/serving. This approach appears to be more effective for cats versus dogs, as cats tend to control their intake based on volume.
- If the client is not willing to use a therapeutic diet, severe calorie restriction should be avoided. A food diary can be used to record current intake over 3–7 days. Subsequently, the pet should be fed 10–20% less than it previously received.

Treats

- Treats are often part of the owner-pet bond.
- Complete avoidance of treats is a hurdle to compliance with weight loss programs.
- Instead, offer a “treat allowance” of 10% of the daily calories and provide a list of low-calorie treats suitable for dogs or cats.

ACTIVITY

- Calorie restriction results in compensatory decreases in basal energy expenditure. Increased activity helps compensate for this and provides alternate opportunities for owner-pet interactions. Provide several suggestions suitable for each client and patient. For example:
 - Leash walking for dogs and trained cats—at least 15 minutes twice daily.
 - Activities such as “fetch,” interactive toys for cats, or playing with a laser light.
 - Food balls—built to hold treats or kibbles and randomly release them while the dog or cat plays. The food inside must be part of the daily calorie allowance.



MEDICATIONS

DRUG(S) OF CHOICE

No approved medications for management of obesity are currently available in the United States.



FOLLOW-UP

- Frequent client communication is important during the weight management program.
- 1 week—telephone call from clinic to address any minor questions and to reinforce the importance of the program.
- Monthly—patient should be weighed in clinic on a monthly basis. If needed, adjustments in food allowance guidelines should be made at this time.
- Upon achieving target weight—once the patient has achieved an ideal BCS, guidelines should be provided for weight maintenance.
- Energy needs will be lower than before weight loss, although this may increase somewhat with time.
- Clients should continue to measure food, monitor BCS or body weight, and adjust food allowance as needed to maintain the loss.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Osteoarthritis
- Diabetes mellitus or insulin resistance
- Dermatoses
- Feline hepatic lipidosis
- Feline lower urinary tract diseases
- Decreased lifespan

AGE-RELATED FACTORS

- MER decreases with age in dogs, which increases the risk for obesity.
- In cats, MER decreases with age until about 10–12 years of age, then increases.
- The highest prevalence of obesity occurs between 5 and 10 years of age in both dogs and cats.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

- Obesity may interfere with a female's ability to become pregnant or deliver healthy offspring.
- Calorie restriction during pregnancy or lactation is discouraged, as nutrient restriction can have long-term adverse effects on offspring.

SYNONYM

Overweight

ABBREVIATIONS

- BCS = body condition score
- LBM = lean body mass
- MER = maintenance energy requirements

Suggested Reading

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Author Dorothy P. Laflamme

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Client Education Handout
available online



BASICS

OVERVIEW

- Odontoma—oral mass that arises from odontogenic epithelial and mesenchymal origin.
 - Ameloblastic fibro-odontoma (AFO) (formerly ameloblastic odontoma)—radiolucent, mass with osteolysis and varying amounts of intralesional mineralization.
 - Complex odontoma—radiodense mass with fully differentiated dental components (more organized than AFO), but unorganized at the cellular level with no tooth-like structures.
 - Compound odontoma—mass with fully differentiated dental components resulting in the presence of denticles (tooth-like structures, see clinical features below).
- Hamartoma—proliferation of normal cellular components with an abnormal organization—not a true neoplasm (applicable to complex and compound odontoma types).
 - A definition to help delineate the three types of odontoma, not a type in itself.

SIGNALMENT

Typically found in young animals.

SIGNS

- Oral swelling or mass
- Delayed deciduous tooth exfoliation or delayed or abnormal tooth eruption at site
- AFO
 - Most lesions are radiolucent with single or multiple (multilocular) expansile lesions of irregular configurations of dental components.
 - Some lesions are associated with impacted teeth.
 - Neoplastic mechanism, may recur (WHO—benign neoplasm).
- Complex
 - Disorganized tissues within a thin, fibrous capsule.
 - Radiographically, often a radial structure of hard tissue particles inside a radiolucent zone, embedded in the maxilla or mandible.
 - Erupted teeth in that area may allow for communication between the odontoma and oral cavity, with a potential for bacterial contamination and infection.
- Compound
 - The presence of denticles is pathognomonic.
 - Small, rudimentary teeth with crown formed, but the roots are often misshapen (dilacerated).
 - Denticles often associated with radiolucency.
 - May be embedded or have some extent of eruption.

CAUSES AND RISK FACTORS

AFO

- Mixed odontogenic tumor with differentiation of odontoblasts, ameloblasts and cementoblasts embedded in cellular mesenchymal tissue.
- Reciprocal inductive interaction of epithelial and mesenchymal tissues.
- WHO classification as a benign neoplasm with possible reoccurrence.

Complex Odontoma

Inductive processes resulting in dental components but not fully organized.

Compound Odontoma

Differentiation of dental components into varying levels of organization—denticles.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infection
- Foreign body
- Dentigerous cyst
- Other oral masses
 - Ameloblastic fibroma—similar to AFO but would contain no hard tissue.
 - CEOT—Calcifying epithelial odontogenic tumor. Osteolysis but not mineralization or dental (mesenchymal) aspect. Slow, not inductive, non-invasive.
 - APOT—Amyloid producing odontogenic tumor. Similar to CEOT, but amyloid producing. Shares biologic features with ameloblastoma.
 - Peripheral odontoma (4 human cases diagnosed). Develops in gingiva or alveolar mucosa with no attachment to bone. Associated with impacted or retained teeth. Similar to erupted odontoma.

CBC/BIOCHEMISTRY/URINALYSIS

Typically not affected

IMAGING

- Intraoral radiography
- Advanced imaging typically not warranted

DIAGNOSTIC PROCEDURES

- Histopathology
- Complete oral examination



TREATMENT

SURGICAL CONSIDERATIONS

Procedures

- Appropriate antimicrobial and pain management therapy when indicated.
- Appropriate patient monitoring and support during anesthetic procedures.
- AFO
 - More aggressive excision may be necessary due to neoplastic classification.

- Monitor for local recurrence.

- Complex and compound odontoma
 - Enucleation and intracapsular excision with aggressive debridement of cyst. More aggressive surgical excision can decrease the chance of recurrence.
 - No chemotherapeutic regimens recommended.
 - Rarely radiotherapy may be beneficial by treating microscopically recurring disease.



MEDICATIONS

None indicated



FOLLOW-UP

PATIENT MONITORING

Typical postoperative—pain management, nutrition

POSSIBLE COMPLICATIONS

Recurrence, local infection, fragile jaw structure

EXPECTED COURSE AND PROGNOSIS

- AFO—fair to guarded prognosis, as there is a chance of recurrence.
- Complex and compound odontoma—short- and long-term prognosis good with adequate therapy.



MISCELLANEOUS

ABBREVIATIONS

- AFO = ameloblastic fibro-odontoma
- APOT = amyloid-producing odontogenic tumor
- CEOT = calcifying epithelial odontogenic tumor
- WHO = World Health Organization

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OLIGURIA AND ANURIA



BASICS

DEFINITION

- Oliguria—production of an abnormally small amount of urine (variably described as urine production rate < 0.27 , < 0.5 , or $< 1.0\text{--}2.0 \text{ mL/kg/h}$). In euvolemic or hypervolemic patients with good perfusion, urine production $< 1.0 \text{ mL/kg/h}$ = absolute oliguria. Hydrated dogs and cats receiving fluids should produce at least 1.0 mL/kg/h .
- Anuria—limited/no urine formation (urine production rate $< 0.08 \text{ mL/kg/h}$).

PATOPHYSIOLOGY

- Physiologic (prerenal) oliguria: kidneys limit water loss during episodes of reduced renal perfusion to preserve fluid and electrolyte balance. High plasma osmolality or low circulating fluid volume stimulate ADH synthesis and release. ADH acts on the kidneys to induce formation of small quantities of concentrated urine.
- Pathologic (renal) oliguria: severe renal parenchymal impairment. Factors include: high resistance in afferent glomerular vessels, low glomerular permeability, back leak of filtrate from damaged renal tubules, renal intratubular obstruction, extensive loss of nephrons resulting in marked reduction of glomerular filtrate produced.
- Anuria: may be renal or post-renal origin. Severe renal disease occasionally causes anuria. True anuria is more indicative of urinary obstruction. Mechanisms are the same as for pathologic oliguria (e.g., UTO or excretory pathway rupture).

SYSTEMS AFFECTED

- Renal—inability to adequately eliminate wastes and water; hyperkalemia.
- Urologic—obstruction-induced distension of the collecting system. Increased risk of urinary tract infection due to failure to empty the bladder.

SIGNALMENT

- Dog and cat.
- Young adult cats: higher incidence of anuria associated with UTO.
- Risk of acute kidney injury increases with age.

SIGNS

- Reduction in quantity of urine voided.
- Enlarged urinary bladder, straining to void, increased frequency of attempted voiding with urethral obstruction.
- Systemic signs of uremia if oliguria/anuria persists.

CAUSES

- Physiologic oliguria—renal hypoperfusion (caused by low blood volume or hypotension) or hypertonicity (usually caused by hypernatremia).
- Pathologic oliguria—acute oliguric kidney injury (renal failure), advanced CKD.
- Anuria—complete UTO, urinary excretory pathway rupture, or severe primary kidney disease.

RISK FACTORS

- Physiologic oliguria—causes include: dehydration, decreased cardiac output, hypotension, ECF volume contraction.
- Pathologic oliguria and anuria: caused by primary kidney disease, preexisting kidney disease, nephrotoxin exposure, dehydration, low cardiac output, hypotension, ECF volume contraction, electrolyte imbalance, acidosis, advanced age, fever, sepsis, liver disease, multiple organ failure, trauma, diabetes mellitus, hypoalbuminemia, hyperviscosity syndrome.
- Anuria—caused by urolithiasis, urinary tract neoplasia, idiopathic feline lower urinary tract disease, functional micturition disorder, trauma, gross hematuria.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Physiologic oliguria: poor tissue perfusion (e.g., dehydration; prolonged capillary refill time; pale mucous membranes; weak, rapid, irregular pulse; cool extremities); history of recent fluid loss (vomiting, diarrhea, polyuria, hemorrhage); signs of uremia are typically absent. Oliguria resolves rapidly when renal hypoperfusion is corrected.
 - Suspect pathologic oliguria and renal anuria with detection of any of the risk factors; (risk factors are additive). Patients with pathologic oliguria caused by CKD have a history of progressive kidney disease (including long-standing polyuria, polydipsia, poor appetite, weight loss). Patients with CKD are at risk of developing acute kidney injury. Signs of uremia are commonly observed; fluid therapy and other measures to restore adequate renal perfusion often fail to increase urine flow.
 - Suspect anuria due to UTO or rupture of the excretory pathway with repeated straining to void but inability to produce urine. Patients may have a history of pollakiuria, dysuria, stranguria, hematuria, urolithiasis, trauma, instrumentation of the urinary tract. Physical exam UTO patient may reveal: enlarged urinary bladder, painful posterior abdomen, masses or uroliths in the urethra or bladder. Physical exam of patients with rupture of the urinary tract may reveal ascites, fluid infiltration in tissues, painful caudal abdomen, masses or uroliths in the bladder or urethra, or evidence of trauma (e.g., pelvic fracture).
 - UTO caused by functional urinary obstruction: suspect in patients with urinary bladder enlargement, increased resistance to manual bladder expression, and neurologic signs affecting the hind limbs and/or tail. Signs of uremia may develop. Restoring urinary flow/correcting rents in the excretory pathway rapidly restores adequate urine flow.
- CBC/BIOCHEMISTRY/URINALYSIS**
- Serum urea nitrogen/creatinine concentrations: elevated unless onset of

oliguria or anuria is very recent.

- Hyperkalemia: common with pathologic oliguria and anuria, less common/less severe in animals with physiologic oliguria (except with hypoadrenocorticism).
- Physiologic oliguria: characterized by high USG (> 1.030 , cats > 1.035). Oliguria associated with lower USG suggests renal parenchymal disease or UTO. Patients with urine-concentrating defects due to other diseases or drugs are the exception to this rule.
- Renal parenchymal anuria is typically characterized by USG < 1.030 (dogs) or < 1.035 (cats). USG varies in patients with post-renal anuria. Adequate urine-concentrating ability often lost after UTO.

IMAGING

- Abdominal radiographs and ultrasound are useful to rule out UTO/excretory pathway rupture.
- Excretory urography, retrograde urethrocytography, pyelography, or vaginourethrocytography may provide definitive proof of UTO/excretory pathway rupture.
- Distension of the excretory pathway or detection of uroliths in the ureters, bladder neck, urethra suggest UTO.
- Detection of fluid within the peritoneum supports a diagnosis of excretory pathway rupture. Contrast media leakage confirms a rupture.

DIAGNOSTIC PROCEDURES

- Electrocardiography: to identify significant hyperkalemia (see Hyperkalemia).
- Urethrocytostomy: may provide evidence for UTO/ urinary tract rupture.
- Urinary catheterization: may provide information about the integrity of the lower urinary tract. Not recommended as a diagnostic procedure because it may be misleading and may cause additional trauma, iatrogenic UTI.



TREATMENT

- Oliguria and anuria are emergencies. Untreated, may lead to death within hours to days. Death results from uremia, hyperkalemia, acidosis, sepsis.
- Persistent hypovolemia may lead to ischemic renal injury.
- Correct renal hypoperfusion rapidly by intravenous administration of normal saline or lactated Ringer's solution.
- Therapy for primary renal oliguria/anuria is limited to symptomatic, supportive care while awaiting spontaneous renal function recovery. Elimination of causative factors may slow or stop further renal injury (e.g., terminating aminoglycoside therapy, correcting hypercalcemia, or restoring adequate renal perfusion); however, once pathologic oliguria/anuria has developed, few kidney diseases will be amenable to specific treatment (exception = leptospirosis).
- Correct post-renal causes for anuria by non-surgical/surgical methods including retrograde

(CONTINUED)

OLIGURIA AND ANURIA

urohydropropulsion of uroliths/urethral plugs; placement of transurethral catheters to restore low-pressure urinary flow; removal of uroliths, polyps, neoplastic tissue; or surgical repair of rents, strictures, malposition of kidneys, ureters, bladder, urethra.

**MEDICATIONS****DRUG(S)**

- Diuretics: indicated after establishing euvoolemia in patients with renal oliguria. Diuretic-induced increased urine production facilitates fluid and electrolyte therapy and implies less severe kidney injury.
- Administration of diuretics before restoring adequate renal perfusion is counterproductive and may promote renal injury.
- Avoid diuretic-induced dehydration.
- Furosemide (2–4 mg/kg IV): often used first in patients with renal oliguria. Urinary flow should increase within 1 hour if not, repeat at the same or double dosage. If diuresis ensues, administer CRI of furosemide to sustain diuresis (0.25–1 mg/kg/h or 2–4 mg/kg IV q8h). Bolus injection followed by CRI may be most effective.
- Mannitol (0.25–1 g/kg IV) can be given as a 10% or 20% solution over 15–20 minutes. Urinary flow should increase within 1 hour. Do not repeat if diuresis does not ensue; may cause excessive volume expansion. If diuresis ensues, mannitol may be continued as CRI (1–2 mg/kg/h) or intermittent IV doses (0.25–0.5 g/kg every 4–6 hours) to sustain diuresis. Avoid mannitol when overhydration, pulmonary edema, congestive heart failure present.
- Dogs, dopamine (0.5–3 µg/kg/min) may increase urine flow by increasing renal blood flow, glomerular filtration, renal sodium excretion. Higher doses may cause renal vasoconstriction, tachycardia, and cardiac arrhythmias and are contraindicated in AKI. Dopamine is generally administered concurrent with furosemide. Diuresis should ensue within 1–2 hours. If diuresis ensues, dopamine should be continued until fluid and electrolyte balance can be maintained without further drug therapy. If urine flow does not increase within 2 hours, discontinue dopamine. Dopamine has not been established to be an effective treatment for

oliguria in dogs. Dopamine is not appropriate for oliguric cats.

- Fenoldopam (0.1–0.6 µg/kg/min), a selective dopamine A1 receptor antagonist, promotes a delayed (4- to 6-hour) diuresis in normal cats; however, its effectiveness in oliguric cats has not been established.

CONTRAINDICATIONS

Nephrotoxic drugs

PRECAUTIONS

- Administer fluids carefully to patients that are persistently oliguric or anuric to avoid overhydration. Do not continue to administer fluids to oliguric/anuric patients after their fluid volume deficit has been restored absent a plan to prevent development of overhydration. In patients with unresponsive renal oliguria; peritoneal dialysis/hemodialysis may be required to correct iatrogenic fluid-induced volume overexpansion.
- Failure to correct fluid deficits before initiating diuretic administration may cause further renal hypoperfusion and ischemic renal injury.
- Use drugs requiring renal excretion with caution.
- Avoid electrolyte solutions containing more than 4 mEq of potassium per liter in most animals. However, some hypokalemic patients may require cautious administration of higher doses of potassium.
- Dopamine can cause cardiac arrhythmias, particularly in animals with hyperkalemia. ECG monitoring is recommended when high dosages are used and in animals with hyperkalemia.

POSSIBLE INTERACTIONS

Furosemide may promote the nephrotoxicity associated with aminoglycoside antibiotics.

**FOLLOW-UP****PATIENT MONITORING**

- Urinary flow rate—determine early during the course of case management. When unclear, consider transurethral catheterization to accurately determine urine production. Place catheters using aseptic technique. Intermittent catheterization is less likely to cause UTI than indwelling catheter. Short catheter indwelling time lowers the risk of UTI. Properly placed/managed indwelling

catheters are usually safe for at least 48 hours. Use a closed, sterile drainage system.

- Creatinine, serum urea nitrogen, and potassium concentrations should be reevaluated after 12–24 hours; patients with severe hyperkalemia may need more frequent monitoring.
- ECG should be performed at appropriate intervals to assess cardiac effects of drugs and hyperkalemia and to monitor response to therapy.

PREVENTION/AVOIDANCE

- Avoid nephrotoxic drugs and substances.
- Avoid dehydration and volume contraction.

POSSIBLE COMPLICATIONS

- Hyperkalemia and associated cardiotoxicity
- Uremia leading to death
- Dehydration
- Overhydration
- Bacterial UTI and sepsis

EXPECTED COURSE AND PROGNOSIS

- Oliguria and anuria are poor prognostic signs in acute or CKD; unless urine outflow can be corrected, survival is not expected.
- Anuria associated with UTO is often reversible if urethral patency is restored.

**MISCELLANEOUS****SEE ALSO**

- Azotemia and Uremia
- Hyperkalemia
- Nephrotoxicity, Drug-Induced
- Renal Failure, Acute
- Renal Failure, Chronic
- Urinary Tract Obstruction

ABBREVIATIONS

- ADH = antidiuretic hormone
- AKI = acute kidney injury
- CKD = chronic kidney disease
- CRI = constant rate infusion
- ECG = electrocardiogram
- USG = urine specific gravity
- UTI = urinary tract infection
- UTO = urinary tract obstruction

Suggested Reading

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OLLULANUS INFECTION



BASICS

OVERVIEW

A trichostrongyloid nematode—adult worms are found in the stomach wall of cats, causing chronic gastritis resulting in anorexia, vomiting, and weight loss. Females are oviparous and larvae may mature to adults without leaving the stomach. It is thought that the main mode of transmission is through vomitus to other cats.

SIGNALMENT

- Colony cats—predisposed, probably because they have close access to other cats' vomitus.
- Stray cats living in urban areas heavily populated with cats—high incidence of infection.
- Captive cheetahs, lions, tigers, cougars—susceptible to infection.

SIGNS

- Chronic vomiting, anorexia, weight loss
- Death from chronic gastritis

CAUSES & RISK FACTORS

- *Ollulanus tricuspis*—adults (only up to 1 mm in length) coil into the gastric mucosa, causing superficial erosions.
- Over time, gastric erosions can become severe with marked inflammation, accumulation of lymphoid aggregates, and fibrous changes in the mucosa and submucosa.
- Eggs—hatch within the female worms and larvae develop to infective L3 larvae within the stomach.
- L3 larvae—vomited; infective to other cats.
- Adult male and female worms passed in the vomitus—can also infect other cats.
- Distributed throughout North America, Australia, New Zealand, Europe, Argentina, Chile.
- Germany—up to 40% of free-roaming cats may be infected.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of vomiting including:
 - Dietary
 - Toxins—lead, ethylene glycol

- Metabolic—diabetes mellitus, renal disease, liver disease, acidosis, heat stroke, hypoadrenocorticism, hyperthyroidism
- Gastric abnormalities—inflammatory bowel disease, neoplasia, obstruction, atrophic gastritis, ulcers, dilatation/volvulus, parasitic such as *Physaloptera*
- Gastroesophageal junction disorders—hiatal hernia
- Small intestinal disorders—inflammatory bowel disease, neoplasia, fungal, viral, obstruction, paralytic ileus
- Large intestinal disorders—colitis, obstipation, inflammatory bowel disease
- Abdominal disorders—pancreatitis, gastrinoma, peritonitis, steatitis, pyometra, diaphragmatic hernia, neoplasia
- Neurologic disorders—psychogenic, motion sickness, vestibular lesions, head trauma, brain neoplasia
- Miscellaneous—heartworm disease and heart disease.

CBC/BIOCHEMISTRY/URINALYSIS

Reflects diarrhea/vomiting—dehydration

OTHER LABORATORY TESTS

- Larvae (or eggs)—seldom found in feces as they are digested within the GIT.
- Vomitus—examine with Baermann method for L3 larvae.
- Vomiting can be induced in the cat using xylazine (0.5 mg/kg IV, or 1 mg/kg IM)—successful in about 70% of cases.

IMAGING

Abdominal ultrasound—may show gastric thickening; rarely see parasites.

DIAGNOSTIC PROCEDURES

- View worms through an endoscope—difficult due to size of worms.
- Gastric lavage—using saline collection followed by centrifugation to precipitate L3 larvae, or use Baermann technique.
- Histopathology—gastric biopsy occasionally shows parasites.



TREATMENT

Few treatments have been reported.



MEDICATIONS

DRUG(S)

- Tetramisole—give as a 2.5% formulation at 5 mg/kg PO once; effective but not available in the United States.
- Fenbendazole, oxfendazole, and pyrantel pamoate are recommended but there is little data available regarding treatment success.

CONTRAINdications/POSSIBLE INTERACTIONS

Tetramisole—at this dose should not cause any side effects in cats.



FOLLOW-UP

Warn owner to watch for further vomiting—treat with another round of tetramisole if it occurs.



MISCELLANEOUS

Ollulanus infection has been identified in a cat with concurrent gastric adenocarcinoma.

ABBREVIATION

- GIT = gastrointestinal tract

Suggested Reading

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OPHTHALMIA NEONATORUM



BASICS

OVERVIEW

- Infection of the conjunctiva and/or cornea before or just after the separation of the eyelids in the neonate.
- Occurs in puppies and kittens.
- Associated with *Staphylococcus* spp. or *Streptococcus* spp. in dogs and cats, and with herpesvirus in cats.
- Potentially vision threatening.
- Source of infection—believed to be from an intrauterine infection, a vaginal infection of the dam at the time of birth, or from a non-hygienic environment.

SIGNALMENT

- Affects all breeds of cats and dogs.
- Neonates before the time that the eyelids open (10–14 days postpartum).

SIGNS

- Upper and lower eyelid margins are fused (physiologic ankyloblepharon) and the lids bulge outward because of the accumulation of debris and discharge within the conjunctival sac.
- May note a mucous to mucopurulent discharge extruding through a patent opening at the medial canthus.
- Cornea and conjunctiva may be ulcerated.
- May note adhesions (symplepharon) of the conjunctiva to the cornea or to other areas of the conjunctiva (including that of the nictitans).
- Perforation of the cornea with iris prolapse and collapse of the globe is occasionally seen.

CAUSES & RISK FACTORS

- Intrauterine or vaginal infections in the dam near the time of birth.
- Unclean environment for the neonates.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Neonates with entropion in which the eyelids have already separated—mucous to mucopurulent discharge may be present; view of the cornea may be obscured; may have appearance of ankyloblepharon; differentiated by age (patients older than 10–14 days) and ability to separate the eyelids.

CBC/BIOCHEMISTRY/URINALYSIS

Normal unless there is a concurrent systemic infection.

OTHER LABORATORY TESTS

- Cultures of neonate's ocular discharge and/or dam's vaginal discharge—may help diagnose bacterial infection and guide antibacterial therapy.
- Cytology of the affected tissues—may help diagnose bacterial infection and guide antibacterial therapy.
- Immunofluorescent antibody or polymerase chain reaction tests (cats)—feline herpesvirus.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Full physical examination of the dam and neonate.
- Fluorescein staining—corneal or conjunctival ulceration.



TREATMENT

- Separation of the eyelids—cornerstone of treatment; can be accomplished by manual traction beginning at the medial canthus or introduction of a closed hemostat, small blunt scissor blade or the blunt, butt end of a scalpel blade into the patent opening or groove of the future lid fissure at the medial canthus and gently separating (not cutting) the eyelids.
- Lavage of conjunctival sac and cornea with warm saline or a 1:50 diluted povidone-iodine aqueous solution to remove the discharge.
- Warm compresses may aid in separating the eyelids and preventing readherence.
- Systemic support as needed.



MEDICATIONS

DRUG(S)

- Broad-spectrum, topical antibiotics—e.g., neomycin/bacitracin/polymyxin B; applied 4 times daily for at least 1 week; antibiotic chosen on basis of bacterial culture and sensitivity, if available.
- Antiviral therapy in the case of herpesvirus infection in cats.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Tetracycline—do not use in neonates because of the risk of affecting bone or teeth; topical ofloxacin or ciprofloxacin is drug of choice for *Chlamydophila*.
- Topical corticosteroids—contraindicated.



FOLLOW-UP

PATIENT MONITORING

- Warm compresses—may be necessary for a few days to keep the eyelids from readhering.
- Topical antibiotics—continued for a minimum of 7 days.
- Observe littermates that are not initially affected.
- Treat vaginal infections in the dam with appropriate medications.

PREVENTION/AVOIDANCE

- Keep the external environment and the dam's nipples clean.
- Treat vaginal infection in the dam before delivery, if possible.

POSSIBLE COMPLICATIONS

- Severe keratitis with scarring and symblepharon.
- Rupture of the cornea with secondary phthisis; blindness may be irreversible.

EXPECTED COURSE AND PROGNOSIS

Favorable with correct and timely diagnosis and treatment and if no major complications occur.



MISCELLANEOUS

Suggested Reading

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Author Simon A. Pot

Consulting Editor Paul E. Miller

OPTIC NEURITIS AND PAPILLEDEMA



BASICS

DEFINITION

- Optic neuritis—Inflammation of one or both optic nerves, resulting in reduction of visual function.
- Papilledema is edema of the optic nerve head that does not obviously affect the function of the optic nerve.

PATHOPHYSIOLOGY

- Optic neuritis may be a primary disease or secondary to CNS disease because the optic nerve communicates with the subarachnoid space.
- Papilledema occurs when CSF pressure is elevated.
- Papilledema may occur separately from optic neuritis.
- Optic neuritis may also feature papilledema.

SYSTEMS AFFECTED

- Nervous
- Ophthalmic

GENETICS

No genetic basis

INCIDENCE/PREVALENCE

Occasional cause of blindness in dogs; rare in cats

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species
Dog and cat

Breed Predilections
None

Mean Age and Range
Middle-aged

Predominant Sex
None

SIGNS

Historical Findings

- Optic neuritis—acute blindness, may report other neurologic signs such as ataxia, seizures or behavior changes.
- Papilledema—no clinically detectable visual abnormalities but may report other neurologic signs.

Physical Examination Findings

- Optic neuritis—may be unilateral or bilateral; absent menace, absent dazzle, mydriatic and nonresponsive pupil, may have anisocoria if unilaterally affected, usually normal anterior segment, hyperemia, congestion, and hemorrhages of the optic nerve head, retina surrounding optic nerve may be detached, may have chorioretinitis concurrently.

- Papilledema—usually bilateral, menace present, dazzle present, normal pupillary light reflexes, normal anterior segment, swelling and elevation of optic nerve head, loss of physiologic cup in center of optic nerve head, retina usually normal.

CAUSES

Optic neuritis

- Idiopathic (dogs)
- Systemic mycoses
- Canine distemper (dogs)
- FIP (cats)
- Neoplasm—primary or metastatic
- Toxoplasmosis
- *Neosporum caninum*
- Granulomatous meningoencephalomyelitis
- Ehrlichiosis
- Orbital cellulitis
- Hepatozoonosis
- Toxicity—lead
- Tick-borne encephalitis virus

Papilledema

- CNS neoplasia (primary or metastatic)
- Hepatic encephalopathy
- Hydrocephalus
- Distemper (dogs)
- FIP (cats)
- Systemic mycoses
- Toxoplasmosis
- Granulomatous meningoencephalitis
- Trauma

RISK FACTORS

None



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Papilledema is differentiated from optic neuritis by presence of normal pupillary light reflexes and no obvious visual deficits.
- Cortical blindness—normal pupillary light reflex; normal fundus examination; possibly other neurologic deficits; normal electroretinogram.
- SARDS (dogs)—normal to absent pupillary light reflex; normal fundus (early in course); flat electroretinogram.

CBC/BIOCHEMISTRY/URINALYSIS

No specific abnormalities

OTHER LABORATORY TESTS

Specific viral, protozoal, or fungal serologic tests on serum

IMAGING

Neuroimaging—MRI and/or CT

DIAGNOSTIC PROCEDURES

- CSF analysis.
- Electroretinogram—investigate retinal function; normal in optic neuritis and papilledema, flat in SARDS.
- Measure intracranial pressure.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient—most cases will need to be hospitalized for workup and medical therapy depending on primary disease process.

NURSING CARE

Depending on degree of neurologic impairment, special attention to patient cleanliness, passive range of motion.

ACTIVITY

Activity may need to be restricted if visual deficits are present and depending on degree of neurologic impairment.

DIET

May need to be altered depending on degree of neurologic impairment.

CLIENT EDUCATION

Optic neuritis—important to emphasize that vision may not return, particularly in idiopathic cases, and treatment may be life-long (immunosuppressive therapy).

SURGICAL CONSIDERATIONS

Surgery infrequently indicated with the exceptions of resectable CNS disease.



MEDICATIONS

DRUG(S) OF CHOICE

Optic neuritis

- Depends on primary disease process when identifiable, always treat any infectious process identified.
- Idiopathic—prednisone 2 mg/kg q12h for 14 days; then 1 mg/kg q12h for 14 days; then gradual reduction to maintenance dosage.

Papilledema

- Mannitol 1 g/kg IV over 20 minutes; repeated as necessary.
- Hypertonic saline 3 mL/kg IV over 10 minutes.
- Corticosteroids—prednisone (0.5 mg/kg PO q12h) or dexamethasone SP 0.25 mg/kg IV q8–12h); not indicated for head trauma.

CONTRAINDICATIONS

Immunosuppressive drugs may be contraindicated in patients where disease etiology is unknown.

PRECAUTIONS

Ensure patients receiving mannitol can urinate; immunosuppressive agents should be used cautiously in infectious processes.

POSSIBLE INTERACTIONS

None

(CONTINUED)

**FOLLOW-UP****PATIENT MONITORING**

Serial ophthalmic examinations should be performed, including fundic exam; careful attention to visual deficits; visual deficits resolving indicate improvement in disease, but patient may also adapt to vision loss, making client's reports of vision unreliable.

PREVENTION/AVOIDANCE

None

POSSIBLE COMPLICATIONS

- Optic neuritis—vision loss may be permanent.
- Papilledema—increased CSF pressure may be associated with brain herniation.

EXPECTED COURSE AND PROGNOSIS

- Optic neuritis—guarded to poor prognosis for return of vision, but idiopathic cases have good prognosis for life.
- Papilledema—guarded to poor prognosis for life.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Optic neuritis—chorioretinitis, CNS disease
- Papilledema—CNS disease

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

Zoonotic infectious CNS disease is rare.

PREGNANCY/FERTILITY/BREEDING

Infectious diseases such as canine distemper may be associated with fetal disease and congenital abnormalities.

SEE ALSO**ABBREVIATIONS**

- CNS = central nervous system
- CSF = cerebrospinal fluid

- CT = computed tomography
- FIP = feline infectious peritonitis
- MRI = magnetic resonance imaging
- SARDS = sudden acquired retinal degeneration syndrome

Suggested Reading

Montgomery KW, van der Woerdt A, Cottrill NB. Acute blindness in dogs: sudden acquired retinal degeneration syndrome versus neurological disease (140 cases, 2000–2006). *Vet Ophthalmol* 2008, 11:314–320.

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ORAL CAVITY TUMORS, UNDIFFERENTIATED MALIGNANT TUMORS



BASICS

OVERVIEW

- Uncommon, highly aggressive, rapidly growing tumor typically located in the caudal maxilla and orbit of young dogs.
- Most are highly bone-invasive and are non-encapsulated with a smooth to slightly nodular surface (mistaken as benign); may become ulcerated.
- Biopsy—reveals undifferentiated malignancy of undetermined histogenesis.
- Highly metastatic.
- Cervical lymphadenopathy common.

SIGNALMENT

- Dog
- Primarily a disease of large breeds
- All dogs < 2 years old; range, 6–22 months
- No sex predilection

SIGNS

Historical Findings

- Excessive salivation
- Halitosis
- Dysphagia, dysorexia
- Bloody oral discharge
- Weight loss

Physical Examination Findings

- Oral mass
- Loose teeth
- Facial deformity, exophthalmia
- Cervical lymphadenopathy—occasionally
- Pain upon palpating or opening the mouth

CAUSES & RISK FACTORS

None identified



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other aggressive oral malignancy including melanoma and squamous cell carcinoma
- Acanthomatous ameloblastoma
- Abscess

CBC/BIOCHEMISTRY/URINALYSIS

May be normal

OTHER LABORATORY TESTS

- Cytologic evaluation of primary tumor and draining lymph node—may provide tentative diagnosis.
- Histopathology consistent with an undifferentiated tumor without characteristic morphologic features of mesenchymal or epithelial origin.
- Immunocytochemistry (various markers) required to rule out other tumors, including rhabdomyosarcoma (aggressive tumor also seen in young dogs).

IMAGING

- Skull radiography—detect bone invasion deep to the mass.
- Thoracic radiography—detect lung metastasis.
- Advanced sectional imaging (CT or MRI)—define local and regional extent of disease, and facilitate therapeutic planning.

DIAGNOSTIC PROCEDURES

- Carefully palpate regional lymph nodes (mandibular, retropharyngeal).
- Large, deep tissue biopsy required to differentiate from other oral malignancies.



TREATMENT

DIET

Soft foods—may be recommended to prevent tumor ulceration or after radical oral excision.

SURGICAL CONSIDERATIONS

Radical surgical excision—often ineffective because of extensive local disease or regional metastasis at diagnosis; if attempted, must have margins of at least 2 cm into normal bone and soft tissues and ideally be planned with the help of contrast enhanced advanced sectional imaging.

RADIATION

- Efficacy unreported.
- Undifferentiated tumors often poorly responsive to megavoltage radiation therapy.
- Considered for palliation (hypofractionated protocol).



MEDICATIONS

DRUG(S)

- Chemotherapy—efficacy unreported; undifferentiated tumors often poorly responsive to systemic chemotherapy.
- Pain management with multimodal analgesic therapy is mandatory (NSAID, opioid, adjuvant analgesic drugs, aminobisphosphonate if osteolytic).

CONTRAINdications/POSSIBLE INTERACTIONS

Chemotherapy can be toxic; seek advice of a medical oncologist before initiating treatment if you are unfamiliar with cytotoxic drugs.



FOLLOW-UP

Most dogs have detectable metastatic dissemination at diagnosis; usually euthanized within 30 days of diagnosis because tumor growth is progressive and uncontrolled, resulting in decreased quality of life and condition.



MISCELLANEOUS

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

Caserto BG. A comparative review of canine and human rhabdomyosarcoma with emphasis on classification and pathogenesis. *Vet Pathol* 2013; 50:806–826.

Patnaik AL, Lieberman PH, Erlandson RA, et al. A clinicopathologic and ultrastructural study of undifferentiated malignant tumors of the oral cavity in dogs. *Vet Pathol* 1986; 23:170–175.

Author Louis-Philippe de Lorimier
Consulting Editor Timothy M. Fan



BASICS

DEFINITION

- Oral cavity growth that may be benign or malignant.
- Fourth most common area of malignancy in dogs and cats.
- The majority of oral malignancies are locally aggressive and slow to metastasize.

PATHOPHYSIOLOGY

Cat

- Squamous cell carcinoma—age range, 3–21 years (mean, 12.5); sites include gingival, sublingual and tonsillar; common presenting signs include excessive drooling and/or bleeding from the mouth; frequently invades bone, loosening teeth; morbidity and mortality result from local disease rather than distant metastasis. There is speculation that a viral association maybe possible.
- Fibrosarcomas—age range, 1–21 years (mean, 10.3); no particular predilection site; all associated with local tissue destruction; muscle and bone invasion are occasionally seen.

Dog

- Epulis is a general term referring to a gingival mass of any type (see Epulis).
 - Previous categorization of fibromatous epulis (FE) has been subdivided into FFH—focal fibromatous hyperplasia (no odontogenic epithelium) and POF—peripheral odontogenic fibroma (with odontogenic epithelium and varying degrees of ossification).
 - Previous categorization of acanthomatous epulis now termed CAA—canine acanthomatous ameloblastomas—locally aggressive.
- Malignant melanoma (see Melanocytic Tumors, Oral)—the most common oral malignant tumor in the dog; cocker spaniels, German shepherds, chow chows, and dogs with heavily pigmented mucous membranes are predisposed; masses can be amelanotic, males more frequently affected than females. Occurs in many places in the oral cavity (the most common site in order of occurrence is gingival, buccal mucosa, lip, tongue, and palate); locally invasive and metastasize to lungs and regional lymph nodes; common presenting complaints are oral bleeding, ptalism, or halitosis; tumor size on presentation is important to patient survival; in the dog, melanomas < 2 cm carry a better survival rate (median 511 days) than those > 2 cm (median 164 days); tumors located rostrally have better prognosis than those located distally.

- Squamous cell carcinoma (see Squamous Cell Carcinoma, Gingiva; Squamous Cell Carcinoma, Tongue; Squamous Cell Carcinoma, Tonsil)—the next most common oral malignancy; originates from the gingival epithelium; red, ulcerated, and may have cauliflower projections; large-breed dogs are predisposed; prognosis depends on location in the oral cavity; those located rostrally carry a better prognosis than those at the base of the tongue or occurring in the tonsils; lesions on the lips and buccal mucosa have a low metastatic rate; gingival lesions infiltrate readily to the underlying bone; lesions on the tongue (due to movement) and tonsils tend to metastasize and are the most aggressive.
- Papillary squamous cell carcinoma—a rapidly growing tumor typically in young dogs (< 1 year), but has been identified in mature dogs; in the papillary gingiva; locally aggressive but does not metastasize; treatment of choice is excision. There is speculation that papillary squamous cell carcinoma is associated with papilloma virus.
- Fibrosarcoma (see Fibrosarcoma, Bone; Fibrosarcoma, Gingiva; Fibrosarcoma, Nasal and Paranasal Sinus)—the third most common oral malignancy in dogs (and the second most common in cats); fibrosarcomas have a predilection for the maxilla of large, male, older dogs; the gingiva is commonly affected, especially around the maxillary fourth premolar, followed by the hard palate and oral mucosa; slowly invasive but rarely metastasize.
- Osteosarcoma—primarily occurs in middle-aged medium- to large-breed dogs. Local bone invasion results in significant facial swelling and is locally aggressive with a low rate of metastasis.
- Odontoma (see Odontoma)
 - Complex odontoma—rare benign tumor composed of disorganized dental components not forming toothlike structures. They are locally destructive with no metastasis and are enclosed in a cystic capsule.
 - Compound odontoma—similar to complex odontomas with the exception that it is composed of organized dental components forming toothlike structures.
- Plasmacytoma—plasma cell origin; occurring primarily in older dogs; aggressive and can metastasize.
- Other tumor types include undifferentiated carcinoma, lymphoma, fibroma, melanocytoma, papilloma, mast cell tumor, giant cell tumor, neurofibroma, myxofibrosarcoma, and rhabdomyosarcoma.

SYSTEMS AFFECTED

Gastrointestinal—oral cavity

GENETICS

N/A

INCIDENCE/PREVALENCE

- Not uncommon. Varies with type of mass. See “Pathophysiology.”
- The oral cavity is the fourth most common site for tumor localization in dogs and cats.

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dogs and cats

Breed Predilections

Golden retrievers, German shorthaired pointers, Weimaraners, Saint Bernards, and cocker spaniels are more prone to oral tumors; dachshunds and beagles less prone to oral tumors; boxer, gingival hyperplasia.

Mean Age and Range

- Older animals are affected most often.
- Complex odontoma, compound odontoma, papilloma, and papillary squamous cell carcinoma usually occur in dogs less than 2 years of age.

Predominant Sex

- Males are more commonly affected with oral melanomas and fibrosarcomas than females.
- Females are more commonly affected with osteosarcomas than males.

SIGNS

Historical Findings

- Weight loss
- Anorexia
- Can eat only soft food
- Reluctance or pain to chew
- Chews only on one side

Physical Examination Findings

- Often no signs
- Halitosis
- Tooth displacement
- Malocclusion
- Oral hemorrhage
- Dysphasia
- Abnormal salivation
- Inability to open or close the mouth
- Abnormal facial symmetry
- Facial swelling
- Head shyness
- Tooth mobility
- Tooth loss

CAUSES

- Unknown
- Papilloma—papilloma virus

RISK FACTORS

- Tonsillar squamous cell carcinoma occurs 10 times more commonly in dogs from urban settings than in rural dogs.

ORAL MASSES

(CONTINUED)

- Squamous cell carcinoma—more prevalent in white dogs in one study.
- Any chronic oral irritation (periodontal disease, secondhand smoke) increases the risk of oral tumor development.
 - It has been suggested that the FE category develop in response to chronic inflammation/irritation
- Viral papillomas can undergo malignancy to become squamous cell carcinoma.
- It has been reported that FeLV, FIV, or FSV may play a role in squamous cell carcinoma development.
- Some researchers showed that cats that wore flea collars had 5 times the risk of developing oral squamous cell carcinoma than non-users.
- Secondhand smoke may be associated with squamous cell carcinoma in cats.
- Immunosuppressed dogs (puppies) are more commonly affected with papillomas.
- Acanthomatous ameloblastoma can very rarely transform into squamous cell carcinoma with radiation therapy.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infection—viral/bacterial/fungal
- Odontoma
- Dentigerous cyst
- Radicular cyst
- Apical granuloma
- Nasopharyngeal polyps
- Eosinophilic granuloma
- Calcinosis circumscripta
- Proliferative gingival hyperplasia
- Oral ulceration (uremic ulcers, autoimmune disease, gum-chewer syndrome)
- Hypercementosis
- Apical granuloma
- Ranula
- Tonsillitis
- Lymphocytic plasmacytic stomatitis

CBC/BIOCHEMISTRY/URINALYSIS

Used to rule out other primary or secondary complications; e.g., anemia, uremia.

OTHER LABORATORY TESTS

Molecular staging of malignant melanomas can be achieved by screening lymph node aspirates for canine melanoma-associated antigens mRNA; aiding in detection of metastatic disease.

IMAGING

• Radiographs of the affected jaw for bony invasion, lungs for metastases (make sure to take three views: VD, right lateral, and left lateral).

- MRI or CT of the mass area to determine the extent of the lesion.
- MRI provides more accurate information regarding the size of the masses and invasion of adjacent structures. Since melanomas have a hyperintense signal on T1 weighted images and a hypointense signal on T2 weighted images, it facilitates identification of the extent of the local growth.
- CT provides better images of calcification and cortical bone erosion. CT images can be enhanced with the use of contrast medium (e.g., iohexol) to delineate the tumor.

DIAGNOSTIC PROCEDURES

Aspirate, biopsy, or surgically remove enlarged regional lymph nodes for cytology and/or histology to evaluate for metastasis.

PATHOLOGIC FINDINGS

- Must biopsy; sample deep tissue surrounding the mass; use excision, wedge, or needle-punch techniques.
- Cytology may also be helpful but is not as definitive as histopathology.



TREATMENT

APPROPRIATE HEALTH CARE

- Depends on the tumor type.
- Benign tumors are treatable with long-term success via surgery and sometimes with radiation therapy.
- Malignant tumors are treated surgically with varying success depending on tumor type, location, and metastasis at presentation.
- In advanced circumstances, combined therapy (surgery, chemotherapy, and radiation) may provide the best care.
- Molecularly targeted therapies provide oncologists with tools to treat cancers with greater specificity. These modalities can be used further to classify tumors, aid in predicting the prognosis, and help determine the exact treatment plan.

NURSING CARE

- Pain control
- Supportive care

ACTIVITY

N/A

DIET

Nutritional support is essential in any treatment plan. Gastrostomy, esophagostomy, nasal gastric tube placement, or peg tube placement may be required for proper nutritional support.

CLIENT EDUCATION

N/A

SURGICAL/RADIATION/

CHEMOTHERAPY CONSIDERATIONS

- Early diagnosis and treatment offer the best chance for a successful outcome.
- The first surgical resection offers the best chance for complete resection.
- Complete en bloc excision is the treatment of choice, with surgical margins ranging from 1 to 2 cm dependent on the tumor type.
- Radiation therapy should be offered in cases where complete excision is not possible and/or the mass is located in the caudal aspect of the oral cavity and precludes complete surgical excision.
- Megavoltage radiation therapy is presently considered the standard of care for treatment of oral tumors; however, intensity-modulated radiation therapy is a relatively new technology that is quickly being adopted.
- Chemotherapy is warranted in oral round cell sarcomas or in high-grade metastatic malignancies.
- Papilloma—marginal excision is the treatment of choice (mainly for histologic evaluation to rule out other forms of tumors); most will spontaneously regress in time and the use of autogenous vaccines is an effective treatment, especially when the masses are affecting mastication.
- Peripheral odontogenic fibroma (ossifying epulis)—marginal excision with removal of full-thickness gingiva down to the alveolar bone has shown success; rapid recurrence may necessitate extraction of involved tooth or slow recurrence may be managed with excising it on a yearly basis.
- Acanthomatous ameloblastoma—excision with at least 1 cm margins is usually curative; radiation has also been used successfully; the combination of surgery and radiation may be most effective (requiring less aggressive surgery), but if radiation is not readily available, surgery may be the only option; surgery must be aggressive with 2 cm margins in cases where the margins are ill defined and that extent of resection is possible; the best chance to resolve the problem surgically is the first time; extract any teeth that may impede incision healing; if the tumor reoccurs it is more aggressive and has been reported to reoccur as squamous cell carcinoma. Multiple (up to 10) injections of bleomycin (5 mg) injected at the tumor site have been effective in a small number of reported cases.
- Malignant melanoma—prognosis improves if the tumor is small and located in the rostral mandible; if surgery is chosen for therapy, it should be aggressive; typically mandibulectomy or maxillectomy; median

(CONTINUED)

ORAL MASSES

survival times average 8 months; combination of surgery, radiation, and chemotherapy (low-dose cisplatin) yielded a median survival of 14 months in one study; pigmentation does not affect the prognosis; relatively radioresistant; one study showed a median survival time of 14 months after radiation only; the problem with melanoma is not local disease management but metastasis; research indicates that vaccination is a promising cure. The DNA-based vaccine is indicated for TNM stage II—III malignant melanomas after local surgical control has been achieved. Single-agent platinum analogues used alone or with piroxicam have been shown to have antitumor activity for malignant melanoma.

- Squamous cell carcinoma—better long-term prognosis than malignant melanoma or fibrosarcoma in the dog; may be widely surgically excised or irradiated in the dog, especially if the lesion is rostral (better prognosis than those located caudally); perform a maxillectomy or mandibulectomy with a 2 cm clean surgical margin as a goal; in dogs, radiation alone delivers a median survival rate of 15–17 months; in dogs, prognosis for survival following treatment of lingual involvement is poor; dogs tolerate partial glossotomy involving 40–60% of the tongue; for tumors larger than 2 cm or those with incomplete resections, surgery, radiation, and chemotherapy (mitoxantrone or cisplatin with piroxicam) may be the best options. In cats, surgical resection gives a mean survival rate of 1 year for resectable tumors. One can use carboplatin or mitotantrone for palliative treatment. Radiation treatment locally along with aminobisphosphonate treatment is considered a good palliative treatment for cats with squamous cell carcinoma. A recent study by Fidel et al. looked at combining accelerated radiation therapy and carboplatin with better results, particularly with tonsillar SCC.
- Fibrosarcoma—surgical excision with at least 2 cm margins usually results in a 12-month median survival rate; usually requires a maxillectomy or mandibulectomy; surgical excision in combination with radiation therapy and chemotherapy offers the best prognosis; radiation or chemotherapy alone offers a poorer median survival rate than surgery alone; palatine fibrosarcomas carry the poorest prognosis because of the inability to surgically resect. Radiation therapy can be useful after surgical removal.

- Osteosarcoma—wide surgical removal with 2 cm margins is ideal. Reoccurrence can occur at metastatic sites. Radiation therapy should be considered post-surgery for microscopic disease. Palliative radiation therapy can be used alone.
- Plasmacytoma—rare; accounts for 5% of oral tumors in the dog; are locally aggressive but rarely metastasize. Surgical removal is the treatment of choice.
- Complex/compound odontoma—surgical resection en bloc is curative if all structures are removed. Surgery can be very extensive and one must remove the cystic walls of the tumor.

**MEDICATIONS****DRUG(S) OF CHOICE**

Chemotherapeutic drugs (see “Surgical/Radiation/Chemotherapy Considerations”).

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

Varies with nature of mass.

PREVENTION/AVOIDANCE

Remove or treat any oral irritation.

POSSIBLE COMPLICATIONS

- Surgical removal of part of the tongue may result in avascular necrosis if the tongue is transected just caudal to the origin of dorsal branches of the lingual arteries.
- Postoperative complications of mandibulectomy include wound dehiscence, prehension dysfunction, tongue lag, medial drift, excessive drooling, palatal ulceration secondary to malocclusion, and pressure necrosis.

- Mandibulectomies can be performed in cats, but they result in greater complications (tongue swelling, ranula formation) than in dogs. Surgery can result in aesthetic complications.

- Low-dose radiation can within the first few weeks cause diarrhea, nausea, vomiting, and hair loss (regrowth of hair is usually white); high dose has the above as well as oral ulceration/necrosis, mucositis, cataracts (these lesions occur in almost all cases and are self-limiting with supportive care), and radiation-induced tumors (mainly in young dogs that underwent radiation therapy for radioresponsive tumors). Late radiation effects can occur with bone and muscle necrosis but are unlikely. IMRT offers a more accurate dose distribution and is rapidly being accepted as the best form of radiation therapy with fewer side effects.

- Complications of chemotherapy are varied depending on the drug used.

EXPECTED COURSE AND PROGNOSIS

- Dogs with inadequate tumor-free surgical margins were 2.5 times more likely to die of the tumor than those with complete histologic excision; some surgical patients need gastrostomy tubes to facilitate nutritional supplementation during the treatment period.
- Dogs with tumors located caudal to the first premolar had 3 times greater risk of dying from the disease than those with tumors located rostral to the first premolar.
- Vaccination of dogs with malignant melanoma seems to be curative and is offered at a number of sites throughout North America.

- Staging of oral tumors using the TNM (primary Tumor, regional distant Lymph Nodes {cervical, submandibular, and parotid nodes}, and Metastasis) classification system allows for a more accurate prognosis; the higher the stage (I–IV) the worse the prognosis.

- Fibrosarcomas have four histologic types: a low-grade malignancy (best prognosis), an intermediate malignancy, a high malignancy, and a histologically low-grade yet biologically high-grade fibrosarcoma that is reported in large-breed dogs (mainly golden retrievers) and that offers a poor prognosis due to its rapid growth and metastasis.

ORAL MASSES

(CONTINUED)



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

ABBREVIATIONS

- CT = computed tomography
- FeLV = feline leukemia virus

- FIV = feline immunodeficiency virus
- FSV = feline sarcoma virus
- IMRT = intensity-modulated radiation therapy
- MRI = magnetic resonance imaging

Suggested Reading

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Client Education Handout available online

ORAL ULCERATION



BASICS

DEFINITION

Focal or multifocal loss of mucosal integrity of the superficial epithelial layers in specific areas of the oral cavity—oral mucosal ulceration.

PATHOPHYSIOLOGY

Oral mucosal ulceration usually coincides with oropharyngeal inflammation. Oral and oropharyngeal inflammation is classified by location as:

- Gingivitis—inflammation of gingiva.
- Periodontitis—inflammation of non-gingival periodontal tissues (i.e., the periodontal ligament and alveolar bone).
- Alveolar mucositis—inflammation of alveolar mucosa (i.e., mucosa overlying the alveolar process and extending from the mucogingival junction without obvious demarcation to the vestibular sulcus and to the floor of the mouth).
- Sublingual mucositis—inflammation of mucosa on the floor of the mouth.
- Labial/buccal mucositis—inflammation of lip/cheek mucosa.
- Caudal mucositis—inflammation of mucosa of the caudal oral cavity, bordered medially by the palatoglossal folds and fauces, dorsally by the hard and soft palate, and rostrally by alveolar and buccal mucosa.
- Palatitis—inflammation of mucosa covering the hard and/or soft palate.
- Glossitis—inflammation of mucosa of the dorsal and/or ventral tongue surface.
- Cheilitis—inflammation of the lip (including the mucocutaneous junction area and skin of the lip).
- Osteomyelitis—inflammation of the bone and bone marrow.
- Stomatitis—inflammation of the mucous lining of any of the structures in the mouth; in clinical use the term should be reserved to describe widespread oral inflammation (beyond gingivitis and periodontitis) that may also extend into submucosal tissues (e.g., marked caudal mucositis extending into submucosal tissues may be termed “caudal stomatitis”).
- Tonsillitis—inflammation of the palatine tonsil.
- Pharyngitis—inflammation of the pharynx.

SIGNALMENT

Species

Dogs and cats

Breed Predilections

- Canine ulcerative stomatitis: Maltese, Cavalier King Charles spaniels, cocker spaniels, Bouvier des Flandres.
- Feline stomatitis/lymphocytic plasmacytic stomatitis (LPS)—may have predilection for Somali and Abyssinian cats (see Stomatitis, Caudal—Cats).

- Idiopathic osteomyelitis—may have predilection for cocker spaniels; complication associated with canine ulcerative stomatitis.

Mean Age and Range

None

Predominant Sex

None

SIGNS

- Halitosis.
- Gingivitis.
- Pharyngitis.
- Buccitis/buccal mucosal ulceration.
- Ptyalism (thick, ropey saliva).
- Pain.
- Anorexia.
- Mucosal ulceration—“Contact ulcers” or “kissing ulcers” common in ulcerative stomatitis.
- Plaque—with or without calculus.
- Exposed, necrotic bone—with alveolar osteitis and idiopathic osteomyelitis.
- Behavior changes secondary to oral sensitivity.
- Scar formation on lateral margins of tongue—may be seen with canine ulcerative stomatitis.
- Note: sometimes these signs will start following a routine dental cleaning on a previously “normal” patient; probably would have occurred eventually, just exacerbated by manipulation and antigenic stimulation in the oral cavity.

CAUSES

Metabolic

- Diabetes mellitus
- Hypothyroidism
- Renal disease—uremia

Nutritional

- Protein-calorie malnutrition
- Riboflavin deficiency

Neoplastic

- Dog—malignant melanoma, squamous cell carcinoma, fibrosarcoma, acanthomatous ameloblastoma, ulcerated benign tumors
- Cat—squamous cell carcinoma, fibrosarcoma, malignant melanoma

Immune Mediated

- Pemphigus vulgaris—90% have oral involvement
- Bullous pemphigoid—80% have oral involvement
- Systemic lupus erythematosus—50% have oral involvement
- Discoid lupus erythematosus
- Drug induced—toxic epidermal necrolysis, erythema multiforme
- Immune-mediated vasculitis

Infectious

- Retrovirus—FeLV/FIV
- Calicivirus—cat
- Herpesvirus—cat
- Leptospirosis—dog
- Periodontal disease—dog and cat

Traumatic

- Foreign body—bone or wood fragments
- Electric cord shock
- Malocclusion
- Gum-chewer’s disease—chronic chewing of cheek

Chemical/Toxic

- Caustic chemical ingestion
- Thallium

Idiopathic

- Eosinophilic granuloma—cats, Siberian huskies, Samoyeds
- Feline stomatitis complex—cats
- Ulcerative stomatitis—dogs; allergic, hypersensitivity reaction to plaque
- Idiopathic osteomyelitis—dogs

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- History and oral examination—foreign bodies; malocclusions; chemical, toxic, and electrical burns
- Idiopathic conditions—clinical signs; history; breed predispositions; response to therapy

CBC/BIOCHEMISTRY/URINALYSIS

- Hyperglycemia if diabetes mellitus; azotemia and isosthenuria if renal disease; leukocytosis if infections.
- Chronic conditions may have elevated serum total protein and elevated globulin levels due to chronic antigenic stimulation; T4 may be decreased secondarily.

OTHER LABORATORY TESTS

- T₄—may be low if hypothyroid or secondary to chronic inflammation
- Free T₄—may be better assessment of true thyroid function
- Serology—FeLV/FIV test, titers for specific infections
- Cultures—usually nonspecific; oral flora contaminants

IMAGING

Radiography—helps determine osseous involvement and extent of idiopathic osteomyelitis.

DIAGNOSTIC PROCEDURES

Biopsy/cytology—neoplasia, immune-mediated disease, and chronic inflammation result in predominant lymphocytes and plasmacytoid lymphocytes (feline stomatitis complex and ulcerative stomatitis in dogs).

PATHOLOGIC FINDINGS

Histopathology typically reveals nonspecific inflammation: neutrophils, macrophages, lymphocytes with varying levels of loss of mucosal epithelial integrity.

ORAL ULCERATION

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

- Supportive therapy—soft diet, fluids, hospitalization in severe cases.
- Pain management—topical analgesics/covering of ulcers, oral narcotics, serotonin reuptake inhibitors, NMDA antagonists, gabapentin.
- Nutritional support—via pharyngostomy or esophagostomy feeding tube.
- Canine ulcerative stomatitis—continuous, meticulous homecare to prevent plaque accumulation; dental cleaning initially and frequently; periodontal therapy; extraction of diseased teeth.
- Underlying metabolic or other disease—treat systemic illness appropriately.

CLIENT EDUCATION

- Warn client that prognosis is guarded, response to therapy depends on underlying cause, and prolonged treatment and/or further extractions may be necessary.
- In canine ulcerative stomatitis or feline stomatitis complex, any level of homecare that can be provided is encouraged (brushing or topical antimicrobials). Caution, these patients may have very sensitive and painful mouths.

SURGICAL CONSIDERATIONS

- Select extractions (partial, caudal, or full mouth)—may be indicated for chronic idiopathic conditions, e.g., canine ulcerative stomatitis and feline stomatitis complex, to remove the source of reaction (plaque/teeth).
- Removal of entire tooth structure—essential in extraction treatment for feline stomatitis.
- Removal of necrotic/avascular bone, gingival flap closure, and broad-spectrum antibiotics—indicated for idiopathic osteomyelitis; monitor for recurrence.



MEDICATIONS

DRUG(S) OF CHOICE

- Antimicrobials—treat primary and secondary bacterial infections; may be used intermittently between dental cleanings for therapeutic assistance, but the owner must be cautioned that chronic use could lead to antibiotic resistance; clindamycin (11 mg/kg PO q12h); amoxicillin-clavulanate (12.5–25 mg/kg PO q12h); tetracycline (10–22 mg/kg PO q8h).
- Anti-inflammatory/immunosuppressive drugs—the comfort of the patient must be weighed against potential long-term side effects of corticosteroid usage; prednisone (0.5–1 mg/kg PO q12–24h, taper dosage).

- Mucosal protectants—for chemical insults; sucralfate (1–25 kg PO q8h); cimetidine (5–10 mg/kg PO q8–12h).
- Analgesics—post-extraction; carprofen (0.5 mg/kg PO q12–24h); hydrocodone (0.22 mg/kg PO q8–12h); tramadol (2.2 mg/kg PO q8–12h).
- Topical therapy—chlorhexidine solution or gel (antibacterial): CET Oral Hygiene Rinse; zinc gluconate/ascorbic acid: Maxi/Guard Gel.

CONTRAINDICATIONS

- Do not use these medications in patients with known hypersensitivities.
- Corticosteroids are contraindicated in patients with systemic fungal infections.

PRECAUTIONS

- Some antimicrobials may upset the gastrointestinal tract.
- Avoid corticosteroids in patients that may already be immunocompromised (e.g., those with FeLV or FIV).

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

Frequent oral examination to evaluate for resolution or recurrence

PREVENTION/AVOIDANCE

Meticulous homecare to prevent plaque accumulation

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

- Response to therapy depends on underlying cause, and prolonged treatment and/or further extractions may be necessary.
- Inflammation may take 4–6 weeks to subside after extractions due to plaque retention of sutures and tongue.
- In cats with feline stomatitis following partial (premolars and molars) and full dentition extractions: 60% significant improvement, 25% some improvement, and 15% refractory.



MISCELLANEOUS

ASSOCIATED CONDITIONS

None

AGE-RELATED FACTORS

None known

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Avoid medications known to interact adversely with pregnant females or developing fetuses.

SYNOMYS

- Necrotizing stomatitis
- Ulcerative stomatitis
- Vincent's stomatitis

ABBREVIATIONS

- CUPS = chronic ulcerative paradental stomatitis
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- LPS = lymphocytic-plasmacytic stomatitis
- NMDA antagonists = anesthetics that work to antagonize the N-methyl d-aspartate receptor
- T₄ = thyroxine

INTERNET RESOURCES

<http://www.avdc.org/Nomenclature.html>.

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Client Education Handout
available online

ORBITAL DISEASES (EXOPHTHALMOS, ENOPHTHALMOS, STRABISMUS)



BASICS

DEFINITION

- Abnormal position of the globe.
- Exophthalmos—anterior displacement of the globe.
- Enophthalmos—posterior displacement of the globe.
- Strabismus—deviation of the globe from the correct position of fixation, which the patient cannot correct.

PATHOPHYSIOLOGY

- Orbit cannot be examined directly; orbital disease manifested by signs that alter the position, appearance, or function of the globe and adnexa.
- Malpositioned globe—caused by changes in volume (loss or gain) of the orbital contents or abnormal extraocular muscle function.
- Exophthalmos—caused by space-occupying lesions posterior to the equator of the globe.
- Enophthalmos—caused by loss of orbital volume or space-occupying lesions anterior to the equator of the globe.
- Strabismus—usually caused by an imbalance of extraocular muscle tone or lesions that restrict extraocular muscle mobility.

SYSTEMS AFFECTED

- Ophthalmic.
- Respiratory—because of the close proximity, the nasal cavity and frontal and maxillary sinuses may be involved.

SIGNALMENT

- Dog and cat.
- Orbital abscess or cellulitis and myositis—more common in young adult dogs.
- Myositis—predisposed breeds: German shepherd, golden retriever, Weimaraner.
- Orbital neoplasia—more common in middle-aged to old dogs.

SIGNS

Exophthalmos

- Secondary signs of space-occupying orbital disease.
- Difficulty in retropulsing the globe.
- Serous to mucopurulent ocular discharge.
- Chemosis.
- Eyelid swelling.
- Lagophthalmos—inability to close the eyelids over the cornea adequately during blinking.
- Exposure keratitis—with or without ulceration.
- Pain on opening the mouth.
- Third eyelid protrusion is due to extraconal mass or late in progression of intraconal mass.
- Visual impairment caused by optic neuropathy.
- Fundic abnormalities, including retinal detachment.
- Retinal vascular congestion.
- Focal inward deviation of the posterior globe.
- Optic disk swelling.
- Neurotropic keratitis after damage to the ophthalmic branch of cranial nerve V.
- Fever and malaise—with orbital abscess or cellulitis.
- IOP—rarely high.

Enophthalmos

- Ptosis
- Third eyelid protrusion
- Extraocular muscle atrophy
- Entropion—with severe disease

Strabismus

- Deviation of one or both eyes from the normal position
- May note exophthalmos or enophthalmos

CAUSES

Exophthalmos

- Neoplasm—primary or secondary.
- Abscess or cellulitis—bacterial or fungal; fungal more likely in cats; look for foreign bodies.
- Zygomatic mucocele—not described in cats.
- Myositis—muscles of mastication or extraocular muscles (eosinophilic or extraocular polymyositis).
- Orbital hemorrhage secondary to trauma.
- Arteriovenous fistula or varix—rare.

Enophthalmos

- Ocular pain.
- Microphthalmia.
- Phthisis bulbi.
- Collapsed globe.
- Horner's syndrome.
- Dehydration.
- Loss of orbital fat or muscle.
- Conformational enophthalmos in dolichocephalic breeds.
- Neoplasia—especially those originating from rostral orbit.

Strabismus

- Abnormal innervation of extraocular muscle.
- Restriction of extraocular muscle mobility by scar tissue from previous trauma or inflammation.
- Destruction of extraocular muscle attachments after proptosis.
- Convergent strabismus—congenital; results from abnormal crossing of visual fibers in the CNS (Siamese cats).
- Shar-Pei strabismus.

RISK FACTORS

Proptosis—more readily occurs in brachycephalic dogs with shallow orbits.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Similar Signs

- Buphtalmic globe—may simulate a space-occupying mass and cause the eye to be displaced anteriorly owing to its size in relationship to the orbital volume; IOP usually high; corneal diameter is greater than normal, corneal edema, mydriatic pupil, optic nerve cupping (i.e., signs of glaucoma), blindness.
- Episcleritis—may cause severe diffuse or focal thickening of the fibrous tunic, often imitating a buphtalmic globe; corneal edema; normal or low IOP; aqueous flare.

Causes

- Acute onset of exophthalmos—often inflammatory orbital disease. Pain, especially on opening the mouth, is more likely due to inflammatory orbital disease than orbital neoplasia.
- Mucocles—more variable in speed of onset and degree of patient discomfort.
- Extraocular or eosinophilic myositis—bilateral diseases; *Neospora caninum* has caused extraocular polymyositis in a litter of German shorthaired pointers.

- Neoplasia—usually slowly progressive, not painful, unilateral exophthalmos.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal.
- Leukogram—may show inflammation with abscess or cellulitis or myositis.
- Peripheral eosinophilia—occasionally seen in dogs with eosinophilic (masticatory muscle) myositis.

IMAGING

- Orbital ultrasonography, CT, and MRI—extremely helpful in defining the extent of the lesion(s) and distinguishing between types of myositis.
- Skull radiographs (especially of the frontal sinuses and nasal cavity).
- Thoracic radiographs—may help identify metastatic disease.

DIAGNOSTIC PROCEDURES

- Lack of globe retropulsion—confirms a space-occupying mass.
- Oral examination, ocular ultrasound, and fine-needle aspiration of the orbit—may be completed after anesthetizing the patient.
- Fine-needle aspiration (18- to 20-gauge)—submit samples for aerobic and anaerobic bacterial and fungal cultures, gram staining, and cytologic examination.
- Cytology—often diagnostic for abscess or cellulitis, zygomatic salivary gland mucocele, and neoplasia.
- Biopsy—indicated if needle aspiration is non-diagnostic.
- Biopsy of masseter, temporal, or extraocular muscle if myositis suspected; assays for type 2M fibers may be helpful.
- Forced duction of the globe (strabismus)—grasp the conjunctiva with a fine pair of forceps following topical anesthesia; differentiates neurologic disease (in which the globe moves freely) from restrictive condition (in which the globe cannot be moved manually).



TREATMENT

PROPTOSIS

See Proptosis.

ORBITAL ABSCESS OR CELLULITIS

- Drainage is seen in less than half of patients, usually because the lesion is at the cellulitis stage and a true abscess has not yet formed.
- If an obvious swelling of the oral mucosa behind the last molar is not present and an ultrasound does not show an abscess, it is best to avoid incising the oral mucosa and treat with systemic antibiotics and anti-inflammatory medications; the affected globe should also be kept moist with topical lubricants q6h.
- Severe cases may require intravenous fluids to maintain hydration and replace fluid deficits until patient is able to eat.
- If a swelling of the oral mucosa behind the last molar is evident, establish ventral orbital drainage while the patient is anesthetized.
- Incise the surgically prepared mucosa approximately 1 cm behind the last

ORBITAL DISEASES (EXOPHTHALMOS, ENOPHTHALMOS, STRABISMUS)

molar. • Push a blunt-tipped forceps (e.g., Kelly or Carmalt) into the orbital space and open; in general, advance the forceps until the abscess drains, to the level of the box lock, or until movement of the eye occurs with forceps opening. • Take care to minimize retrobulbar trauma and optic nerve damage; use only blunt dissection; never cut or crush tissue. • Complications that can occur with aggressive dissection include damage to the optic nerve and ciliary nerves. • Collect samples for bacterial culture and cytologic examination through this port. • Feed soft food until globe is back in normal position and pain appears resolved. • Hot packing—q6h; helps decrease swelling and cleans discharge.

ORBITAL NEOPLASMS

- Usually primary and malignant. • Early exenteration or orbital exploratory surgery and debulking of the mass via a lateral approach to the orbit to save the globe are rational therapeutic choices. • Adjunctive chemotherapy or radiotherapy—depending on neoplasm type and extent of the lesion.
- Without adjunct therapy—survival is weeks to months if malignant because the patient is usually examined late in the course of disease.
- Consultation with an oncologist is recommended once the diagnosis is made.

ZYGOMATIC MUCOCELE

May resolve with antibiotic and corticosteroid administration; if not, surgical excision of the cyst and associated gland is usually curative.

STRABISMUS

- Neurologic—best treated by identifying the underlying cause and addressing that, if possible. • Restrictive or post-traumatic—may be treated surgically; repositioning or excising the attachments of the extraocular muscles; relieving excessive tension on those muscles; usually a very difficult procedure.



MEDICATIONS

DRUG(S) OF CHOICE

- Exophthalmos (all patients)—lubricate cornea (e.g., artificial tear ointment or gel

q6h) to prevent desiccation and ulceration.

- Ulceration—topical antibiotic (e.g., bacitracin, neomycin, polymyxin q8h) and cycloplegic (e.g., 1% atropine q12–24h), to prevent infection and reduce ciliary spasm, respectively.

Orbital Abscess or Cellulitis

- Oral or intravenous antibiotics—sodium ampicillin (20 mg/kg q6–8h) or drugs with an anaerobic spectrum (amoxicillin with clavulanic acid or metronidazole) should be considered while awaiting results of bacterial culture and cytologic examination or if client declines diagnostic testing. • Bacterial orbital infections—may be mixed; *Pasteurella multocida* and *Enterobacteriaceae* common.
- Most patients recover within approximately 2–3 weeks of treatment. • Fluconazole (2.5 mg/kg q12h or 5 mg/kg q24h) or posaconazole (5 mg/kg q12h) may be considered for orbital aspergillosis.
- Prednisone—1 mg/kg SC or IM q24h, once or twice; minimize optic neuritis and reduce orbital swelling and globe exposure.
- Alternatively, systemic NSAIDs (e.g., carprofen or meloxicam) can be used in place of prednisone but should be administered for several weeks.

Acute Myositis

- Difficult prehension—systemic corticosteroids (prednisone 2 mg/kg SC or IM); then oral corticosteroids for the following 4–6 weeks (prednisone 2 mg/kg q24h) until the swelling subsides; then taper.
- Azathioprine 1–2 mg/kg PO q24h for 3–7 days; then q48h and taper; with or without corticosteroids, may be used chronically to manage recurrent disease.

PRECAUTIONS

- Systemic corticosteroids—use with extreme caution with deep fungal orbital disease.
- Azathioprine—may be hepatotoxic and cause myelosuppression. Follow CBC platelet count and liver enzymes every 1–2 weeks for 8 weeks, then periodically thereafter.



FOLLOW-UP

PATIENT MONITORING

- Inflammatory orbital disease—examine at least weekly until clinical signs abate. • Advise client to watch for recurrence of signs, especially if an orbital foreign body is likely.
- Treat fungal infections for 60 days after signs cease.

POSSIBLE COMPLICATIONS

- Vision loss • Loss of the eye • Permanent malposition of the globe • Death



MISCELLANEOUS

AGE-RELATED FACTORS

Give a course of antibiotic therapy first prior to attempting ventral orbital drainage.

PREGNANCY/FERTILITY/BREEDING

Avoid systemic corticosteroids, antifungal medications, and azathioprine in pregnant animals.

SEE ALSO

- Proptosis • Red Eye

ABBREVIATIONS

- CNS = central nervous system • CT = computed tomography • IOP = intraocular pressure • MRI = magnetic resonance imaging • NSAID = nonsteroidal anti-inflammatory drug

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ORGANOPHOSPHORUS AND CARBAMATE TOXICOSIS



BASICS

DEFINITION

- Results from exposure to organophosphorous compounds or carbamates. Since 2003, calls to the ASPCA APCC regarding exposure to organophosphorous compounds have decreased significantly. Currently, organophosphate and carbamate exposures represent only 4.5% of insecticide-related exposure calls to the ASPCA APCC.
- The decrease is likely related to EPA cancellations of various registrations and approval of new, less toxic formulations. Canceled products, however, often remain in homes and businesses for years.
- Animal products—organophosphate: chlorpyrifos, coumaphos, cythioate, diazinon, famphur, fenthion, phosmet, and tetrachlorvinphos; carbamate: carbaryl and propoxur (*many animal products containing phosmet, tetrachlorvinphos, carbaryl, chlorpyrifos, diazinon [all] have been discontinued*).
- Agricultural, lawn, and garden products—organophosphate: acephate, chlorpyrifos, diazinon, disulfoton, fonofos, malathion, parathion, terbufos, and others; carbamate: carbofuran and methomyl (*same comment as above for environmental products*).

PATHOPHYSIOLOGY

- Cause nervous system effects by inhibiting cholinesterase, which includes acetylcholinesterase, pseudocholinesterase, and other esterases.
- Acetylcholinesterase—normally hydrolyzes the neurotransmitter acetylcholine in nervous tissue, RBCs, and muscle, resulting in termination of nervous transmission.
- Pseudocholinesterase—found in plasma, liver, pancreas, and nervous tissue, mainly in cats.
- Cholinesterase inhibition—allows acetylcholine accumulation at the post-synaptic receptor; causes stimulation of effector organs; spontaneous reactivation after organophosphorous compound binding is very slow and once aging occurs is virtually non-existent; reversible after carbamate binding.

SYSTEMS AFFECTED

Nervous—results from overriding stimulation of parasympathetic pathways; may also result from sympathetic stimulation; acetylcholine stimulates nicotinic receptors of the somatic nervous system (skeletal muscle), parasympathetic preganglionic nicotinic and post-ganglionic muscarinic receptors (cardiac muscle, pupil, blood vessels, smooth muscles in lung and gastrointestinal tract, exocrine glands), and sympathetic preganglionic nicotinic receptors (adrenal and indirectly

cardiac muscle, pupil, blood vessels, smooth muscles in lung and gastrointestinal tract, exocrine glands).

GENETICS

- Animals with inherently low cholinesterase activity—more susceptible to cholinesterase depression.
- Cholinesterase activity—more easily inhibited in cats than in dogs.

INCIDENCE/PREVALENCE

Common in small animals

GEOGRAPHIC DISTRIBUTION

More common in areas of high flea prevalence and intense agricultural activity.

SIGNALMENT

Species

- Dog and cat
- Cats most susceptible

Breed Predilections

Lean dogs (e.g., sight hounds and racing breeds) and lean longhaired cats—more susceptible to cholinesterase inhibition because of lack of fat; many organophosphorous compounds and metabolites are stored in fat and slowly released into circulation.

Mean Age and Range

Young animals—more likely intoxicated due to lower detoxification capability.

Predominant Sex

Intact males more susceptible to some organophosphates

SIGNS

General Comments

- Parasympathetic stimulation—usually predominates.
- Sympathetic stimulation—may result in lack of specific expected signs; may note opposite signs from those expected.

Historical Findings

- Medical history—often discloses heavy or repeated applications of flea and tick insecticides; evidence of exposure to an agricultural or home and garden product.
- Carbamate insecticides (methomyl and carbofuran)—may cause rapid onset of seizures and respiratory failure and death; treat aggressively without delay.
- Organophosphate insecticides (cats, especially chlorpyrifos)—chronic anorexia, muscle weakness, and muscle twitching, with or without episodes of acute toxicosis, which may last for days to weeks.

Physical Examination Findings

- Hypersalivation
- Vomiting
- Diarrhea
- Miosis
- Bradycardia
- Depression
- Ataxia
- Muscle tremors

- Seizures
- Hyperthermia
- Dyspnea
- Respiratory failure
- Death
- Patient may not exhibit all signs
- Sympathetic stimulation—signs reversed

CAUSES

- Overuse, misuse, or use of multiple cholinesterase-inhibiting insecticides.
- Misuse of organophosphate insecticides in cats (e.g., organophosphate-containing dips labeled for dogs only, inappropriately applied to cats).
- Intentional dermal application of house or yard insecticides.

RISK FACTORS

- Concurrent exposure to multiple organophosphate- and/or carbamate-containing products.
- Exposure to floors that are damp with organophosphorous premise products.
- Incorrect dilution of insecticides.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- History of exposure, amount of exposure, and clinical signs—should be consistent with toxicosis.
- Exposure to other insecticidal products—pyrethrin/pyrethroids (flea and tick); d-limonene (citrus flea and tick); fipronil (flea and tick); imidacloprid (flea).
- Other pesticides—strychnine; fluoroacetate (1080); 4-aminopyridine (avicide); metaldehyde (snail bait); zinc/aluminum phosphide (rodenticide); bromethalin (rodenticide).
- Other toxicants—chocolate; caffeine; cocaine; amphetamine; tremorgenic mycotoxins.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

Cholinesterase Activity

- Reduced to < 25% of normal in whole blood, retina, or brain—suggests exposure to a cholinesterase-inhibiting compound, must compare to normal reference values in that species generated by the same laboratory.
- Test results—must be interpreted in context of the amount of exposure and the clinical signs and the time of their onset.
- Use laboratories experienced in handling animal samples.
- Chlorpyrifos—experimentally exposed animals may remain clinically normal with no detectable cholinesterase activity.
- Carbamate inhibition—reactivation can occur during sample transport, storage, and testing, giving false-negative results.

ORGANOPHOSPHORUS AND CARBAMATE TOXICOSIS

(CONTINUED)

DIAGNOSTIC PROCEDURES

- Atropine response test—administer atropine at preanesthetic dose 0.02 mg/kg IV. Antimuscarinic response (tachycardia, mydriasis) suggests lack of anticholinesterase exposure.
- Detection of insecticides—tissue (e.g., brain, liver, kidney, and fat); stomach contents; gastrointestinal tract; fur or hair; negative results do not rule out toxicosis.
- May find pieces of chewed containers in the gastrointestinal tract.

PATHOLOGIC FINDINGS

- Histopathologic lesions—rare, no characteristic lesions likely in acute toxicosis.
- Delayed neuropathy—not usually associated with commercially available organophosphorous compounds.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—mild signs from exposure to flea and tick collars and powders; treat by simply removing the collar or brushing excess powder from the coat.
- Inpatient—continued salivation, tremors, or dyspnea.

NURSING CARE

- Basics—stabilization; decontamination; antidotal treatment with atropine (and pralidoxime chloride for organophosphate toxicosis); supportive care.
- Control seizure activity, tremors.
- Oxygen—if necessary, until respiration returns to normal.
- Fluid therapy—may be needed in anorexic cats and dehydrated animals.
- Bathing (dermal exposure)—use hand dish-washing detergent; rinse with copious amounts of water.

ACTIVITY

N/A

DIET

Chronically anorexic cats—maintain nutritional and fluid requirements.

CLIENT EDUCATION

- Stress the importance of following insecticide label directions.
- Caution client that cats with chronic anorexia and weakness may need days to weeks of supportive care for full recovery.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

- Diazepam (0.05–1 mg/kg IV to effect) used initially for seizures. Pentobarbital

(5–15 mg/kg IV to effect) added for persistent seizure activity. Phenobarbital (3–30 mg/kg IV to effect, low dosage in cats) or propofol (3–6 mg/kg IV or 0.1 mg/kg/min CRI) can be used for refractory seizures.

- Atropine sulfate—0.2 mg/kg one-quarter IV, remaining SC, as needed; administered immediately; repeated only as needed to control life-threatening clinical signs from muscarinic stimulation.

• Pralidoxime chloride (Protopam) 10–15 mg/kg IM, SC q8–12h until recovery; discontinue after three doses if no response; reduces muscle fasciculations; most beneficial against organophosphorous insecticides when started within 24 hours of exposure; even several days after dermal exposure may stimulate anorexic cats (with or without tremors) to resume eating; if refrigerated and wrapped in foil, reconstituted bottles may be successfully used for up to 2 weeks.

Emesis

- Ingestion of liquid insecticidal solution—avoid inducing emesis; risk of aspiration because many solutions contain hydrocarbon solvents.
- Liquid solvent *not* ingested, no clinical signs, and very recent ingestion—induce emesis with 3% hydrogen peroxide (2.2 mL/kg PO to a maximum of 45 mL) after feeding a moist meal.

Activated charcoal

- Evacuation of the stomach for patient with clinical signs—gastric lavage with the patient intubated, under anesthesia, with a large-bore stomach tube; then administration of activated charcoal (2 g/kg PO) containing sorbitol as a cathartic in a water slurry.
- Diarrhea—do not administer sorbitol-containing products.

CONTRAINDICATIONS

Phenothiazine tranquilizers may potentiate organophosphate toxicosis.

PRECAUTIONS

Atropine—avoid overuse; may cause tachycardia, CNS stimulation, seizures, disorientation, drowsiness, and respiratory depression.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

Monitor heart rate, respiration, and fluid and caloric intake.

PREVENTION/AVOIDANCE

- Closely follow directions on insecticide labels.

- Avoid use on sick or debilitated animals.
- Avoid simultaneous use of organophosphate and carbamate products.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

- Chronic organophosphate insecticide-induced weakness and anorexia (cats, chlorpyrifos exposure)—may last 2–4 weeks; most patients fully recover with aggressive nursing care.
- Acute toxicosis treated promptly—good prognosis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

Young animals have lower detoxification ability

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

Poisoning (Intoxication) Therapy

ABBREVIATIONS

- ASPCA APCC = American Society for the Prevention of Cruelty to Animals Animal Poison Control Center
- CNS = central nervous system
- RBC = red blood cell

Suggested Reading

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Client Education Handout
available online

ORONASAL FISTULA



BASICS

OVERVIEW

- A defect between the oral and nasal cavity.
- Communication between the mouth and nasal cavity can occur from pathology of any of the tissues surrounding the maxillary teeth or hard palate.
- The maxillary canines are most commonly involved.
- The palatal root of the maxillary fourth premolar is the next most common area involved.

SIGNALMENT

- Dogs—dolichocephalic head types are affected most often, especially dachshunds.
- Cats—rare

SIGNS

- Chronic rhinitis—with or without blood.
- Sneezing—common, especially when the maxillary canines are digitally palpated.

CAUSES & RISK FACTORS

- Usually associated with advanced -periodontitis (PD4) of the maxillary canine tooth leading to destruction of the bone separating the nasal and oral cavities.
- Other causes include trauma, penetration of a foreign body, bite wounds, traumatic tooth extraction, electrical shock, or oral cancer.
- Fistula width is related to the size of the tooth affected; fistula depth to the chronicity of the periodontal infection.
- Dogs with uncorrected lingually displaced (base-narrow) mandibular canines and those with marked mandibular distocclusion (overbite) causing the mandibular canines to penetrate the hard palate are predisposed.
- Dachshunds predisposed.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Periodontal disease
- Oral neoplasia
- Trauma
- Foreign body penetration

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

- Skull radiographs rarely helpful in diagnosing oronasal fistula because the lesions are generally isolated to the palatal surface.
- Intraoral radiographs are highly recommended to evaluate the periodontal status of the patient's teeth.
- Radiographs may show foreign body entrapment or lysis consistent with neoplasia.

DIAGNOSTIC PROCEDURES

Periodontal probing—results in direct extension into the nasal cavity or epistaxis.



TREATMENT

- Extract the tooth and close the defect; after extraction, the goal of surgical closure is to place an epithelial layer in both the oral and nasal cavities.
- Full-thickness flap—after tooth extraction, a mucoperiosteal pedicle flap may be elevated from the dorsal aspect of the fistula, released, advanced to cover the defect, and sutured in place; a successful full-thickness flap requires at least 2 mm attached gingiva above the defect, sutures at the edge of the defect (not over the void), without tension on the suture line.
- Double reposition flap—used for large fistulas or repair failures where no attached gingiva remains or where periosteal tissue cannot be included; after extraction, the first flap is harvested from the hard palate and inverted so that the oral epithelium is toward the nasal passage; the second flap is mucobuccal and harvested from the alveolar mucosa and underside of the lip rostral to the fistula; it is sutured over the first flap and donor site.
- Guided tissue regeneration of the maxillary canine—may be used for repair of a deep palatal pocket if not yet fistulated; a palatal flap is elevated to approach the infrabony defect; soft tissue and calculus are removed from the defect with a curette.
- In deep infrabony pockets before fistulation, bone grafts such as PerioGlas, Consil, synthetic and natural hydroxyapatite, autogenous and heterologous bone, polylactic

acid, and Osteoallograft, (freeze dried canine cadaver bone) have been used to exclude regrowth of gingival connective tissue and epithelium, promoting regeneration of bone and periodontal ligament. Implant materials should not be used if an oronasal fistula is present.

- Oronasal fistulas located in the central portion of the hard palate may be surgically repaired with a transposition flap of the hard palate mucoperiosteum from tissue adjacent to the defect.



MEDICATIONS

DRUG(S)

N/A

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

Normal postoperative monitoring

EXPECTED COURSE AND PROGNOSIS

Even with adequate tissue, excellent release of tension on the flap, and good technique, a persistent opening may occur due to constant tension on the site during each breath. With inadequate tissue or technique, the prognosis decreases, and additional surgeries with advanced flaps may be required.



MISCELLANEOUS

INTERNET RESOURCES

<http://www.avdc.org/Nomenclature.html>

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Author Jan Bellows

Consulting Editor Heidi B. Lobprise

OSTEOCHONDRODYSPLASIA



BASICS

OVERVIEW

- A developmental abnormality of cartilage and bone; encompasses many disorders involving bone growth.
- Results from abnormal endochondral ossification.
- Skeletal defects—usually involve the appendicular skeleton; specifically the metaphyseal growth plates.
- Achondroplasia—failure of cartilage growth; characterized by a proportionate short-limbed dysplasia; evident soon after birth.
- Hypochondroplasia—less severe form of achondroplasia.
- Characteristic breeds—result of selection of certain desirable traits.
- Affects musculoskeletal and possibly ophthalmic systems.

SIGNALMENT

- Achondroplastic breeds—bulldog; Boston terrier; pug; Pekingese; Japanese spaniel; shih tzu.
- Hypochondroplastic breeds—dachshund; basset hound; beagle; Welsh corgi; Dandie Dinmont terrier; Scottish terrier; Skye terrier.
- Reported non-selected chondrodysplastic abnormalities—Alaskan malamute; Samoyed; Labrador retriever; English pointer; Norwegian elkhound; Great Pyrenees; cocker spaniel; Scottish terrier; Scottish deerhound; beagle; miniature poodle; French bulldog; Scottish fold cat.
- Ocular-skeletal dysplasia—diagnosed in Labrador retriever and Samoyed.

SIGNS

Historical Findings

- Phenotypically normal at birth, retardation of growth recognized in first few months of life.

Physical Examination Findings

- Usually affects the appendicular skeleton; may affect axial skeleton.
- Long bones—appear shorter than normal; often bowed.
- Major joints (elbow, stifle, carpus, tarsus)—appear enlarged.
- Radius and ulna—often severely affected owing to asynchronous growth.
- Lateral bowing of the forelimbs.
- Enlarged carpal joints.
- Valgus deformity of the paws.
- Shortened maxilla—relative mandibular prognathism.
- Spinal deviations—due to hemivertebrae.
- Retina—dysplasia; partial to complete detachment.

CAUSES & RISK FACTORS

- Achondroplastic and hypochondroplastic breeds—autosomal dominant trait.
- Nonselected chondrodysplastic breeds—autosomal recessive or polygenic trait.
- Littermates often affected.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Premature closure of the ulnar or radial physes—history of trauma; no other bones affected; unilateral or bilateral abnormalities.
- Pituitary dwarfism.

IMAGING

- Radiography of affected limbs—irregular flattening of the metaphysis; widening of the physal line; retained endochondral cores; irregularities in ossification of the affected long bone; degenerative joint disease and joint laxity owing to abnormal stress and weight-bearing on the limbs.
- Radiography of the spine—hemivertebrae; wedge-shaped vertebrae.

DIAGNOSTIC PROCEDURES

Bone biopsy of growth plate—definitive diagnosis

PATHOLOGIC FINDINGS

Histologic findings: disorganization of the proliferative zone, abnormalities within the hypertrophic zone, abnormal formation of the primary and secondary spongiosa.



TREATMENT

- Achondroplasia—considered a normal abnormality in some (chondrolystrophic) breeds.
- Surgery—usually of little benefit for non-selected chondrodysplasia.
- Corrective osteotomy to realign limb(s) or joint(s)—may have limited benefit.



MEDICATIONS

DRUG(S)

- Analgesics and anti-inflammatory agents—palliative use warranted.
 - Deracoxib (1–2 mg/kg PO q24h).
 - Carprofen (2.2 mg/kg PO q12h or q24h).
 - Etodolac (10–15 mg/kg PO q24h).
 - Meloxicam (load 0.2 mg/kg PO, then 0.1 mg/kg PO q24h—liquid).
 - Firocoxib (5 mg/kg PO q24h).
 - Tepoxalin (load 20 mg/kg, then 10 mg/kg PO q24h).
 - Tramadol (1–4 mg/kg PO q8–12h).
- Chondroprotective agents—polysulfated glycosaminoglycans, glucosamine, and chondroitin sulfate; may have limited benefit in preventing articular cartilage changes.



FOLLOW-UP

PREVENTION/AVOIDANCE

- Do not repeat dam-sire breedings that resulted in affected offspring.
- Discourage breeding affected animals.

POSSIBLE COMPLICATIONS

Intra-articular and periarticular joint structures—degenerate owing to abnormal conformation of the appendicular skeleton; leads to altered biomechanics; results in poor quality of life.

EXPECTED COURSE AND PROGNOSIS

Depends on severity



MISCELLANEOUS

SYNONYMS

- Cherubism • Dwarfism

ABBREVIATION

NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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OSTEOCHONDROSIS



BASICS

DEFINITION

A pathologic process in growing cartilage, primarily characterized by a disturbance of endochondral ossification that leads to excessive retention of cartilage.

PATHOPHYSIOLOGY

- Cells of the immature articular joint cartilage and growth plates do not differentiate normally.
- For articular cartilage, the process of endochondral ossification is retarded, presumably due to localized, focal disruption of blood supply. If blood supply is reestablished, healing occurs. Alternatively, if blood supply is not reestablished, cartilage remains thick and there is separation between the cartilage and subchondral bone. Eventually a fissure occurs through the articular cartilage that allows communication with the joint cavity. The result is creation of a cartilage flap that is separated from the underlying subchondral bone; this condition is known as osteochondritis dissecans.
- Bilateral disease common.
- Most commonly affected joints—shoulder (caudocranial humeral head); elbow (medial aspect of the humeral condyle); stifle (femoral condyle: lateral more often than medial); hock (ridge of the talus: medial more common than lateral).
- Other reported locations—femoral head; dorsal rim of the acetabulum; glenoid cavity (scapula); patella; distal radius; medial malleolus; cranial end plate of the sacrum; vertebral articular facets; cervical vertebrae.

Immature Joint Cartilage

- Thickened cartilage results in impaired metabolism, leading to degeneration and necrosis of the poorly supplied cells.
- Fissure within the thickened cartilage—may result from mechanical stress; eventually leads to the formation of a cartilage flap or OCD; may cause lameness.
- Lameness (pain)—usually becomes evident once osteochondritis dissecans develops; osteochondrosis is often asymptomatic.

Retention of Cartilage in Growth Plates

- Usually does not lead to necrosis, probably owing to nutrition provided by vessels within the cartilage.
- Failure of endochondral ossification can lead to decreased longitudinal bone growth. When this is severe and occurs in the distal ulnar physis, angular limb deformity may result.

SYSTEMS AFFECTED

Musculoskeletal

GENETICS

- Polygenic transmission—expression determined by an interaction of genetic and environmental factors.

- Heritability index—depends on breed; 0.25–0.45.

INCIDENCE/PREVALENCE

Frequent and serious problem in many dog breeds

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

- Dog

Breed Predilections

Large and giant breeds—Great Dane, Labrador retriever, Newfoundland, Rottweiler, Bernese mountain dog, English setter, Old English sheepdog.

Mean Age and Range

- Onset of clinical signs—typically 4–8 months
- Diagnosis—generally 4–18 months
- Symptoms of secondary DJD—any age

Predominant Sex

- Shoulder—males (2:1)
- Elbow, stifle, and hock—none

SIGNS

General Comments

Depend on the affected joint(s) and concurrent DJD.

Historical Findings

Lameness—most common; sudden or insidious in onset; one or more limbs; becomes worse after exercise; duration of several weeks to months; slight, moderate, or severe.

Physical Examination Findings

- Pain—usually elicited on palpation by flexing, extending, or rotating the involved joint.
- Generally a weight-bearing lameness.
- Joint effusion with capsular distention—common with OCD of elbow, stifle, and hock.
- Muscle atrophy—consistent finding with chronic lameness.
- Hock OCD—hyperextension of the tarsocrural joint.

CAUSES

- Developmental
- Nutritional

RISK FACTORS

- Diet containing three times the recommended calcium levels
- Rapid growth and weight gain
- Overfeeding



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Soft tissue trauma
- Intra-articular (osteochondral) fractures

- Elbow dysplasia

- Panosteitis

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

Radiography

- Standard craniocaudal and mediolateral views—necessary for all involved joints.
- Failure of normal endochondral ossification results in radiolucency. Thus the normal bone contour is lost, which radiographically appears as flattening of the subchondral bone or as a subchondral lucency.
- Cannot be differentiated from OCD on plain radiographs unless the cartilage flap is mineralized.
- Sclerosis of the underlying bone—common in chronic OCD lesions;
- Calcified bodies within the joint (joint mice)—indicate dislodged cartilage flap.
- Contralateral joint—comparison; check for involvement.
- Oblique views—may improve visualization, especially for hock, elbow, and shoulder lesions.
- Skyline views of the talar ridges of the hock joint—help identify medial and lateral lesions.

CT and MRI

Useful for visualizing extent of subchondral lesions. Magnetic resonance imaging is the most accurate method of detecting OC/OCD lesions, flaps, and fragments.

Ultrasonography

Can be used to detect lesions, but is very operator dependent and is the least accurate diagnostic imaging method.

Positive Contrast Arthrography

Useful for differentiating from OCD of the shoulder.

DIAGNOSTIC PROCEDURES

- Diagnosis most frequently made based on physical examination and diagnostic imaging.
- Joint tap and analysis of synovial fluid—confirms involvement; should note straw-colored fluid with normal to decreased viscosity; from cytology, should note > 90% mononuclear cells. Not specific for osteochondrosis.
- Arthroscopy—minimally invasive; excellent method for differentiating from OCD and for corrective treatment.

PATHOLOGIC FINDINGS

- Articular cartilage—initially may appear yellowish.
- Retention of articular cartilage extending into subchondral bone surrounded by increased amount of trabecular bone.
- Clefts between the underlying subchondral bone and the degenerated and necrotic deep layer of the overlying thickened (retained) cartilage.

OSTEOCHONDROSIS

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

N/A

NURSING CARE

- Cryotherapy (ice packing) of affected joint—immediately post-surgery; 5–10 minutes q8h for 3–5 days.
- Range-of-motion exercises—initiated as soon as patient can tolerate.

ACTIVITY

- Restricted.
- Avoid hard concussive activities (e.g., running on concrete).

DIET

Weight control—important for decreasing load and, therefore, the stress on the affected joint(s).

CLIENT EDUCATION

- Discuss the heritability of the disease.
- Warn client that DJD may develop.
- Discuss the influence of excessive intake of nutrients that promote rapid growth.

SURGICAL CONSIDERATIONS

- Osteochondrosis of articular cartilage is generally a nonsurgical condition..
- May progress to OCD as the patient grows. If OCD develops, surgery is generally recommended.
- Surgery is performed by arthrotomy or arthroscopy, and is indicated for most OCD patients.
- Surgical treatment usually involves removal of the cartilage flap.
- Osteochondral autografts have been described for treatment of OCD of the caudal humeral head, medial aspect of the humeral condyle, and femoral condyles. Benefit beyond surgical debridement by flap removal requires further investigation.
- Shoulder—indicated for all OCD lesions; exploratory procedure indicated for pain and lameness with radiographic evidence of osteochondrosis.
- Elbow—indicated for all OCD lesions; indicated to assess for other conditions (see Elbow Dysplasia).
- Stifle—controversial; patients develop DJD even with procedure; arthroscopy may improve the recovery rate and long-term function.
- Hock—remove osteochondral flap; controversial; all patients develop severe DJD even with procedure. Arthrodesis is considered an option for patients with severe disease.
- Sacrum—remove fragment if impinging on the cauda equina.



MEDICATIONS

DRUG(S) OF CHOICE

Anti-inflammatory drugs (NSAIDs) and analgesics—may be used to symptomatically treat DJD associated with OCD; does not promote healing of the cartilage flap (thus surgery is still indicated).

CONTRAINDICATIONS

Avoid corticosteroids owing to potential side effects and articular cartilage damage associated with long-term use.

PRECAUTIONS

NSAIDs—gastrointestinal irritation may preclude their use.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Chondroprotective drugs (e.g., polysulfated glycosaminoglycans, glucosamine, and chondroitin sulfate)—may help limit cartilage damage and degeneration; may help alleviate pain and inflammation.



FOLLOW-UP

PATIENT MONITORING

- Periodic monitoring until patient is skeletally mature—recommended to assess progression to an OCD lesion.
- Post-surgery for OCD—limit activity for 4–6 weeks; encourage early, active movement of the affected joint(s).
- Yearly examinations—recommended to assess progression of DJD.

PREVENTION/AVOIDANCE

- Discourage breeding of patients.
- Do not repeat dam-sire breedings that resulted in affected offspring.
- Restricted weight gain and growth in young dogs—may decrease incidence.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

- Shoulder—good to excellent prognosis for return to full function; minimal osteoarthritis development with OC and after OCD surgery.
- Elbow, stifle, and hock—fair prognosis for OC, guarded for OCD; depends on size of lesion (most important), DJD, and age at diagnosis and treatment; progressive osteoarthritis development, even after surgery.
- Sacrum—good after fragment removal.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

Elbow Dysplasia

ABBREVIATIONS

- CT = computed tomography
- DJD = degenerative joint disease
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug
- OC = osteochondrosis
- OCD = osteochondritis dissecans

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Client Education Handout
available online

OSTEOMYELITIS



BASICS

DEFINITION

Acute or chronic inflammation of cortical bone, endosteum, periosteum, medullary cavity and vascular channels that is usually caused by bacteria. Less common causes include fungi, parasites, viruses, foreign bodies and corrosion of metallic implants.

PATOPHYSIOLOGY

- Extension of soft tissue infections to bone—uncommon in small animals.
- Hematogenously disseminated microorganisms—from infectious foci at a distant site in the body. Bacteria localize in the metaphyseal region of long bones in young animals and vertebrae of adults. Inflammation and thrombus formation produce an ischemic environment that promotes bacterial proliferation. Mycotic infections are often due to hematogenous dissemination of inhaled spores.
- Direct inoculation of bone with pathogenic bacteria (post-traumatic)—most common route of infection. May not initiate infection unless local tissue environmental factors are affected e.g. poor vascularity due to concurrent soft tissue injury or fracture instability, necrotic bone or soft tissue, sequestration, altered tissue defenses or systemic immune response, foreign material, or surgical implants. Diminished blood supply allows for potentiation of infection as neither inflammatory cells nor antimicrobials gain access to the site of infection.
- Bacteria produce a matrix of exopolysaccharides (glycocalyx) that together with host-derived proteins and cellular debris forms a biofilm that protects bacteria from phagocytes, antibacterials and antibodies. Bacterial adherence to implants and sequestra and biofilm protection allow reinfection once antibiotic therapy is stopped.
- Resorption of bone due to infection and instability causes widening of the fracture gap and implant loosening, contributing to persistence of infection and inhibiting revascularization.

SYSTEMS AFFECTED

Musculoskeletal

GENETICS

Breeds with heritable immunodeficiency or hematogenous diseases

INCIDENCE/PREVALENCE

- Hematogenous disease—rare. • Prevalence of fracture-associated osteomyelitis—radius/ulna 41.5%; femur 28.5%.
- Discospondylitis in adult dogs and cats and fungal disease—not uncommon.

GEOGRAPHIC DISTRIBUTION

- Actinomycosis—grass awns contaminated by passage through mucous membranes or gastrointestinal tract usually cause soft tissue infections. Osteomyelitis may be an extension

of soft tissue infection. • Blastomycosis—central and eastern regions of the United States: Great Lakes region and the Mississippi and Ohio river valleys; Canadian provinces of Quebec, Manitoba and Ontario.

- Coccidioidomycosis—southwestern United States, Mexico, and Central and South America. • Histoplasmosis—Ohio, Missouri, and Mississippi river valleys and tributaries.

SIGNALMENT

Species

Dog and cat

Breed Predilections

Breeds with immunodeficiency and hematogenous diseases

Mean Age and Range

Hematogenous metaphyseal infection—young dogs

Predominant Sex

Male dogs—for post-traumatic infection; blastomycosis

SIGNS

General Comments

- Acute postoperative wound infections after orthopedic surgery—may be indistinguishable from acute condition; may progress to chronic disease.
- Most patients have chronic disease at time of examination and diagnosis.

Historical Findings

- Lameness.
- Draining tracts.
- Previous trauma.
- Fracture or surgery—posttraumatic disease.
- Hind limb weakness and difficulty in rising—discospondylitis or vertebral osteomyelitis.
- Travel to regions endemic for mycotic infections—fungal infection.

Physical Examination Findings

- Acute hematogenous disease (dogs)—sudden onset of systemic illness; soft tissue swelling over affected site; lameness; pyrexia; lethargy; limb pain.
- Chronic condition—localized disease, usually no systemic component; chronic draining tracts, pain, muscle atrophy, muscle contracture.
- Non-union fracture with concurrent infection—instability, crepitus, limb deformity.
- Fungal infections—limb swelling, lameness, and intermittently draining tracts.
- Bone infections of the spine—pain and neurologic deficits.

CAUSES

- Open fracture.
- Traumatic injury.
- Open reduction and internal fixation of closed fracture.
- Elective orthopedic surgery.
- Prosthetic joint implant.
- Gunshot wound.
- Penetrating foreign body.
- Bite and claw wounds.
- Extension to bone of soft tissue infection—periodontitis; rhinitis; otitis media; paronychia.
- Hematogenous infection.
- *Staphylococcus* spp. reported in up to 60% of bone infections, usually *S. intermedius*; often monomicrobial infection. Polymicrobial bone infections are common—may include Gram-negative

aerobes: *E. coli*, *Pseudomonas*, *Proteus*, and *Klebsiella* spp.

- Anaerobic bacterial isolates can be as high as 70% and include *Actinomyces*, *Clostridium*, *Peptostreptococcus*, *Bacteroides*, and *Fusobacterium*.
- Fungal infection generally results from hematogenous spread—*Coccidioides immitis*, *Blastomyces dermatitidis*, *Histoplasma capsulatum*, *Cryptococcus neoformans*, *Aspergillus*.

RISK FACTORS

- Open fracture and bone contamination
- Soft tissue trauma
- Penetrating wounds
- Migrating foreign body
- Orthopedic surgery/implants
- Cortical bone allograft
- Immunodeficiency
- Nosocomial infection



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Panosteitis
- Neoplasia
- Bone cysts
- Delayed fracture union due to instability
- Hypertrophic osteodystrophy
- Hypertrophic osteopathy
- Medullary bone infarction

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram—inflammatory left shift with acute disease
- Fungal hyphae may be present in the urine of systemically ill patients with aspergillosis.

OTHER LABORATORY TESTS

- Serology—confirms some fungal infections.
- Blood cultures in dogs with suspected hematogenous infection.
- Urine excretion of antigen for blastomycosis.

IMAGING

Radiology

- Acute disease—bone architecture normal; gas may be evident if anaerobic infection present.
- Chronic disease—sequestra (avascular segment of cortical bone); periosteal new bone formation; involucrum formation (reactive bone surrounding sequestrum); bone resorption—widening of fracture gaps; cortical thinning; generalized osteopenia; implant loosening.
- Fistulogram—can help identify sequestra or radiolucent foreign bodies.

Other

- Ultrasonography—localize large fluid accumulations; guide fluid sampling by needle aspiration.
- Scintigraphy—^{99m}Tc-labeled methylene diphosphonate; highly sensitive for detecting increased vascularity of bone; not specific for osteomyelitis.

DIAGNOSTIC PROCEDURES

- Fluid aspirates of fluctuant areas or Jamshidi needle tissue biopsies for aerobic and anaerobic culture—collected by sterile techniques; identify microorganisms; determine in vitro antimicrobial drug susceptibility.
- Open surgical biopsy—indicated when needle aspirates are negative

OSTEOMYELITIS

(CONTINUED)

or when debridement is necessary for treatment; culture samples of necrotic tissue, sequestra, implants, and foreign material; histopathologic examination for suspected fungal infection and to rule out neoplasia. Request special fungal stains on pathology samples. • Samples for anaerobic culture—immediately place into appropriate transport medium. Avoid culturing purulent fluid from draining tracts—results misleading as often get contaminants from skin. • Blood cultures—indicated in acute hematogenous osteomyelitis or chronic disease with septicemia. • Urine culture to rule out urinary tract infections as a source for hematogenous disease.

PATHOLOGIC FINDINGS

- Bone sequestration—virtually diagnostic.
- Inflammation and necrosis of bone and the adjacent tissues—pyogenic bacteria.
- Cytologic or histopathologic examination of smears or sections—usually leads to diagnosis of fungal infection.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—surgical debridement, drainage, culturing, irrigation, and wound management until infection begins to resolve; infected fractures (surgical stabilization).
- Outpatient—long-term oral antimicrobial drug therapy.

NURSING CARE

- Depends on severity, location, and degree of associated soft tissue injury. • Avoid pathogen contamination to other patients. • Physical therapy.

ACTIVITY

Restricted—with any danger of a pathologic fracture developing; with an unhealed fracture.

DIET

No restriction

CLIENT EDUCATION

- Warn the client about cost of treatment, likelihood of recurrence, possibility of repeated surgical intervention, and long duration of therapy. • Discuss prognosis.

SURGICAL CONSIDERATIONS

- Chronic disease—surgical debridement; sequestrectomy; establishment of drainage.
- Infected stable fracture—leave preexisting implants in place during healing. • Infected unstable fracture—remove implants; stabilize with external or internal skeletal fixation.
- Bone deficits—graft with autologous cancellous bone either acutely or after infection has abated and granulation tissue is present. • Large segmental deficits in long bones—bridge by Ilizarov technique or other bone segment transport. • Localized chronic infection—consider amputation (tail, digit, limb) or en bloc resection (sternum, thoracic

wall, mandible, maxilla) and primary wound closure. • Remove all implants after the fracture has healed; bacteria harbored by implant biofilm may lead to recurrence or be a pathogenic factor for fracture-associated sarcoma. • Muscle flap coverage of exposed bone early in the course of treatment greatly reduces contamination of bone and promotes fracture healing.



MEDICATIONS

DRUG(S) OF CHOICE

- Administer a broad-spectrum bactericidal antimicrobial intravenously for 3–5 days while awaiting culture and susceptibility results. Eventual antimicrobial should be selected based on in vitro determination of susceptibility of microorganisms; also consider possible toxicity, frequency, route of administration, and expense; most penetrate normal and infected bone well; must be given for 4–8 weeks; continue for at least 2 weeks beyond radiographic and clinical resolution of infection. • Staphylococci (dogs)—usually *S. intermedius*, are resistant to penicillin because of β -lactamase production; highly susceptible to cloxacillin, amoxicillin-clavulanate, cefazolin, and clindamycin.
- Antibiotics effective against anaerobes that are also available for parenteral administration: ampicillin sodium, metronidazole, and clindamycin.
- Aminoglycosides and quinolones (ciprofloxacin and enrofloxacin)—effective against gram-negative aerobic bacteria.
- Quinolones—may give orally; not nephrotoxic; to protect against resistance, use only for infections caused by gram-negative organisms or *Pseudomonas* that are resistant to other oral antimicrobial drugs. • Chronic disease—continuous local delivery of antimicrobial drugs by antibiotic-impregnated methylmethacrylate beads or biodegradable substances. • Fungal osteomyelitis—long-term therapy (months); treat at least a month beyond resolution of clinical signs; e.g., itraconazole 5–10 mg/kg PO q24h; given continuously may control disseminated aspergillosis long-term.
- Analgesics—injectable narcotics and/or nonsteroidal anti-inflammatory drugs are important to encourage limb use.

CONTRAINDICATIONS

Quinolones—avoid in immature dogs; potential for cartilage injury.

PRECAUTIONS

Aminoglycosides—may cause nephrotoxicity, especially in dehydrated patients and with electrolyte losses or preexisting renal disease.

ALTERNATIVE DRUG(S)

Identify other antimicrobial drugs by repeating cultures and susceptibility

determination if the infection becomes unresponsive to the initial agent.



FOLLOW-UP

PATIENT MONITORING

- Radiography—2–3 weeks after intervention and then sequentially as needed to monitor bone healing (every 4–6 weeks). • Reculture bone—suspected persistent infection.

POSSIBLE COMPLICATIONS

- Recurrence. • Progression to chronic disease. • Malignant neoplasia—rare sequela to chronic infection of fractures repaired by internal fixation.

EXPECTED COURSE AND PROGNOSIS

- Favorable response to treatment in 90% of affected dogs; recurrence is possible, particularly with chronic infections. • Acute infection and chronic bacterial discospondylitis—may be cured by 4–8 weeks of antimicrobial drug therapy if there is limited bone necrosis and no fracture.
- Chronic disease—resolution with antimicrobial drug therapy alone unlikely; provide appropriate surgical treatment.
- Recurrence of chronic infection weeks, months, or years after the last treatment may require repeated sequestrectomy. • Consider amputation in severe chronic cases with irreversible loss of limb function.



MISCELLANEOUS

SYNONYM

Bone infection

SEE ALSO

Discospondylitis

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Client Education Handout
available online



BASICS

DEFINITION

Osteosarcoma (OS) is a cancer derived from malignant osteoblast or stem cell, and is the most common primary bone tumor in dogs. Large to giant breed dogs most commonly develop appendicular OS, while axial OS can also affect smaller breeds. The biologic behavior of this neoplasm is malignant, with presumed microscopic lung metastases present in $\geq 85\%$ of dogs at diagnosis. This disease is less common in cats, and the biologic behavior in this species is less malignant than in dogs.

PATOPHYSIOLOGY

Genetic predisposition is likely a major contributor for the development of OS. Other factors contributing to OS development include chronic inflammation associated with metallic implants, history of prior radiation therapy to the site of tumorigenesis, and rapid bone turnover, all associated with the development of OS in dogs.

SYSTEMS AFFECTED

- Musculoskeletal—the appendicular skeleton (metaphyseal region of long bones) is most commonly affected in dogs. OS may also occur in the axial skeleton.
- Respiratory—this neoplasm metastasizes through a hematogenous route; the most common metastatic site is the lung parenchyma; however, other sites include bones, regional lymph node, skin, and visceral organs (liver, kidney).

GENETICS

There is a strong breed predilection, with some degree of heritability being identified in giant breeds such as Scottish deerhound, rottweiler, golden retriever, and Irish wolfhound.

INCIDENCE/PREVALENCE

- Dogs—OS accounts for up to 85% of primary bone tumors in dogs, representing $\sim 5\%$ of all reported malignancies in dogs.
- Cats—OS is the most common primary bone tumor in cats, accounting for $< 7\%$ of all reported cancers in this species.

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Dogs—large to giant breed
- Cats—domestic shorthair cats

Mean Age and Range

- Dogs—bimodal peak at 2 years and 7 years, reported to occur as young as 6 months
- Cats—average age of 8.5 years, range of 4–18 years

Predominant Sex

Dogs and cats—no strong sex predilection

SIGNS

General Comments

- Because OS occurs most commonly in the appendicular skeleton of dogs and cats, lameness and pain are common clinical findings.
- Clinical symptoms associated with OS affecting the axial skeleton can be variable depending upon the anatomic site involved.

Historical Findings

- Lameness (acute or chronic) is the most common problem.
- Signs of axial skeletal OS vary, depending on the site of the lesion.

Physical Examination Findings

- A firm, painful swelling of the affected site is common with axial skeletal OS.
- Degree of lameness varies from mild to non-weight-bearing.
- Animals can present with a pathologic fracture.
- Soft tissue swelling secondary to tumor infiltration and hemorrhage may be observed.

CAUSES

Unknown in both species

RISK FACTORS

- Dogs—large- to giant-breed dogs at greater risk
- Neutering at an early age
- Metallic implants at fracture repair sites
- History of exposure to ionizing radiation
- Cats—unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other primary bone tumor (i.e., fibrosarcoma, chondrosarcoma)
- Metastatic bone tumor (i.e., prostatic, mammary, other carcinoma)
- Infectious (i.e., fungal or bacterial osteomyelitis)

CBC/BIOCHEMISTRY/URINALYSIS

Elevated alkaline phosphatase is a poor prognostic factor.

IMAGING

Radiography of Primary Site

- At least two views of the primary lesion should be made (i.e., anterior-posterior and a lateral for appendicular sites).
- Typical findings include mixed osteolytic/osteoproducing effects involving the metaphyseal region of long bones.
- Soft tissue swelling overlying diseased bone.

Thoracic Radiography

- Three radiographic views of the thorax (right and left lateral and a dorsoventral view) should always be performed; although visible macroscopic metastatic disease is present in $< 10\%$ of cases at the time of presentation.
- If pulmonary metastases are identified at initial diagnosis, the prognosis is considered poor for long-term survival.
- Metastatic lesions typically appear as discrete, round, soft tissue density nodules.

Nuclear Bone Scans

Might be useful and more sensitive for identifying bony metastatic disease or contemporaneous primary lesions than plain radiography.

OTHER DIAGNOSTIC PROCEDURES

Bone Aspirate

- A relatively non-invasive, potentially high-yield procedure using an 18-gauge needle to withdraw cells from the tumor site.
- Cytologic evaluation may give a diagnosis of malignant mesenchymal neoplasia.
- Concurrent alkaline phosphatase positivity on cytology is sensitive and specific for OS diagnosis.

Bone Biopsy

- The gold standard for diagnosis.
- Performed with the patient under light general anesthesia or moderate sedation.
- Samples should be taken through the center of the lesion; peripheral biopsies are often nondiagnostic and contain reactive osteoblasts.
- Biopsy may be performed using a Michele trephine, jamshidi bone biopsy needle, or open (i.e., wedge) biopsy technique.

PATHOLOGIC FINDINGS

- Gross—mild to severe destruction of cortical bone with new bone proliferation.
- Histologic—malignant population of mesenchymal cells that are plump, polygonal to spindlyoid in shape. The finding of osteoid production is necessary and diagnostic for OS. Subclassifications such as osteoblastic, chondroblastic or telangiectatic have not consistently been shown to be prognostic. Parosteal (juxtacortical) OS is a rarely seen soft tissue variant that may have a less aggressive biologic behavior than other forms of OS.



TREATMENT

DIET

No specific dietary management is required, although weight loss may benefit amputees in general.

CLIENT EDUCATION

- Long-term prognosis is poor; however, a subpopulation (15%) of patients achieve long-term survival.
- Clients must understand that treatment goals are to relieve discomfort and prolong life; a cure is unlikely.
- Clients should be prepared for possible chemotherapy-induced side effects.

SURGICAL CONSIDERATIONS

Dogs—Appendicular Sites

- Conventional surgical management involves amputation of the affected limb (forequarter or hip disarticulation).
- Limb salvage therapy is available at a limited number of referral hospitals. This technique is appropriate only

OSTEOSARCOMA

(CONTINUED)

for locally confined and small distal radial lesions. The primary tumor is surgically removed, replaced by an allograft or metal prosthesis, and stabilized with a bone plate.

- Adjuvant chemotherapy recommended with either surgical procedure (see below).

Dogs—Axial Sites

• Depending on location, aggressive surgical excision and adjuvant chemotherapy are recommended (see below). • Mandibular OS may have a less aggressive biologic behavior than other sites; one study reported a 71% 1-year median survival time with surgery alone. However, recent studies would suggest that OS arising from the mandible is still highly metastatic and warrants treatment with adjunctive chemotherapy. • If surgical resection is not possible, palliative radiation is effective for the alleviation of osteolytic bone pain.

Cats—Appendicular Sites

- Amputation alone is considered appropriate.
- Adjuvant therapy not typically necessary.

Cats—Axial Sites

• Depending on site of lesion, aggressive surgical excision should be attempted. • Local recurrence appears to be the main reason for treatment failure. • If surgical resection is not possible, palliative radiation is effective for the alleviation of osteolytic bone pain.

Metastatectomy

• Pulmonary metastatectomy has been described for dogs with OS; however, is not routinely practiced. • Selection criteria for dogs to undergo this procedure include a long disease-free interval (> 300 days) and only 1–2 pulmonary nodules based on thoracic radiographs.

Inoperable Neoplasms

- Palliative (coarse fractionation) radiotherapy. • Stereotactic radiosurgery in combination with systemic chemotherapy and aminobisphosphonate therapy can provide prolonged survival times with acceptable pain control (10–12 months). • Pain management with nonsteroidal anti-inflammatory drugs, opioids or bisphosphonates may improve quality of life and thus prolong survival.



MEDICATIONS

DRUG(S) OF CHOICE

Definitive Therapy

- Chemotherapy with either platinum-based drugs (cisplatin or carboplatin) or doxorubicin is the current standard of care; a minimum of four doses is recommended.
- Cisplatin, carboplatin, or doxorubicin are standard of care. • Cisplatin 70 mg/m² IV q 3 weeks. Must be given with a saline induced diuresis to prevent nephrotoxicity: 18.3 mL/kg/h for 4 hours, administer

chemotherapy over 20 minutes, then continue diuresis for another 2 hours. Cisplatin will cause vomiting within 2 hours of administration. Antiemetics must be given before cisplatin, and the patient may need to be sent home with antiemetic therapy.

- Carboplatin 300 mg/m² IV q3 weeks.
- Doxorubicin 30 mg/m² IV q3 weeks for 5 doses is a less expensive option; may be used in combination with cisplatin.
- Chemotherapy is not effective against gross disease, less than 5% expected response rate.
- Chemotherapy typically initiated within 2 weeks of surgery.

CONTRAINdications

- Patients with preexisting renal dysfunction should not be treated with platinum-based chemotherapy drugs. • Do not give cisplatin to cats.

ALTERNATIVE DRUG(S)

Palliative Therapy

- Pain management must be addressed in patients whose owners decline definitive therapy. • Manage pain with nonsteroidal anti-inflammatory drugs, ± tramadol (2–5 mg/kg q8–12h), ± acetaminophen with codeine (0.5–2 mg/kg q8–12h), ± transdermal fentanyl (as per package instructions) ± gabapentin (3–10 mg/kg q8–24h). • Euthanasia when quality of life declines.



FOLLOW-UP

PATIENT MONITORING

- Monitor CBC for evidence of myelosuppression 7–14 days following chemotherapy. • Doxorubicin—periodic echocardiography and ECGs as cumulative cardiotoxicity may occur at > 180 mg/m².
- Thoracic radiographs every 2–3 months after surgery to assess for metastasis.
- Radiograph surgical site every 2–3 months to monitor for local recurrence following limb salvage.

POSSIBLE COMPLICATIONS

- Metastatic disease is very likely; sites of spread include lungs, other bones, soft tissue.
- Animals that undergo limb salvage may develop recurrent infections, local recurrence, or implant failure.

EXPECTED COURSE AND PROGNOSIS

Dogs

- Without treatment, with amputation alone, or with palliative radiotherapy alone, median survival is approximately 4 months. When conventional palliative radiotherapy is combined with intravenous aminobisphosphonates and oral analgesics, acceptable quality of life can be extended up to 6–9 months. The use of stereotactic radiosurgery in combination with

chemotherapy and aminobisphosphonates can extend survival times to 10–12 months.

- With surgery and chemotherapy, median survival is extended to a median of 10 months.

Cats

- Appendicular OS, with surgery, median survival of > 2 years. • Axial OS, with surgery, median survival of 5.5 months.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Do not breed animals that are undergoing chemotherapy.

SYNONYMS

- Osteogenic sarcoma

SEE ALSO

- Chondrosarcoma, Bone
- Fibrosarcoma, Bone
- Hemangiosarcoma, Bone

ABBREVIATIONS

- CT = computed tomography
- ECG = electrocardiogram
- OS = osteosarcoma

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Client Education Handout
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OTITIS EXTERNA AND MEDIA



BASICS

DEFINITION

- Otitis externa: inflammation of the external ear canal; includes anatomic structures of the pinna, horizontal and vertical canals, and the external wall of the tympanic membrane.
- Otitis media: inflammation of the middle ear; includes anatomic structures of the medial wall of the tympanic membrane, bulla (tympanic cavity), auditory ossicles, and auditory tube. • The terms are descriptions of clinical signs; they are not diagnoses.

PATOPHYSIOLOGY

- Otitis externa—chronic inflammation results in alterations in the environment of the canal; the normal external ear canal is lined with epithelium containing modified apocrine (cerumen) glands; with inflammation, glands enlarge and produce excessive wax; the epidermis and dermis thicken and become fibrotic; thickened canal folds effectively reduce canal width; calcification of auricular cartilage is the end-stage result.
- Otitis media—often an extension of otitis externa; frequently occurs without rupture of tympanum; can occur from polyps or neoplasia within the middle ear or auditory tube; may be caused by an increase in fluid retention within the bulla or extension of infection into the bulla.

SYSTEMS AFFECTED

- Skin/Exocrine • Nervous

GEOGRAPHIC DISTRIBUTION

Environmental humidity may predispose to infection.

SIGNALMENT

Species

Dogs and cats

Breed Predilections

- Pendulous-eared dogs—especially spaniel and retriever
- Dogs with hirsute external canals—terrier and poodle
- Stenosis of the external ear canal—Shar-Pei and bulldog
- Primary secretory otitis media—Cavalier King Charles spaniel

SIGNS

Historical Findings

- Pain—shying from touching of the head, or refusing to open the mouth.
- Head shaking.
- Scratching at the pinnae.
- Malodor from canals.
- Peripheral vestibular deficits or facial nerve deficits from extension to inner ear.

Physical Examination Findings

Otitis Externa

- Redness and swelling of the external canal, leading to stenosis.
- Scaling and exudation—may result in malodor and canal obstruction.
- Vestibular signs indicate development of otitis interna.
- Deafness from obstruction.
- Purulent and malodorous exudates.

- Inflammation, pain, pruritus and erythema of the pinnae and external canals.
- Aural hematoma.
- Palpable scarring and calcification of the auricular cartilage.
- Holding of the pinna down and/or head tilt toward the affected side (if unilateral).

Otitis Media

- Chronic otitis externa (dogs)—can result in tympanic membrane rupture (71% of cases) and otitis media (82% of cases).
- Intact tympanic membrane: bulging pars flaccida.
- Evidence of fluid and/or gas behind the pars tensa; membrane may be opaque; fluid may be purulent or hemorrhagic.
- Ruptured tympanic membrane: discharge into canal or bullae filled with debris.
- Deafness.
- Pain on palpation or opening of the mouth.
- Pharyngitis, tonsillitis, or discharge through auditory tube.
- Lymphadenopathy if severe or chronic.

CAUSES

Predisposing Causes

- Predisposing causes change the environment of the ear canal facilitating inflammation and encouraging secondary infection:
 - Abnormal or breed-related conformation of the canal restricts proper air flow—see “Breed Predilections”
 - Excessive moisture (e.g., from swimming or overzealous cleaning)
 - Topical drug reaction and irritation and trauma from abrasive cleaning techniques.
 - Underlying systemic disease produces abnormalities in the environment and ear canal immune response.
 - Obstructions—neoplasia, polyps, cerumen gland hyperplasia, and accumulation of hair; may also be a secondary event.
 - Trauma to the canal.

Primary Causes

- Primary causes directly initiate or cause inflammation within the ear canal:
 - Parasites (*otitis externa*)—*Otodectes cynotis*, *Demodex* spp., *Sarcoptes* and *Notoedres*, and *Otobius megnini*.
 - Hypersensitivities—atopy, food, contact, and systemic or local drug reaction.
 - Foreign bodies—plant awns.
 - Unilateral and persistent/recurrent otitis externa/media more suspicious of an obstruction, foreign body, or growth.
 - Keratinization disorders and increased cerumen production—functional obstruction of the ear canal.
 - Endocrinopathy.
 - Auto-immune diseases may affect the pinnae and external canal.
 - Primary secretory otitis media.

Perpetuating Causes

- Perpetuating causes prevent resolution of the inflammation and/or infection of the ear canal:
 - Chronic change: stenosis of the canal, swelling from inflammation, scarring and calcification; increased retention of debris in the ear by increased cerumen production and decreased removal by epidermal migration and physical obstruction.
 - Bacterial infection: *Staphylococcus pseudintermedius*, *Pseudomonas aeruginosa*, *Enterococcus* spp., *Proteus mirabilis*, *Streptococcus* spp.,

Corynebacteria spp., and *Escherichia coli*.

- *Pseudomonas aeruginosa* commonly cultured in otitis media.
- Fungal/yeast infection: *Malassezia pachydermatis*, *Candida albicans*, and rarely other fungi (*Sporothrix schenckii*, *Cryptococcus neoformans*).



DIAGNOSIS

CBC/BIOCHEMISTRY/URINALYSIS

May indicate a primary underlying disease.

OTHER LABORATORY TESTS

Allergy Testing

- Food-elimination diet—determine cutaneous adverse reaction to food.
- Intradermal allergy testing—atopy.

IMAGING

- Bullae radiographs: may be normal; bullae may appear cloudy if filled with exudate; thickening of bulla and petrous temporal bone with chronic disease; presence of bone lysis with osteomyelitis or neoplastic disease.
- CT or MRI: detailed evidence of fluid or tissue density in the bulla, adjacent tissues, or auditory tube.

DIAGNOSTIC PROCEDURES

- Direct- or video-otoscopy: visualization of the external canal, tympanic membrane, and bulla (if tympanum ruptured).
- Skin scrapings from pinnae: parasites.
- Skin biopsy: auto-immune disease, neoplasia, cerumen gland hyperplasia.
- Culture of exudate: useful with persistent infection; most indicated when rod bacteria seen in cytology.
- Microscopic evaluation of exudate: single most important diagnostic tool after complete examination of the ear canal; physical appearance of the exudate does not permit accurate diagnosis of the type of infection; microscopic examination is necessary.
- Infections within the canal can change with prolonged or recurrent therapy; repeat examination of exudate is required in chronic cases.
- Myringotomy: spinal needle or sterile catheter is inserted through the tympanic membrane to sample fluid within the bulla for cytologic examination and culture.

Microscopic Examination

- Preparations: examine from both canals (canal contents may differ); examine both unstained and modified Wright-stained samples.
- Mites: presumptive diagnosis.
- Type(s) of bacteria or yeast: assist in the choice of therapy as well as determine if culture is needed.
- Note findings (type of organisms; cells present) in the record; rank the number of organisms and cell types present on a standardized scale (e.g., 0–4) for treatment monitoring.
- White blood cells within the exudate: indicates active infection; systemic therapy may be required.

OTITIS EXTERNA AND MEDIA

(CONTINUED)



TREATMENT

CLIENT EDUCATION

Demonstrate proper method for cleaning and medicating ears (e.g., volume of medication to instill).

SURGICAL CONSIDERATIONS

- Indicated when the canal is severely stenotic or obstructed or when neoplasia or a polyp is diagnosed.
- Severe, unresponsive otitis media may require a bullae osteotomy or total ear canal ablation.



MEDICATIONS

DRUG(S) OF CHOICE

Cleansing Solutions

- Tympanum integrity should be assessed prior to introduction of solutions and/or medications into the external ear canal.
- Tympanum not intact: saline solution or 2.5% acetic acid (1:1 vinegar/water) rinses.
- Ceruminolytics—should not be introduced into the tympanic bulla; diethyl sodium sulfosuccinate, squaline, propylene glycol.
- Antiseptics—acetic acid or 0.2% chlorhexidine gluconate. Tris-EDTA has antibacterial and synergistic properties with certain antibiotics.
- Astringents—isopropyl alcohol, boric acid, salicylic acid.
- Anti-infective/parasiticide agents specific to identified organism(s).

Ear Flushing

- Sedation may be required.
- Gentle solutions should be used initially.
- Bulb syringe or properly trimmed French red rubber catheter is used to flush in solution and remove debris.
- Repeat cleansing at a tapering frequency during therapy.

Systemic

- Cytologic examination of exudates will help to determine type of systemic medication needed.
- Otitis media and chronic/severe otitis externa should be treated with systemic medication for at least 4–6 weeks.
- Antibiotic—should be based on culture/sensitivity if recurrent.
- Coccal bacteria—cephalexin (22 mg/kg q12h), amoxicillin trihydrate-clavulanate potassium (10–15 mg/kg q12h), and chloramphenicol (25–50 mg/kg q8–12h). Clindamycin (11 mg/kg q12–24h) for bone involvement.
- Rod bacteria—based on culture/sensitivity: fluoroquinolones: enrofloxacin (dogs, 10–20 mg/kg q12h; cats, 5 mg/kg/day), marbofloxacin (5.5 mg/kg/day); Aminoglycoside: amikacin (20 mg/kg/day).
- Antifungal—should always be used with topical antifungal therapy. Ketoconazole (5 mg/kg q12–24h), fluconazole (5–10 mg/kg q24h) and itraconazole (5 mg/kg/day).

- Anti-inflammatory—often required to reduce swelling and cerumen production: tapering dosages: prednisolone (0.5–1 mg/kg/day), dexamethasone (0.1 mg/kg/day), triamcinolone (0.1 mg/kg/day).
- Antiparasite—ivermectin (300 µg/kg SC or PO 1–2 weeks for four treatments), selamectin, moxidectin (see “Contraindications” below).

Topical

- Topical therapy paramount for resolution and control of otitis externa.
- Completely clean the external ear canal of debris.
- Continue cleanings until symptoms resolve and then routinely to maintain control.
- Apply appropriate topical medications in sufficient quantity to completely treat the entire canal.
- Ointments and lotions may be occlusive unless used judiciously.
- Antibiotic—based on cytologic evaluation, culture/sensitivity, and/or empiric choice. Gentamicin, neomycin, amikacin, enrofloxacin, and silver sulfadiazine. Also chloramphenicol and tobramycin.
- Antifungal—imidazoles: clotrimazole, ketoconazole, miconazole, thiabendazole. Also nystatin, terbinafine.
- Anti-inflammatory—corticosteroids: dexamethasone, fluocinolone, betamethasone, triamcinolone, hydrocortisone aceponate, and mometasone.
- Antiparasite—ivermectin, amitraz, and thiabendazole.

CONTRAINDICATIONS

- Ruptured tympanum—use caution with topical cleansers other than sterile saline or dilute acetic acid, and aminoglycoside antibiotics; potential for ototoxicity is a concern; controversial.
- Ivermectin—not FDA approved for use systemically; herding (dog) breeds have increased sensitivity (*MDR1/ABCB1* gene mutation) to avermectins.

PRECAUTIONS

- Use caution when cleaning the external ear canals of all animals with severe and chronic otitis externa; the tympanum can easily be ruptured.
- Post-flushing vestibular complications are more common in cats, although usually temporary; warn clients of possible complications and residual effects.

POSSIBLE INTERACTIONS

- Topical medications infrequently induce contact irritation or allergic response; reevaluate all worsening cases.
- Corticosteroid use controversial with otitis media/interna.



FOLLOW-UP

PATIENT MONITORING

Repeat exudate examinations can assist in monitoring infection.

PREVENTION/AVOIDANCE

- Routine ear cleaning by the client • Control of underlying diseases

POSSIBLE COMPLICATIONS

- Deafness, vestibular disease, cellulitis, facial nerve paralysis, progression to otitis interna, and rarely meningoencephalitis.
- Post-external ear canal flushing complications in cats (vestibular signs) are not uncommon; clients should be warned of possible residual effects.

EXPECTED COURSE AND PROGNOSIS

- Otitis externa—with proper therapy, most cases resolve in 3–4 weeks; failure to correct underlying primary cause results in recurrence.
- Perpetuating factors (e.g., stenosis of the ear canal and calcification of the auricular cartilage) will not resolve and may cause recurrence.
- Otitis media—may require 6 or more weeks of systemic antibiotics until all signs resolve and the tympanic membrane has healed.
- Osteomyelitis of petrous temporal bone and bulla may require 6–8 weeks of antibiotics.
- Vestibular signs usually improve within 2–6 weeks (often with residual symptoms).



MISCELLANEOUS

ZOONOTIC POTENTIAL

- *Sarcopes* or *Notoedres* mite infestations can cause transient pruritus and dermatitis in human beings.
- Fungal infection (dermatophytosis, sporotrichosis) possible transmission to humans.

ABBREVIATIONS

- CT = computed tomography
- EDTA = ethylene diamine tetra-acetate
- MRI = magnetic resonance imaging

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Client Education Handout
available online

OTITIS MEDIA AND INTERNA



BASICS

DEFINITION

Inflammation of the middle (otitis media) and inner (otitis interna) ears, commonly caused by bacterial infection.

PATOPHYSIOLOGY

- Media—from extension of infection of the external ear through the tympanic membrane; may extend from the oral and nasopharyngeal cavities via the Eustachian tube.
- Interna—may also result from hematogenous spread of a systemic infection.

SYSTEMS AFFECTED

Nervous

- Impaired balance—from damage to the vestibular apparatus in the inner ear or to vestibular portion of vestibulocochlear nerve.
- Nausea—from dizziness due to impaired balance.
- Hearing loss—from damage to hair cells in the cochlea or to the cochlear portion of vestibulocochlear nerve.

Ophthalmic

- Corneal ulcer—from inability to blink due to damage to facial nerve.
- Keratoconjunctivitis sicca (dry eye)—from damage to parasympathetic branch of the facial nerve that travels to the lacrimal gland.
- Horner's syndrome—from damage to sympathetic nerve in middle ear.

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Dogs.
- Cocker spaniels and other long-ear breeds.
- Poodles with chronic otitis or pharyngitis from dental disease.
- Primary secretory otitis media (PSOM) in Cavalier King Charles spaniels.

Mean Age and Range

Any age

SIGNS

General Comments

Depend on severity and extent of inflammation; range from none to those related to bulla discomfort and nervous system involvement.

Historical Findings

- Pain when opening the mouth; reluctance to chew; shaking the head; pawing at the affected ear.
- Vestibular deficits—may be persistent, transient, or episodic.
- Unilateral involvement—head tilt, leaning, veering, or rolling.
- Bilateral involvement—wide head excursions, truncal ataxia; ± deafness.

- Vomiting and nausea—may occur during the acute phase.
- Saliva and food dropping from corner of the mouth; inability to blink; ocular discharge.
- Anisocoria (smaller pupil on affected side), protrusion of the third eyelid, enophthalmos and ptosis (Horner's syndrome) may be noted.

Physical Examination Findings

- Aural erythema, discharge, and thick and stenotic canals supports otitis externa.
- Gray, dull, opaque, and bulging tympanic membrane on otoscopic examination indicates middle ear exudate.
- Dental tartar, gingivitis, tonsillitis, or pharyngitis may be associated.
- Ipsilateral mandibular lymphadenopathy may occur with severe infections.
- Pain upon mouth opening or bulla palpation.
- Corneal ulcer—from inability to blink or keratoconjunctivitis sicca.

Neurologic Examination Findings

- Unilateral damage to vestibular portion of cranial nerve VIII—ipsilateral head tilt, leaning, veering, falling, or rolling may occur.
- Nystagmus—resting or positional and rotary or horizontal, fast phase characteristically opposite the affected side, and does not change in direction.
- Vestibular strabismus—ipsilateral ventral deviation of eyeball with neck extension.
- Bilateral damage of vestibular portion of cranial nerve VIII—patient reluctant to move, may stay in a crouched posture, wide head excursions; physiologic nystagmus poor to absent.
- Facial nerve damage—ipsilateral paresis/paralysis of the ear, eyelids, lips, and nares; reduced tear production (indicated by Schirmer tear test).
- Chronic facial paralysis—contracture of the affected face caused by fibrosis of denervated muscles.
- Deficits may be bilateral.
- Sympathetic nerve damage—ipsilateral Horner's syndrome; always miosis; may also note protrusion of third eyelid, ptosis, and enophthalmos.
- Same signs in PSOM but associated with recurrent accumulation of viscous mucus in the middle ear.

CAUSES

- Bacteria—*Staphylococcus* spp., *Streptococcus* spp., *Proteus* spp., *Pseudomonas* spp., *Pasteurella* spp., and *E. coli* and obligate anaerobes.
- Yeast (*Malassezia* spp., *Candida* spp.) and *Aspergillus*.
- Mites—predispose to secondary bacterial infections.
- Foreign bodies (e.g., grass awns, foxtail awns, or spear grass in endemic areas),

trauma, polyps, tumors (e.g., fibromas, squamous cell carcinoma, ceruminous gland carcinoma, primary bone tumors).

- Iatrogenic damage during cleaning or investigation of otitis externa.

RISK FACTORS

- Recurrent otitis externa.
- Nasopharyngeal polyps and inner, middle, or outer ear neoplasia—may predispose to bacterial infection.
- Upper respiratory infection in cats and dental disease—may be linked to otitis media.
- Vigorous ear flush.
- Ear-cleaning solutions (e.g., chlorhexidine)—may be irritating to middle/inner ear; avoid if tympanum is ruptured.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Congenital vestibular anomalies—signs present from birth.
- Hypothyroidism—associated with cranial nerves VII and VIII deficits; abnormal thyroid profile supports diagnosis.
- Neoplasia and nasopharyngeal polyps—common causes of refractory and relapsing otitis media and interna; diagnosed by oral and otic exam, and imaging of the head.
- Idiopathic vestibular disease (old dogs and young to middle-aged cats), idiopathic facial paralysis, and idiopathic Horner's syndrome—diagnoses made by exclusion.
- Cryptococcus*—reported in association with peripheral vestibular disease in cats.
- Trauma—history and physical evidence of injury.
- Thiamin deficiency (cats)—bilateral central vestibular signs; history of an all-fish diet or persistent anorexia.
- Metronidazole toxicity—bilateral cerebellar involvement (vestibular portion) after high dosage or prolonged use.
- Central vestibular disease—presence of lethargy, somnolence, and other brainstem signs.

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis with left-shift may be noted.
- Globulins—may be high if chronic infection.

OTHER LABORATORY TESTS

- Blood, urine cultures—may be positive with a hematogenous source of infection.
- Low T₄, free T₄ with normal or high TSH level with hypothyroidism.

IMAGING

- Video otoscopy—detailed examination of external ear canal and tympanic membrane; membrane may appear cloudy with middle ear exudate. Helps evaluate the integrity of

OTITIS MEDIA AND INTERNA

(CONTINUED)

the tympanic membrane, obtaining samples for cytology and culture/sensitivity, and performing therapeutic lavages of the ear canal and middle ear cavity.

- Bullae radiographs—not as sensitive a test; may see thickening of the bullae and petrous temporal bone with chronic disease; may see lysis of the bone with severe cases of osteomyelitis; may be normal.
- CT or MRI—detailed evidence of fluid and soft tissue density within the middle ear and extent of involvement of adjacent structures; CT better at revealing associated bony changes; MRI better for evaluating soft tissue structures including brainstem and cerebellum.

DIAGNOSTIC PROCEDURES

- Myringotomy—insert a spinal needle (20-gauge; 2.5- to 3.5-inches) through the otoscope and tympanic membrane to aspirate middle ear fluid for cytologic examination and culture and sensitivity. Examine for bacterial and fungal causes of infection.
- BAER—test the peripheral and central auditory pathways; detect hearing loss.
- CSF analysis—if indication of intracranial extension, perform culture and sensitivity.

PATHOLOGIC FINDINGS

Purulent exudate within the middle ear cavity surrounded by a thickened bullae and microscopic evidence of degenerative neutrophils with intracellular bacteria.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—severe debilitating infection; neurologic signs.
- Outpatient—stable patients, pending further diagnostics and surgery, if indicated.

NURSING CARE

- Fluid therapy—if unable to eat or drink due to vomiting and disorientation.
- Concurrent otitis externa—culture and clean the ear; use warm normal saline if the tympanum is ruptured.

ACTIVITY

Restrict with marked vestibular signs to avoid injury.

DIET

- Vomiting from vestibulitis— withhold food and water for 12–24 hours.
- Severe disorientation—hand-feed and water small amounts frequently; sternal during feeding to avoid aspiration pneumonia.

CLIENT EDUCATION

- Inform client that most bacterial infections resolve with an early aggressive course of

long-term broad-spectrum antibiotics and do not recur.

- Warn client that relapsing signs may occur and may require surgical drainage.

SURGICAL CONSIDERATIONS

- Do not rely on severity of neurologic signs as an indication for surgical intervention.
- Surgical treatment—for patients with evidence of middle ear exudate, osteomyelitis refractory to medical management, and nasopharyngeal polyps or neoplasia.
- Bullae osteotomy—allows drainage of the middle ear cavity.
- Ablation of ear canal—when otitis media is associated with recurrent otitis externa or neoplasia.
- Cytologic examination and culture/sensitivity of middle ear effusion and histopathology of abnormal tissue at time of surgery.



MEDICATIONS

DRUG(S) OF CHOICE

- Topical water, saline or TrizEDTA-based otic antimicrobial preparations, if tympanum is ruptured; treatment specific for bacteria, yeast, or mites present.
- Antibiotics—long-term (6–8 weeks); topical and systemic antibiotics are selected on basis of culture and sensitivity, if available.
- Amoxicillin/clavulanic acid (12.5–22 mg/kg q12h PO)—good first-choice antibiotic.
- Fluoroquinolone or third-generation cephalosporin—good second alternatives or can be used in combination, if culture and sensitivity unavailable; enrofloxacin (Baytril) 5–10 mg/kg q24h (dogs), 5 mg/kg q24h (cats), or marbofloxacin (Zeniquin 5 mg/kg q24h), or cefpodoxime (Simplicef 10 mg/kg q12h); clindamycin (Cleocin 5–30 mg/kg q12h), if anaerobes are suspected.
- Antinausea preparations—meclizine (Antivert, Antrizine, Bonine, Dramamine Less Drowsy Formula): 12.5 mg PO q24h (dogs < 10 kg and cats), 25 mg PO q24h (dogs > 10 kg); or maropitant citrate (Cerenia) 1 mg/kg SC or 2 mg/kg PO q24h (dogs), 1 mg/kg SC or 1 mg/kg PO q24h (cats); or dolasetron mesylate (Anzemet) 0.6 mg/kg IV q24h (dogs, cats).

CONTRAINDICATIONS

- Ruptured tympanum or associated neurologic deficits—avoid oil-based or irritating external ear preparations (e.g., chlorhexidine) and aminoglycosides, which are toxic to inner ear structures.
- Otitis media or interna—use topical and systemic corticosteroids judiciously; may

exacerbate infection. Reserve for cases in which flushing of the ear canal is prevented by inflammation, or to treat edema associated with intracranial spread of infection.

PRECAUTIONS

Avoid vigorous external ear flush.



FOLLOW-UP

PATIENT MONITORING

Evaluate for resolution of signs after 10–14 days or sooner if the patient is deteriorating.

PREVENTION/AVOIDANCE

- Parasite control—ear mites predispose to secondary bacterial infection.

POSSIBLE COMPLICATIONS

- Residual signs associated with vestibular (head tilt) and facial nerve damage or Horner's syndrome.
- Severe middle/inner ear infections—may spread to brainstem. Clinical signs indicate central vestibular lesion, typically preceded by peripheral vestibular or middle/inner ear signs. Aggressive surgical debridement and antibiotic therapy are required.
- Osteomyelitis of the petrous temporal bone and middle ear effusion—common sequela to severe, chronic otitis externa.
- Bulla osteotomy—postoperative complications include Horner's syndrome, facial paralysis, and onset or exacerbation of vestibular dysfunction, or deafness.

EXPECTED COURSE AND PROGNOSIS

- Otitis media-interna—usually responsive to medical management; 2- to 4-month course of antibiotic to avoid relapse.
- When medical management of otitis externa is ineffective, consider lateral ear resection.
- Vestibular signs—improvement in 2–6 weeks.



MISCELLANEOUS

AGE-RELATED FACTORS

Ear mites more common in kittens and puppies.

SEE ALSO

- Facial Nerve Paresis/Paralysis
- Head Tilt
- Horner's Syndrome
- Otitis Externa and Media

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ABBREVIATIONS

- BAER = brainstem auditory evoked response
- CSF = cerebrospinal fluid
- CT = computed tomography
- MRI = magnetic resonance imaging
- PSOM = primary secretory otitis media
- T₄ = thyroxine
- TSH = thyroid stimulating hormone

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**Client Education Handout
available online**

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OVARIAN REMNANT SYNDROME



BASICS

OVERVIEW

- Ovarian remnant syndrome is the presence of behavioral and/or physical signs of an estrous cycle in a female dog or cat having previously undergone ovariohysterectomy.
- Caused by the presence of functional residual ovarian tissue.
- Ovarian remnant syndrome is reported to be responsible for 17% of all post-OHE complications.

SIGNALMENT

- Female dog and cat; more common in cat.
- No breed predisposition or geographic distribution.
- Signs of an estrous cycle usually occur months to years after OHE but can begin within days after surgery.

SIGNS

Bitches

Estrogen Influence

- Attraction of male dogs.
- Swelling of the vulva.
- Mucoid to sanguineous vaginal discharge.
- Passive interaction with male dogs.
- Flaggging.
- May allow copulation.
- Signs of proestrus last an average of 9 days; signs of estrus last an average of 9 days; average interval between signs of estrous cycles is 7 months.
- Signs are usually cyclical or periodic (i.e., q6 months).

Progesterone Influence

- Prominent vulva compared to patients with complete OHE.
- Enlargement of the uterine stump.
- Uterine stump pyometra can develop due to progesterone effect.

Queens

Estrogen Influence

- Vocalization.
- Lordosis.
- Restlessness.
- Head rubbing.
- Rolling.
- Tail deviation and treading the hind limbs.
- May allow copulation.
- Demonstrate typical behavioral signs of estrus in a cyclical (seasonally polyestrous) fashion.
- Estrus lasts 2–19 days, followed by an interestrous interval that lasts for 8–10 days unless ovulation and luteinization occurred, in which case the interestrous interval is at least 45 days.

Progesterone Influence

- Enlargement of the uterine stump.
- Uterine stump pyometra can develop due to the effects of progesterone.

CAUSES & RISK FACTORS

- Failure to remove both ovaries completely.
- No correlation with age at OHE, difficulty of surgery, obesity of patient, or experience of surgeon.
- Presence of anatomically abnormal ovarian tissue (fragmentation into the broad ligament) is possible, more common in queens.
- Supernumerary ovary (rare).
- Experimentally, functionality returns to ovarian tissue removed from its vascular supply and replaced into or onto the lateral abdominal wall, mesentery, or serosal surface.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Inflammation or infection of the genitourinary tract.
- Vaginal hemorrhage due to foreign body (grass awn).
- Trauma.
- Uterine stump granuloma secondary to local pathology (foreign body reaction to suture material or grass awn).
- Neoplasia of a remnant portion of the tubular tract (uterine stump leiomyoma or leiomyosarcoma).
- Neoplasia of an ovarian remnant (granulosa cell tumor, carcinoma, luteoma, functional teratoma).
- Neoplasia of the urinary tract (transitional cell carcinoma).
- Vascular anomalies of the genitourinary tract.
- Coagulopathy.
- Exogenous estrogen administration (as for sphincter incompetence associated with urinary incontinence).
- Exposure to human transdermal hormone replacement therapy (most commonly small lap dogs).
- Endogenous extraovarian source of estrogen: adrenal pathology (rare).

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal.
- Chronic blood loss anemia if vaginal hemorrhage is profound; uncommon unless concurrent ovarian neoplasia, follicular cysts, coagulopathy, or other systemic disease.
- Pancytopenia is possible from estrogen toxicity.
- An inflammatory leukogram and isosthenuria can occur subsequent to uterine stump pyometra.

OTHER LABORATORY TESTS

- Observation of behavioral and physical signs of estrus together with vaginal cytology and/or measurement of serum progesterone or estradiol concentrations confirming the presence of functional ovarian tissue.
- Vaginal cytology: vaginal mucosal cornification is a bioassay for elevated plasma estradiol concentrations (see Breeding, Timing).
 - Vaginal cytology (bitch): epithelial cell cornification is generally > 90% during estrus (superficial and pyknotic or anuclear cells).
 - Vaginal cytology (queen): epithelial cell cornification ranges from 10% to 40%; clearing (absence of debris and clumping of cells) occurs in 90% of smears during estrus.
- Serum progesterone (bitch): a serum progesterone concentration > 2 ng/mL (measured 1–3 weeks after behavioral estrus) is consistent with functional luteal tissue. GnRH (50 µg IM), hCG (400 IU IV), or hCG (1,000 IU “1/2 IV, 1/2 IM”) can be used to attempt to induce ovulation or luteinization for diagnostic purposes; serum progesterone concentration is measured 2–3 weeks later. Note: pathologic ovarian tissue may not be responsive to either hormone.
- Serum progesterone (queen): ovulation and/or luteinization is stimulated most commonly by coital stimulation during behavioral estrus, and serum progesterone concentration is measured 2–3 weeks later; post-stimulation serum progesterone concentrations > 2 ng/mL are consistent with adequate coital stimulation and functional luteal tissue. GnRH (25 µg IM) can be used to attempt to induce ovulation or luteinization for diagnostic purposes; serum progesterone concentration is measured 2–3 weeks later. Pathologic ovarian tissue may not be responsive.
- Serum estradiol: peak levels triggering behavioral estrus range from 20 to > 70 pg/mL; serum estradiol concentrations are confirmatory to the diagnosis of ovarian remnant syndrome based on vaginal cytology.
- Luteinizing hormone assay (Witness LH, Zoetis): the LH assay should be positive (> 1 ng/mL) in a gonadectomized dog due to lack of pituitary feedback from a gonad. When a positive result is obtained, consider repeating in 24 hours to rule out detection of the 12–24h LH surge in an intact, estrual bitch (should have representative vaginal cytology with superficial cells predominating). If both are positive, then the dog has been gonadectomized. A negative test (< 1 ng/L) is found with intact dogs unless performed at the moment of the LH surge during estrus. The assay is licensed for use in the bitch, but

(CONTINUED)

OVARIAN REMNANT SYNDROME

likely is applicable in male dogs, toms and queens, provided that the queen is exposed to 14 hours of light/day. Note: exogenous estrogen exposure in a gonadectomized dog can cause the LH to become misleadingly negative.

- Anti-müllerian hormone (AMH) testing: A positive test in a bitch > 6 months of age supports the presence of ovarian tissue (SpayCheck®; offered by multiple endocrine laboratories in cases with a negative AMH but convincing clinical evidence supporting remnant syndrome. Some investigators advise obtaining a progesterone to identify persistent luteal structures lacking AMH).
- Cytology of vulvar discharge can be suppurative if a uterine stump granuloma or pyometra exists.
- Provocative adrenal testing (pre- and post-ACTH administration).

IMAGING

Ultrasonography

- Can be used to support a diagnosis of ovarian remnant syndrome that is based on cytology and hormonal profiles.
- Remnant ovarian tissue may be visible only during the follicular phase (anechoic, cystic structures) or the luteal phase (hypo or isoechoic cystic structures).
- Ultrasonographic imaging of ectopic ovarian tissue requires technical expertise and is best accomplished with a higher frequency, linear transducer (8–10 mHz). Ovarian remnants containing follicular or luteal structures often cause distal enhancement due to their fluid content; this can be used to locate them caudolateral to the ipsilateral kidney (Web Figure 1).
- Evaluate the region dorsal to the bladder for a uterine remnant, which can enlarge under hormonal influence or with pathology. (Web Figures 2a, 2b).
- Evaluate the adrenal glands for normal size and shape. Normal canine adrenal glands are < 0.51–0.74 cm in sagittal (Web Figures 3, 4).

DIAGNOSTIC PROCEDURES

- Exploratory laparotomy—removal of residual ovarian tissue confirms and resolves the problem.
- Identification of residual ovarian tissue is facilitated by the presence of follicles or corpora lutea; schedule procedure during times of elevated progesterone or during behavioral estrus. Unlike a routine ovariohysterectomy, this laparotomy is facilitated by hormone influence.

- Histopathology—always submit visible ovarian tissue; if no visible ovarian tissue is identified, submit all residual tissue at the ovarian pedicles. This helps confirm the diagnosis and screens for malignancy. Submit revised uterine stump tissue for aerobic and anaerobic cultures and histopathology (hormone influence, inflammatory response, malignancy).



TREATMENT

- Referral to a board-certified surgeon should be considered.
- Surgical removal of residual ovarian tissue.
- Surgical removal of significantly diseased uterine stump.
- Although not curative, restricting light exposure to < 8 hours per day can suppress signs of estrus in some, but not all, cats with ovarian tissue.



MEDICATIONS

DRUG(S)

- Progestational or androgenic compounds to suppress follicular ovarian activity—not recommended because of undesirable side effects (mammary neoplasia, diabetes, undesirable behavior, hepatopathy, dermatopathy).
- Immunocontraception or GnRH agonist (Suprelorin, Peptech Animal Health Pty Limited, Australia; Virbac, Vienna) administration will offer a viable alternative or adjunctive therapy to laparotomy when perfected and commercially available in the United States.



FOLLOW-UP

POSSIBLE COMPLICATIONS

- Removal of functional luteal tissue may induce transient signs of pseudopregnancy in dogs and cats postoperatively (see False Pregnancy).
- The use of oral antiprogestin agents (cabergoline) can be considered for pseudopregnancy.

EXPECTED COURSE AND PROGNOSIS

- Successful removal of remnant ovarian tissue should result in cessation of clinical signs of estrus/diestrus.
- Adjunctive therapy for pyometra (systemic antibiotics, supportive care) as indicated.
- Adjunctive therapy for functional ovarian neoplasia as indicated.



MISCELLANEOUS

SEE ALSO

- Breeding, Timing
- False Pregnancy

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- GnRH = gonadotropin-releasing hormone
- hCG = human chorionic gonadotropin
- LH = luteinizing hormone
- OHE = ovariohysterectomy

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OVARIAN TUMORS



BASICS

OVERVIEW

- Epithelial (carcinoma), germ cell (dysgerminoma and teratoma), and sex cord stromal (granulosa cell tumor, Sertoli-Leydig cell tumor, thecoma, and luteoma) tumors.
- Dogs—rare (0.5–1.2% of tumors); 40% carcinomas, 10% germ cell, and 50% sex cord.
- Cats—rare (0.7–3.6% of tumors); 15% germ cell, and 85% sex cord.
- Metastasis common for malignant epithelial and germ cell tumors in the dog and all tumors in cats.
- Some tumors produce hormones resulting in paraneoplastic syndrome.

SIGNALMENT

- Dog and cat
- Middle-aged to old animals
- Teratoma develops in young patients

SIGNS

- Bilaterally symmetrical alopecia; pancytopenia; masculinization (hormone-secreting tumors)
- Malignant ascites or pleural effusion—occasionally
- Other signs associated with mass effects of the tumor

CAUSES & RISK FACTORS

- Intact sexual status
- Dogs: pointer, English bulldog, boxer, German shepherds and Yorkshire terrier at risk



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of abdominal effusion including vasculitis and pancreatitis.
- Other mid-abdominal masses
- Ovarian cysts, paraovarian cysts, cystic rete tubules, vascular hematomas, metastatic neoplasia

CBC/BIOCHEMISTRY/URINALYSIS

- No consistent abnormalities
- Pancytopenia in dogs with functional tumors

OTHER LABORATORY TESTS

Serum progesterone—levels > 2 mg/mL with functional tumors

IMAGING

- Abdominal radiography—may reveal unilateral or bilateral mid-abdominal mass at the caudal pole of the kidney or effusion, mineralization of tumor may be seen.
- Abdominal ultrasonography—confirm abdominal radiographic findings and provide greater certainty for the origin of mass effect.
- Advanced imaging—CT or MRI can provide detailed assessment for origin and associated tissues that might be involved in disease process.
- Thoracic radiography—may reveal distant metastasis.

DIAGNOSTIC PROCEDURES

- Cytologic evaluation of pleural or abdominal fluid—may be diagnostic for malignant effusion.
- Cytologic evaluation of tumor—tumor cells may readily implant on the body wall via fine-needle aspirate. Therefore, excisional biopsy is often recommended over fine-needle aspirate of the mass.
- Histopathologic examination—necessary for definitive diagnosis.



TREATMENT

- Ovariohysterectomy—treatment of choice for a solitary mass.
- Peritoneal transplantation during surgical removal is possible; change gloves and surgical instruments during procedure.



MEDICATIONS

DRUG(S)

- Chemotherapy—little information for dogs and cats, no standard therapy.
- Cyclophosphamide, chlorambucil, lomustine, and bleomycin—successful treatment in one patient (dog).
- Cisplatin—successful treatment reported in three dogs.

CONTRAINdications/POSSIBLE INTERACTIONS

- Cisplatin—do not use in dogs with renal disease; do not use without appropriate and concurrent diuresis; do not use in cats (fatal).
- Chemotherapy may be toxic; seek advice if unfamiliar with these agents.



FOLLOW-UP

- Abdominal and thoracic radiography—every 3 months; monitor for recurrence and metastasis.
- Ovariohysterectomy—prevention.
- Prognosis—guarded.
- Chemotherapy—has potential to lengthen survival.

ASSOCIATED CONDITIONS

- Pyometra
- Ovarian cysts
- Cystic endometrial hyperplasia
- Ovarian remnant syndrome

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OVULATORY FAILURE



BASICS

OVERVIEW

- Ovulatory failure is a breakdown in the process of the release of oocytes from follicles with resultant corpus luteum formation and progesterone production.
- Ovulatory failure may present with nymphomania or prolonged anestrus.
- Bitches with nymphomania, decreased interestrous interval, have prolonged estrogen production and may present with signs of estrogen toxicity, including dermatologic or hematologic abnormalities.

SIGNALMENT

- Intact bitch or queen of any age, but there is a greater predisposition in older females.
- Ovulatory failure is reported in 1.2% of bitches presented for breeding management.
- No reported breed predisposition for anovulation; follicular cysts reported more commonly in Malamute, German shepherd, golden retriever, Bouvier des Flandres, and Labrador retriever.
- Heritability unknown.

SIGNS

- Prolonged proestrus or estrus
- Edematous vulva
- Sanguineous vulvar discharge (bitch)
- Nymphomania
- Anestrus
- Decreased interestrous interval
- Bilaterally symmetrical alopecia (progressive, non-pruritic)
- If neoplasia: enlarged abdomen ± palpable cranial-midabdominal mass ± ascites
- If chromosome abnormality: genitalia ranges from infantile or ambiguous to normal to enlarged clitoris or os clitoris; small stature; anestrus

CAUSES & RISK FACTORS

- Failure of release of gonadotropin-releasing hormone or luteinizing hormone from the hypothalamus or pituitary, respectively.
- Failure of receptors on the follicular wall to respond to LH.
- Failure of the follicles to produce adequate estrogen to illicit a surge in GnRH.
- Functional follicular cysts: may mimic a normal estrous cycle initially, but estrus persists and ovulation does not occur.
- Immune-mediated oophoritis.
- Cachexia or obesity.
- Stress (performance, travel, kennel).
- Addison's disease.
- Cushing's disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Prolonged proestrus (up to 30 days) or estrus (up to 30 days).
- Split heat: the anovulatory cycle will be followed by a normal, fertile, ovulatory cycle in 1–8 weeks.
- Hypoluteoidism.
- Granulosa cell tumor or serous cystadenoma: ± palpable abdominal mass; enlarged ovary on ultrasound, often

with a honeycomb appearance; ± ascites; ± bilaterally symmetrical alopecia, hyperpigmentation, lichenification if endocrinologically functional.

- Ovarian senescence.
- Immune-mediated oophoritis
- Chromosomal abnormality: intersex, hermaphrodites, pseudohermaphrodites, chimeras, mosaics may develop follicles that either go on to ovulate or simply regress.
- Exogenous estrogen administration or exposure.

CBC/BIOCHEMISTRY/URINALYSIS

If estrogen toxicity exists: normochromic, normocytic anemia; thrombocytopenia; initial leukocytosis followed by leukopenia

OTHER LABORATORY TESTS

- Progesterone < 4–10 ng/mL over multiple samplings once vaginal cytology exceeds 70% anucleated superficial cells. It often hovers around 3–5 ng/mL for a prolonged period of time and never exceeds 10–12 ng/mL.
- Karyotyping is indicated in cases of suspected chromosomal abnormality.

IMAGING

• Radiology may be beneficial if an ovarian mass is present. A large soft tissue density may be noted mid-abdomen. If ascites is present, a loss of general abdominal detail or ground glass appearance may be present.

• Ultrasonography is extremely helpful to evaluate ovarian structures: multiple anechoic structures on the ovary may be considered follicles; anechoic structures > 1 cm are considered cystic; enlarged ovaries may be neoplastic; anechoic structures with thickened walls may indicate luteinization (partial or complete) of follicular structures; serial (daily) ultrasonography is necessary to document ovulation; use of color doppler to assess ovarian follicular blood flow (increased with follicles, minimal with luteal structures).

DIAGNOSTIC PROCEDURES

Exploratory laparotomy to examine the ovaries or to obtain ovarian biopsies: the ovarian bursa must be opened to visualize the ovary.



TREATMENT



MEDICATIONS

DRUG(S)

- Ovulation induction may be attempted once cytology reaches > 70% anucleated cells and follicles are > 4–5 mm (toy to small-breed canine), 5–7 mm (medium to large-breed canine), 7–10 mm (giant-breed canine), or 2–3 mm (feline).
- Ovulation-inducing agents: GnRH 1.1–2.2 µg/kg IM or IV or 25 µg/cat IM. May repeat daily for 1–3 days in bitches, single dose for queens; hCG

500–1,000 IU/dog IM or 500 IU/queen IM, may repeat in 2–3 days if ovulation does not occur; GnRH and hCG may be given concurrently; deslorelin implant (2.1 mg implant; Ovuplant®) placed in the mucosa of the vulvar lip using a lidocaine block and removed with a similar block and sharp dissection, remove implant once ovulation is documented (progesterone > 10 ng/mL); cervical stimulation in queens, may be performed starting at the time of initial induction medication and repeated several times daily for 24–48 hours.



FOLLOW-UP

- Monitoring of progesterone concentrations during pregnancy is advised as luteal failure or hypoluteoidism are more common with induced ovulation.
- Progesterone should be monitored after induction medications are administered to confirm a normal rise in progesterone.
- Serial ultrasound examinations (using color doppler) may be useful to document ovulation.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Bilaterally symmetrically non-pruritic alopecia with significantly prolonged estrus.

PREGNANCY/FERTILITY/BREEDING

- Depending on etiology, anovulation may be hereditary; discuss with owner prior to breeding.
- The cycle after an anovulatory cycle may be normal, necessitating no treatments.

SEE ALSO

- Infertility, Female—Dogs
- Sexual Development Disorders

ABBREVIATIONS

- GnRH = gonadotropin-releasing hormone
- hCG = human chorionic gonadotropin
- LH = luteinizing hormone

INTERNET RESOURCES

Concannon PW, England G, Verstegen III J, Linde-Forsberg C, eds., Recent Advances in Small Animal Reproduction. International Veterinary Information Service, Ithaca NY, www.ivis.org.

Suggested Reading

Johnston SD, Root Kustritz MV, Olson PNS. Disorders of the feline ovary. In: Canine and Feline Theriogenology. Philadelphia: Saunders, 2001, pp. 453–462.

Meyers-Wallen VN. Unusual and abnormal canine estrous cycles. Theriogenology 2007, 68:1205–1210.

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PAIN (ACUTE, CHRONIC, AND POSTOPERATIVE)



BASICS

DEFINITION

- Unpleasant sensory or emotional experience associated with actual or potential tissue damage (adaptive pain) or altered sensory neurobiology (chronic pain).
- The inability for the animal to communicate does not negate presence of pain and the need for appropriate pain-relieving treatment.

PATHOPHYSIOLOGY

- With physiologic pain, an application of a noxious stimulus activates specialized nerve endings called nociceptors; nociceptors transduce noxious chemical, mechanical, or thermal stimuli into electrochemical potentials that are transmitted via sensory nerves, from the affected tissue to the spinal cord.
- In the dorsal horn of the spinal cord, the incoming first-order peripheral nerve synapses with ascending spinal neurons, which terminate in the brainstem. Incoming noxious information can be modulated in the dorsal horn by other incoming information, descending inhibitory nerve impulses, or pharmacologic inhibition by several classes of drugs. The ascending neurons synapse in the brainstem to form ascending tracts that end in the cortex, where sensation occurs.
- Neuroendocrine and physiologic responses (e.g., tachycardia, elevated cortisol) to noxious stimuli may originate from the brainstem and do not necessarily correlate with the perceived intensity of pain.
- Nociceptive processes (i.e., transduction, transmission, and modulation) appear to be similar anatomically and physiologically in most mammalian and many non-mammalian species. The perception of pain may vary between species and individuals of the same species since anatomic differences in cortical development exist and integration of past experiences and learned behaviors varies.
- Prolonged activity in nociceptive pathways (e.g., days, weeks, or months) from chronic injury or disease, or injury to nervous system tissues, may cause altered neuroprocessing resulting in sensitization of these pathways and hyper-responsiveness. This may cause an increased response to a stimulus not normally considered noxious (allodynia).

SYSTEMS AFFECTED

- Pain may originate from any tissue, including the nervous system itself. In humans, certain pain syndromes may be associated with fear, anxiety, or depression in the absence of any observable injury.
- The physiologic response to pain can include decreased immune function, increased catabolism, and elevated neuroendocrine markers of stress. Pain can result in a loss of function of affected tissues.

GENETICS

Age, sex, breeding strain, and species can influence responses to noxious stimuli. Genes have been described that modify individual behavioral responses to noxious stimuli in several species. Genes may also be variably expressed depending on stimulus intensity and duration, which can lead to altered neuroprocessing and maladaptive or chronic pain.

INCIDENCE/PREVALENCE

- Evolutionarily, aversion to noxious stimuli was protective to organisms, keeping them away from harm.
- While acute pain is beneficial to warn or teach an animal about potential harmful objects in its environment, persistent acute pain associated with surgery or injury does not benefit the patient and should be treated appropriately.
- Any form of chronic pain syndrome does not serve a protective function and should be treated.

SIGNS

- Behavioral signs of pain and distress vary considerably among individuals.
- Experience, environment, age, species, and other factors can modify the intensity of the reaction to noxious stimuli or to an altered neurobiology associated with maladaptive or chronic pain.
- The most obvious clinical signs of distress in the dog and cat can include vocalization, agitation, abnormal posture or gait, thrashing, hyperesthesia or hyperalgesia.
- More subtle signs shared by many conditions include trembling, lethargy, reduced appetite, stupor, and biting.
- Tachypnea, tachycardia, mydriasis, and hypertension are signs observed with the stress response that may also accompany pain; these are nonspecific and present in many

non-painful conditions. The stress response is often not associated with chronic pain due to adaptation.

- Clinical signs associated with chronically painful conditions may be very subtle or difficult to evaluate since homeostatic mechanisms tend to help the animal compensate. Chronically painful conditions are often associated with decreased activity, lameness, and/or depression.

CAUSES

- Physiologic or adaptive pain can be caused by perceived or actual tissue disruption associated with trauma or surgery and also by chronic degenerative changes and inflammation associated with conditions such as osteoarthritis.
- Pain that extends beyond the initial tissue damage and healing processes is pathologic (maladaptive) and may indicate that the initiation of altered nervous system processing has occurred.

RISK FACTORS

- All animals that experience surgical or traumatic tissue damage or have recently altered behavior should be evaluated for the presence of pain.
- Due to the increasing prevalence of degenerative diseases in older patients, routine examination should include evaluation for pain.
- Pain intensity may not always correlate with the degree of tissue damage. However, more invasive soft tissue and orthopedic procedures or inflammatory disease progression in older patients are likely associated with greater pain.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Identifying pain in veterinary patients is a diagnosis, and the medical record should reflect the veterinarian's clinical diagnostic and treatment plan.
- Acute pain is almost always accompanied by tissue damage or disease, and diagnosis and treatment of the primary disorder should be done before or concomitantly with treatment of pain. The presence or absence of pain is sometimes used as a way of monitoring and diagnosing some conditions, and treatment should be in accordance with good medical

(CONTINUED)

PAIN (ACUTE, CHRONIC, AND POSTOPERATIVE)

practice. Pain should be differentiated from distress associated with other factors, such as restraint, restrictive bandaging, and separation from owners. Drugs used to treat pain, particularly opioids and dissociative anesthetics, may cause dysphoria, which often resembles and can be confused with signs of pain and distress.

CBC/BIOCHEMISTRY/URINALYSIS

- Cortisol release associated with acute pain may appear as a stress leukogram.
- Hyperglycemia may also be observed in some patients, but can also be seen with anesthesia in the absence of tissue trauma.
- Normal laboratory test values do not rule out the presence of pain.

OTHER LABORATORY TESTS

N/A

IMAGING

- Many painful patients have underlying changes in anatomic structures observable on ultrasound, radiography, computed tomography or magnetic resonance imaging.
- Chronic pathologic tissue changes such as the degree of osteophyte formation with osteoarthritis do not necessarily always correlate with the degree of pain and dysfunction experienced by the patient. Some patients can be painful without observable tissue or structural changes.

DIAGNOSTIC PROCEDURES

- Perform a thorough diagnostic evaluation for an underlying condition (e.g., ruptured cruciate ligament) when an animal appears painful. If an underlying condition is diagnosed it should be treated appropriately. Pain is most commonly caused by an underlying medical or surgical condition that when properly treated will eventually alleviate pain associated with the abnormality.
- Begin evaluation of pain with the signalment, history, and physical examination. Next, the animal's behavior is observed from a distance, and then behavior is noted during human interaction. Finally, gentle palpation of the body region of interest is performed, if necessary, to determine the animal's response.
- When analgesics are administered, the process should be repeated periodically to assess effectiveness. Do not assume administration of an analgesic will result in acceptable relief of pain.

- Complete abolition of pain may not be possible or desirable if analgesic administration results in excessive adverse effects. Therapy should aim to make pain tolerable.



TREATMENT

APPROPRIATE HEALTH CARE

- Analgesic drug selection depends on species, pain intensity, and underlying cause.
- Treat the underlying cause at the same time if possible.
- Acupuncture, prescribed activity (e.g., physical therapy), mesenchymal stromal cell or platelet-rich plasma injection, and physical manipulation (massage, trigger point manipulation, chiropractic) may be useful adjunctive treatment modalities for certain types of painful musculoskeletal conditions.
- If the patient's quality of life is not acceptable after all reasonable therapeutic options have been explored, euthanasia may be the most humane option.

NURSING CARE

- General good nursing practices.
- Non-pharmacologic, including bandaging and hydrotherapy, may be appropriate.

ACTIVITY

- Rehabilitation medicine and weight loss is a useful adjunct for some musculoskeletal conditions.
- Cage rest or limited activity may be useful for certain types of pain.

DIET

- Dietary changes to help treat the underlying condition (e.g., weight reduction for hip dysplasia) may be beneficial.
- Many supplements and nutriceuticals have been marketed that may have beneficial effects on articular cartilage or modify inflammatory disease progression.
- Commercial veterinary diets are marketed specifically for animals with mobility issues.

CLIENT EDUCATION

- When pain medication is dispensed, educate the client on what to look for with effective treatment, as well as adverse effects.
- Inform the client that analgesic effectiveness varies and several drugs may need to be tried

before an effective treatment is found. Pain management must be individualized because of the neurobiologic complexity of pain perception.

- Clients should be asked to participate in evaluation of their pet's pain, especially chronic pain. Simplified assessment tools for both acute and chronic pain in dogs and acute pain in cats are now available and can help document treatment effectiveness.

SURGICAL CONSIDERATIONS

- Surgical treatment of the underlying condition causing pain may be the best treatment in some circumstances.
- Ablative procedures (neurectomy) to halt pain transmission is not always associated with positive results and may result in worsening of the painful condition. These procedures are rarely performed in veterinary patients.



MEDICATIONS

DRUG(S) OF CHOICE (SEE APPENDIX VII)

- Opioids, alone or in combination with other classes of drugs, such as sedative/tranquilizers or NSAIDs, are widely used for the management of acute postoperative pain. Full μ -opioid receptor agonists, such as morphine, hydromorphone, and fentanyl, are usually effective for moderate to severe pain. Partial agonist or agonist-antagonist drugs, such as buprenorphine and butorphanol, are usually reserved for mild to moderate pain. Opioids generally have poor oral bioavailability, and oral doses should be adjusted accordingly. Full μ -opioid receptor agonists can be used safely in cats. However, doses are usually reduced relative to dog doses. Should dysphoria develop, tranquilization with an α_2 -agonist or acepromazine may be beneficial.
- NSAIDs are used most commonly for the chronic treatment of painful conditions in dogs. NSAIDs can be safe when administered chronically, but gastrointestinal, hepatic and renal adverse effects are possible. The best strategy appears to be reducing the dose to the lowest effective dose in an individual. If chronic administration is anticipated serum chemistries should be considered to monitor for hepatic and renal adverse effects.

PAIN (ACUTE, CHRONIC, AND POSTOPERATIVE)

(CONTINUED)

• Most NSAIDs have not been approved for cats (exceptions include robenecoxib and meloxicam in the US and ketoprofen, carprofen, and tolfenamic acid in Canada and Europe). Additional information is available for many drugs and should be referred to when considering extra-label use. Owners should be informed of the risks of analgesic drug therapy in their pet before consenting to treatment.

• Treatment of neuropathic pain is a subcategory of pathologic pain. It may originate from brain or spinal masses, injury (such as with intervertebral disc disease), inflammation, or the repetitive stimulation of the pain transmission system by a chronic injury outside the central nervous system. Classic signs that accompany neuropathic pain are allodynia and hyperalgesia. Neuropathic pain does not always respond well to traditional analgesics, such as NSAIDs and opioids, although these drugs are usually tried initially (except for NSAIDs when neurosurgery is imminent). Tricyclic antidepressants, antiepileptic drugs (e.g., gabapentin), *N*-methyl-d-aspartate (NMDA) receptor antagonists, and other alternative (complementary) therapies may be effective. Most of these treatments consist of extra- or off-label use of human medications and require careful client communication and approval.

CONTRAINDICATIONS

• Opioids may be associated with severe respiratory depression in human patients, but in most dogs and cats cause only minimal respiratory depression. In patients with severe respiratory compromise or intracranial hypertension, opioids may be contraindicated. Most μ -opioid receptor agonists can also alter gastrointestinal and urinary tract motility, resulting in constipation, urinary retention, and vomiting.

• NSAIDs can cause gastrointestinal ulceration, hepatopathies, and impaired renal function. Preexisting gastrointestinal, hepatic, or renal disease may be a contraindication to their use. Concomitant glucocorticoid therapy, severe stress, or anorexia may predispose many animals to adverse effects. NSAIDs that significantly inhibit cyclooxygenase (COX-1) may also alter platelet function and may result in increased

surgical blood loss. Acetaminophen or acetaminophen-containing analgesics should not be used in cats.

PRECAUTIONS

- Carefully monitor patients for adverse effects and clinical effectiveness following administration of analgesic drugs.
- Opioid-induced hyperthermia has been reported in feline patients, most commonly after fentanyl patch application or hydromorphone administration.
- Opioid administration may result in altered gastrointestinal motility (constipation), inappetence, and urine retention. These signs usually appear soon after initiation of opioid therapy and should resolve within 12–36 hours of stopping opioid administration. In the interim supportive care such as passing a urinary catheter may be necessary.
- In consultation with the pet owner, the veterinarian may feel the need to prescribe NSAIDs to a particular patient even if the risk for adverse events is deemed increased due to disease or preexisting conditions. The veterinarian should strive to ethically balance the long-term therapeutic risk of drugs such as NSAIDs against the benefit of improved quality of life.

POSSIBLE INTERACTIONS

- Opioids can reduce the anesthetic requirements for most species, especially when combined with α_2 -agonists or acepromazine as a premedication before anesthesia. In humans the combination of certain opioids such as meperidine with serotonin altering drugs may result in toxicity (e.g., l-deprenyl, amitriptyline, tramadol, trazadone) and are occasionally prescribed to veterinary patients.
- Concurrent glucocorticoid therapy may enhance NSAID toxicity.
- Other drugs that predispose animals to gastrointestinal or renal impairment, such as aminoglycoside antimicrobials, should be used with caution when NSAIDs are also being administered.

ALTERNATIVE DRUG(S)

- Adjunctive analgesic drugs (e.g., gabapentin, amantadine, amitriptyline, tramadol) may be beneficial for patients that have altered neuroprocessing associated with chronic disease changes or nervous system

injury. To select and administer an adjuvant analgesic properly, the veterinarian should be aware of the drug's clinical pharmacology. The following information about the drug is necessary: (1) approved indication, (2) unapproved indication (e.g., as an analgesic) widely accepted in veterinary medical practice, (3) common side effects and potentially serious adverse effects, (4) pharmacokinetic features, and (5) specific dosing guidelines for pain (see Appendix VII).

- Non-traditional medical treatments are common, but should be evaluated for safety and effectiveness before recommendation.
- Regenerative medicine (i.e., mesenchymal stromal cell therapy) has become more common. The effectiveness of many therapies used for chronic painful conditions appears to be unpredictable, but in a small number of patients the results can be life-altering.



FOLLOW-UP

PATIENT MONITORING

- Frequent evaluation of analgesic drug effectiveness should be performed.
- Patients receiving chronic analgesic medication, especially NSAIDs, should be evaluated periodically to monitor gastrointestinal, liver, and renal function.
- It is the responsibility of the veterinarian to ensure that the information about the effects of prescribed drugs is disseminated to clients.

PREVENTION/AVOIDANCE

Although some degree of pain is usually an unavoidable consequence of surgery or trauma, when possible, the preemptive administration of analgesic drugs may provide better pain control and reduce the potential for central nervous system wind-up. Use of proper anesthetic techniques incorporating analgesic premedications and local and regional analgesic techniques where appropriate, are effective ways of practicing preemptive analgesia.

EXPECTED COURSE AND PROGNOSIS

Acute pain associated with surgery or trauma usually resolves with tissue healing. Opioids may be most effective for the 12–24 hours

(CONTINUED)

PAIN (ACUTE, CHRONIC, AND POSTOPERATIVE)

following surgery, whereas NSAIDs may be better after that period. Some NSAIDs are effective analgesics immediately after surgery. When pain signs persist beyond the normal course of a few days to weeks, suspect persistent disease, injury, or central nervous system changes and consult an anesthesiologist or a board-certified specialist trained in pain management for suggestions about appropriate therapy.

**MISCELLANEOUS****PREGNANCY/FERTILITY/BREEDING**

- Opioids may cause fetal respiratory depression following delivery. NSAIDs may alter maternal or fetal prostaglandin production, resulting in pregnancy complications.

- The effects on the fetus of many of the analgesic drugs approved for use in dogs and cats are not widely reported.

ABBREVIATIONS

- COX = cyclooxygenase
- NMDA = *N*-methyl-d-aspartate
- NSAID = nonsteroidal anti-inflammatory drug

INTERNET RESOURCES

- American College of Veterinary Anesthesia and Analgesia's position paper on pain management:
http://acvaa.org/docs/Pain_Treatment.
- International Veterinary Academy of Pain Management:
<http://www.ivapm.org>.

Suggested Reading

AAHA/AAFP Pain Management Guidelines
Task Force Members, Peter Hellyer, Ilona Rodan, Jane Brunt, Robin Downing, James

E. Hagedorn, and Sheilah Ann Robertson. AAHA/AAFP Pain Management Guidelines for Dogs & Cats. *J Am Anim Hosp Assoc* 2007, 43:235–248.

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Fox S. *Pain Management in Small Animal Medicine*. Boca Raton, FL: CRC Press, 2013.

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Authors Kurt A. Grimm, Leigh A. Lamont, and William J. Tranquilli

Consulting Editor Joane M. Parent



Client Education Handout available online

PANCREATITIS—CATS



BASICS

DEFINITION

• Inflammation of the pancreas most often of unknown cause(s). • Acute pancreatitis— inflammation of the pancreas that occurs abruptly with little or no permanent pathologic change. • Chronic pancreatitis— continuing inflammatory disease that is accompanied by irreversible morphologic change such as fibrosis.

PATHOPHYSIOLOGY

• Host defense mechanisms normally prevent pancreatic autodigestion by pancreatic enzymes, but under select circumstances, these natural defenses fail; autodigestion occurs when these digestive enzymes are activated within acinar cells. • Local and systemic tissue injury is due to the activity of released pancreatic enzymes and a variety of inflammatory mediators such as kinins, free radicals, and complement factors are released by infiltrating neutrophils and macrophages. The most common pathologies involving the feline pancreas include acute necrotizing pancreatitis (ANP) and acute suppurative pancreatitis.

SYSTEMS AFFECTED

• Gastrointestinal—altered GI motility (ileus) due to regional chemical peritonitis; local or generalized peritonitis due to enhanced vascular permeability; concurrent inflammatory bowel disease may be seen in some cats. • Hepatobiliary—lesions due to shock, pancreatic enzyme injury, inflammatory cellular infiltrates, hepatic lipidosis, and intra/extrahepatic cholestasis. Feline gastrointestinal inflammatory disease (concurrent cholangitis ± inflammatory bowel disease) may be seen in some cats. • Respiratory—pulmonary edema or pleural effusion. • Cardiovascular—cardiac arrhythmias may result from release of myocardial depressant factor. • Hematologic—activation of the coagulation cascade and systemic consumptive coagulopathy (DIC) occur.

GENETICS

No genetic basis for disease pathogenesis in cats has been identified.

INCIDENCE/PREVALENCE

• True prevalence is unknown but is a relatively common clinical disorder in cats. • Necropsy surveys suggest an increased prevalence in cats with cholangitis, and inflammatory bowel disease. The unique feline pancreaticobiliary anatomy and intestinal microbiota likely contribute to multi-organ inflammatory disease in this species.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Cat of any age

Breed Predilections

Siamese cats

Mean Age and Range

Mean age for acute pancreatitis is 7.3 years.

Predominant Sex

None

SIGNS

General Comments

Vague, nonspecific, and nonlocalizing signs. Anorexia, lethargy, and vomiting are reported most frequently.

Historical Findings

- Lethargy/anorexia
- Vomiting
- Weakness
- Abdominal pain
- Diarrhea – small bowel and large bowel diarrhea and fever are less common in cats than dogs

Physical Examination Findings

- Severe lethargy.
- Dehydration—common; due to GI losses.
- Abdominal pain—may adopt a “prayer position” and/or resist abdominal palpation. Abdominal pain is recognized much less frequently in cats compared to dogs.
- Mass lesions may be palpable.
- Fever—Observed in 25% of cats.

CAUSES

Etiology is most often unknown; possibilities include:

- Hepatobiliary tract disease—both inflammatory and degenerative (hepatic lipidosis)
- Pancreatic trauma/ischemia
- Duodenal reflux
- Drugs/toxins (organophosphates)
- Pancreatic duct obstruction
- Hypercalcemia
- Inflammatory gastrointestinal disease
- Nutrition—excessive lean body mass is associated with ANP

RISK FACTORS

- Breed?
- Obesity?
- Organophosphate poisoning
- Concurrent hepatic/intestinal inflammatory disease
- See “Causes”



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other causes of acute abdomen:

- GI disease (obstruction, foreign body, perforation, infectious gastroenteritis, ulcer disease)—exclude with CBC/biochemistry/urinalysis, diagnostic imaging, and paracentesis. Gastrointestinal or hepatic neoplasia—exclude with tissue biopsy.
- Urogenital disease (pyelonephritis, prostatitis or abscessation, pyometra, urinary tract rupture or obstruction, acute renal failure)—exclude with CBC/biochemistry/urinalysis, urine culture/sensitivity, and imaging.
- Hepatobiliary disease (cholangitis and EHBO) exclude with CBC/biochemistry/urinalysis, bile acids, imaging, and liver

biopsy.

- Abdominal neoplasia—exclude with imaging and cytology or biopsy.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—often reveals nonregenerative anemia (40%), leukocytosis (38%), and/or leukopenia (15%).
- Serum biochemistries—often show prerenal azotemia; liver enzyme activities (ALT, ALP) are often elevated because of hepatic ischemia or exposure to pancreatic enzymes; hyperbilirubinemia with intra/extrahepatic biliary obstruction; hyperglycemia with necrotizing pancreatitis due to hyperglucagonemia; hypoalbuminemia, hypercholesterolemia and hypertriglyceridemia are common.
- Hypocalcemia is more common in cats than dogs, and a low ionized calcium concentration is a negative prognostic indicator in cats.
- Urinalysis—increased urine SG associated with dehydration or can be unremarkable.

OTHER LABORATORY TESTS

- Serum amylase and lipase activities are unreliable serologic markers—may be elevated, but are nonspecific; can also increase with hepatic, renal, or neoplastic disease in the absence of pancreatitis.
- Serum pancreatic lipase immunoreactivity (fPL) is a highly sensitive and specific serologic marker of acute pancreatic inflammation. A cage-side fPL assay (SNAP fPL) has been developed as a useful screening tool. Elevation in SNAP fPL should be followed up by laboratory measurement of serum Spec fPL to quantitate the degree of elevation.

IMAGING

- Abdominal radiographs—may include increased soft tissue opacity in the right cranial abdominal compartment; loss of visceral detail (“ground glass appearance”) due to abdominal effusion; static gas pattern in the proximal duodenum.
- Abdominal ultrasound—nonhomogeneous solid or cystic mass lesions suggest pancreatic abscess; may be a pancreatic mass or altered echogenicity (hypoechoic) in the area of the pancreas; pancreas is usually enlarged with irregular borders, surrounding mesentery may be hyperechoic due to focal peritonitis, may see peritoneal effusion and extrahepatic biliary obstruction.
- fPL assay and pancreatic ultrasound in combination have the highest specificity for an antemortem diagnosis of acute pancreatitis.

DIAGNOSTIC PROCEDURES

- Ultrasound-guided needle-aspiration biopsy may confirm inflammation (cytology), abscess, or cyst.
- Laparoscopy with pancreatic forceps biopsy for histologic diagnosis.
- Histopathologic evaluation may miss focal or segmental pancreatic inflammation and results should be interpreted with caution.

PATHOLOGIC FINDINGS

- Gross findings (acute pancreatitis)—mild swelling with edematous pancreatitis.
- Gross

(CONTINUED)

findings (chronic pancreatitis)—pancreas is reduced in size, firm, gray, and irregular; may contain extensive adhesions to surrounding viscera. • Microscopic changes (acute pancreatitis)—include edema, parenchymal necrosis, hemorrhage, and neutrophilic cellular infiltrate with acute lesions. • Microscopic changes (chronic pancreatitis)—pancreatic fibrosis around ducts, ductal epithelial hyperplasia, atrophy, and mononuclear cellular infiltrate.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient medical management most often.
- Aggressive IV fluid therapy. • Fluid therapy goals—correct hypovolemia and maintain pancreatic microcirculation. • A balanced electrolyte solution such as lactated Ringer's solution (LRS) is the first-choice rehydration fluid. • Correct initial dehydration (mL = % dehydration × weight in kg × 1,000) and give over 4–6 hours. • May need colloids (oxyglobin, hetastarch) to improve pancreatic circulatory needs and prevent ischemia.
- Following replacement of deficits, give additional fluids to match maintenance requirements (2.5 × weight in kg) and ongoing losses (estimated). • Potassium chloride (KCl) supplementation usually needed because of potassium loss in the vomitus; base potassium supplementation on measured serum levels (use 20 mEq of KCl/L of IV fluid if serum potassium levels are not known; do not administer faster than 0.5 mEq/kg/h).

ACTIVITY

Restrict

DIET

- Continue to feed orally unless vomiting is intractable; feeding maintains intestinal epithelial integrity and minimizes bacterial translocation. • Initiate enteral feeding via esophagostomy, gastrostomy enteral feeding device, or nasoesophageal tube placement.
- NPO in animals with persistent vomiting for the shortest time possible; when there has been no vomiting for 12 hours, offer small volumes of water; if tolerated, begin small, frequent feedings of a diet that does not contain excessive amounts of dietary fat. Most nutritionists agree that excessive dietary fat restriction is not necessary in cats with pancreatitis.

CLIENT EDUCATION

- Discuss the need for extended hospitalization. • Discuss the expense of diagnosis and treatment. • Discuss possible short-term and long-term complications (see "Associated Conditions").

SURGICAL CONSIDERATIONS

- May need surgery to remove pseudocysts, abscesses, or devitalized tissue seen with necrotizing pancreatitis. • May need laparotomy and pancreatic biopsy to confirm pancreatitis and/or rule out other, nonpancreatic diseases such as hepatic cholangitis, lipidosis, and/or IBD.
- Extrahepatic biliary obstruction from pancreatitis requires ductal decompression with surgical correction.



MEDICATIONS

DRUG(S)

- Animals with intermittent vomiting should be treated with antiemetics—chlorpromazine (0.2–0.4 mg/kg IM or SC q8h) or ondansetron (0.1–0.2 mg/kg IV q12h) are reasonable first-choice options. Maropitant (Cerenia) is approved for parenteral administration in cats older than 16 weeks and is given IV at 1 mg/kg q24h for 5–7 consecutive days. • Antibiotics if evidence of sepsis from bacterial translocation and to prevent pancreatic infection—cefotaxime (50 mg/kg IM q8h). • Analgesics to relieve abdominal pain, e.g., butorphanol (0.2–0.4 mg/kg SC q6h), buprenorphine (0.01–0.02 mg/kg IM, IV, or SC q6–12h) or fentanyl CRI (2–4 µg/kg/h) as needed.

CONTRAINdications

- Anticholinergics (e.g., atropine)
- Azathioprine • Chlorothiazide • Estrogens
- Furosemide • Tetracycline • L-asparaginase

PRECAUTIONS

Only use antibiotics if a clear clinical condition exists, such as infection.



FOLLOW-UP

PATIENT MONITORING

- Evaluate hydration status closely during first 24 hours of therapy; twice daily check physical examination, body weight, hematocrit, total plasma protein, BUN, and urine output. Evaluate the effectiveness of fluid therapy after 24 hours and adjust flow rates and fluid composition accordingly; repeat biochemistries to assess electrolyte/acid-base status. • Watch closely for systemic complications involving a variety of organ systems; perform appropriate diagnostic tests as needed (see "Associated Conditions").
- Gradually taper fluids down to maintenance requirements if possible. Maintain oral alimentation or enteral nutrition as described above, being careful to feed diets that do not contain excessive amounts of dietary fat.
- Monitor for clinical evidence of IBD and treat accordingly. • Monitor for progression to diabetes mellitus, exocrine pancreatic

PANCREATITIS—CATS

insufficiency (EPI), and/or hepatic lipidosis in cats with ANP.

PREVENTION/AVOIDANCE

- Weight reduction if obese • Avoid high-fat diets

POSSIBLE COMPLICATIONS

- Failed response to supportive therapy.
- Life-threatening associated conditions such as EPI, diabetes mellitus, and hepatic lipidosis. • Progression of acute pancreatitis to chronic pancreatitis.

EXPECTED COURSE AND PROGNOSIS

- Guarded for most patients with ANP; cats with multi-organ inflammation may be less responsive to treatment. • More guarded to poor for patients with severe necrotizing pancreatitis, decreased ionized calcium fraction, and systemic conditions.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Life-Threatening

- Pulmonary edema (e.g., adult respiratory distress syndrome) • Cardiac arrhythmias
- Peritonitis • DIC

Non-Life-Threatening

- Diabetes mellitus • EPI • Chronic pancreatitis • Cholangitis and hepatic lipidosis • Inflammatory bowel disease

SEE ALSO

- Acute Abdomen • Cholangitis/Cholangiohepatitis Syndrome • Exocrine Pancreatic Insufficiency • Inflammatory Bowel Disease

ABBREVIATIONS

- ALP = alkaline phosphatase • ALT = alanine aminotransferase • ANP = acute necrotizing pancreatitis • DIC = disseminated intravascular coagulation
- EHBO = extrahepatic biliary obstruction
- EPI = exocrine pancreatic insufficiency
- FPL = feline pancreatic lipase immunoreactivity • GI = gastrointestinal
- IBD = inflammatory bowel disease
- NPO = nothing per os

INTERNET RESOURCES

<http://www.vin.com/VIN.plx> Veterinary Information Network

Suggested Reading

Stockhaus C, Teske E, Schellenberger K, et al. Serial serum feline pancreatic lipase immunoreactivity concentrations and prognostic variables in 33 cats with pancreatitis. J Am Vet Med Assoc 2013, 243:1713–1718.

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Consulting Editor Stanley L. Marks



Client Education Handout
available online

PANCREATITIS—DOGS



BASICS

DEFINITION

- Inflammation of the pancreas most often of unknown cause(s). Acute pancreatitis— inflammation of the pancreas that occurs abruptly with little or no permanent pathologic change. Chronic pancreatitis— continuing inflammatory disease that is accompanied by irreversible morphologic change such as fibrosis and atrophy.

PATHOPHYSIOLOGY

- Local and systemic tissue injury is due to the activity of released pancreatic enzymes and a variety of inflammatory mediators such as kinins, free radicals, and complement factors are released by infiltrating neutrophils and macrophages.

SYSTEMS AFFECTED

- Gastrointestinal—altered GI motility (ileus) due to regional chemical peritonitis; local or generalized peritonitis due to enhanced vascular permeability.
- Hepatobiliary—lesions due to shock, pancreatic enzyme injury, inflammatory cellular infiltrates, hepatic lipidosis, and intra/extrahepatic cholestasis.
- Respiratory—pulmonary edema or pleural effusion; adult respiratory distress syndrome is an uncommon but potentially fatal sequela with systemic complications.
- Cardiovascular—cardiac arrhythmias may result from release of myocardial depressant factor.
- Hematologic—activation of the coagulation cascade and systemic consumptive coagulopathy (DIC) occur.

GENETICS

Possible genetic basis in miniature schnauzers where select mutations in the *SPINK1* gene may confer increased susceptibility.

INCIDENCE/PREVALENCE

- True prevalence is unknown but a relatively common clinical disorder.
- Up to 1% of normal dogs may have histologic evidence of pancreatitis.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog of any age

Breed Predilections

- Miniature schnauzer • Yorkshire terrier
- Cocker spaniel

Mean Age and Range

Acute pancreatitis is most common in middle-aged and older (> 7 years) dogs; mean age at presentation is 6.5 years.

Predominant Sex

Female

SIGNS

General Comments

- Predominantly GI tract signs that are

nonlocalizing and abdominal pain. Dogs with chronic pancreatitis may not exhibit abdominal pain.

Historical Findings

- Lethargy/anorexia • Vomiting • Weakness
- Abdominal pain • Diarrhea—small or large bowel type

Physical Examination Findings

- Severe lethargy. • Dehydration—common; due to GI losses.
- Abdominal pain—may adopt a “prayer position” and/or resist abdominal palpation.
- Mass lesions may be palpable.
- Fever—common with more severe acute pancreatitis.
- Less common systemic abnormalities include respiratory distress, bleeding disorders, and cardiac arrhythmias.

CAUSES

Etiology is most often unknown; possibilities include:

- Nutritional factors (e.g., dietary indiscretion, hyperlipoproteinemia)
- Pancreatic trauma/ischemia • Duodenal reflux • Drugs/toxins (see “Contraindications”)
- Pancreatic duct obstruction • Hypercalcemia • Infectious agents—babesiosis

RISK FACTORS

- Breed (potential genetic predisposition—miniature schnauzers) • Obesity
- Concurrent disease (e.g., diabetes mellitus, hyperadrenocorticism, hypothyroidism, chronic renal failure, and neoplasia) • Recent drug administration (see “Contraindications”)
- See “Causes”



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other causes of acute abdomen:

- GI disease (obstruction, foreign body, perforation, gastroenteritis, ulcer disease)—exclude with CBC/biochemistry/urinalysis, diagnostic imaging, and paracentesis.
- Splenic torsion—exclude with imaging.
- Hypoadrenocorticism—exclude with CBC/biochemistry/urinalysis, resting cortisol, ACTH stimulation test.
- Urogenital disease (pyelonephritis, prostatitis or abscessation, pyometra, urinary tract rupture or obstruction, acute renal failure)—exclude with CBC/biochemistry/urinalysis, urine culture/sensitivity, and imaging.
- Hepatobiliary disease—exclude with CBC/biochemistry/urinalysis, bile acids, ultrasound imaging, and liver biopsy.
- Abdominal neoplasia—exclude with ultrasound imaging and cytology or biopsy.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—acute pancreatitis often associated with hemoconcentration with increased PCV, leukocytosis with a left shift, and toxic neutrophils with severe inflammation; thrombocytopenia.
- Serum biochemistries—

often show prerenal azotemia; liver enzyme activities (ALT, ALP) are often increased because of hepatic ischemia or exposure to pancreatic toxins; hyperbilirubinemia with intra/extrahepatic biliary obstruction; electrolyte abnormalities associated with vomiting; hyperglycemia with necrotizing pancreatitis due to hyperglucagonemia; hypoalbuminemia; hypercholesterolemia and hypertriglyceridemia are common.

- Urinalysis—increased urine SG associated with dehydration. Urinalysis may show evidence of proteinuria or may be unremarkable.

OTHER LABORATORY TESTS

- Serum amylase and lipase activities are unreliable serologic markers—may be elevated but are nonspecific; also increase with hepatic, renal, or neoplastic disease in the absence of pancreatitis; dexamethasone may increase serum lipase concentrations in dogs.
- Serum pancreatic lipase immunoreactivity (cPL) is a highly sensitive and specific serologic marker of acute pancreatic inflammation, although is less sensitive for detecting chronic pancreatic inflammation. A cage-side cPL assay (SNAP cPL) has been developed as a useful screening tool. Elevation in SNAP cPL should be followed up by laboratory measurement of serum Spec cPL to obtain a quantitative value.

IMAGING

- Abdominal radiographs—may include increased soft tissue opacity in the right cranial abdominal compartment; loss of visceral detail (“ground glass appearance”) due to abdominal effusion; static gas pattern in the proximal duodenum; widened angle between pyloric antrum and proximal duodenum.
- Abdominal radiographs are a relatively insensitive diagnostic procedure for pancreatitis and are of greater value for helping to rule out other causes of chronic vomiting in the dog such as gastric or intestinal foreign bodies.
- Thoracic radiographs—may reveal mild pleural effusion or more severe pulmonary complications.
- Abdominal ultrasound—nonhomogeneous solid or cystic mass lesions suggest pancreatic abscess; pancreas is usually enlarged with an irregular border, may be a pancreatic mass or altered echogenicity (hypoechoic) in the area of the pancreas secondary to edema; surrounding mesentery is typically hyperechoic secondary to focal peritonitis; may see peritoneal effusion and extrahepatic biliary obstruction.
- cPL assay and pancreatic ultrasound in combination have the highest sensitivity for an antemortem diagnosis of acute pancreatitis.

DIAGNOSTIC PROCEDURES

- Ultrasound-guided needle-aspiration biopsy may confirm inflammation (cytology), abscess, or cyst.
- Laparoscopy with pancreatic biopsy forceps for histologic diagnosis.
- Histopathologic evaluation may

(CONTINUED)

miss focal or segmental pancreatic inflammation; thus this diagnostic tool must be interpreted with caution.

PATHOLOGIC FINDINGS

- Gross findings (acute pancreatitis)—mild swelling with edematous pancreatitis; grayish yellow areas of pancreatic necrosis with varying amounts of hemorrhage with necrotizing pancreatitis.
- Gross findings (chronic pancreatitis)—pancreas is reduced in size, firm, gray, and irregular; may contain extensive adhesions to surrounding viscera.
- Microscopic changes (acute pancreatitis)—include edema, parenchymal necrosis, hemorrhage, and neutrophilic cellular infiltrate with acute lesions.
- Microscopic changes (chronic pancreatitis)—pancreatic fibrosis around ducts, ductal epithelial hyperplasia, atrophy, and mononuclear cellular infiltrate.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient medical management most often required.
- Aggressive IV fluid therapy.
- Fluid therapy goals—correct hypovolemia and maintain pancreatic microcirculation.
- A balanced electrolyte solution such as lactated Ringer's solution (LRS) is the first-choice rehydration fluid.
- Correct initial dehydration ($\text{mL} = \% \text{ dehydration} \times \text{weight in kg} \times 1,000$) and give over 4–6 hours.
- May need colloids (oxyglobin, hetastarch) to improve pancreatic circulatory needs and prevent ischemia.
- Following replacement of deficits, give additional fluids to match maintenance requirements ($2.5 \times \text{weight in kg}$) and ongoing losses (estimated).
- Potassium chloride (KCl) supplementation usually needed because of potassium loss in the vomitus; base potassium supplementation on measured serum levels (use 20 mEq of KCl/L of IV fluid if serum potassium levels are not known; do not administer faster than 0.5 mEq/kg/h).

ACTIVITY

Restrict

DIET

- Continue to feed orally unless vomiting is intractable; feeding maintains intestinal epithelial integrity and minimizes bacterial translocation.
- Initiate enteral feeding via esophagostomy, gastrostomy enteral device, or nasoesophageal tube placement.
- NPO in animals with persistent vomiting for the shortest time possible; when there has been no vomiting for 12 hours, offer small volumes of water; if tolerated, begin small, frequent feedings of a carbohydrate (e.g., boiled rice); gradually introduce a protein source of high biologic value such as cottage cheese or lean meat.
- Avoid high-protein and high-fat diets and use fat-restricted low-residue diets.

CLIENT EDUCATION

- Discuss the need for extended hospitalization.
- Discuss the expense of diagnosis and treatment.
- Discuss possible short-term and long-term complications (see "Associated Conditions").

SURGICAL CONSIDERATIONS

- May need surgery to remove pseudocysts, abscesses, or devitalized tissue seen with necrotizing pancreatitis.
- May need laparotomy and pancreatic biopsy to confirm pancreatitis and/or rule out other, nonpancreatic diseases.
- Extrahepatic biliary obstruction from pancreatitis requires surgical correction.



MEDICATIONS

DRUG(S)

- Animals with intermittent vomiting should be treated with antiemetics—maropitant (1 mg/kg SC q24h for 5 days maximum) or ondansetron (0.1–0.2 mg/kg IV q12h) are reasonable first choice options.
- Anti-inflammatory agents—corticosteroids are indicated for treatment of shock. Anti-inflammatory doses of corticosteroids can be used for management of acute pancreatitis, although published evidence for benefit is lacking.
- Antibiotics if evidence of sepsis—penicillin G (20,000 U/kg q6h), ampicillin sodium (20 mg/kg q8h), and enrofloxacin (10 mg/kg IV q24h in dogs).
- Analgesics to relieve abdominal pain, e.g., buprenorphine (0.01–0.02 mg/kg IM, IV, or SC q6–12h) or fentanyl CRI (2–5 µg/kg/h) as needed.

CONTRAINdications

- Anticholinergics (e.g., atropine)
- Azathioprine
- Chlorothiazide
- Estrogens
- Furosemide
- Tetracycline
- L-asparaginase

PRECAUTIONS

Only use antibiotics if a clear clinical condition exists, such as infection.



FOLLOW-UP

PATIENT MONITORING

- Evaluate hydration status closely during first 24 hours of therapy; twice daily check physical examination, body weight, hematocrit, total plasma protein, BUN, and urine output.
- Evaluate the effectiveness of fluid therapy after 24 hours and adjust flow rates and fluid composition accordingly; repeat biochemistries to assess electrolyte/acid-base status.
- Repeat plasma enzyme concentrations (cPL assay) after 7 days to evaluate the inflammatory process and response to therapy.
- Watch closely for systemic complications involving a variety of organ systems; perform appropriate diagnostic tests as needed (see "Associated Conditions").

PANCREATITIS—DOGS

- Gradually taper fluids down to maintenance requirements if possible.
- Maintain oral alimentation or enteral nutrition as described above being careful to feed only low-fat diets.
- A clinical index for pancreatitis may be used to define initial disease severity and response to treatment.

PREVENTION/AVOIDANCE

- Weight reduction if obese.
- Avoid high-fat diets.
- Avoid drugs that may precipitate disease (see "Contraindications").

POSSIBLE COMPLICATIONS

- Failed response to supportive therapy
- Life-threatening associated conditions
- Progression of acute pancreatitis to chronic pancreatitis

EXPECTED COURSE AND PROGNOSIS

- Good for most patients with acute pancreatitis; these patients usually respond to appropriate symptomatic therapy.
- More guarded to poor for patients with necrotizing pancreatitis and systemic conditions



MISCELLANEOUS

ASSOCIATED CONDITIONS

Life-Threatening

- Pulmonary edema (e.g., adult respiratory distress syndrome)
- Cardiac arrhythmias
- Peritonitis
- DIC

Non-Life-Threatening

- Diabetes mellitus
- EPI
- Chronic pancreatitis

AGE-RELATED FACTORS

Most common in middle-aged animals

SEE ALSO

- Acute Abdomen
- Exocrine Pancreatic Insufficiency

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- cPL = canine pancreatic lipase immunoreactivity
- DIC = disseminated intravascular coagulation
- EPI = exocrine pancreatic insufficiency
- GI = gastrointestinal
- NPO = nothing per os

INTERNET RESOURCES

<http://www.vin.com/VIN.plx> Veterinary Information Network

Suggested Reading

- Watson P. Chronic pancreatitis in dogs. Top Companion Anim Med 2012, 27:133–139.
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Client Education Handout
available online

PANCYTOPENIA



BASICS

DEFINITION

Simultaneous leukopenia, nonregenerative anemia, and thrombocytopenia; not a disease itself—rather, a group of laboratory findings that can result from multiple causes.

PATHOPHYSIOLOGY

- Mechanisms may include decreased production of cells in the bone marrow or increased peripheral use, destruction, or sequestration; one or more of these mechanisms may occur together.
- Decreased production occurs when pluripotent, multipotent, or committed stem cells are destroyed, their proliferation or differentiation is suppressed, or the maturation of differentiated cells is delayed or arrested.
- If pluripotent stem cells are affected, pancytopenia develops; if committed stem cells are involved, cytopenia of the specific cell type develops.
- Increased use and destruction of cells typically results in increased production in the bone marrow. At least 2–3 days are required before increased production begins to have an effect on peripheral blood cell counts, and peak output usually takes about a week; thus, the rate of use or destruction necessary to cause cytopenia is not as great during the first few days of disease as it is later.
- Sequestration of cells in the microcirculation, especially that of the spleen, intestine, and lungs, can cause cytopenia of the cell type involved.

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SYSTEMS AFFECTED

Hemic/Lymphatic/Immune—bone marrow, spleen, lymph nodes, and other lymphocytic tissues; depending on the cause, these organs can be affected by cellular depletion, degeneration, necrosis, hyperplasia, dysplasia, or dyscrasia; changes may occur alone or in combination.

INCIDENCE/PREVALENCE

Pancytopenia is an uncommon occurrence and does not always occur with the causes listed below. One study (Weiss et al. 1999) determined an incidence of 2.4% in dogs.

GEOGRAPHIC DISTRIBUTION

Unless the cause of pancytopenia is due to an infectious agent that is localized to a certain region (e.g., leishmaniasis, histoplasmosis), no specific geographic distribution exists.

SIGNALMENT

- Dogs and cats
- No age, sex, or breed predilection

SIGNS

Historical Findings

- History reflects the underlying cause.
- Lethargy or pallor from anemia.
- Petechial hemorrhage or mucosal bleeding from thrombocytopenia.
- Repeated febrile episodes or frequent or persistent infections from leukopenia.

Physical Examination Findings

- Lethargy, weakness
- Pale mucous membranes
- Petechial hemorrhages
- Mucosal hemorrhage (e.g., hematuria, epistaxis, hemoptysis, melena)
- Fever

CAUSES

Infectious Diseases/Agents

- FeLV
- FIV
- FIP
- ICH
- Canine and feline parvovirus
- Histoplasmosis
- Ehrlichiosis
- Cytauxzoonosis
- Leishmaniasis
- Endotoxemia or septicemia

Drugs, Chemicals, and Toxins

- Chloramphenicol
- 2nd generation cephalosporins
- Trimethoprim-sulfadiazine
- Albendazole
- Fenbendazole
- Griseofulvin
- ACE inhibitors (e.g. captopril)
- Methimazole
- Phenobarbital
- Phenylbutazone
- Estrogen (exogenous administration, Sertoli cell tumor, interstitial cell tumor)
- Chemotherapeutic drugs (azathioprine, carboplatin, cyclophosphamide, cytosine arabinoside, doxorubicin, hydroxyurea, vinblastine)
- Fusarium* T-2 toxin
- Thallium
- Ionizing radiation

Proliferative and Infiltrative Diseases

- Hematopoietic neoplasia (e.g., acute and chronic leukemias, lymphoma, histiocytic tumors, myelodysplasia)
- Myelofibrosis
- Myelophthysis
- Osteosclerosis

Immune-Mediated Diseases

- Aplastic anemia (also known as aplastic pancytopenia).
- Immune-mediated hemolytic anemia and thrombocytopenia (when precursor cells are targeted by the immune system).

RISK FACTORS

Vary with individual cause



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute onset with severe clinical signs—more consistent with conditions that cause necrosis, destruction, or sequestration of cells.
- Slow, insidious onset—more consistent with conditions that cause bone marrow suppression.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

Glucocorticoids often mildly to moderately increase the segmented neutrophil count, which may then obscure the presence of neutropenia.

Disorders That May Alter Laboratory Results

Phlebotomy technique may result in platelet clumping and hemolysis, leading to spuriously low platelet count and PCV, respectively.

CBC/BIOCHEMISTRY/URINALYSIS

- Leukopenia—characterized by neutropenia with or without lymphopenia.
- Nonregenerative anemia—severity depends on duration and underlying cause.
- Thrombocytopenia.
- Blood smear evaluation—may reveal infectious agents (e.g., *Ehrlichia* spp. *Histoplasma capsulatum*); may reveal abnormal cells of any lineage, suggesting myeloproliferative or lymphoproliferative diseases.
- Toxic changes in leukocytes—may suggest bone marrow injury (e.g., from parvovirus or chemical agent), septicemia, or endotoxemia.
- Biochemical alterations—depends on organ and degree of involvement (e.g., increased liver enzymes may be seen with certain infectious diseases, toxins, and infiltrative diseases).

OTHER LABORATORY TESTS

- Reticulocyte count—a regenerative response to anemia suggests destruction, use, or sequestration of RBCs; a nonregenerative response suggests bone marrow suppression and merits bone marrow examination.
- Immunologic tests for infectious diseases (e.g., FeLV, FIV, *Ehrlichia* spp.).
- PCR for infectious agents.

DIAGNOSTIC PROCEDURES

- Bone marrow examination—indicated when cause of pancytopenia cannot be determined with other tests.

(CONTINUED)

PANCYTOPENIA

- Hypercellular bone marrow associated with myelodysplasia, neoplasia, myelophthisis, or recovery from parvovirus.
- Hypocellular bone marrow associated with necrosis, myelofibrosis, and suppression (e.g., drugs, estrogen, aplastic anemia).
- If a bone marrow aspirate cannot be obtained, myelofibrosis, necrosis, or marked hypocellularity should be suspected and a core biopsy should be evaluated.

PATHOLOGIC FINDINGS

Bone marrow core biopsy—may see replacement of normal hematopoietic tissue with necrotic, neoplastic, fibrous, or adipose tissue, depending on the underlying cause.

**TREATMENT**

- Supportive treatment depends on the clinical situation and includes aggressive antibiotic therapy and blood component transfusions.
- Treatment of the underlying condition is paramount.

**MEDICATIONS****DRUG(S) OF CHOICE**

Treatment should be appropriate for the clinical situation (i.e., the degree to which each cell population is decreased, presence of fever or infection, and established or suspected specific diagnoses); see specific causes.

CONTRAINDICATIONS

- Drugs that may suppress hematopoiesis further (see "Causes").
- NSAIDs, clopidogrel, or other drugs that may interfere with platelet function.

PRECAUTIONS

Because of the patient's compromised immune status, glucocorticoids and other immunosuppressive drugs should be used only when absolutely necessary and with extreme care and frequent monitoring.

ALTERNATIVE DRUG(S)***Recombinant Hematopoietic Growth Factors***

- rhG-CSF—1–5 µg/kg/day SC; stimulates neutrophil production.
- rhEPO—initial dosage: 100 U/kg SC 3 times/week; stimulates erythropoiesis.

**FOLLOW-UP****PATIENT MONITORING**

- Daily physical examination, including frequent monitoring of body temperature.
- Periodic CBC—frequency depends on severity of cytopenia, age, general physical condition of the patient, and underlying cause.

PREVENTION/AVOIDANCE

- Castration of cryptorchid males.
- Vaccination for infectious diseases.
- Frequent monitoring of CBC in cancer patients receiving chemotherapy or radiation.

POSSIBLE COMPLICATIONS

- Hemorrhage
- Sepsis

EXPECTED COURSE AND PROGNOSIS

- Depends on the underlying cause
- Often a guarded prognosis is warranted

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Secondary infections—in patients with neutropenia.

ZOONOTIC POTENTIAL

- Tularemia.
- An owner can contract histoplasmosis from the same source as the patient.

PREGNANCY/FERTILITY/BREEDING

Stress of underlying disease may cause abortion; see respective topics for the effects of different causes on pregnancy.

SEE ALSO

- Anemia, Aplastic
- Anemia, Nonregenerative
- Anemia, Regenerative
- Neutropenia
- Specific causes of pancytopenia
- Thrombocytopenia

ABBREVIATIONS

- ACE = angiotensin-converting enzyme
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- ICH = infectious canine hepatitis
- PCR = polymerase chain reaction
- PCV = packed cell volume
- RBC = red blood cell
- rhEPO = recombinant human erythropoietin
- rhG-CSF = recombinant human granulocyte colony-stimulating factor

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Client Education Handout available online

PANNICULITIS/STEATITIS



BASICS

OVERVIEW

Inflammation of the subcutaneous fat tissue.

SYSTEMS AFFECTED

Skin/Exocrine

SIGNALMENT

Species

Steatitis—predominantly cats, but can occur in dogs with concurrent diseases.

Mean Age and Range

- Panniculitis—any age.
- Steatitis—young to middle-aged cats; older dogs.

SIGNS

- Uncommon in dogs and cats.
- Single or multiple subcutaneous nodules or draining tracts.
- May be painful and fluctuant to firm.
- Nodules—few millimeters to several centimeters in diameter.
- Involved fat may necrose.
- Exudate—usually a small amount of oily discharge; yellow-brown to bloody.
- Multiple lesions (dogs and cats)—systemic signs common (e.g., anorexia, pyrexia, lethargy, and depression).

CAUSES & RISK FACTORS

- Infectious—bacterial, fungal (deep mycosis or dermatophyte), opportunistic mycobacteria, *Nocardia*, viral.
- Immune-mediated—lupus panniculitis, erythema nodosum, vasculitis or drug reaction.
- Idiopathic—sterile nodular panniculitis, thromboembolism.
- Trauma.
- Neoplastic—multicentric mast cell tumors, cutaneous lymphoma, pancreatic carcinoma.
- Foreign bodies.
- Post-injection—corticosteroids, vaccines, other subcutaneous injections.
- Nutritional—vitamin E deficiency in cats, oily fish-based diet (steatitis).

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DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Infectious

- More common than sterile/immune-mediated panniculitis.
- Deep pyoderma.
- FIP.

Cutaneous Cyst

- Usually non-painful, non-inflamed
- Well demarcated

Lipoma

- Soft; usually well demarcated
- No inflammation or draining tracts
- Usually solitary

Mast Cell Tumors/Epitheliotropic Lymphoma

- Multifocal
- Often erythematous
- Variable presentations

Sterile Nodular Panniculitis

Diagnosis made by ruling out other causes of panniculitis.

CBC/BIOCHEMISTRY/URINALYSIS

- Panniculitis—no abnormalities.
- Most steatitis cases and occasional panniculitis: moderate to severe neutrophilia with mild eosinophilia; mild to moderate leukocytosis; mild nonregenerative anemia; hypoalbuminemia and proteinuria, possible hypocalcemia.

OTHER LABORATORY TESTS

- Antinuclear antibody—lupus panniculitis
- Serum protein electrophoresis • Serum lipase/amylase levels • FeLV/FIV testing

IMAGING

- Abdominal ultrasound:
- Panniculitis—pancreatitis may be a contributing factor.
- Steatitis—may see mottled subcutaneous, inguinal or falciform fat, loss of contrast in abdominal cavity.

DIAGNOSTIC PROCEDURES

- Aspirates and impression smears:
- Pyoderma—numerous neutrophils and variable numbers of mononuclear cells and bacteria.
- Fungal infections—fungal organisms and variable numbers of mononuclear cells may be noted.
- Blastomycosis—urine antigen testing.
- Bacterial culture and sensitivity testing (tissue)—necessary for identifying primary or secondary bacterial infection.
- Fungal and opportunistic mycobacteria culture (tissue).
- Biopsy with negative cultures for diagnosis of sterile nodular panniculitis.
- Special stains of histopathologic samples—may help identify causative agent.

PATHOLOGIC FINDINGS

- Surgical excisional biopsies—more accurate than punch biopsy specimens in most cases.
- Histopathology required for diagnosis:
- Panniculitis—lobular or diffuse infiltrate (granulomatous, pyogranulomatous, suppurative, eosinophilic, necrotizing or fibrosing) of panniculus; may identify if vasculitis present. Special stains will aid in identifying infectious agents.
- Steatitis—lumpy, granular fat, normal to yellowish/orange coloration of body fat may be noted.



TREATMENT

Diet: Steatitis—remove fish products from diet; feed nutritionally complete, balanced commercially prepared food; may require parenteral feeding (e.g., PEG tube, esophagostomy feeding tube).



MEDICATIONS

DRUG(S)

Positive culture results require appropriate antibacterial, antifungal, or antimycobacterial treatment.

Sterile nodular panniculitis

- Systemic treatment with corticosteroids; prednisone (2.2 mg/kg daily in dogs or 4.4 mg/kg daily in cats; taper based on response: may require low dose to maintain remission). • Oral vitamin E—200 IU q12h < 10 kg, 400 IU q12h > 10 kg.
- Azathioprine (Dogs: 1 mg/kg PO daily initially)—can be used if corticosteroids are contraindicated or insufficient response to corticosteroids alone.
- Cyclosporine can be beneficial in some dogs (initially 5 mg/kg q24h for 4–8 weeks, then tapered).

Steatitis

Oral vitamin E—200 IU q12h < 10 kg, 400 IU q12h > 10 kg; corticosteroids at an anti-inflammatory dosage; S-adenosylmethionine PO on an empty stomach.



FOLLOW-UP

- Depends on underlying etiology type and duration of treatment.
- Monitor CBC, platelet count, chemistry profile, and urinalysis/urine bacterial culture and sensitivity if immune-suppressive agents or long-term corticosteroids are used.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Pancreatic carcinoma, chylous ascites, peritonitis

ABBREVIATIONS

- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- PEG tube = percutaneous endoscopically-placed gastrostomy tube

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Consulting Editor Alexander H. Werner

PANOSTEITIS



BASICS

DEFINITION

A self-limiting, painful condition affecting one or more of the long bones of young, medium- to large-breed dogs that is characterized clinically by lameness and radiographically by high density of the marrow cavity.

PATHOPHYSIOLOGY

- Cause unknown.
- Attempts to isolate microorganisms have failed.
- Metabolic, allergic, or endocrine aberrations—without support.
- Pain—may owe to the disturbance of endosteal and periosteal elements, vascular congestion, or high intramedullary pressure.

SYSTEMS AFFECTED

Musculoskeletal—lameness of variable intensity; may affect a single limb or become a shifting leg lameness.

GENETICS

- No proven transmission.
- Predominance of German shepherds in the affected population strongly suggests an inheritable basis.

INCIDENCE/PREVALENCE

No reliable estimates; common

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog

Breed Predilections

- German shepherds and German shepherd mixes—most commonly affected.
- Medium to large breeds—most commonly affected.

Mean Age and Range

- Usually 5–18 months of age
- As young as 2 months and as old as 5 years

Predominant Sex

Male

SIGNS

General Comments

Lameness—if no distinct abnormalities noted on physical examination or radiographs, repeat examinations 4–6 weeks later.

Historical Findings

- No associated trauma.
- Lameness—varying intensity; usually involves the forelimbs initially; may affect the hind limbs; may see shifting leg lameness; may be non-weight-bearing.
- Severe disease—mild depression; inappetence; weight loss.

Physical Examination Findings

- Pain—on deep palpation of the long bones (diaphysis) in an affected limb; distinguishing characteristic; palpate firmly along the entire shaft of each bone while carefully avoiding any pinching of nearby muscle.
- Bones—ulna most commonly affected; may affect radius, humerus, femur, and tibia (in decreasing order of frequency) either concurrently or subsequently.
- May note low-grade fever.
- May see muscle atrophy.

CAUSES

Unknown

RISK FACTORS

Purebred German shepherd or German shepherd mix



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Always consider the diagnosis with lameness in a young German shepherd or German shepherd mix.
- May occur alone or with other juvenile orthopedic diseases.
- Osteochondritis dissecans.
- Fragmented medial coronoid process.
- Un-united anconeal process.
- Hip dysplasia.
- Fractures and ligamentous injuries from unobserved trauma.
- Shifting leg lameness—immune-mediated arthritides; Lyme disease; bacterial endocarditis.
- Coccidioidomycosis.
- Bacterial osteomyelitis.
- Hypertrophic osteodystrophy.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal
- May note eosinophilia early in disease

OTHER LABORATORY TESTS

N/A

IMAGING

- Radiographic densities within the medulla of long bones—characteristic; confirm diagnosis.
- Early, middle, and late radiographic lesions.
- Early—trabecular pattern of the ends of the diaphysis becomes more prominent; may appear blurred; may see granular opacities.
- Middle—patchy sclerotic opacities first around the nutrient foramen and later throughout the diaphysis; widened cortex; thickened periosteum with increased opacity.
- Late—during resolution, diminished overall opacity of the medullary canal (toward normal); a coarse trabecular pattern and some granular opacity may remain; may be a period in which the medullary canal becomes more lucent than normal.

- Bone scintigraphy may reveal subtle lesions that later become more apparent on follow-up radiographs.

DIAGNOSTIC PROCEDURES

Bone biopsy—occasionally indicated to rule out neoplasia and bacterial or fungal osteomyelitis that have similar radiographic appearances.

PATHOLOGIC FINDINGS

- Biopsy or necropsy—rarely performed because of excellent prognosis for recovery.
- No gross pathologic lesions.
- Degeneration of the marrow adipocytes surrounding the nutrient foramen followed by proliferation of vascular stromal cells within the marrow sinusoids.
- Osteoid formation and endosteal new bone formation—progress proximally and distally.
- Vascular congestion—may accompany the proliferation of new bone, secondarily stimulating endosteal and periosteal reaction.
- Remodeling of the endosteum—occurs during resolution; reestablishes normal endosteal and marrow architecture.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient

NURSING CARE

Maintenance and replacement fluid therapy—occasionally owing to prolonged periods of inappetence and pyrexia.

ACTIVITY

- Limited—not shown to hasten recovery; lessens pain.
- Moderate to severe disease—pain may cause self-limited movement leading to muscle atrophy.

CLIENT EDUCATION

- Warn client that patient may develop other juvenile orthopedic diseases.
- Inform client that signs of pain and lameness may last for several weeks.
- Warn client that recurrence of clinical signs is common up to 2 years of age.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

NSAIDs

- Minimize pain; decrease inflammation.
- Symptomatic therapy has no bearing on the duration of the disease.
- Carprofen (2.2 mg/kg PO q12h), etodolac (10–15 mg/kg PO q24h), meloxicam

PANOSTEITIS

(CONTINUED)

(0.2 mg/kg PO, IV, or SC first day—then 0.1 mg/kg q24h), deracoxib (1–2 mg/kg PO q24h for OA, 3–4 mg/kg for postoperative pain PO q24h; do not exceed 7 days), firocoxib (5 mg/kg PO q24h), buffered or enteric-coated aspirin (10–25 mg/kg PO q8–12h).

- Glucocorticoids.
- May give anti-inflammatory dosage—prednisone (0.1–0.5 mg/kg PO).
- Potential side effects well documented.
- Goal for chronic use—low-dose and alternate-day therapy.

PRECAUTIONS

NSAIDs—gastrointestinal upset may preclude use.

PRECAUTIONS

NSAIDs—most cause some degree of gastric ulceration.

POSSIBLE INTERACTIONS

NSAIDs—do not use in conjunction with glucocorticoids; risk of gastrointestinal tract ulceration; consider appropriate washout times when switching from one NSAID to another.

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

Recheck lameness every 2–4 weeks to detect more serious concurrent orthopedic problems.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

- Self-limiting disease.
- Treatment—symptomatic; appears to have no influence on duration of clinical signs.
- Multiple limb involvement—common.
- Lameness—typically lasts from a few days to several weeks; may persist for months.
- Occasional case has unrelenting pain and lameness that is unresponsive to therapy. Euthanasia has been recommended in these dogs.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

Typically affects immature and young dogs

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Females reported to be more susceptible to panosteitis during estrus; no proven relationship to reproductive hormones or pregnancy.

SYNOMYS

- Enostosis
- Eosinophilic panosteitis
- Fibrous osteodystrophy
- Juvenile osteomyelitis

ABBREVIATION

- NSAID = nonsteroidal anti-inflammatory drug

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Consulting Editor Walter C. Renberg



Client Education Handout
available online

PANTING AND TACHYPNEA



BASICS

DEFINITION

- Tachypnea—increased respiratory rate.
- Panting—rapid, shallow, open-mouth breathing that is usually not associated with gas exchange issues.

PATHOPHYSIOLOGY

• Respiratory rate, rhythm, and effort are controlled by the respiratory center in the brainstem in response to numerous afferent pathways, both central and peripheral in origin. These include the cerebral cortex, central chemoreceptors, peripheral chemoreceptors, stimulation of mechanoreceptors in the airways that sense lung inflation and deflation, stimulation of irritant receptors of the airways, stimulation of C-fibers in the alveoli and pulmonary blood vessels that sense interstitial congestion, and baroreceptors that sense changes in blood pressure. • Tachypnea and panting can occur in response to stimulation of any of the above receptor pathways.

SYSTEMS AFFECTED

Respiratory

SIGNALMENT

- Dog and cat; no age, or sex predilection.
- Older, large breed dogs predisposed to panting associated with laryngeal paralysis.
- Brachycephalic dogs prone to panting due to upper airway obstruction.

SIGNS

Historical Findings

- Patients with primary respiratory or cardiac disease usually have associated coughing or exercise intolerance.
- Non-respiratory causes—clinical complaints associated with the primary disease, e.g., PU/PD/PP with hyperadrenocorticism, intermittent signs of systemic hypertension with pheochromocytoma.

Physical Examination Findings

- Brachycephalic syndrome (stenoic nares, stertorous respirations associated with soft palate elongation or saccular eversion) may be observed.
- Stridor can be evident on inspiration with upper airway diseases.
- Lower airway disease—cough, expiratory wheezes on auscultation, abdominal effort.
- Pulmonary parenchymal disease—may have crackles on auscultation; harsh or moist lung sounds common, may be normal.
- Cardiogenic pulmonary edema—heart murmur or arrhythmia, tachycardia, gallop sound, hypothermia, pale mucous membranes, poor capillary refill time.
- Pleural space disease—diminished breath sounds: ventrally—fluid; dorsally—air; unilaterally—space-occupying lesions, pyothorax, chylothorax.
- Thoracic wall disease—visible and/or palpable trauma.

- Non-respiratory diseases—findings will depend on the other diseases, e.g., pale mucous membranes if anemic, hepatomegaly with hyperadrenocorticism.
- Other signs could indicate trauma.

CAUSES & RISK FACTORS

Panting

- Pain, anxiety, hyperthermia.
- Brachycephalic airway syndrome.
- Central nervous system disease causing abnormal ventilatory control.
- Cardiovascular compromise (shock), hypertension, arrhythmia.
- Drug therapy (opioids)
- Metabolic acidosis.
- Laryngeal disease.
- Cortisol or norepinephrine excess.
- Can be a normal behavioral pattern in some dogs.

Tachypnea

- Hypoxemia, hypercapnia, hypotension, hyperthermia, anemia, acidosis, systemic inflammation, brainstem disease.
- Airway pathology—inhaled irritant, bronchoconstriction, airway compression, airway infection.
- Interstitial pathology—edema, hemorrhage, inflammation, neoplasia, fibrosis.
- Larynx—laryngeal paralysis, edema, collapse, foreign body, neoplasia, inflammation, trauma, webbing.
- Trachea—collapse, stenosis, trauma, foreign body, neoplasia, parasites.
- Lower airway disease—allergic disease, inflammation, infection (*Mycoplasma*), parasites, neoplasia.
- Pulmonary parenchymal disease—edema (cardiogenic or non-cardiogenic), pneumonia or pneumonitis, neoplasia (primary or metastatic), hemorrhage.
- Pulmonary thromboembolism associated with—IMHA, PLE, PLN, cardiac disease, neoplasia, heartworm disease.
- Pericardial effusion.
- Pleural effusion or pneumothorax.
- Abdominal distention—organomegaly; neoplasia, pregnancy; obesity; ascites; gastric dilatation, torsion.
- CNS disease—compression or infarct near the respiratory center.
- Metabolic acidosis—diabetic ketoacidosis, diarrhea, uremia, renal tubular acidosis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Tachypnea without respiratory distress—may be a non-respiratory problem.
- Stertor and stridor are features of upper airway disease—auscultation over the trachea can help delineate upper airway noises from lower airway noises.
- Thoracic auscultation and percussion—most useful for distinguishing pleural disease (dampened lung sounds, dull percussion) from parenchymal disease (normal, harsh or moist lung sounds, crackles on auscultation).
- Wheezes on auscultation are suggestive of narrowed lower airway (bronchi, bronchioles).
- Crackles on auscultation are features of airway collapse, bronchitis, edema, or other pulmonary parenchymal diseases.
- Congestive heart failure—murmur, tachycardia, poor pulse quality, jugular pulses.

auscultation are features of airway collapse, bronchitis, edema, or other pulmonary parenchymal diseases.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia—can cause non-respiratory tachypnea.
- Polycythemia—chronic hypoxia.
- Inflammatory leukogram—pneumonia, pneumonitis, pyothorax, or non-respiratory causes (SIRS, sepsis).
- Eosinophilia—hypersensitivity or parasitic airway disease.
- Thrombocytosis—hyperadrenocorticism predisposes to PTE; alternatively, could indicate iron deficiency anemia.
- Sodium: potassium ratio < 27 —can be seen with pleural or abdominal effusions.
- High alkaline phosphatase—hyperadrenocorticism predisposes to panting and PTE.
- Hypoproteinemia—may suggest protein losing disease that can predispose to PTE.
- Proteinuria—can predispose to PTE.
- Azotemia—if severe can lead to uremic pneumonitis.
- Hyperglycemia, glucosuria, and ketonuria—could indicate ketoacidosis as cause of tachypnea.

OTHER LABORATORY TESTS

- Fecal examinations if indicated.
- Low dose dexamethasone suppression test to assess adrenal cortical function, if indicated.
- Pleural fluid analysis.
- Serum antigen or antibody titers—heartworm, toxoplasmosis, distemper, FeLV, FIV.
- Pulse oximetry or arterial blood gas—can help differentiate pulmonary from non-respiratory causes.
- Hemoglobin saturation with oxygen $< 95\%$ supportive of hypoxemia.
- PaO_2 —partial pressure of oxygen dissolved in arterial blood; normoxemia: PaO_2 80–120 mmHg (room air, sea level), hypoxemia: $\text{PaO}_2 < 80$ mmHg; F_1O_2 —fraction of inspired oxygen ranges from 0.21 (room air) to 1.0; $\text{PaO}_2/\text{F}_1\text{O}_2$ ratio—measure of lung efficiency; $\text{PaO}_2/\text{F}_1\text{O}_2 \geq 500$ —normal lung efficiency; 300–500—mild insufficiency; 200–300—moderate insufficiency; < 200 —severe insufficiency.
- Reduction in lung efficiency is most commonly due to pulmonary parenchymal disease.
- PaCO_2 or PvCO_2 —partial pressure of CO_2 dissolved in arterial or venous blood; measure of ventilation; normal 30 mmHg $< \text{PCO}_2 < 40$ mmHg.
- Hypercapnia = hypoventilation = decreased alveolar minute ventilation.
- Hypocapnia = hyperventilation = increased alveolar MV.
- Hypoventilation can be due to upper airway obstruction, pleural space disease, thoracic wall disease and abdominal distention; respiratory muscle fatigue from a prolonged period of tachypnea can lead to hypoventilation.
- Blood gas may reveal metabolic acidosis as a cause.
- Coagulation testing—if suspect hemothorax and/or pulmonary hemorrhage.

PANTING AND TACHYPNEA

(CONTINUED)

IMAGING

- Cervical and thoracic radiography: *laryngeal disease*—increased density could suggest edema or soft tissue mass lesion. Also can see large airway narrowing, lymphadenopathy, intraluminal abnormalities. *Lower airway disease*—bronchial thickening, middle lung lobe consolidation (cats), atelectasis, hyperinflation and diaphragmatic flattening (primarily cats). *Pneumonia*—alveolar infiltrates; aspiration pneumonia usually cranoventral distribution or middle lobe affected. *Cardiogenic pulmonary edema*—enlarged cardiac silhouette, pulmonary venous distention, enlarged left atrium with perihilar pulmonary infiltrates in dogs; infiltrates can be of any distribution in cats. *Noncardiogenic pulmonary edema*—caudodorsal distribution. ARDS—diffuse, symmetrical alveolar infiltrates. *Pulmonary vascular abnormalities*—PTE, heartworm disease. *Pleural space disease*—pneumothorax, pleural effusion, mass lesions, diaphragmatic hernias. *Thoracic wall disease*—rib fractures, neoplasia.
- Thoracic ultrasonography: evaluation of distribution of pleural effusion (excellent as guide for thoracocentesis), pneumothorax (absence of “glide sign”), and parenchymal disease (presence of “comet tail” artifact). Pulmonary mass identification—guide fine-needle aspiration; mediastinal evaluation.
- Echocardiography: evaluate cardiac function if cardiogenic pulmonary edema or pleural effusion suspected; elevated pulmonary artery pressure and right ventricular overload can support diagnosis of PTE; visualize heart-based masses, rule out pericardial effusion.
- Abdominal ultrasound: evaluation of abdominal distention, assess adrenal gland size. • Fluoroscopy: evaluate tracheal and/or large airway collapse; evaluate diaphragmatic function.
- Computed tomography: airway, pulmonary parenchymal, and pleural space disease can be evaluated; can detect lesions not clearly defined on radiographs but requires general anesthesia.
- Pulmonary vascular angiography: gold standard for diagnosis of PTE but requires general anesthesia.
- Perfusion scintigraphy: abnormal perfusion scan is considered supportive of PTE.
- May need CNS imaging.

DIAGNOSTIC PROCEDURES

- Laryngoscopy/nasopharyngoscopy/tracheoscopy—to evaluate laryngeal function and visualize foreign bodies and masses; visualize caudal nasopharyngeal region with flexible endoscope or spay hook and dental mirror.
- Bronchoscopy—evaluate large and small airways; take biopsies; perform bronchoalveolar lavage for cytology and culture.
- Thoracocentesis—fluid analysis and culture.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient care if life-threatening; therapy depends on underlying cause.
- Administer oxygen and see if tachypnea resolves—this would be supportive of a primary respiratory problem.
- Upper airway disease—use sedation to reduce inspiratory effort. Check body temperature frequently and actively cool patients as needed. Severe upper airway disease requires intubation to stabilize; if the problem cannot be immediately cured, placement of a temporary tracheostomy tube is indicated. Remove foreign bodies; perform surgical excision/biopsy of masses, surgical correction for laryngeal paralysis and brachycephalic syndrome; give anti-inflammatory medications for laryngeal edema.
- Lower airway disease—bronchodilators; oxygen therapy until stable; systemic corticosteroids may be required to stabilize cats with acute bronchoconstriction.
- Pulmonary parenchymal disease—oxygen therapy, antibiotics if pneumonia; treat coagulation disorders; cardiogenic edema requires furosemide ± vasodilators. Non-cardiogenic edema requires oxygen therapy, may require positive-pressure ventilation if oxygen therapy alone is not adequate to stabilize the patient.
- Pleural space disease—thoracocentesis for air and fluid. Place a chest tube if repeated chest taps are needed to keep patient stable.
- Abdominal distention—drain ascites only as needed to keep the patient comfortable; relieve gastric distention.
- Non-respiratory diseases—treat primary problem.

NURSING CARE

- Oxygen therapy via cage, nasal cannula, E-collar covered in plastic wrap, mask, or flow-by. Humidify oxygen source if giving oxygen therapy for more than a few hours.
- Monitor temperature regularly, as hyperthermia will worsen respiratory difficulty.

DIET

Weight-reducing diet if obesity is a contributing cause.

SURGICAL CONSIDERATIONS

- Anesthesia must be carefully tailored to the patient. Securing an airway is essential and rapid intravenous induction is important. Have multiple sizes of endotracheal tubes available if upper airway obstruction is suspected.
- If laryngeal paralysis or

brachycephalic syndrome is suspected, prepare for surgical correction at the time of diagnosis. Warn owners of increased likelihood of aspiration pneumonia in dogs with laryngeal disease.



MEDICATIONS

DRUG(S)

Varies with underlying cause (see “Appropriate Health Care”).



MISCELLANEOUS

SEE ALSO

- Acidosis, Metabolic • Acute Respiratory Distress Syndrome • Asthma, Bronchitis—Cats • Brachycephalic Airway Syndrome • Congestive Heart Failure, Left-Sided • Hyperadrenocorticism chapters • Laryngeal Diseases • Pneumonia chapters • Pneumothorax • Pulmonary Edema, Noncardiogenic

ABBREVIATIONS

- ARDS = acute respiratory distress syndrome
- CNS = central nervous system
- FeLV = feline leukemia virus • FIV = feline immunodeficiency virus • IMHA = immune-mediated hemolytic anemia • MV = minute ventilation • PLE = protein-losing enteropathy • PLN = protein-losing nephropathy • PTE = pulmonary thromboembolism • PU/PD/PP = polyuria, polydipsia, polyphagia • SIRS = systemic inflammatory response syndrome

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PAPILLOMATOSIS



BASICS

OVERVIEW

- Cutaneous mucous membrane lesions of dogs and cats caused by various papilloma viruses.
- Dogs: oral papillomatosis, venereal papillomatosis, exophytic cutaneous papillomas, cutaneous inverted papillomas, multiple papillomas of the footpad, canine pigmented viral plaques.
- Cats: feline cutaneous papillomas, feline cutaneous fibropapillomas (feline sarcoids), feline viral plaques.
- Viral plaques may progress to BISC, SCC or invasive carcinoma.

SIGNALMENT

Dogs

- Puppies and young adult dogs—oral papillomatosis, venereal papillomatosis, multiple papillomas of the footpad, cutaneous inverted papillomas, canine pigmented viral plaques (breed predisposition).
- Older dogs—exophytic cutaneous papillomas, cutaneous inverted papillomas.
- Miniature schnauzers and pugs—pigmented viral plaques; associated with immunosuppression in other breeds.

Cats

- More common in older cats; associated with immunocompromise (e.g., FIV).
- Feline sarcoids: younger cats, especially those with outdoor exposure.

SIGNS

Dogs

- Cutaneous papillomas—pedunculated, fronds of epithelium, up to 1 cm in diameter located anywhere.
- Canine papillomavirus—most often oral mucosa, hard palate, epiglottis; may interfere with prehension, swallowing; trauma results in halitosis and ptalism; may be confined to genital or eyelid regions.
- Cutaneous inverted papillomas—less common, multiple lesions often found with a central pore; on ventral abdomen; caused by distinctly different papilloma virus from COPV.
- Multiple papillomas affecting footpads in younger dogs—firm, hyperkeratotic lesions causing discomfort and lameness.
- Canine pigmented viral plaques—miniature schnauzers, pugs; Boston terriers, French bulldogs; rarely transform to SCC; ventral abdomen and inner thigh region.

Cats

- Feline cutaneous papillomas—rare.
- Feline viral plaques—more common; may progress to BISC or invasive carcinoma.
- Feline sarcoid lesions—uncommon.
- Cats 10 years or older; other systemic disease causing immunosuppression (e.g., FIV).

CAUSES & RISK FACTORS

- Oral papillomas affecting naive dogs and recovered animals develop lifelong immunity.
- Dogs—cutaneous papillomas thought to

involve cell-mediated immunologic defects.

- Older, immunosuppressed cats develop plaques and BISC.
- Canine pigmented viral plaques—strong breed predisposition.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Dogs

- Oral cavity, oropharynx—fibromatous epulis, transmissible venereal tumor, SCC.
- Cutaneous—sebaceous hyperplasia, acrochordon.
- Pigmented plaque—melanocytoma.
- Inverted—infundibular keratinizing acanthoma.

Cats

Eosinophilic granuloma, complex, actinic keratoses, cutaneous lesions of FeLV, multicentric SCC *in situ*, SCC.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

Cats: FeLV, FIV

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Gross lesions have a typical appearance.
- Biopsy for histopathology; immunohistochemistry demonstrates viral antigens within lesions; PCR not definitive.

PATHOLOGIC FINDINGS

- Dependent upon syndrome; all lesions share cytopathic effects of papillomavirus infection: hyperkeratosis, acanthosis, koilocytes in stratum spinosum, abnormal, large keratohyalin granules in stratum granulosum.
- Viral pigmented plaques may lack koilocytes and viral inclusion bodies.



TREATMENT

- Most lesions regress spontaneously (especially oral forms).
- Surgery if needed (excision, cryosurgery, or electrosurgery).
- Persistent disease (dogs)—COPV vaccine reported to induce epithelial tumors and SCC at vaccination sites; latency period 11–34 months; autogenous vaccination: treatment controversial.
- Cats—diagnosis for visceral diseases or causes of immunosuppression.



MEDICATIONS

DRUG(S)

- α -Interferon—30 units/cat PO q24h.
- Imiquimod—applied to individual lesions three times/week for 4 weeks.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Imiquimod—potential for human exposure when applying to patient; causes severe localized reaction; use with caution at mucocutaneous junctions.



FOLLOW-UP

PATIENT MONITORING

Monitor for signs of malignant transformation to SCC.

PREVENTION/AVOIDANCE

- Separate dogs with oral papillomas from susceptible animals.
- Commercial kennels—may consider autogenous vaccination.

EXPECTED COURSE AND PROGNOSIS

- Dogs—prognosis good; incubation period 1–8 weeks; regression usually 1–5 months; lesions persist 24 months or more.
- Cats—long-term prognosis for plaques and BISC depends on concurrent diseases.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

Dependent upon viral strain

ZOONOTIC POTENTIAL

Papillomaviruses: species specific

PREGNANCY/FERTILITY/BREEDING

- Venereal lesions may preclude breeding.
- Transmission of viral infection likely; especially when active lesions present.

P

SEE ALSO

Dermatoses, Viral (Non-papillomatosis)

SYNOMYMS

Bowen's disease = BISC

ABBREVIATIONS

- BISC = bowenoid *in situ* carcinoma
- COPV = canine oral papillomavirus
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- PCR = polymerase chain reaction
- PV = papilloma virus
- SCC = squamous cell carcinoma

Suggested Reading

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Author Elizabeth R. May

Consulting Editor Alexander H. Werner

PARALYSIS



BASICS

DEFINITION

- Paresis—weakness of voluntary movement.
- Paralysis—lack of voluntary movement.
- Quadripareisis (tetraparesis)—weakness of voluntary movements in all limbs.
- Quadriplegia (tetraplegia)—absence of all voluntary limb movement.
- Paraparesis—weakness of voluntary movements in pelvic limbs.
- Paraplegia—absence of all voluntary pelvic limb movement.
- Schiff-Sherrington syndrome may occur with severe spinal cord trauma below T2—patient in lateral recumbency, front limbs and neck in extension, with paralysis of pelvic limbs; front limb function is normal; prognosis based on presence or absence of pain perception in pelvic limbs.
- Spinal shock may occur with severe spinal cord trauma, usually located near the thoracolumbar spine—paralyzed pelvic limbs with initially areflexic pelvic limb reflexes that become exaggerated (and more indicative of a T3–L3 lesion localization) within minutes to a few hours after the trauma.

PATOPHYSIOLOGY

- Weakness—caused by lesions in the upper motor neuron (UMN) or lower motor neuron (LMN) systems.
- UMN system—cell bodies or nuclei located within the brain and responsible for initiating voluntary movement; axons from these cell bodies form the tracts (rubrospinal, corticospinal, vestibulospinal, reticulospinal) that descend from the brain to synapse on the interneurons in the spinal cord. Interneuronal axons synapse on large alpha motor neurons in the ventral gray matter of the spinal cord; these are cell bodies of origin for the LMN system, which is responsible for spinal reflexes.
 - LMN system—collections of lower motor neurons in the cervical and lumbar intumescences that give rise to axons that form the ventral nerve roots, spinal nerves, and (ultimately) the peripheral nerves that innervate limb muscles.
 - Evaluation of limb reflexes—determines which system (UMN or LMN) is involved.
 - UMN and their axons—have inhibitory influence on the large alpha motor neurons of the LMN system; maintain normal muscle tone and normal spinal reflexes.
 - If UMN is injured, spinal reflexes are no longer inhibited or controlled and spinal reflexes become exaggerated or hyperreflexic.
 - If LMN system is injured, spinal reflexes cannot be elicited (areflexic) or are reduced (hyporeflexic). Large alpha motor neurons or their processes (peripheral nerves) also maintain normal muscle tone. With LMN injury, muscle wasting is usually severe and within 5–7 days of injury.

SYSTEMS AFFECTED

Nervous

SIGNALMENT

Dog and cat

SIGNS

General Comments

Limb weakness—acute or gradual onset

Historical Findings

- Owner may describe the patient as being “down,” unable to move, walk, or get up.
- Many focal compressive spinal cord diseases begin with ataxia and progress to weakness, then to paralysis.

Physical Examination Findings

- Usually normal, unless the disease is systemic.
- If in pain, patient may resent handling and manipulation.
- Aortic emboli (ischemic neuromyopathy)—patient may be paraplegic and areflexic or hyporeflexic; femoral pulses absent; limbs often cold; nail beds often blue.

Neurologic Examination Findings

- Confirm that the problem is weakness or paralysis.
- If limbs are paralyzed—likely bladder is also paralyzed, negating voluntary urination.
- Localize problem to either LMN or UMN system.
- Tetraparesis with exaggerated spinal reflexes in all limbs—lesion located at C1–C5 spinal segments or in the brain.
- Tetraparesis with normal or depressed front limb spinal reflexes and exaggerated pelvic limb spinal reflexes—lesion located at C6–T2 spinal segments.
- Tetraparesis with depressed spinal reflexes and muscle tone in all limbs—lesion is diffuse involving muscles or peripheral nerves, or, the cervical (C6–T2 spinal cord segments) and lumbar spinal cord intumescences (L4–S2 spinal segments).
- Normal front limbs but paraparesis/paraplegia with exaggerated pelvic limb spinal reflexes—lesion located at T3–L3 spinal segments.
- Normal front limbs but paraparesis/paraplegia with depressed to absent pelvic limb spinal reflexes—lesion located at L4 spinal segment and caudally.
- Normal front limb and pelvic limb motor activity but flaccid tail/anus and urinary and/or fecal incontinence—lesion located at S2 spinal segment and caudally.
- Normal front limbs but paraparesis/paraplegia and depressed patellar reflexes—lesion involves spinal segments L4–6, located in vertebral bodies L3–4.
- Normal front limbs but paraparesis/paraplegia, exaggerated patellar reflexes, and weak flexor and sciatic reflexes—if only the spinal cord is affected (no root involvement), lesion involves spinal segments L6–S2, located in vertebral bodies L4–L6.

CAUSES

Quadriplegia

- If LMN system—acute onset: coonhound paralysis, botulism, tick paralysis, fulminating form of myasthenia gravis, protozoal

myoneuritis.

- If LMN system—more gradual onset: polyneuropathies and polymyopathies from toxicity, infection, inflammation, endocrinopathy, metabolic disease, or congenital/inherited disease.
- If UMN system—acute onset: disc herniation; fibrocartilaginous embolism; trauma; neoplasia; myelitis of many causes.
- If UMN system—gradual onset: disc herniation; discospondylitis; neoplasia; myelitis of many causes; malformations of the spine or spinal cord.

Paraplegia

- If UMN system—disc herniation; discospondylitis; fibrocartilaginous embolism; neoplasia; trauma; congenital malformations of spine or spinal cord; degenerative myelopathy.
- If LMN system—fibrocartilaginous embolism; disc herniation; lumbosacral instability; discospondylitis; trauma; neoplasia; spina bifida.

Quadriplegia with Cranial Nerve Deficits, Seizures, or Stupor

- UMN system—diseases of the brainstem: encephalitis; neoplasia; trauma; vascular accidents; congenital or inherited disorders.

RISK FACTORS

- Degenerative disc disease—dachshunds, poodles, cocker spaniels, and beagles.
- Hunting dogs—coonhound paralysis.
- Roaming animals—spinal cord and vertebral trauma.
- Atlantoaxial luxation—toy and small breeds.
- Lumbosacral instability—large breeds; working breeds; German shepherds.
- Cervical spondylomyelopathy (wobbler syndrome)—large breeds; Doberman pinschers; Great Danes.
- Syringomyelia—Cavalier King Charles spaniels, brachycephalic toy breeds and many others.
- Spinal arachnoid diverticulum: rottweilers, pugs, small breeds.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Weak or paralyzed pelvic limbs—ensure femoral pulses are present and normal; aortic or femoral artery emboli may lead to LMN paraparesis or paraplegia.
- Spinal reflexes—localize weakness to the cervical, thoracolumbar, or lower lumbar cord segments.
- Acute onset—be careful when moving patient if possibility of trauma.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal, unless inflammatory diseases involved.

OTHER LABORATORY TESTS

- Urinary tract inflammation—urine culture may be positive in discospondylitis or in any dog that has had chronic bladder paralysis or repeated urinary catheterizations.
- Discospondylitis—diagnose by spinal

(CONTINUED)

PARALYSIS

radiography (intervertebral disc space lysis); perform *Brucella* titer; consider blood and urine bacterial cultures. • Exercise-induced weakness—determine acetylcholine receptor antibody titers (test for myasthenia gravis); check serum creatine kinase concentration (polymyositis or polymyopathy), RBC count (anemia or polycythemia), and blood glucose concentration (hypoglycemia); check for cardiac arrhythmia and hypoxia via ECG, thoracic radiography, Holter monitoring, and echocardiography; muscle biopsy. • LMN weakness or muscle pain, muscle atrophy, or hypertrophy—determine creatine kinase concentration to help diagnose polymyositis; perform muscle and nerve biopsy; evaluate *Neospora caninum* and *Toxoplasma gondii* serum titers. • Myelitis or meningitis—dog: perform titers for *N. caninum*, *T. gondii*, Rocky Mountain spotted fever, *Ehrlichia* spp., and canine distemper virus; cat: perform serum titers for *T. gondii* and *Cryptococcus neoformans* and evaluate spinal fluid for signs of feline infectious peritonitis virus and *C. neoformans*.

IMAGING

- Spinal radiography—may reveal disc herniation, discospondylitis, bony tumor, congenital vertebral malformation, and fracture or luxation.
- Myelography—required if survey radiography not diagnostic and CT or MRI not available.
- CT or MRI—has replaced myelography where technology is available.

DIAGNOSTIC PROCEDURES

- CSF—before myelography to detect myelitis and meningitis; if high protein or cell numbers consider infectious disease titer analysis.
- Needle electromyography and motor nerve conduction velocity—may help with diagnosis and characterization of generalized LMN.
- Muscle and nerve biopsy—generalized LMN weakness.
- Aspirate intervertebral disc space under fluoroscopy; perform cytology and culture to isolate an infectious agent if discospondylitis is observed on imaging studies.

**TREATMENT**

- Inpatient—with severe weakness or paralysis until bladder function can be ascertained.
- Hand feeding—with diffuse LMN, swallowing can be affected.
- Feeding from an elevated platform or installation of a feeding

tube—recommended for animals with megaesophagus until resolution occurs.

- Activity—restrict until spinal trauma and disc herniation can be ruled out.
- Physical therapy—important for paralyzed patients; tone muscles and keep joints flexible.
- Bedding—check and clean frequently to prevent urine scalding and superficial pyoderma; use padded bedding or waterbed to help prevent decubital ulcer formation.
- Turn quadriplegic patients from side to side four to eight times daily—prevents hypostatic lung congestion and decubital ulcer formation.
- Surgery—for disc herniation, fracture, and some neoplasias and congenital conditions; often the quickest and most effective method of improving the neurologic status.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Medications depend on underlying cause of weakness.
- Corticosteroid use, even in known diseases like spinal trauma or disc herniation, is controversial. May help to allay pain associated with some causes of paralysis, but do not expedite spinal cord recovery.
- Dexamethasone 0.1–0.2 mg/kg q48h for pain relief for two to three doses.
- Prednisolone 0.5–1 mg/kg q12–24h for pain relief for 3–5 days.
- Pyridostigmine bromide 0.5–3 mg/kg PO q8–12h for suspected myasthenia gravis; administer cautiously at low dose while waiting for titer results.
- If acute generalized LMN signs—check for ticks; use appropriate insecticides.

CONTRAINdicATIONS

Corticosteroids—do not use with discospondylitis or fungal or protozoal myelitis/meningitis; do not use with myasthenia gravis if aspiration pneumonia is present.

PRECAUTIONS

Corticosteroids—associated with gastrointestinal ulceration and hemorrhage, delayed wound healing, and heightened susceptibility to infection.

ALTERNATIVE DRUG(S)

- NSAIDS for spinal diseases associated with bone discomfort or pain.
- Tramadol 2 mg/kg q12h PO (dogs or cats), up to 4–5 mg/kg q12h (dogs only) for pain relief. Avoid using with antidepressants.
- Gabapentin 3–10 mg/kg q12h PO for neuropathic pain.
- Butorphanol 0.2–0.6 mg/kg q2–4h for pain control.

**FOLLOW-UP****PATIENT MONITORING**

- Neurologic examinations—daily to monitor status.
- Bladder—evacuate (via manual expression or catheterization) three to four times a day to prevent overdistention and subsequent bladder atony; once bladder function has returned, patient can be managed at home.

POSSIBLE COMPLICATIONS

- Urinary tract infection, bladder atony, urine scalding and pyoderma, constipation, decubital ulcer formation.
- Aspiration pneumonia—with generalized LMN disease or in any quadriplegic patient.
- Myelomalacia—with severe spinal cord trauma or disc herniations.
- Respiratory compromise or paralysis—with myelomalacia or generalized LMN disease.

**MISCELLANEOUS****SEE ALSO**

- Schiff-Sherrington Phenomenon
- Neck and Back Pain
- Syringomyelia and Chiari-like Malformation
- Exercise-Induced Weakness/Collapse in Labradors

P

ABBREVIATIONS

- CSF = cerebrospinal fluid
- CT = computed tomography
- ECG = electrocardiogram
- LMN = lower motor neuron
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug
- RBC = red blood cell
- UMN = upper motor neuron

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**Client Education Handout
available online**

PARANEOPLASTIC SYNDROMES



BASICS

OVERVIEW

Paraneoplastic syndromes (PNS) are a diverse group of systemic disorders resulting from the metabolic effects of cancer in tissues remote from the tumor. These disorders are usually caused by production and release of substances not normally released by the tumor cell of origin or in amounts not normally produced by those cells. Other etiologies of PNS aside from production of metabolically active substances include autoimmune disease stimulation, immune complex formation, immunosuppression, and ectopic receptor production/competitive blockade of normal hormones. PNS may also occur secondary to substances produced by normal cells due to the presence of the tumor (e.g., tumor necrosis factor production by reticuloendothelial cells contributing to cancer cachexia). Many PNS in veterinary medicine have an unknown etiology. Pathophysiology depends on the specific PNS (see Table 1).

SIGNALMENT

Any dog or cat with a histologically malignant (most common) or benign cancer (rare).

SIGNS

Vary with tumor type and organ systems affected but include:

- Alopecia (feline paraneoplastic syndrome)
- Anemia
- Cachexia
- Cutaneous flushing
- Diencephalic syndrome
- Disseminated intravascular coagulation
- Eosinophilia
- Gastroduodenal ulceration
- Hypercalcemia
- Hypertrophic osteopathy
- Hypoglycemia
- Myelofibrosis
- Neutrophilic leukocytosis
- Nodular dermatofibrosis
- Polycythemia
- Superficial necrolytic dermatitis
- Thrombocytopathy
- Thrombocytopenia
- Thrombocytosis

P

CAUSES & RISK FACTORS

Production and release of substances not normally released by the tumor cell of origin or in amounts not normally produced by those cells and the substances' subsequent effects on target tissues.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Varies with syndrome

CBC/BIOCHEMISTRY/URINALYSIS

Helpful in identifying and monitoring several of the reported syndromes.

OTHER LABORATORY TESTS

Ionized calcium and parathormone levels—assess patients with hypercalcemia; hypercalcemia of malignancy usually characterized by high ionized calcium and low PTH, may occasionally have elevated PTH-rP.

IMAGING

- Radiography—detect hypertrophic osteopathy
- Advanced imaging (CT or MRI)—detect occult tumor

DIAGNOSTIC PROCEDURES

Biopsy—diagnose paraneoplastic skin lesions



TREATMENT

- Varies based on the underlying tumor and the clinical manifestations of the paraneoplastic syndrome.
- The only definitive treatment is to treat the underlying neoplasia rather than to try to control the clinical signs of the paraneoplastic syndrome. If the primary tumor cannot be treated, then management of clinical signs, as best as possible, is indicated for palliation.



MEDICATIONS

DRUG(S)

Depends on underlying tumor type



FOLLOW-UP

PATIENT MONITORING

As for underlying tumor type



MISCELLANEOUS

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging
- PTH = parathormone

Suggested Reading

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(CONTINUED)

PARANEOPLASTIC SYNDROMES

Table 1

Syndrome	Primary Tumor Association (Dog)	Primary Tumor Association (Cat)	Primary Mechanism
Alopecia	Adrenal carcinoma		Dogs: due to an excess of cortisol production; most often associated with hyperadrenocorticism Cats: mechanism unknown. See Adenocarcinoma, Pancreas; Hyperadrenocorticism (Cushing's Syndrome—Cats); and Feline Paraneoplastic Alopecia
Alopecia (feline paraneoplastic alopecia)		Pancreatic carcinoma and carcinoma of the biliary tree	
Cachexia	Assorted—true cancer cachexia is relatively rare	Assorted—true cancer cachexia is relatively rare	Severe metabolic derangements likely caused by cytokines and hormones; may result from alterations in lipid, protein, and carbohydrate metabolism that create a net energy loss in spite of adequate caloric intake; anaerobic metabolic pathways of cancer cells may play a role. See Weight Loss and Cachexia
Cutaneous flushing syndrome	Pheochromocytoma; mast cell tumor	Not reported	Inappropriate release of vasoactive substances, such as histamine, causes paroxysmal flushing of the skin
Diencephalic syndrome	Astrocytoma, anaplastic ependymoma	Not reported	Tumor is present in the diencephalon region of the brain; excess of growth hormone results in dramatic weight loss (without acromegaly) despite adequate caloric intake
Disseminated intravascular coagulation	Hemangiosarcoma; many others	Myeloproliferative disease	See Disseminated Intravascular Coagulation
Eosinophilia	Assorted, including lymphoma and mast cell tumors	Assorted, including lymphoma and mast cell tumors	May be due to stimulation of eosinophil precursors by products such as interleukin-2, -3, and -5 and granulocyte-macrophage colony-stimulating factor
Exfoliative dermatitis (feline thymoma associated exfoliative dermatitis)	Not reported	Thymoma	Not completely elucidated, likely due to the induction of autoreacting T-lymphocytes
Feminization syndrome	Testicular tumors—especially Sertoli cell tumors		Due to hyperestrogenism or a relative testosterone:estrogen imbalance that is uncomplicated by myelosuppression
Gastroduodenal ulceration	Non-islet cell pancreatic neoplasia; mast cell tumor	Rare	Inappropriate gastrin secretion (non-islet cell tumor) or excess histamine secretion (mast cell)
Hypercalcemia	Lymphoma; apocrine gland adenocarcinoma of the anal sac (AGASACA); multiple myeloma; others	Relatively rare; lymphoma; squamous cell carcinoma; others	Dogs: multiple secreted factors involved; with lymphoma and AGASACA may involve parathyroid hormone-related protein (PTHrP) production Cats: mechanisms unexplored. See Hypercalcemia
Hypertrophic osteopathy	Metastatic and primary tumors of the lung, intra-abdominal tumors also	Metastatic and primary tumors of the lung, intra-abdominal tumors also	Characterized by distal limb soft tissue swelling followed by periosteal new bone growth. The etiology is unknown. Several mechanisms likely play a role, including vagally-mediated changes in limb perfusion, cytokine and growth factor secretion, immune mechanisms, vascular thrombi caused by platelets and antiphospholipid antibodies, and interaction between activated platelets and the endothelium

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PARANEOPLASTIC SYNDROMES

(CONTINUED)

Table 1

(Continued)

Syndrome	Primary Tumor Association (Dog)	Primary Tumor Association (Cat)	Primary Mechanism
Hyperviscosity syndrome	Immunoglobulin-secreting tumor (e.g., multiple myeloma, lymphoma)	Immunoglobulin-secreting tumor	Accumulation of large immunoglobulin proteins or polymerized small immunoglobulin proteins in the blood that result in decreased blood flow from increased viscosity. See Multiple Myeloma and Paraproteinemia
Hypoglycemia	Insulinoma; benign and malignant smooth muscle tumors; large mesenchymal tumors; others	Rare; insulinoma	Involves the excess production of insulin or insulin-like factors or excessive glucose utilization. See Insulinoma
Immune complex disorders	Lymphocytic leukemia; primary erythrocytosis	Lymphoma	Secondary to antigen-antibody-immune complex activation; glomerulonephritis is most recognized problem
Myasthenia gravis	Thymoma; others	Very rare; thymoma	Exact mechanism is unknown, likely immune-mediated, may be due to effects of follicular helper T-cells. See Myasthenia Gravis
Myelofibrosis	Assorted	Assorted	See Myelodysplastic Syndromes
Neutrophilic leukocytosis	Hemangiosarcoma; lymphoma; others	Assorted; lymphoma, carcinomas and sarcomas	Production of a granulocyte-monocyte stimulating cytokine is likely cause
Nodular dermatofibrosis	Renal cystadenoma or cystadenocarcinoma primarily in German shepherds and shepherd crosses. Also reported in one golden retriever	Not reported	Mechanism is unknown but involves proliferation of fibroblasts. Propensity to develop is inherited in an autosomal dominant pattern. May be linked to chromosome 5. Loss of heterozygosity/function of the <i>FLCN</i> gene may contribute to neoplastic transformation of renal epithelial cells. Renal tumors are usually slowly progressive and almost always bilateral
Pemphigus	Rare, reported in one case of mediastinal lymphoma and one splenic sarcoma	Not reported	Autoimmunity to target antigens (periplakin and envoplakin) in the skin
Peripheral nerve syndromes	Various	Not reported	Unknown, but usually subclinical and secondary to changes in myelination
Polycythemia	Renal sarcoma and carcinoma; others	Renal carcinoma	Inappropriate secretion of erythropoietin or erythropoietin-like peptides. See Polycythemia and Polycythemia Vera
Superficial necrolytic dermatitis (metabolic epidermal necrosis, hepatocutaneous syndrome, necrolytic migratory erythema)	Hepatic neoplasia; pancreatic neoplasia (glucagonoma)	Pancreatic neoplasia (glucagonoma)	Many names used to describe similar clinical entities; usually observed in patients with hepatic disease and less commonly with glucagon-secreting pancreatic tumors; sometimes referred to as glucagonoma syndrome; exact mechanism is unclear; may see associated glucose intolerance or diabetes mellitus
Thrombocytopenia	Immunoglobulin-secreting tumors	Immunoglobulin-secreting tumors	Immunoglobulin molecules inhibit normal platelet aggregation. See Thrombocytopathies
Thrombocytopenia	Lymphoma, multiple myeloma, hemangiosarcoma, others	Lymphoma, others	Thrombocytopenia, primary immune mediated or secondary to myelophthisis. See Thrombocytopenia
Thrombocytosis	Myeloproliferative disorders	Myeloproliferative disorders	Overproduction of cytokines that stimulate thrombopoietin production (e.g., interleukin-1, -3, -6, -11)

PARAPHIMOSIS, PHIMOSIS, AND PRIAPIST



BASICS

OVERVIEW

- Phimosis—inability to protrude the penis beyond the preputial orifice.
- Paraphimosis—exteriorized penis cannot be retracted back into the sheath. • Priapism—prolonged extrusion of an erect penis not associated with sexual arousal; can result from excessive parasympathetic stimulation or decreased venous outflow from the corpus cavernosum penis; relatively uncommon condition in dogs and rare in cats.

SIGNALMENT

- Dog and cat. • German shepherd and golden retriever—observed congenital preputial stenosis causing phimosis; possibly hereditary. • Siamese cat—one report noted six of seven cases of priapism were Siamese.

SIGNS

- Phimosis—may be undetected until unsuccessful in attempts to copulate; severe defects in the neonate interfere with urination; may cause pooling of urine in preputial cavity, can lead to balanoposthitis, and even septicemia. • Paraphimosis—if recent only sign may be licking of an exteriorized penis; after hours of exposure, may see ischemic necrosis and urethral obstruction; edema and swelling may make differentiation from priapism difficult.
- Priapism—persistent penile erection lasting > 4 hours; bulbus glandis firm and swollen.

CAUSES & RISK FACTORS

- Phimosis—abnormally small preputial orifice; congenital or acquired (e.g., caused by injury or disease); may be associated with a persistent penile or preputial frenulum (thin band of connective tissue joining the penis and prepuce along the ventral glans).
- Paraphimosis—usually associated with erection and/or copulation; preputial hair at the orifice can entrap the penis, especially the bulbus glandis, preventing retraction; moderately stenotic preputial orifice may contribute; injuries; os penis fractures; neurologic disease (encephalomyelitis, intervertebral disc disease); balanoposthitis; penile swelling (neoplasia, strangulation with foreign body); incompetent preputial muscles.
- Priapism—non-ischemic: (arterial, high flow) trauma, vasoactive drugs, neurologic conditions, canine distemper; ischemic (veno-occlusive, low flow): trauma during mating, chronic distemper encephalomyelitis, penile thromboembolism, amphetamine use, penile neoplasia, perineal abscess, cause often unknown; humans (sickle cell disease, hematologic dyscrasias, hemodialysis, fluid therapy, heparin therapy, vasoactive drugs,

spinal cord injury, anesthesia, urethral obstruction due to uroliths).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Paraphimosis—exposure of the glans penis caused by abnormality of the retractor penis muscles or prepuce muscles, large preputial opening, short prepuce, or priapism.
- Priapism—urethral obstruction by uroliths (dysuria).

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal. • Phimosis in neonates—may note severe balanoposthitis and evidence of septicemia (e.g., leukocytosis, neutrophilia progressing to neutropenia, positive urine cultures).

OTHER LABORATORY TESTS

- Penile blood gas analysis to differentiate types of priapism in dogs: ° Ischemic: pH < 7.25, a P_{O_2} < 30 mmHg, P_{CO_2} > 60 mmHg ° Non-ischemic: pH of 7.4, a P_{O_2} > 90 mmHg, P_{CO_2} < 40 mmHg.

DIAGNOSTIC PROCEDURES

- Ultrasonography—visualization of engorged penile vessels. • Neurologic exam, radiographs, magnetic resonance imaging—to evaluate spinal cord.



TREATMENT

PHIMOSIS

- Surgical enlargement of the preputial orifice. • Persistent penile frenulum (dogs)—remove band of tissue holding the glans penis to the parietal lamina of prepuce.

PARAPHIMOSIS

- Requires immediate treatment—after 24 hours, tissue damage and urethral obstruction may necessitate penile amputation; goal: replace the penis in a normal position. • Indwelling urinary catheter—if urethral patency is in question.
- Remove foreign objects. • Lubricate the penis. • Compresses of hypertonic glucose solutions. • Surgically enlarge the preputial orifice, if necessary. • Phalloplasty has reportedly been successful in correcting the condition. • Castration not effective; paraphimosis is not testosterone-dependent.

PRIAPIST

- Aspiration of penile blood may be therapeutic (temporary pain relief) and diagnostic (blood gas analysis to differentiate ischemic from non-ischemic conditions).
- Identifying the underlying cause is often not possible before ischemia of the penis occurs;

penile amputation and perineal urethrostomy usually required due to irreparable ischemic necrosis of the penis; castration not effective.

- Penile amputation and perineal urethrostomy—indicated for cats with difficulty urinating. • Abdominal compression bandage and indwelling urinary catheter—maintain the penis within the prepuce; may also reduce localized edema. Ischemic priapism may be treated with intrapenile injections of phenylephrine (100–500 µg diluted into 1 mL of saline solution).



MEDICATIONS

DRUG(S)

- Antibiotic ointments—maintain treatment; prevent adhesions between penis and prepuce.
- None approved or proven safe.



FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS

- Phimosis—fair to good if identified prior to development of septicemia. • Paraphimosis and priapism—guarded to poor for return to breeding activity; fair to good for life with early successful medical and/or surgical management.



MISCELLANEOUS

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PARAPROTEINEMIA



BASICS

OVERVIEW

- The presence in the blood of an abnormal protein (paraprotein or M component) produced by a single clone of cells. The paraprotein may be composed of whole immunoglobulin molecules, subunits, light chains, or heavy chains. This disorder is commonly seen with plasma cell neoplasms, such as multiple myeloma, or other immunoglobulin secreting B-cell lymphoproliferative diseases, such as CLL or lymphoma.
- Primary signs are related to the underlying neoplasm and could be related to bony invasion or bone marrow infiltration.
- Markedly elevated serum paraprotein levels can produce signs of HVS.

SYSTEMS AFFECTED

- Musculoskeletal—bone lysis by the neoplastic cells can cause lameness and pathologic fractures.
- Nervous—bone lysis of the vertebrae can cause neurologic signs; disorientation, seizures, cranial nerve deficits, or vestibular signs may be associated with HVS.
- Hemic/Lymphatic/Immune—myelophthisis and secondary immune-mediated destruction may cause anemia, leukopenia, or thrombocytopenia. Hemostasis may be compromised by paraprotein interference with platelet and coagulation factor function; inhibited normal immunoglobulin production leads to decreased immunoglobulin levels, thus an increased susceptibility to infection.
- Ophthalmic—HVS can cause dilated and tortuous retinal vessels, retinal detachment, or retinal hemorrhage.
- Cardiovascular—HVS can cause tachycardia, hypertrophic cardiomyopathy, and gallop rhythm, as well as cardiac failure in cats more often than dogs.
- Renal/Urologic—renal failure is possible secondary to tumor infiltration, HVS causing renal hypoxia, proteinuria, hypercalcemia of malignancy, or infection.

SIGNALMENT

- Dogs—middle-aged to older
- Cats (rare)—older
- No sex predilection

SIGNS

- Lethargy and weakness
- Lameness, paresis
- Epistaxis or gingival bleeding
- Petechia or ecchymoses
- Blindness or retinal hemorrhage
- Polyuria and polydipsia
- Seizures

CAUSES & RISK FACTORS

- Factors contributing to multiple myeloma—genetic predisposition, viral infections, chronic immune stimulation, and exposure to carcinogens have been suggested.
- Retroviruses in cats.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Monoclonal gammopathy—extramedullary plasmacytoma, lymphoma, chronic and acute lymphocytic leukemia, ehrlichiosis, leishmaniasis, bartonellosis, dirofilariasis, plasmacytic gastroenteritis, feline stomatitis and FIP.
- Polyclonal gammopathy—chronic infectious/inflammatory disorders (e.g., hepatitis/hemoparasites/FIP/fungal), stomatitis, chronic autoimmune disease, and neoplasia.
- Bleeding—in most cases, due to paraproteinemia and thrombocytopenia; other possibilities: paraneoplastic, infectious, or autoimmune immune-mediated thrombocytopenia/pathia and vasculitis.
- HVS—see Hyperviscosity Syndrome.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia/leukopenia/thrombocytopenia—secondary to myelophthisis or autoimmune mechanisms; marked lymphocytosis associated with CLL or lymphoma within the bone marrow.
- Total protein and globulin—elevated.
- Albumin—may be low.
- Calcium—may be high secondary to malignancy, renal failure, or bone lysis.
- Urea and creatinine—may be elevated secondary to primary renal azotemia.
- Proteinuria—caused by light chains (i.e., Bence-Jones protein); not detected on routine test; immunoassay or electrophoresis on the urine sample is needed.

OTHER LABORATORY TESTS

- Protein electrophoresis—identify a monoclonal spike/oligoclonal/polyclonal pattern.
- Immunoelectrophoresis—helps to define the type of gammopathy (i.e., IgG, IgA, or IgM).
- Infectious disease testing.
- Flow cytometry—lymphocytosis.

IMAGING

- Radiology of affected bones—to identify a potential site to aspirate or biopsy.
- Skeletal survey or bone scan—to define extent of lytic lesions. Most common location for multiple myeloma lesions includes vertebral bodies, ribs, pelvis, skull, and proximal long bones.
- Thoracic and abdominal radiography or abdominal ultrasonography—for evidence of enlarged lymph nodes or organomegaly suggestive of lymphoma.

OTHER DIAGNOSTIC PROCEDURES

- Bone marrow aspiration/biopsy—plasma cells < 5% is considered normal, > 20% in dogs or > 10% with special attention to cell morphology in cat is consistent with multiple myeloma; myelophthisis associated with other lymphoproliferative diseases.
- Bone biopsy of lytic lesion—rarely required to diagnose multiple myeloma.
- Lymph node aspiration—to identify neoplastic population of lymphocytes with lymphoma; to identify

amastigotes of *Leishmania* or morulae of *Ehrlichia*.

- Organ cytology, PARR or histopathology and immunohistochemistry—for neoplastic populations of cells, infectious agents (e.g., immunofluorescence for FCoV in macrophages), or amyloid; note: coagulopathies may prevent invasive diagnostics.



TREATMENT

- Supportive care depending on the manifestation of disease and the organ systems affected.
- HVS—see Hyperviscosity Syndrome.
- Chemotherapy for neoplastic processes, such as multiple myeloma.



MEDICATIONS

DRUG(S)

- See specific diseases for appropriate chemotherapy or antibiotic choices.



FOLLOW-UP

- See specific diseases.
- Electrophoresis may be monitored as an indication of response to therapy.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Immunologic incompetence

SYNOMYMS

- Monoclonal gammopathy
- M protein

SEE ALSO

- Hyperviscosity Syndrome
- Lymphoma—Cats
- Lymphoma—Dogs
- Multiple Myeloma

ABBREVIATIONS

- CLL = chronic lymphocytic leukemia
- FCoV = feline coronavirus
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- HVS = hyperviscosity syndrome
- PARR = PCR for antigen receptor rearrangement
- PCR = polymerase chain reaction

Suggested Reading

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Author Julie Armstrong

Consulting Editor Alan H. Rebar

PATELLAR LUXATION



BASICS

DEFINITION

Medial or lateral displacement of the patella from its normal anatomic position in the femoral trochlea.

PATHOPHYSIOLOGY

- Clinical signs may be mild to severe; different degrees of clinical and pathologic changes; classified into grades I—IV.
- Common musculoskeletal changes—tibial rotation on its long axis; bowing of the distal femur and proximal tibia; shallow to absent femoral trochlea; dysplasia of the femoral and tibial epiphysis; displacement of the quadriceps muscle group.

SYSTEMS AFFECTED

Musculoskeletal

GENETICS

- Recessive, polygenic, and multifocal inheritances proposed.
- Hereditary factor in Devon Rex cats.

INCIDENCE/PREVALENCE

- One of the most common stifle joint abnormalities in dogs.
- Medial—> 75% of cases (large and small dogs and cats).
- Bilateral involvement—50% of cases.
- Uncommon in cats, but may be more common than suspected because most affected cats are not lame.

SIGNALMENT

Species

- Predominantly dog
- Rarely cat

Breed Predilections

- Most common in toy and miniature dog breeds.
- Dogs—miniature and toy poodles; Yorkshire terriers; Pomeranians; Pekingese; Chihuahuas; Boston terriers.

Mean Age and Range

Clinical signs—may develop soon after birth; generally after 4 months of age.

Predominant Sex

Risk for females 1.5 times that for males

SIGNS

General Comments

Clinical expression depends on grade (severity), amount of degenerative arthritis, chronicity of disease, and occurrence of other stifle joint abnormalities (e.g., cruciate ligament rupture).

Historical Findings

- Persistent abnormal hind limb carriage and function in neonates and puppies.
- Occasional skipping or intermittent hind limb lameness—worsens in young to mature dogs.

- Sudden signs of lameness—owing to minor trauma or worsening DJD in mature animals.

Physical Examination Findings

- Grade I—patella can be manually displaced from the trochlea, but immediately resumes a normal position when pressure is released.
- Grade II—patella can be manually displaced or can spontaneously do so with flexion of the stifle joint; patella remains malpositioned until it is manually reduced or the patient extends the stifle joint. Patient intermittently carries the affected limb with the stifle joint flexed.
- Grade III—patella remains luxated most of the time but can be manually reduced with the stifle joint in extension; movement of the stifle joint results in relaxation of the patella.
- Grade IV—patella is permanently luxated and cannot be manually repositioned; may be up to 90° of rotation of the proximal tibial plateau; shallow or missing femoral trochlea.
- Grades III and IV—crouching, bowlegged (genu varum) or knock-kneed (genu valgum) stance for medial or lateral luxations, respectively; most of the body weight is transferred to the front limbs.
- Pain—occurs as the patella relocates or if abrasion creates contact with exposed bone.

CAUSES

- Congenital
- Rarely, traumatic

RISK FACTORS

Coxa vara—lateral displacement of the proximal femur; vastus medialis pulls patella medially.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cranial cruciate ligament rupture—positive cranial drawer; concurrent in 15–20% of cases.
- Avulsion of the tibial tubercle—patellar alta.
- Rupture of the patellar tendon—patella alta.
- Malunion and malalignment of fractures of the femur or tibia—may result in displacement of the quadriceps muscle group.

IMAGING

Patella luxation is diagnosed based on clinical signs and physical examination. Computed tomography or orthogonal radiography of the femur and tibia may be indicated in Grade III and IV luxations to assess bowing and torsion of the femur and tibia.

DIAGNOSTIC PROCEDURES

Palpation of patellar position and movement during flexion and extension of the stifle. Medial and lateral force exerted on patella to relocate the patella into the trochlear groove (if luxated) or luxate the patella (in Grade I or II luxations).

PATHOLOGIC FINDINGS

- Gross—cartilage wear lesions of the patella and femoral trochlea; joint capsule redundancy on the side opposite to luxation; fibrosis and contracture on the side of luxation.
- Microscopic—cartilage fibrillation and loss of glycosaminoglycan content; synovitis.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—all grade I and some grade II luxations.
- Inpatient (surgery)—most grade II and all grade III and IV luxations.

NURSING CARE

- Cryotherapy (ice packing)—immediately after surgery; 5–10 minutes q8h for 3–5 days.
- Passive stifle range-of-motion exercises—as soon as tolerated.

ACTIVITY

Normal to restricted, depending on severity and if surgical correction was performed.

DIET

Weight control—decreases the load and stress on the patella support mechanism.

CLIENT EDUCATION

- Discuss the heritability of the condition.
- Warn about relapse potential after surgery. Retrospective studies indicate that 8%–19.8% of patellas relaxate after surgery. Revision surgery is necessary in 13% of cases.
- Inform about increased risk of cranial cruciate ligament disease.
- Warn that the condition could worsen over time (e.g., from grade I to grade II).

P

SURGICAL CONSIDERATIONS

- Malalignment is the underlying cause—tibial crest transposition is the definitive realignment procedure, but often needs to be combined with other techniques such as sulcoplasty.
- Retinacula and joint capsule tension on the side of luxation prevents realignment—medial capsulotomy (release) is essential.
- Shallowness of the trochlea sulcus is assessed and managed with one of the following:
 - Trochleoplasty—rasp or burr to deepen the sulcus.
 - Trochlea chondroplasty—only indicated in very young dogs; lift the surface hyaline cartilage and curette out cancellous bone to deepen the sulcus; lay the cartilage back over exposed bone.
 - Recession sulcoplasty—remove a pie-shaped wedge; deepen the defect, replace the wedge; preferred technique for most patients since the surface cartilage is mostly intact.

PATELLAR LUXATION

(CONTINUED)

- Block recession sulcoplasty—remove a block instead of a wedge; increases surface area of cartilage in contact with patella.
- Transposition of the tibial tubercle—realign the longitudinal axis of the quadriceps mechanism so that it is centered over the femoral trochlea; osteotomize the tibia tubercle leaving it attached distally, transpose it opposite the direction of luxation, and stabilize it with K-wires and, in larger dogs, a tension band wire.
- Imbricate the joint capsule and supporting soft tissues on the side opposite the luxation—to help keep the patella in the sulcus. Imbrication as a sole procedure is not sufficient to permanently correct the position.
- Corrective osteotomies of the distal femur and proximal tibia—realigns the longitudinal axis of the hind limb; generally indicated for only grade IV luxations with significant bowing and torsion.



MEDICATIONS

DRUG(S) OF CHOICE

- NSAIDs—minimize pain; decrease inflammation; meloxicam (load 0.2 mg/kg PO, then 0.1 mg/kg daily PO—liquid), carprofen (2.2 mg/kg PO q12h), etodolac (10–15 mg/kg PO q24h), deracoxib (3–4 mg/kg PO q24h—chewable) for 7 days (for postoperative pain).

CONTRAINDICATIONS

Avoid corticosteroids because of potential side effects and articular cartilage damage associated with long-term use.

P

PRECAUTIONS

NSAIDs—gastrointestinal irritation may preclude their use.

ALTERNATIVE DRUG(S)

Supplementation with omega-3 fatty acids (fish oils) is useful to decrease joint inflammation. Chondroprotective drugs (e.g., polysulfated glycosaminoglycans, glucosamine, and chondroitin sulfate)—may help limit cartilage damage and degeneration, but recent evidence suggests they are not or are only minimally efficacious.



FOLLOW-UP

PATIENT MONITORING

- Post-trochleoplasty—encourage early, active use of the limb.
- Leash walk exercise for 4 weeks; prevent jumping. When corrected with tibial crest transposition, cage rest is indicated until follow-up radiographs indicate the crest is healed in its new position.
- Yearly examinations—to assess progression.

PREVENTION/AVOIDANCE

- Discourage breeding of affected animals.
- Do not repeat dam-sire breedings that result in affected offspring.

POSSIBLE COMPLICATIONS

Infection, recurrence, tibial crest avulsion, pin migration.

EXPECTED COURSE AND PROGNOSIS

- With surgical treatment—> 90% of patients are free from lameness and clinical dysfunction.
- DJD—radiographic evidence in almost all affected stifle joints after surgery. Clinical impact appears minimal in small dogs.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Cranial cruciate ligament disease

SEE ALSO

Arthritis (Osteoarthritis)

ABBREVIATIONS

- DJD = degenerative joint disease
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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Client Education Handout
available online

PATENT DUCTUS ARTERIOSUS



BASICS

DEFINITION

Persistent patency of the fetal ductus arteriosus connecting the descending aorta to the pulmonary artery.

PATHOPHYSIOLOGY

The ductus arteriosus fails to close following birth permitting persistent communication between the aorta and pulmonary artery. Blood typically shunts from left to right. Hemodynamic consequences depend on the size of the shunt, pulmonary vascular resistance, and concurrent heart defects. Small shunt volumes are well tolerated; moderate-to-large shunt volumes cause left-sided CHF from volume overload of the left ventricle. Much less frequently, a large-diameter PDA causes severe pulmonary vascular injury, high pulmonary vascular resistance, pulmonary hypertension, and reversal of the shunt (Eisenmenger's pathophysiology or "reversed" PDA), with bidirectional shunting across the ductus. Patients affected with right-to-left shunting suffer from arterial desaturation and hypoxia-triggered erythrocytosis.

SYSTEMS AFFECTED

- Cardiovascular—volume overload (left-to-right shunt) or pulmonary vascular disease and erythrocytosis (right-to-left shunt).
- Hemic/Lymph/Immune—increased red cell mass and hyperviscosity if erythrocytosis develops.
- Respiratory—symptoms of cough or labored breathing if pulmonary edema or pulmonary hypertension develop.

GENETICS

Genetically transmitted ("polygenic" model) defect in many canine breeds, including the bichon frise, Cavalier King Charles spaniel, Chihuahua, cocker spaniel, collie, English springer spaniel, German shepherd, Labrador retriever, Maltese, miniature (and toy) poodle, Pomeranian, Shetland sheepdog, and others.

INCIDENCE/PREVALENCE

Very common congenital heart defect in dogs; prevalence estimated to be up to 2.5 cases/1,000 live births. Uncommon in cats.

SIGNALMENT

Species

Dog and cat

Breed Predilections

See "Genetics"

Mean Age and Range

- Vast majority are identified during the initial vaccination sequence
- Onset of signs related to CHF—weeks to many years

Predominant Sex

Dogs—females predisposed in many breeds

SIGNS

General Comments

- Onset of reversed PDA—quite sudden in dogs (usually before 4 months of age); might develop more gradually in cats.
- No significant documentation that shunt reversal begins after 6 months of age in dogs, but signs related to reversed shunting might be overlooked for years. The onset of clinical signs has been reported in dogs older than 5 years of age.

Historical Findings

- Most affected animals are asymptomatic at initial evaluation.
- Respiratory distress, coughing, exercise intolerance with development of CHF.
- Stunted growth in some.
- Right-to-left shunting PDA—exertional rear limb weakness and complications of erythrocytosis and hyperviscosity (seizures or sudden death related to arrhythmias or microvascular thrombi).
- Signs usually precipitated by or worsened by exercise.

Physical Examination Findings

- Typically, continuous, machinery-type murmur loudest over pulmonary artery at the left craniodorsal cardiac base; localized in some dogs; murmur can be loud near the manubrium sterni in small dogs; often a concurrent systolic murmur of mitral regurgitation at the left apex. The murmur in puppies < 6 weeks of age or in cats of any age might not be obviously continuous, but more resemble a long systolic and early diastolic murmur.
- Loud murmurs—associated with a palpable precordial thrill.
- Arterial pulses—hyperkinetic ("waterhammer").
- Caudodorsal displacement of the ventricular apex indicating LV enlargement.
- Tachypnea, respiratory distress, and inspiratory crackles—can indicate left-sided CHF or concurrent primary respiratory disease such as pneumonia.
- Rapid, irregular cardiac rhythm with variable-intensity arterial pulses if atrial fibrillation develops—this is more common in larger breed dogs.
- In right-to-left shunting ("reversed") PDA the findings differ—no continuous murmur, normal arterial pulses, and a prominent right ventricular impulse; systolic ejection murmur and a tympanic, or split, second heart sound might be evident; jugular pulse is possible.
- Classic feature of right-to-left shunting PDA is differential cyanosis—pink cranial, but cyanotic caudal, mucous membranes. Severe secondary erythrocytosis or an intracardiac shunt (septal defect or patent foramen ovale) can cause cyanosis of the cranial mucous membranes.

CAUSES

Genetically predisposed in most cases

RISK FACTORS

Genetic (breed) predisposition in dogs; risk

factors in cats are unknown; a large diameter PDA is a risk factor for shunt reversal.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Principal auscultatory differentials are congenital aortic stenosis with aortic insufficiency (to-and-fro systolic/diastolic murmurs) and ventricular septal defect with aortic valve prolapse into the defect (causing a systolic murmur of VSD and diastolic murmur of aortic regurgitation).
- Other rare causes of continuous thoracic murmurs—arteriovenous fistula of the lung, aortopulmonary communication, rupture of the aorta into the right atrium or right ventricle, or coronary artery fistula.
- Systemic arterial to pulmonary artery fistula(s) can result in similar imaging findings to those of PDA; murmurs are often soft or absent.
- Rear limb weakness of right-to-left shunting PDA if often misdiagnosed as a neuromuscular disease, especially myasthenia gravis.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal unless right-to-left shunting in which case variable degrees of erythrocytosis (PCV 58–80%) might be present.

OTHER BLOOD TESTS

Reversed PDA—low femoral arterial pO_2 compared to a pO_2 obtained by careful puncture of the carotid or brachial artery using a 25-gauge needle. This is rarely if ever needed for diagnosis. Pulse oximetry of the cranial membranes compared to the rectum might document the disparity in hemoglobin saturation.

IMAGING

Thoracic Radiographic Findings

- Lateral projection—left heart enlargement; typically pulmonary overcirculation; frequently the lobar pulmonary veins are slightly larger than the attendant arteries.
- Dorsoventral view (preferable to accentuate the descending aorta) demonstrates cardiac elongation (left ventricular enlargement), left auricular enlargement, and dilation of the descending aorta (called a "ductus bump"); the main pulmonary artery is dilated.
- Left-sided CHF—distended pulmonary veins, increased interstitial/alveolar densities.
- Reversed PDA—heart usually normal sized, but the contour of the right cardiac border is more prominent on the DV view, and the pulmonary circulation appears normal to reduced; the main pulmonary artery and proximal lobar branches are dilated; a ductus bump often is evident on the DV view; lung fields are clear.

PATENT DUCTUS ARTERIOSUS

(CONTINUED)

Echocardiographic Findings

- Left atrium, left ventricle, and main pulmonary artery are dilated; right ventricle is normal, except in cats, in which it is more likely to be hypertrophied; the ductal ampulla and the distal ductus can generally be imaged from the right and left cranial hemithorax.
- Left ventricular systolic function (fractional shortening) is normal to reduced; can be markedly decreased in large dogs with long-standing PDA.
- Doppler studies demonstrate continuous flow into the main pulmonary artery (from the ductus); often concurrent pulmonary insufficiency from dilation of the pulmonary artery, and mitral regurgitation caused by left-sided cardiac dilatation; transmural flow velocity and transaortic flow velocity are high because of increased volume and left atrial pressure; aortic velocities can be augmented substantially (up to 2.5–3 m/second), mimicking findings of mild subvalvular aortic stenosis. Trivial aortic regurgitation often evident likely from aortic dilatation and increased flow across the valve.
- Right-to-left shunting PDA—small left heart chambers, right atrial dilation, right ventricular hypertrophy, and dilation of the main and branch pulmonary arteries; contrast echocardiography is useful to confirm the diagnosis; inject saline in the cephalic vein while imaging the abdominal aorta. Color and spectral Doppler studies can identify low velocity bidirectional shunting across ductus. High velocity pulmonary and tricuspid regurgitation jets indicative of pulmonary hypertension might be detected.

Angiographic Findings

- Echocardiography has completely supplanted angiography for the diagnosis.
- Standard angiography is useful for the differential diagnosis of rare aortic or coronary arterial malformations, abnormal aortic arch (with right-sided ductus arteriosus), systemic arterial to pulmonary artery fistulas, and during interventional catheterization procedures. Injection of contrast media into the descending aorta demonstrates ductal morphology, information crucial to catheter-based ductal occlusion techniques. Computed tomography angiography is an alternative for delineation of some of these lesions.

DIAGNOSTIC PROCEDURES

Electrocardiography

- ECG—mainly used in PDA to diagnose auscultable arrhythmias. • Typical abnormalities include wide P waves and tall R waves in the caudal leads (II, aVF, III) and left precordial leads.
- Atrial fibrillation—observed infrequently, related to marked dilatation of the left atrium; more common in large-breed dogs.
- Right-to-left shunting PDA—findings of right ventricular

enlargement, S waves in leads I, II, III and right axis deviation are more typical but variable.

PATHOLOGIC FINDINGS

- Persistent patency of the ductus arteriosus between descending aorta and origin of the left pulmonary artery.
- Left-to-right shunting PDA—pulmonary edema, cardiomegaly (left sided), and dilation of the aorta and pulmonary artery.
- Right-to-left shunting PDA—right ventricular hypertrophy, dilation of the pulmonary artery, and prominent bronchial arteries; ductal diameter is invariably very wide, similar to the descending aorta. Pulmonary arterioles are thickened; there are often histologic changes of pulmonary vascular disease (medial hypertrophy, plexiform lesions or necrotizing arteritis).



TREATMENT

APPROPRIATE HEALTH CARE

- Manage pulmonary edema with furosemide and, if necessary, oxygen, nitrates, and cage rest; following stabilization, promptly occlude the PDA.
- Ductal closure involves surgical ligation or occlusion with a canine ductal occluder device, thrombogenic coil, or vascular plug device—refer to an experienced surgeon or to a cardiologist for these procedures.
- Schedule stable animals for elective surgery or device closure without delay; asymptomatic dogs as young as 7–8 weeks of age show no higher operative mortality than older dogs.
- Treat dogs with erythrocytosis caused by right-to-left shunting PDA with rehydration or, if needed, by periodic phlebotomy to maintain the PCV < 65% (typically 62–65%). Rarely hydroxyurea is used for intractable erythrocytosis.

ACTIVITY

- Restrict activity until the ductus is closed and in all dogs with CHF.
- After removal of any sutures and first follow-up examination, resume normal activity.

DIET

Normal; but restrict sodium intake if CHF.

CLIENT EDUCATION

- Surgical or transcatheter ductal closure—do not delay; mortality is higher and left ventricular function impaired if clinical signs or atrial fibrillation develop.
- Following successful closure of the PDA and a 2-week convalescence, the dog can be treated normally.

SURGICAL CONSIDERATIONS

- Closure of a PDA can be achieved through surgical ligation or by placement of a catheter-delivered, occluding or thrombogenic device

within the ductal lumen. Smaller patient sizes (< 2.5 kg) are a limiting factor with current PDA devices, but new, lower-profile devices have been developed and tested recently.

- Surgery can generally proceed within 24–48 hours of medical stabilization.
- Standard therapy involves ductal ligation via left thoracotomy; surgical and perioperative mortality should be < 3% for all cases.
- Mortality with devices is even lower, but some complications including failure to achieve closure are reported.
- Results obtained with catheter-delivered occlusion devices are very good when done by experienced operators.
- Never correct right-to-left PDA surgically; the right ventricle will not be able to eject against the pulmonary vascular resistance without the “pop-off valve” of the PDA.
- PDA with moderate pulmonary hypertension can sometimes be closed, especially in cats, provided pulmonary vascular resistance is not fixed and predominant shunting is left to right. Refer to a cardiologist for evaluation.



MEDICATIONS

DRUG(S) OF CHOICE

- Treat pulmonary edema with furosemide (2–4 mg/kg q6–12h PO, SC, IM, or IV as required); can be discontinued when the PDA is closed.
- When surgery is not an option—if CHF, prescribe furosemide, ACE inhibitor such as enalapril (0.5 mg/kg q12–24h PO), and pimobendan (0.25–0.3 mg/kg q12h PO).
- When atrial fibrillation has developed add digoxin and diltiazem (see Atrial Fibrillation and Atrial Flutter). An alternative is electrical cardioversion—this is a reasonable therapy provided the ductus can be closed—refer to a cardiologist.
- To control severe, life-threatening CHF—can use direct vasodilators such as hydralazine (1–2 mg/kg q12h PO) or sodium nitroprusside (1–5 µg/kg/minute IV) to reduce left-to-right shunting. Maintain systolic blood pressure at 85–90 mmHg.

CONTRAINDICATIONS

- Left-to-right PDA—drugs that increase systemic vascular resistance and arterial blood pressure, except as needed for anesthesia and surgery.
- Right-to-left PDA—drugs that lead to systemic arterial vasodilation and reduce systemic arterial blood pressure, including drugs with arterial vasodilating effects.

PRECAUTIONS

- Measure digoxin levels if prescribed.
- Monitor arterial blood pressure, renal function, and serum electrolytes to identify problems related to diuretic and vasodilator therapies.

(CONTINUED)

PATENT DUCTUS ARTERIOSUS**POSSIBLE INTERACTIONS**

Aggressive diuresis leading to dehydration or hypokalemia exacerbates the risk for digoxin toxicity.

ALTERNATIVE DRUG(S)

- Prostaglandin inhibitors (e.g., indomethacin) do *not* close PDAs effectively in dogs.
- Sildenafil—a minimum 2- to 3-week trial course should be given to dogs with reversed PDA; clinical signs can improve significantly in some dogs on long-term therapy.
- Hydroxyurea—consider for treatment of severe erythrocytosis unresponsive to phlebotomy; not always effective and adverse effects are possible.

**FOLLOW-UP****PATIENT MONITORING**

- Pain management is appropriate post-thoracotomy and shortens the recovery time. Opiate therapy is generally administered perioperatively for 24–48 hours. Instill long-acting local anesthetic in the surgical wound prior to closure. Analgesic therapy following catheter-based closure is less aggressive but also continued for 24–48 hours.
- Postoperative—monitor vital signs and respiratory rate; dyspnea can indicate pneumothorax.
- Cardiac auscultation postoperatively and at suture removal; if heart sounds are normal, no further follow-up or diagnostic studies are required unless preoperative echocardiography showed moderate to severe LV dysfunction. There is no basis for recommending annual cardiac reevaluation of uncomplicated cases.
- Persistent, continuous murmur indicates either incomplete closure of the ductus, recanalization (rule out infection or device migration), or a concurrent cardiac or vascular defect.
- Systolic murmurs are variably heard postoperatively; these should abate by the time of suture removal. Reinvestigate unexpected murmurs by Doppler echocardiography. When only partial ligation at surgery is achieved, consider referral to a cardiologist for device occlusion.
- Sudden illness, fever, or acute respiratory signs postoperatively—consider bacterial infection of the closure site with hematogenous pneumonia; aggressive antibiotic therapy

needed. • An unusual complication is acquired stenosis of the main or branch pulmonary artery following surgery to correct PDA.

PREVENTION/AVOIDANCE

Do not breed affected animals.

POSSIBLE COMPLICATIONS

- Left-sided CHF.
- Cardiac arrhythmias (atrial fibrillation).
- Pulmonary vascular disease with pulmonary hypertension, reversed shunting, exercise intolerance, and erythrocytosis.
- Perioperative death (from torn ductus or aortic aneurysm), bleeding, or infection.
- Recanalization of the ductus.
- Pulmonary or systemic embolization from a dislodged occluding device; hemolysis from device-induced RBC fragmentation; sepsis from infected surgical site or implanted device.

EXPECTED COURSE AND PROGNOSIS

- Infrequently dogs remain asymptomatic for life. PDA closure adds an estimated 10 years to median lifespan in dogs (12 years with closure, 2 years without). In other reports, ~50–60% of dogs died from CHF within 1 year of diagnosis if the PDA is not closed.
- Surgery performed prior to onset of moderate-to-severe CHF—excellent prognosis with approximately 2–3% surgical/perioperative mortality in the most experienced hospitals. Even lower mortality and excellent closure results are obtained in *experienced* hospitals using ductal occluding devices.
- Moderate-to-severe CHF is related to left ventricular myocardial failure or atrial fibrillation—guarded prognosis; referral to a cardiologist is advised.
- Dogs with right-to-left shunting PDA can live for several years but often die suddenly; occasionally, dogs live beyond 5 years of age (especially cocker spaniels).
- Cats—varies from rapidly progressive left-sided CHF to gradual development of pulmonary vascular disease; even right-sided CHF can develop with PDA and pulmonary vascular disease.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Typically an isolated defect, but is recognized in conjunction with other congenital heart

lesions; these seem more likely in larger breeds. Occasionally a vascular ring anomaly is evident, such as persistent right fourth aortic arch.

AGE-RELATED FACTORS

Presentation is typically young animals, median age of presentation reported as 5 months in dogs.

PREGNANCY/FERTILITY/BREEDING

Carries greater risk for CHF in pregnant bitches; offspring carry greater risk for large PDA or reversed shunting due to pulmonary vascular disease; do not breed affected dogs.

SYNOMYNS

Duct of Botallo, or ductus Botalli

SEE ALSO

- Atrial Fibrillation and Atrial Flutter
- Congestive Heart Failure, Left-Sided
- Murmurs, Heart
- Pulmonary Hypertension

ABBREVIATIONS

- CHF = congestive heart failure
- ECG = electrocardiogram
- LV = left ventricle
- PA = pulmonary artery
- PCV = packed cell volume
- PDA = patent ductus arteriosus

INTERNET RESOURCES

Dr. James Buchanan Cardiology Library:
<http://www.vin.com/library/general/JB110pda.htm>,
<http://www.vin.com/library/general/JB103pdaRL.htm>

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Client Education Handout
available online

PECTUS EXCAVATUM



BASICS

OVERVIEW

- Deformity of the sternum and costal cartilages that results in a dorsal to ventral narrowing of the chest, primarily in the caudal aspect.
- Can have secondary abnormalities of respiratory and cardiovascular function from restriction of ventilation and cardiac compression.
- Considered congenital in origin although an acquired case has been reported.
- Upper respiratory obstruction at a young age could cause abnormal respiratory gradients and subsequent pectus excavatum.
- Uncommon defect.
- Concurrent cardiac defects common.
- Some patients demonstrate swimmer syndrome—neonatal dogs lack the ability to posture properly and remain in sternal recumbency, which can lead to invagination of the sternum.

SIGNALMENT

- Dog and cat.
- Brachycephalic breeds and Bengal cats may be predisposed.
- Most common age of presentation: 4 weeks–3 months.
- Male cats more often reported than females, no gender predisposition noted in dogs.

SIGNS

- Thoracic defect, easily palpated or seen.
- Varying degrees of respiratory distress.
- Exercise intolerance.
- Weight loss.
- Recurrent respiratory infections.
- Cough.
- Vomiting.
- Cyanosis.
- Poor appetite.
- Cardiac murmurs associated with concurrent cardiac defects or compression of the heart.
- Muffled heart sounds.
- No correlation between severity of signs and severity of anatomic or physiologic abnormalities.
- Vertebral deformities.
- Swimmer syndrome—limbs not adducted properly; ambulation impaired.

CAUSES & RISK FACTORS

- Genetic predisposition—may exist.
- Unknown etiology—suspected causes include intrauterine pressure abnormalities, shortening of central tendon of the diaphragm, cranial abdominal muscle

deficiency, and abnormal osteogenesis or chondrogenesis.

- Dogs predisposed to respiratory obstructive processes have a higher risk than others.
- Single report in a geriatric Golden retriever with laryngeal paralysis.
- Puppies raised on surfaces causing poor footing may be predisposed to swimmer syndrome.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Congenital diaphragmatic hernia (pleuroperitoneal or pericardioperitoneal)
- Tracheal malformations or collapse
- Congenital heart defects
- Pulmonary edema
- Hemothorax
- Pyothorax
- Pneumonia
- Tracheobronchitis/bronchitis
- Brachycephalic airway syndrome

IMAGING

Thoracic Radiography

- Confirm sternal and costal skeletal abnormalities.
- Decreased thoracic volume.
- Cardiac malpositioning—left and cranial displacement of cardiac silhouette.
- Concurrent secondary pulmonary disease.
- Measure frontosagittal and vertebral indices to characterize degree of deformity as mild, moderate, or severe and help predict response to treatment.

Echocardiography

Rule out concurrent congenital cardiac defects or other cardiac disease.



TREATMENT

- Decision to repair deformities—made on the basis of clinical signs. If incidental finding with minimal to no clinical signs, then intervention may not be indicated.
- Treatment options include external coaptation, partial sternectomy, or both. Decision based on age of the animal and degree of deformity.
- Surgery benefits patients with concurrent respiratory distress; benefits unknown in patients with no respiratory distress but with moderate or severe deformity.
- Non-clinical patients can develop signs at later date; patients with clinical signs of disease may show progression.

- Puppies with swimmer syndrome—place on surfaces with excellent footing; careful toggling of front and rear legs may improve adduction.

- Brachycephalic breeds with concurrent upper airway obstruction may benefit from surgery directed at these problems.
- Anesthesia—patients require constant monitoring; ventilatory support should be available.



MEDICATIONS

DRUG(S)

Treat underlying or secondary medical conditions.



FOLLOW-UP

- Examinations—dictated by clinical signs or when surgical intervention has been precluded.
- No specific actions for avoiding disease; genetic factors may sometimes be involved.
- Progression of respiratory signs—can develop in nonclinical or mildly clinical patients.
- Prognosis—guarded to good depending on properly timed and expertly administered intervention.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Cardiac defects
- Swimmer syndrome

Suggested Reading

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PEDIATRIC BEHAVIOR PROBLEMS AND TRAINING—DOGS



BASICS

DEFINITION

These problems include behaviors that are normal and common to most puppies but not acceptable to the family. They require some degree of modification by training and shaping to become acceptable. Training and behavior issues include confinement training, house training, destructive chewing (see *Destructive Behavior—Dogs*), playbiting, jumping on people (see *Unruly Behaviors: Jumping, Pulling, Chasing, Stealing*), and getting on counters or furniture.

SYSTEMS AFFECTED

Behavioral

GENETICS

- Activity levels and behaviors of young pups are likely to be similar to those of their parents.
- Some problems may be more prevalent in certain breeds such as those with a high need for exercise and mental stimulation.

INCIDENCE/PREVALENCE

Common to most puppies

GEOGRAPHIC DISTRIBUTION

May be more frequent in urban environments or where opportunities to exercise are less available.

SIGNALMENT

Species

Dog

Breed Predilections

Breeds selected for high-energy, stamina, and working functions (e.g., retrieve, hunt, herd).

Mean Age and Range

3–9 months of age but some may persist through adulthood.

Predominant Sex

May be higher frequency and intensity in males.

SIGNS

Confinement training

N/A

House training

N/A

Playbiting

- The pet bites hands, legs, and/or clothing. Bites are usually inhibited but can cause injuries due to sharp teeth or insufficient bite inhibition.
- Growling and barking may be present but usually a higher pitch with lower tones associated with other types of aggression (e.g., fear-related, possessive).
- Attacks are usually triggered by movement or play with a family member but can be spontaneous.

Getting on Counters/Furniture

- The pet gets on furniture and counters to explore and access objects to chew or eat.

- The pet may also climb onto furniture during play, to get attention, or to rest.

CAUSES

General

- Normal puppy play and exploration
- Inadequate owner supervision, management, training, socialization, mental stimulation or environmental enrichment
- Owner responses may reinforce or exacerbate the behaviors.

Confinement training

N/A

Housetraining

N/A

Playbiting

- A normal behavior, but rough play, teasing, and encouraging the pet to bite hands and feet may cause or contribute to problems.

Getting on Counters/Furniture

- Insufficient outlets for normal play and exploration
- Tempting objects or food left on counters/furniture
- Desire for social interaction
- No acceptable alternative bedding on which to rest

RISK FACTORS

See "Causes"



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Confinement training

N/A

House training

N/A (rule out medical)

Playbiting

- Fear-related aggression*—aggressive behavior is accompanied by signs of fear and/or submission (lowered body, ears and tail down/tucked, horizontal retraction of oral commissures). ° The behavior occurs when the pet is in a situation it perceives as threatening. ° Vocalization might include growling or yelping.
- Possessive aggression*—the behavior occurs in specific situations in which there is competition for a resource.
- The pet stiffens and hovers over the guarded object.
- An increase in the speed of eating or quickly grasping an object tightly in the mouth may also be observed.
- Growling has a deep tone.
- Piloerection may occur, as might lunging, snapping, and biting.
- The pet learns that aggressive behavior is effective at achieving goals (avoid being picked up, pushed off couch, restrained by collar, nails trimmed).
- Conflict-related aggression*—the pet bites in situations where it is frustrated or uncertain how to respond due to inconsistent outcomes (reward/punishment).
- Medical*, e.g., viral encephalitis, toxins, congenital disorders, usually accompanied by other signs of illness.

Getting on Counters/Furniture

N/A

CBC/BIOCHEMISTRY/URINALYSIS

Refractory house training problems may require a urinalysis, fecal exams or other testing as suggested by physical exam and history. If neurologic signs or pain, further medical assessment including imaging would be required.

DIAGNOSTIC PROCEDURES

N/A unless showing concurrent signs of illness.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient

NURSING CARE

N/A

ACTIVITY

Provide a regular daily routine of exercise, play, and mental stimulation.

DIET

- Provide sufficient food and chew toys to reduce the motivation to steal and chew.
- Use food-dispensing toys to slow feeding and provide oral and mental stimulation.

CLIENT EDUCATION

General

- Family members should constantly look for and reward acceptable behaviors.
- Avoid harsh verbal or physical punishment (e.g., striking the pet, shaking by the scruff, rolling on the back, squeezing lips against teeth). This may worsen problems, negatively impacts the bond with the pet, and can lead to more serious problems (such as fear, aggression).
- Teach the pet to sit on command by using food-lure training, and ask him to sit prior to getting anything he wants or needs.

Confinement training

- The goal is to acclimate the pup to being confined in a safe, comfortable area to prevent housesoiling, destructiveness, injury, and provide a safe haven for rest, chew toys, and perhaps eating, also accustoms him to confinement for traveling and boarding.
- Choose an appropriate confinement area (CA). A crate is good for intermittent confinement but no longer than the puppy can control its urine and stools (gradually increasing from 1–2 to 4–5 hours). If the pet must be confined for > 5 hours on a daily basis, a larger housing area should be provided with an elimination area within.
- Introduce the pup to the CA early. Place treats, toys, or food in the area so that he is motivated to enter. Whenever the pup is tired or sleepy, place him in his CA. To maintain a positive association, the pup should never be scolded or roughly forced in.
- Some degree of distress

PEDIATRIC BEHAVIOR PROBLEMS AND TRAINING—DOGS (CONTINUED)

vocalization may occur the first few times the pup is confined. A radio, TV or CD may help calm the pet and mask environmental noises that trigger barking. A calming pheromone (Adaptil) sprayed in the crate or a diffuser in the room may help the puppy adapt. Avoid releasing the pup when he cries or whines. Wait until he is quiet, or squeak a toy from out of sight to get the pup to quiet before he is released.

House training

• The puppy should be taken out to eliminate each hour when awake during the daytime when the family is home. If he does not eliminate within 5 minutes, return indoors, supervise closely for 15–30 minutes and try again. Take the pet out when he is most likely to need to eliminate: after play, exercise, naps, eating, drinking, confinement, as well as prior to confinement, as well as when he exhibits pre-elimination circling and sniffing. Offer food 2–3 times each day for 20 minutes at the same time to help establish an elimination routine. • Until the puppy has completed 4 consecutive weeks without soiling, it should either be within eyesight of the family or confined to its CA. A leash will help keep the pet close and can be used to interrupt an attempt to eliminate indoors. Most pups can control elimination through the night by 3–4 months of age. By 4 months of age, most puppies will have 2–3 hours or more of control during the daytime. Soiling can be prevented by closing doors or moving furniture to limit access to areas and by making locations aversive with a motion-activated alarm. • Punishment should not be used. If urine or stool is found in the home after the act, the owner was not sufficiently supervising. If caught in the act of eliminating indoors, the puppy should calmly be interrupted, and taken outdoors. Urine and stool odors should be removed. • If the puppy eliminates in its crate: he may have been left there longer than he can control eliminating; the crate may be so large that he sleeps in one end and eliminates in the other; the puppy did not eliminate prior to confinement; the feeding schedule was not matched to the elimination schedule; there is anxiety about confinement or being left alone (see separation distress); or there is an underlying medical cause. • If it is not practical to take the puppy outside frequently enough (apartment dweller, long work days), indoor training is similar to conventional housetraining, i.e., supervision, confinement, reward desirable behavior, but the elimination site would be on paper or a litter pad. When the family is out of the home, the puppy should be confined to a large enough confinement area (e.g., pen or large crate) with the paper within. • Medical issues may

cause or contribute to house training problems, including problems that cause increased volume of urine or stool (e.g., renal disease, malabsorption), increased frequency of elimination (e.g., lower urinary tract disease, colitis) or CNS problems that interfere with learning or mobility.

Playbiting

- Exercise often enough and with appropriate outlets to meet the pet's needs. • Have toys available at all times to toss and distract the pet. • Use food-laced toys to keep the pet occupied. • Keep a leash attached to the supervised pup to prevent and interrupt undesirable behaviors. • Use confinement if the puppy is out of control and the family cannot effectively engage the pet in alternate acceptable activities. • Avoid games that encourage biting hands or feet. • Make all interactions structured and predictable by training sit before giving toys, food, play, and attention. • Ignore attention-seeking behavior such as whining, barking, or pawing for attention. • Say "Ouch" very loudly and immediately walk away to interrupt any hard bites during play. • Physical corrections should be avoided as they can cause fear, anxiety, and aggression or inadvertently encourage further rough play. • Consider a head halter for difficult pups. • Enroll in puppy classes early (8–10 weeks of age).

Getting on Counters/Furniture

- Keep food and appealing objects off counters and furniture • Constantly supervise
- Confine the pup when he can't be supervised • Block access to potential problem areas • Provide interesting toys on the floor for mental stimulation • Provide a bed/rest area on the floor • Meet the pet's needs for food, chewing, mental stimulation and exploration • Decrease the appeal of furniture or trash bins with bitter tasting sprays, or motion-activated sprays or alarms.



MEDICATIONS

DRUG(S) OF CHOICE

- Drugs are generally not indicated. • If signs of anxiety see other appropriate sections in the text (e.g., Separation Distress Syndrome).

ALTERNATIVE DRUG(S)

A dog-appeasing pheromone may help the pup in stressful situations.



FOLLOW-UP

PATIENT MONITORING

- Phone follow-ups at approximately 10 days, 20 days, and 6 weeks following the initial visit

are usually helpful. • This can be done by a trained support staff member.

PREVENTION/AVOIDANCE

- Discuss supervision and confinement strategies. • Begin food-lure-reward training in the home at 7–8 weeks of age. • Enroll in a puppy class at 8–10 weeks of age. • Provide regular sessions of physical exercise and mental stimulation. • Provide information and guidance about normal behavior to insure needs are adequately met (e.g., mental stimulation, socialization, exercise, object play). • Suggest safe and interesting toys for chewing, play, and mental stimulation.
- Make all interactions predictable by teaching sit before giving anything of value.

Possible Complications

- Damaged household objects and clothing
- Food stealing • Intestinal foreign bodies/obstructions • Minor injuries from play-bites
- A guest is knocked down and injured
- Owner frustration, a weakened bond, and possible relinquishment to a shelter.

EXPECTED COURSE AND PROGNOSIS

- Prognosis is generally good. • The frequency and intensity of the behaviors will decrease with age, consistency and by providing sufficient outlets. • Play-biting can usually be quickly controlled if the family is consistent with training. • Confinement training should take a few days to several weeks to accomplish. • Housetraining can be accomplished in a few weeks, but may take longer if the family is not consistent in supervision and training or the family schedule does not address the dog's needs.



MISCELLANEOUS

Suggested Reading

Dunbar I. Sirius Puppy Training, DVD. Berkeley, CA: James & Kenneth Publishers, 2006.

Landsberg GL, Hunthausen WL, Ackerman L. Handbook of Behavior Problems of the Dog and Cat, 3rd ed. Philadelphia: Elsevier Saunders, 2013.

Seksel K. Preventing behavior problems in puppies and kittens. Vet Clin North Am Small Anim Pract 2008; 38:971–982.

Author Wayne Hunthausen

Consulting Editor Gary M. Landsberg



Client Education Handout
available online

PEDIATRIC BEHAVIOR PROBLEMS—CATS



BASICS

DEFINITION

- Undesirable behaviors exhibited by kittens between birth and puberty.

PATHOPHYSIOLOGY

- Most pediatric behavior problems are normal, species-typical behaviors.
- Lack of appropriate social interactions and environmental stimulation can contribute to abnormal or unwanted behaviors.

SYSTEMS AFFECTED

Behavioral

GENETICS

Paternal influences on friendliness to people and boldness to unfamiliar or novel objects have been supported.

SIGNALMENT

Species

Cats

Mean Age and Range

Generally 6–52 weeks

SIGNS

General Comments

Play Aggression

- Elements of predation including stalking, chasing, attacking, pouncing, swatting, and biting. Play can be solitary, with objects, or social to another kitten, animal or person.
- With normal play, bites are inhibited and claws retracted. Vocalizations are rare compared to other forms of feline aggression.
- Inappropriate play behaviors may be uninhibited, leading to bite and scratch injuries.

Excessive Play/Activity and/or Destructive Play

High level of solitary play (running, jumping, climbing, object play) may result in household damage and disruption of owner sleep.

Scratching

- Use of claws to scratch on household items and/or people.
- Scratching is a normal behavior for both claw maintenance and territorial marking but becomes problematic when scratched objects include walls, furniture, carpets, and other household items.

Fearful Behaviors

Includes hiding, hissing, scratching, unsocial behaviors and can include varying manifestations of aggression to another animal or person.

Historical Findings

Aggressive Play Directed toward People or Other Pets in the Household

- Attacks directed toward people or other pets in the household.
- Ambushes are common and occur without vocalizations. Bites are generally inhibited but may indent the skin and light scratches with claws may occur.

Uninhibited Aggressive Play Directed toward People

- Signs similar to above except more intense.
- Bites and scratches are not as inhibited and can break skin.

Play Directed toward Household Objects

- Bursts of solitary play that include intense running, jumping, climbing across and up household furnishings.
- Knocks or swipes objects from surfaces.

Scratching

Household items and family members.

Fear and Defensive Behaviors Due to Lack of Socialization

- No exposure to people before 7 to 9 weeks of age.
- Behaviors associated with fear, e.g., dilated pupils, piloerection, defensive postures, hissing, hiding, fleeing, aggression.

Fear and Defensive Behaviors Related to Early Trauma

Normal until experienced traumatic event, e.g., abuse, attack by another animal.

Fear and Defensive Behaviors Related to Correction Techniques

- History of punishment by owner(s).
- Kitten shows defensive postures including hissing, fleeing, hiding, dilated pupils, piloerection in presence of owner or in response to corrections.

CAUSES

Aggressive Play Directed toward People or Other Cats in the Household

- Normal species-typical behavior but without appropriate social interaction with conspecifics, the behavior can become uninhibited and injurious.
- Owners may encourage inappropriate interactive play by promoting play with human body parts (fingers, hands, feet).
- Lack of outlets for appropriate play.

Play Directed toward Objects in the Household

Normal species-typical behavior beginning at 7–8 weeks of age.

Fear and Defensive Behaviors Due to Lack of Early Socialization

No or minimal amount of exposure to people before 7–9 weeks of age.

Fear and Defensive Behaviors Related to Early Trauma

Early traumatic event

Fear and Defensive Behaviors Related to Correction Techniques

Normal until “corrected” by person, e.g., spanked, swatted, flicked on nose, yelled at, chased.

RISK FACTORS

Aggressive Play Directed toward People

- Only cat in the household, orphan hand-reared kitten or adoption prior to 6 weeks of age.
- Insufficient appropriate outlets for normal play and exploration.
- Encouragement of inappropriate play (e.g., with hands, fingers, feet).

Play Directed toward Objects in the Household

- Lack of sufficient enrichment including toys and interactive play with people or other animals.
- Only pet in household.

Scratching

Lack of appropriate scratching outlets.

Fear and Defensive Behaviors

- Lack of appropriate socialization with people, use of punishments and other traumatic experience(s).
- Removing kittens less than 2 weeks of age from queen may result in markedly fearful and overly aggressive kittens towards humans and other cats



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Play Aggression toward People

Differentiate normal play from the more serious, uninhibited play aggression.

Excessive Play/Destructive Behaviors

None

Scratching

Nail maintenance, marking, or play-related

Fearful and Defensive Behaviors

Central nervous system diseases, pain, metabolic disorders, endocrinopathies (e.g., hyperthyroidism), pain.

CBC/BIOCHEMISTRY/URINALYSIS

Frightened kittens may have elevated glucose levels.



TREATMENT

ACTIVITY

Many pediatric behavior problems can be alleviated or reduced by enriching the kitten's environment (e.g., provide movable toys, variety of toys, rotating them regularly); engage the kitten in interactive play directed away from the owner's body parts; provide access to window sills, boxes, perches; offer a variety of enticing scratching surfaces; possibly get second kitten.

DIET

Provide multiple small meals.

CLIENT EDUCATION

Most of these problems are normal kitten behaviors that the owners perceive as abnormal or excessive and inappropriate for their lifestyle. Many kittens will mature out of these problem behaviors.

Aggressive Play Directed toward People

- Owner needs to provide and initiate regular interactive play that allows for hunt, stalk and attack behaviors directed at appropriate toys or objects. Ensure owners never use hands, fingers, feet to encourage play.
- Most

PEDIATRIC BEHAVIOR PROBLEMS—CATS

(CONTINUED)

effective treatment may be to acquire an additional kitten of the same size and temperament. • Redirection: Identify the situations in which the attacks may occur. Watch for signs of dilated pupils, stalking, crouching, tail swishing. Be prepared to redirect the play to another object (e.g., tossing a wadded piece of paper or chasing a toy) or to cue and reward alternative desirable behaviors that the kitten has learned (e.g., go to mat, sit/watch, let's eat, let's play). • Educate the client to not hit, or swat, on nose with fingers as this may encourage rougher play from the kitten. • Immediately stop play for inappropriate behaviors. • May use a startling noise or hiss to distract the kitten, then stop all play by withdrawing from and then ignoring the kitten. • Frequent trimming of tips of claws helps reduce damage caused by nails. • If injuries are being caused by claws, declawing may be considered in severe cases where kitten is at risk of relinquishment, or for immunocompromised owners.

Aggressive Play Directed toward Other Cats in the Household

- Acquire additional kitten of the same size and temperament of the problem kitten.
- Watch for signs and redirect into alternative acceptable behaviors (sit/watch, go to mat)
- Problem kitten and other cat should have restricted access to each other at times when problems might arise • Startling, punitive techniques may aversively affect the other cat and are not recommended. • Provide appropriate outlets for predatory behaviors with the problem kitten on a regular, daily basis using toys or objects.

Play That Is Excessive and/or Destructive, and Scratching

- Put valuable, breakable, or dangerous objects away. • Provide appropriate toys for the kitten and rotate every few days to maintain novelty and interest. • Interactive play with kitten using toys or objects on a daily basis. • "Booby traps" may be used to keep kitten from a few select objects or areas. Excessive use of such items might result in generalized anxiety. • Provide scratching posts of variable materials and assure they are long enough and stable enough for the cat to stretch and scratch. • Place scratching stations in commonly used areas and encourage use with catnip, treats, and integrating perches and resting areas. • Make inappropriately scratched areas less desirable (e.g., double sided sticky tape, plastic). • Frequent trimming of claws. • Declawing is a humane concern; however several studies indicate that declawing is not psychologically harmful to cats. Therefore, declawing may be preferable to relinquishment.

Fear and Defensive Behaviors Due to Lack of Early Socialization or from Early Trauma

- Gradual exposure to people without forcing interactions. • The kitten should be housed where it is comfortable and where it can remove itself from view but be frequently aware of people. • Counter-conditioning generally required. Highly enticing food and treats should be offered. Initially, food can be put in or near hiding area. Gradually food is placed farther from hiding area and closer to where a person is stationary. No attempt should be made to grab or hold the kitten. Eventually the food may be given by hand or on the person's lap. Toys on strings can be used to entice the kitten to play. • Important principles to remember are to let the kitten make the advances—not the person—and avoid scaring the kitten by forcing interaction or preventing escape.

Fear and Defensive Behaviors Related to Correction Techniques

Identify and cease inappropriate punishment.



MEDICATIONS

DRUG(S)

- None needed unless extreme fear and anxiety. See also Fears, Phobias, and Anxieties—Cats. • May consider use of feline pheromone products for fearful kittens



FOLLOW-UP

PATIENT MONITORING

- Telephone follow-up support helpful. • Be sure clients are not using aversive techniques that may induce fear and aggression in the kitten and/or exacerbate intensity of play aggression.

PREVENTION/AVOIDANCE

- Kitten behavior problems are often a result of owner's unrealistic expectations and misunderstanding of normal kitten behavior, as well as lack of enrichment and appropriate predatory play outlets. • Most problem behaviors can be prevented or redirected.
- Between 3 and 7 weeks of age, kittens should experience positive interactions with people to reduce fear and develop appropriate social bonds with humans. • Between 4 and 18 weeks, helpful to have exposure to tolerant (and playful) conspecifics to learn effective bite and play inhibition. • Advise family members to avoid roughhousing and body part play with kittens. • Punitive corrections should be discouraged.

EXPECTED COURSE AND PROGNOSIS

Normal Play Behaviors Directed toward People, Other Cats, and Household Objects

Reduction or resolution of problem when appropriate treatment protocols are followed. As the kitten ages, many of these behaviors begin to wane.

Uninhibited Aggressive Play Directed toward People

- Guarded prognosis • Aggression may become more severe and injurious with maturity. A better prognosis is given to those cases that are caught early and appropriately counseled or by obtaining a second compatible cat.

Scratching

Generally, if can successfully divert and reward for using appropriate scratching surfaces, the prognosis is good, and as the kitten matures, the behaviors wane. For cats with a high drive to scratch, long-term management is needed.

Fear and Defensive Behaviors Due to Lack of Early Socialization or Related to Early Trauma

- Kittens will vary in the degree to which they acclimate to people; maximal improvement may take months or even years; some may never be comfortable around people. • The longer the interval from 3 weeks of age to exposure to people, the poorer the prognosis.
- The more intense the early trauma, the poorer the prognosis.

Fear and Defensive Behaviors Related to Correction Techniques

- Can resolve quickly if corrections have not been used frequently, have not been severe, and the clients follow advice to replace these techniques with reward-based, avoidance, and redirection procedures.



MISCELLANEOUS

AGE-RELATED FACTORS

Fear and Defensive Behaviors Due to Lack of Early Socialization

During the sensitive period, between 3–7 weeks, the kitten must be exposed to people to prevent fearful and defensive responses to them.

INTERNET RESOURCES

- www.indoorpet.osu.edu • www.catvets.com
- AAFP and ISFM environmental needs guidelines: <http://bit.ly/14uWTCB>

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Client Education Handout
available online

PELGER-HUËT ANOMALY



BASICS

OVERVIEW

- Congenital hereditary disorder that has been seen in several breeds of dogs and domestic shorthair cats.
- An autosomal dominant inheritance pattern is likely.
- Nuclear hyposegmentation of many to all granulocytes (neutrophils, eosinophils and basophils) is seen.
- Hypolobulation of monocytes and megakaryocytes has also been reported.
- Chromatin patterns of leukocytes are normochromatic, or occasionally hyperchromatic.
- Cytoplasm of cells is unremarkable (i.e., no toxic changes are observed).
- Cellular function remains normal in heterozygotes.
- Heterozygous animals are asymptomatic.
- Care should be taken not to misinterpret a leukogram in a patient with Pelger-Huët anomaly as a severe left shift or vice versa.

SIGNALMENT

- Dogs—Pelger-Huët anomaly has been reported in mixed-breed dogs as well as numerous purebred animals. Overall the incidence is low; however, Australian shepherd dogs have been shown to have a 9.8% incidence rate.
- Cats—Pelger-Huët anomaly has only been reported in domestic shorthair cats. The overall incidence in cats is unknown; however, it is likely rare when compared to dogs.
- An autosomal dominant mode of inheritance is likely; however, incomplete penetrance has been seen in Australian shepherd dogs.

SIGNS

- No clinical signs observed in heterozygous animals, as the leukocytes are fully functional.
- Homozygous animals either die *in utero* or are stillborn with significant chondrodysplastic changes.

CAUSES AND RISK FACTORS

- Caused by an inherited defect of terminal differentiation due to a mutation in the laminin B receptor in humans.
- Australian shepherd dogs may have a higher incidence of the anomaly than other breeds; however, incidence rates in other breeds have not been thoroughly investigated.



DIAGNOSIS

DIFFERENTIAL DIAGNOSES

- The primary differential diagnosis to rule out is a severe regenerative or degenerative left shift, indicating severe inflammation and/or endotoxemia.
- An inflammatory leukogram may show a leukocytosis or leukopenia. Immature leukocytes exhibit an open, pale chromatin pattern.
- Toxic changes (e.g., Döhle bodies, blue foamy cytoplasm, toxic granulation) are frequently seen with severe inflammation and/or endotoxemia.
- Pelger-Huët cells have a nucleus that shows a mature, condensed chromatin pattern and exhibit no toxic changes.
- Animals with Pelger-Huët anomaly are clinically well, whereas animals with severe left shifts tend to be systemically ill and exhibit laboratory test abnormalities consistent with underlying inflammation and/or endotoxemia and possible organ system dysfunction.

CBC/SERUM BIOCHEMISTRY/ URINALYSIS

- The blood smear reveals a persistent varying hyposegmentation of all granulocytes and often monocytes.
- Granulocyte nuclei may be round, oval, peanut, dumbbell, horseshoe and bilobed in shape.
- A key finding is the mature, condensed chromatin pattern.
- The serum biochemistry profile and

urinalysis are unremarkable in cases of Pelger-Huët anomaly.

OTHER LABORATORY TESTS

No other tests are indicated to diagnose Pelger-Huët anomaly.

IMAGING

Imaging is not useful in diagnosing Pelger-Huët anomaly.

DIAGNOSTIC PROCEDURES

- Establishment of a hereditary pattern typically an academic exercise, but potentially useful.
- No additional diagnostic procedures are indicated to diagnose Pelger-Huët anomaly.



TREATMENT

No treatment is indicated for Pelger-Huët anomaly.



FOLLOW-UP

No follow-up is necessary.



MISCELLANEOUS

Suggested Reading

Deshuillers P, Raskin R, Messick J. Pelger-Huët anomaly in a cat. *Vet Clin Pathol* 2014; 43:337–341.

Latimer KS. Pelger-Huët Anomaly. In: Feldman BF, Zinkle JG, Jain NC, eds. Schalm's Veterinary Hematology, 5th ed. Philadelphia: Lippincott Williams & Williams, 2000, pp. 976–983.

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PELVIC BLADDER



BASICS

OVERVIEW

Also known as "intrapelvic bladder," as the urinary bladder neck is caudal to the pubic bone, causing most of the urethra and a variable amount of the bladder to remain inside the bony pelvis. The association of a short urethral length and urethral sphincter mechanism incompetence is common.

SIGNALMENT

- Dog and rarely cat.
- Primarily young female dogs (<1 year of age); incontinence often worsens after ovariectomy/ovariohysterectomy.
- Incontinence usually detected in male dogs after neutering.

SIGNS

- May be asymptomatic
- Incontinence can be continuous or intermittent
- Conscious voiding patterns often present
- Urgency with small volume elimination
- Perineum stained/soaked with urine; urine scalding; wet vulva/prepuce

CAUSES & RISK FACTORS

The position of the bladder in incontinent female dogs has been shown to be more intrapelvic and associated with a shorter urethral length, suggesting that an intrapelvic bladder neck and a short urethra together encourage urinary incontinence.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Urinary incontinence—ectopic ureter, USMI, inappropriate urination, urge incontinence, urinary tract infection, neurogenic incontinence (lower motor neuron disease).
- The degree of incontinence often exceeds that seen with USMI but is not as severe as that seen with ectopic ureters.
- Often associated with ectopic ureters.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC and biochemistries typically unremarkable.
- Urinalysis may reveal evidence of UTI (including pyuria, bacteriuria, and hematuria) or polyuria (USG < 1.035).
- Urine culture and sensitivity via a cystocentesis should be performed. Urine culture is often positive.

IMAGING

- Abdominal radiographs may reveal a caudally displaced bladder, but this should be interpreted carefully without bladder distension.
- Excretory urography may allow visualization of the kidneys, ureteral terminations, urinary bladder, and urethra but does not provide bladder distension. Without appropriate bladder distension, interpretation of bladder neck location should be made with caution.
- Retrograde vaginourethrogram or urethrocystography allows visualization of the vaginal vault, urethra, urethral length, prostate, urinary bladder shape, and bladder neck location.
- If the urinary bladder and urethra are inside the bony pelvis, double contrast cystourethrography may be required for full visualization. After maximum dilation with infusion of carbon dioxide or contrast medium, much of the bladder, bladder neck, and entire urethra remain within the pelvic canal, caudal to the bony pelvic brim. There is often a short wide urethra.
- Ultrasonography of the kidneys, ureters, and urinary bladder can aid in documentation of concurrent urologic anomalies, hydronephrosis concurrent pyelonephritis, or concurrent ectopic ureters.
- The diagnostic combination of choice is urethrocystoscopy and cystourethrography. This combination allows careful investigation of urethral, ureteral, cystic, vaginal, and vestibular defects. It also allows more accurate measurement of urethral length and width and aids in formulating therapy.

DIAGNOSTIC PROCEDURES

- Neurologic exam should be normal.
- Urodynamic procedures—consider cystometrography and urethral pressure profilometry to evaluate urinary bladder and urethral function, as well as urethral functional length. Detrusor function is usually normal, though higher threshold pressures may be generated at lower fluid volumes. The functional urethral length is shortened, and intraurethral pressure is frequently decreased, resulting in USMI.



TREATMENT

- Identify UTI and treat appropriately.
- Goal is to increase urethral resistance (artificial urethral sphincters, intraurethral injections of bulking agents, etc.), increase urethral length (bladder neck reconstruction),

and/or relocate the bladder neck to an intra-abdominal position (colposuspension, urethropexy, prostatoxexy, or vas deferensopexy).

- Detrusor relaxation has been suggested to treat refractory incontinent dogs as an overactive bladder could contribute to incontinence or urgency.
- Medical management for traditional USMI is typically successful in 75–90% of female dogs.

SURGICAL CONSIDERATIONS

- Colposuspension is the traditional surgical approach. A cure rate of 53% has been reported.
- Placement of an artificial urethral sphincter, or hydraulic occluder, has been successful and is the currently surgical treatment of choice if other minimally invasive or medical interventions fail. Experience with this procedure has been limited and the risk of urethral strictures can be up to 20%. Cystopexy can also be considered.

MINIMALLY INVASIVE TREATMENT

Transurethral submucosal bulking agent therapy (e.g., collagen implantation) has been described for the treatment of patients refractory to medical management and is associated with relatively good success. This is accomplished via cystoscopic guidance. This aids in improving incontinence but does not affect the location of the urinary bladder.



MEDICATIONS

DRUG(S)

- Phenylpropanolamine: an α -agonist (1–1.5 mg/kg PO q8h) will improve continence for USMI in a majority of cases.
- Diethylstilbestrol: initially 0.1–0.3 mg/kg q24h for 7 days, then once weekly; 0.1–1 mg PO for 3–5 days, then 1 mg per week thereafter. Gradually reduce to the lowest effective dose. DES can be toxic to the bone marrow in dogs and cats and can cause blood dyscrasias. This can progress, in rare cases, to fatal aplastic anemia. In some dogs, a combination of estrogen and PPA therapy may be more effective.
- Estriol: can be used for estrogen-responsive urinary incontinence. The dose is 2 mg once daily per dog (regardless of body weight) for 14 days, followed by the lowest effective daily dose tapered every 7 days.

(CONTINUED)

PELVIC BLADDER**FOLLOW-UP****PATIENT MONITORING**

- Every 3–6 months for UTI.
- Patients receiving an α -agonist should have serial blood pressure evaluations, as this is contraindicated in hypertensive patients or those with renal or heart disease.
- Patients receiving estrogen therapy should have serial CBC evaluations to monitor for bone marrow dyscrasias.

- Use all medications at the lowest effective dose.

**MISCELLANEOUS****ABBREVIATIONS**

- DES = diethylstilbestrol
- PPA = phenylpropanolamine
- USMI = urethral sphincter mechanism incompetence
- UTI = urinary tract infection

Suggested Reading

Crawford JT, Adams WM. Influence of vestibulovaginal stenosis, pelvic bladder, and recessed vulva on response to treatment for clinical signs of lower urinary tract disease in dogs: 38 cases (1990–1999). J Am Vet Med Assoc 2002, 221(7):995–999.

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Consulting Editor Carl A. Osborne

PEMPHIGUS



BASICS

OVERVIEW

- A group of auto-immune dermatoses characterized by varying degrees of erosion, ulceration, crusting, and pustule and vesicle formation.
- Affects the skin and sometimes mucous membranes.
- Forms identified in animals: pemphigus foliaceus (PF), pemphigus erythematosus (PE), pemphigus vulgaris (PV), panepidermal pustular pemphigus/vegetans (PEP), canine benign familial chronic pemphigus (Hailey-Hailey disease), paraneoplastic pemphigus (PP).

PATHOPHYSIOLOGY

- Tissue-bound auto-antibody directed at intraepidermal cell antigens (desmogleins) and acetylcholine receptors is deposited within the intercellular spaces, causing epidermal cell separation and cell rounding (acantholysis).
- Severity of ulceration and disease—related to depth of auto-antibody deposition within the skin.
- PF—auto-antibody deposition in the superficial layers of the epidermis.
- PV—lesions more severe; mediated by auto-antibody deposition just above the basement membrane zone; rapidly leads to ulcer formation.
- Implicated trigger factors are varied—genetics, hormonal, neoplasia, drugs, nutrition, viral, emotional stress, and physical factors (burns, UV radiation).

P SYSTEMS AFFECTED

Skin/Exocrine

GENETICS

Benign familial chronic pemphigus (Hailey-Hailey disease)—may have a genetic predisposition (autosomal dominant genodermatosis in humans).

INCIDENCE/PREVALENCE

- Uncommon group of diseases.
- PF—most common type.
- PE—relatively common; may be a more benign variant of PF or may be a crossover syndrome of pemphigus and lupus erythematosus.
- PV—second most common type; most severe form.
- PEP—rarest type; course of disease may be more severe than PF.
- PP—rare, clinical signs vary from severe to relatively benign crusted lesions.

SIGNALMENT

Species

- Dogs and cats—PF, PV, PE
- Dog—PEP

Breed Predilections

- PF—Akita, bearded collie, chow chow, dachshund, Doberman pinscher, Finnish spitz, Newfoundland, and schipperke.
- PE—collie, German shepherd dog, and Shetland sheepdog.

Mean Age and Range

Usually middle-aged to old animals

Predominant Sex

None reported

SIGNS

PF

- Scales, crust, pustules, epidermal collarettes, erosions, erythema, alopecia, and footpad hyperkeratosis with fissuring.
- Occasional vesicles are transient.
- Common involvement—head, ears, and footpads; often becomes generalized.
- Mucosal and mucocutaneous lesions uncommon.
- Cats—nipple and nailbed involvement common.
- Lymphadenopathy, edema, depression, fever, and lameness (if footpads involved) when severe or generalized.
- Variable pain and pruritus.
- Secondary bacterial infection possible.

PE

- Similar to PF.
- Lesions usually confined to head, face, and footpads.
- Depigmentation more common than with other forms often precedes crusting.

PV

- Oral ulceration frequent and may precede skin lesions.
- Ulcerative lesions, erosions, epidermal collarettes, blisters, and crusts.
- More severe than PF and PE.
- Affects mucous membranes, mucocutaneous junctions, and skin; may become generalized.
- Axillae and inguinum often involved.
- Positive Nikolsky sign (new or extended erosive lesion created when lateral pressure is applied to the skin near an existing lesion).
- Variable pruritus and pain.
- Anorexia, depression, and fever.
- Secondary bacterial infections common.

PEP

- Pustule groups become eruptive papillomatous lesions and vegetative masses with exudation.
- No oral involvement.
- No systemic illness.

CAUSES

Undetermined—genetics and a possible triggering event (e.g., viral infection, drug).

RISK FACTORS

Undetermined



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

PF

- Bacterial folliculitis
- Dermatophytosis
- Demodicosis
- Candidiasis
- Keratinization disorders
- Lupus erythematosus
- Pemphigus erythematosus
- Subcorneal pustular dermatosis
- Drug eruption
- Zinc-responsive dermatitis
- Dermatomyositis
- Tyrosinemia
- Mycosis fungoides
- Lymphoreticular malignancies
- Metabolic epidermal necrosis
- Sterile eosinophilic pustulosis
- Linear IgA dermatosis

PE

- Pemphigus foliaceus
- Lupus erythematosus
- Mucocutaneous pyoderma
- Demodicosis
- Dermatophytosis
- Epidermolysis bullosa simplex
- Uveodermatologic syndrome

PV

- Bullous pemphigoid
- Systemic lupus erythematosus
- Toxic epidermal necrolysis
- Drug eruption
- Mycosis fungoides
- Lymphoreticular neoplasia
- Ulcerative stomatitis causes
- Erythema multiforme

PEP

- Pemphigus vulgaris
- Bacterial folliculitis
- Pemphigus foliaceus
- Lichenoid dermatoses
- Cutaneous neoplasia

CBC/BIOCHEMISTRY/URINALYSIS

- Abnormalities uncommon.
- Leukocytosis and hyperglobulinemia with chronicity and/or secondary infection.

OTHER LABORATORY TESTS

Antinuclear antibody—may be weakly positive in PE only.

DIAGNOSTIC PROCEDURES

- Cytology of aspirates or impression smears from pustules or crusts—acantholytic keratinocytes and neutrophils; occasionally with eosinophils.
- Bacteriologic culture—identify secondary bacterial infections.

PATHOLOGIC FINDINGS

- Biopsies of lesional or perilesional skin required for diagnosis—acantholysis and

(CONTINUED)

PEMPHIGUS

- intraepidermal clefting; microabscess or pustule formation; rafts of acantholytic keratinocytes.
- Location of epidermal lesions—varies with disease; PF and PE have subcorneal or intragranular clefting and acantholysis; PV and PEP have suprabasilar clefting.
- Immunopathology of biopsied skin via immunofluorescent antibody assays or immunohistochemical testing—may demonstrate positive staining in the intercellular spaces in 50–90% of cases; results can be affected by concurrent or previous corticosteroid (or other immunosuppressive drug) administration; indirect immunofluorescence usually negative; PE may demonstrate staining of basement membranes and intercellular spaces.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Initial inpatient supportive therapy for severely affected patients.
- Outpatient treatment with initial frequent hospital visits (every 1–3 weeks); taper to every 1–3 months when remission is achieved and the patient is on a maintenance medical regimen.

NURSING CARE

Severely affected patients may require antibiotics and hydrotherapy/soaks.

DIET

Low-fat—to avoid pancreatitis predisposed by corticosteroids and (possibly) azathioprine therapy.

CLIENT EDUCATION

Sun avoidance/use of sunblock—ultraviolet light may exacerbate lesions (PE).

**MEDICATIONS****DRUG(S)****PF and PV****Corticosteroids**

- Prednisone or prednisolone—1.1–2.2 mg/kg/day PO divided q12h to initiate control.
- Minimum maintenance—0.5 mg/kg PO q48h to twice weekly.
- Taper dosage at 2- to 4-week intervals by 5–10 mg/week.

Cytotoxic Agents

- Most patients require additional immunomodulating drugs.
- Work synergistically with corticosteroids to allow reduction in dose and side effects.
- Azathioprine 2.2 mg/kg PO q24h, then q48h (dogs); infrequently used in cats, owing to potential for marked bone marrow suppression; feline dose 1 mg/kg q24–48h.

- Chlorambucil 0.2 mg/kg daily; best choice for cats.
- Cyclophosphamide 50 mg/m² BSA PO q48h (dogs).
- Cyclosporine 5–15 mg/kg PO q24h; limited application.
- Dapsone 1 mg/kg PO q8h; then as needed (dogs); limited application.

Chrysotherapy

- Used in conjunction with prednisone; very expensive.
- Auranofin 0.1–0.2 mg/kg PO q12–24h.

PE and PEP

- Oral prednisone or prednisolone 1.1 mg/kg PO q24h; then q48h; then to the lowest maintenance dose possible; may be stopped when in remission.
- Topical steroids may be sufficient in mild cases.

PRECAUTIONS

- Corticosteroids—polyuria, polydipsia, polyphagia, temperament changes, diabetes mellitus, pancreatitis, and hepatotoxicity.
- Azathioprine—pancreatitis, bone marrow suppression.
- Cytotoxic drugs—leukopenia, thrombocytopenia, nephrotoxicity, and hepatotoxicity.
- Chrysotherapy—leukopenia, thrombocytopenia, nephrotoxicity, dermatitis, stomatitis, and allergic reactions.
- Cyclophosphamide—hemorrhagic cystitis.
- Immunosuppression—can predispose animal to demodicosis, cutaneous and systemic bacterial and fungal infection.

ALTERNATIVE DRUG(S)**Alternative Corticosteroids**

- Use instead of prednisone if undesirable side effects or poor response noted.
- Methylprednisolone 0.8–1.5 mg/kg PO q12h; for patients that tolerate prednisone poorly.
- Triamcinolone 0.2–0.3 mg/kg PO q12h; then 0.05–0.1 mg/kg q48–72h.
- Glucocorticoid pulse therapy—11 mg/kg IV methylprednisolone sodium succinate for 3 consecutive days to induce remission; limited application.

Topical Steroids

- Hydrocortisone cream.
- More potent topical corticosteroids—0.1% betamethasone valerate, flucinolone acetonide, or 0.1% triamcinolide; q12h; then q24–48h.

Miscellaneous

- Tetracycline and niacinamide 500 mg PO q8h (dogs > 10 kg); half doses for dogs < 10 kg; limited application (especially PE).

**FOLLOW-UP****PATIENT MONITORING**

- Monitor response to therapy.

- Monitor for medication side effects—routine hematology and serum biochemistry, especially patients on high doses of corticosteroids, cytotoxic drugs, or chrysotherapy; check every 1–3 weeks, then every 1–3 months when in remission.

EXPECTED COURSE AND PROGNOSIS**PV and PF**

- Guarded (PV) to fair (PF): life-long or long-term therapy with corticosteroids and cytotoxic drugs usually needed.
- Regular monitoring necessary.
- Side effects of medications may affect quality of life.
- May be fatal if untreated (especially PV).
- Secondary infections cause morbidity and possible mortality (especially PV).

PE and PEP

- Fair: relatively benign and self-limiting.
- Oral corticosteroids may eventually be tapered to low maintenance doses; may be discontinued in some patients.
- Cutaneous lesions persist if untreated, but systemic symptoms rare.

**MISCELLANEOUS****PREGNANCY/FERTILITY/BREEDING**

Avoid steroids and cytotoxic drugs during pregnancy

ABBREVIATIONS

- BSA = body surface area
- PE = pemphigus erythematosus
- PEP = panepidermal pemphigus
- PF = pemphigus foliaceus
- PP = paraneoplastic pemphigus
- PV = pemphigus vulgaris

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Author Karen Helton Rhodes

Consulting Editor Alexander H. Werner



Client Education Handout
available online

PERIANAL FISTULA



BASICS

OVERVIEW

- Chronic inflammatory condition characterized by multiple, painful, progressive, ulcerating sinuses or, much less frequently, true fistulous tracts involving the perianal region.
- Synonyms: anal furunculosis, perianal sinus, pararectal fistulae, fistulae-in-ano.

SIGNALMENT

- Dog • German shepherd dogs primarily; Irish setters • Middle-aged dogs with mean age of 5–7 years; range, 7 months–14 years
- Males more commonly affected in most studies

SIGNS

- Dyschezia • Tenesmus • Hematochezia
- Constipation • Diarrhea • Malodorous mucopurulent anal discharge • Ulceration of the perianal skin with sinus tract formation
- Licking and self-mutilation • Reluctance to sit; posturing difficulties; personality changes
- Pain on manipulation of tail and examination of perianal area • Fecal incontinence • Anorexia • Weight loss

CAUSES & RISK FACTORS

- Cause not clearly defined, but a multifactorial immune-mediated mechanism is strongly suspected. • Appears to be an inappropriate T-cell mediated response. • An association with colitis has also been proposed, particularly in German shepherd dogs. • A genetic predisposition, based on breed incidence, has been proposed but not proven. • Anatomic factors have been implicated, particularly in German shepherds.
- Low tail carriage and a broad tail. • High density of apocrine sweat glands in the cutaneous zone of the anal canal of German shepherd dogs.

P



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other inflammatory processes—e.g., anusitis, hidradenitis suppurativa • Chronic anal sac abscess • Perianal adenoma or adenocarcinoma with ulceration and drainage
- Squamous cell carcinoma • Atypical bacterial infection • Oomycosis • Rectal fistula

CBC/BIOCHEMISTRY/URINALYSIS

- Usually unremarkable. • Patients with inflammation may have an inflammatory leukogram.

DIAGNOSTIC PROCEDURES

- Presumptive diagnosis—based on clinical signs and results of physical examination.
- Definitive diagnosis—made by biopsy of

the affected area.

- Colonoscopy with biopsy—may reveal associated colitis.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient medical therapy recommended initially in all cases.
- Clipping and cleaning the perianal area facilitates local therapy.
- Bathing with an antimicrobial shampoo may be helpful.

DIET

- Dietary modification—novel protein elimination diet such as venison or fish and potato. Hypoallergenic hydrolyzed diets should also be considered.
- Stool softeners—with pain or tenesmus.

SURGICAL CONSIDERATIONS

- Surgery is primarily indicated for patients with incomplete resolution or pseudohealing of sinuses following appropriate medical therapy.
- Anal sacculectomy—perform if anal sac involvement is confirmed.
- Surgical options—resection of inflammatory tissue and/or ablation of remaining sinuses with carbon dioxide laser is preferred.
- Surgical debridement (deroofing) with fulguration by chemical cautery or electrocautery; surgical resection followed by primary closure or second intention healing are other options.
- Radical excision of the rectal ring with modified rectal pull-through is not commonly necessary and is associated with a higher risk of fecal incontinence.



MEDICATIONS

DRUG(S) OF CHOICE

- Cyclosporine (CsA) ± ketoconazole is treatment of choice but is expensive.
- Cyclosporine A microemulsion as a single agent—give 4–8 mg/kg PO per day as induction dose, then taper dose based on clinical response.
- Cyclosporine A and ketoconazole—give CsA orally at 2–5 mg/kg/day PO and ketoconazole at 5–10 mg/kg/day PO as induction dose and then taper CsA as clinical signs resolve.
- Ketoconazole reduces dose of cyclosporine required by inhibiting CsA metabolizing enzymes.
- Continue treatment at least 4 weeks after complete resolution of fistula(e), but many patients require chronic treatment at reduced frequency to prevent recurrences.
- Tacrolimus (0.1% ointment) applied topically as maintenance therapy may be sufficient to control lesions; begin application as dose of oral medications is reduced.
- Apply topically q12h with gloved hand, then taper to q24–72h.

OR

- Oral prednisone and topical tacrolimus, appears to be efficacious and economical in less severe cases.
- Prednisone—2 mg/kg PO q24h for 2 weeks, decrease to 1 mg/kg q24h for 4 weeks and then 1 mg/kg q48h for 10 weeks.
- 0.1% tacrolimus ointment—(see protocol above)
- Chronic maintenance therapy with tacrolimus and possibly prednisone likely necessary for long-term control.
- Azathioprine alone or combined with prednisone using a decreasing dosage regimen is another treatment option.
- Metronidazole—10 mg/kg q12h for 2 weeks at initiation of therapy to control secondary infection.
- Elimination or hypoallergenic dietary therapy must be strictly enforced.
- Fecal softener if needed.

ALTERNATIVE DRUG(S)

Analgesics may be necessary, especially during induction phase, to facilitate local therapy.



FOLLOW-UP

PATIENT MONITORING

- Assess cyclosporine trough levels especially when ketoconazole is used if toxicity is suspected.
- Re-examine to assess healing, signs of recurrence, and associated complications.

POSSIBLE COMPLICATIONS

- Reversible alopecia • Vomiting, diarrhea, anorexia • Weight loss • Recurrence • Failure to heal • Dehiscence of surgical site
- Tenesmus • Fecal incontinence • Anal stricture • Flatulence • Iatrogenic Cushing's disease from corticosteroids

EXPECTED COURSE AND PROGNOSIS

- Guarded for complete resolution except in mildly affected patients.
- Chronic treatment may be necessary.
- If all treatment is discontinued, patient should be closely monitored for recurrence.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Colitis • Constipation and/or obstipation may develop

Suggested Reading

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Consulting Editor Stanley L. Marks

PERICARDIAL EFFUSION



BASICS

DEFINITION

Abnormally high volume of fluid within the pericardial sac; cardiac tamponade refers to the clinical syndrome that results from reduced cardiac output due to mechanical compression of the heart.

PATOPHYSIOLOGY

Accumulation of effusion exceeds the elastic capabilities of the pericardial sac resulting in elevated intrapericardial pressure. Cardiac tamponade occurs when intrapericardial pressure exceeds cardiac diastolic filling pressures. The compliant right atrium and right ventricle normally have the lowest filling pressures and are thus predominantly affected. The resultant reduction in cardiac venous return diminishes cardiac output. In animals with chronic pericardial disease, low cardiac output activates compensatory mechanisms that lead to fluid accumulation, typically manifested as right-sided CHF. Animals with acutely developing effusions typically exhibit signs of weakness or collapse.

SYSTEMS AFFECTED

- Cardiovascular—signs of low cardiac output and CHF
- Hepatobiliary—chronic passive congestion with mildly to moderately high liver enzymes
- Renal/Urologic—prerenal azotemia
- Respiratory—tachypnea or pleural effusion

INCIDENCE/PREVALENCE

Pericardial disorders comprise approximately 8% of the canine cardiology caseload at referral institutions.

GEOGRAPHIC DISTRIBUTION

Increased incidence of coccidioidomycosis-induced effusive constrictive pericarditis in the southwestern United States, Mexico, and Central and South America.

SIGNALMENT

Species

Dog; pericardial effusion in cat is typically secondary to CHF.

Breed Predilections

- Golden retrievers and German shepherds are predisposed to both right atrial hemangiosarcoma and idiopathic effusion.
- Brachycephalic breeds are predisposed to aortic body tumors.

Mean Age and Range

Middle-aged to older dogs are predisposed.

Predominant Sex

Male dogs may be predisposed to idiopathic effusion.

SIGNS

General Comments

Chronic pericardial effusion often causes

jugular distension and ascites without a cardiac murmur.

Historical Findings

- Lethargy
- Anorexia
- Weakness
- Exercise intolerance
- Abdominal distension
- Respiratory distress; occasionally cough
- Syncope or collapse
- Vomiting

Physical Examination Findings

- Jugular vein distension
- Ascites (especially with chronic effusion)
- Muffled heart sounds
- Weak arterial pulses
- Pulsus paradoxus
- Pallor or slow capillary refill time
- Tachypnea and/or tachycardia

CAUSES

- Neoplasia—hemangiosarcoma, heart base tumor, thyroid adenoma or adenocarcinoma, mesothelioma, metastatic neoplasia, and lymphoma (especially cats)
- Idiopathic—pericarditis (benign hemorrhagic effusion vs. effusive constrictive pericarditis with pericardial fibrosis)
- Coagulopathy—intoxication with vitamin K antagonist rodenticide, other coagulopathies
- CHF (especially cats)
- Infection—feline infectious peritonitis, coccidioidomycosis, bacterial pericarditis
- Congenital disorders—pericardioperitoneal diaphragmatic hernia, intrapericardial cysts
- Left atrial tear or cardiac trauma
- Pericardial foreign body

RISK FACTORS

- Cardiac neoplasia
- Advanced chronic valvular disease
- Coagulopathy



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- CHF secondary to other causes (e.g., valvular disease, cardiomyopathy, congenital heart disease), hepatic failure, abdominal neoplasia with hemorrhage, protein-losing nephropathy or enteropathy, Budd-Chiari-like syndrome.
 - Other causes of ascites (e.g., hepatic failure, hypoproteinemia, intra-abdominal neoplasia, and hemorrhage)—characteristically result in remarkable abnormalities on CBC and biochemistry profile, with a lack of jugular venous distension. Jugular vein examination can be helpful in differentiating these conditions from heart failure.
- CBC/BIOCHEMISTRY/URINALYSIS**
- CBC—usually normal; anemia possible in animals with hemangiosarcoma, lymphoma,

or coagulopathy; red cell morphology may be abnormal; may see thrombocytopenia in animals with neoplasia or DIC.

- Biochemistry profile—often normal; may see mild to moderately elevated liver enzymes (in animals with chronic passive hepatic congestion), mild azotemia (typically prerenal), hypoproteinemia, and mild electrolyte abnormalities (e.g., hyponatremia, hypochloremia, and hyperkalemia).
- Urinalysis—usually normal with normal renal concentrating ability unless a diuretic has been administered.

OTHER LABORATORY TESTS

- Elevated serum concentrations of cardiac troponin I (cTnI) have been demonstrated in dogs with pericardial effusion, especially in those with hemangiosarcoma.
- Clotting times (e.g., activated partial thromboplastin time and one-stage prothrombin time)—prolonged in animals with vitamin K antagonist rodenticide intoxication or DIC.
- Pericardial fluid analysis, although limited in diagnostic sensitivity and specificity, may be helpful in identifying certain neoplastic etiologies (e.g., lymphoma) or infectious causes.
- Feline infectious peritonitis testing or feline leukemia virus testing may be useful in cats.

IMAGING

Thoracic Radiographic Findings

- Mild-to-severe cardiac enlargement; cardiac silhouette often globoid with very sharp edges often evident on the dorsoventral view due to lack of cardiac motion artifact.
- Pleural effusion in some patients.
- Ascites in many patients.
- Large caudal vena cava in some patients.
- Nodular pulmonary infiltrates may be evident in patients with metastatic neoplasia.

Echocardiography

- Superior diagnostic test to evaluate for a cardiac mass; though only moderately accurate in predicting histopathologic diagnosis of mass lesions.
- Echo-free space clearly identified between the parietal pericardium and the epicardial surface of the heart.
- Often demonstrates the cause of pericardial effusion in patients with neoplasia (e.g. right atrial hemangiosarcoma or heart base tumor) or PPDH.
- Left atrial rupture may be suspected based on concurrent findings of pericardial effusion and advanced chronic valvular disease, especially if an intra-atrial or intra-pericardial thrombus is visualized.
- Pericardial effusion facilitates the detection of intrapericardial masses; echocardiography is ideally performed prior to pericardiocentesis if patient stable.
- Diastolic collapse of the right atrium or ventricle are indicative of cardiac tamponade.

PERICARDIAL EFFUSION

(CONTINUED)

Magnetic Resonance Imaging

Cardiac MRI has not been found to be superior to echocardiography in improving the diagnosis of cardiac neoplasia; however, advanced imaging may be helpful in detecting pulmonary, hepatic, or splenic metastases.

DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

- Sinus tachycardia in many patients; occasionally ventricular or supraventricular arrhythmias.
- Low-voltage QRS complexes (< 1 mV in leads I, II, III, aVR, aVL, and aVF) in some.
- ST segment elevation in some patients.
- Electrical alternans, a regular (1:1 or 2:1) variation in QRS-T wave height or morphology, results from the heart swinging back and forth within the pericardial sac in some patients.

PATHOLOGIC FINDINGS

- Pathologic findings will vary based on the underlying cause of pericardial effusion.
- Small cardiac masses may be identified that were not visible on antemortem testing.
- Dogs with left atrial tears will have advanced mitral endocardiosis with thickened and irregular mitral and/or tricuspid valve leaflets, left atrial enlargement and endocardial jet lesions, and possible ruptured chordae tendinae.



TREATMENT

APPROPRIATE HEALTH CARE

Cardiac tamponade warrants immediate pericardiocentesis; if uncomfortable with performing pericardiocentesis, referral to individuals with competence in this technique is strongly advised. Repeated pericardiocentesis may be needed; surgery may be indicated in selected dogs. Pericardiocentesis is rarely required in the cat.

Pericardiocentesis

- Place the patient in sternal recumbency. Clip haircoat on the right thorax between the third and eighth intercostal spaces from above the costochondral junction ventrally to the sternum. The right side of the thorax is preferred over the left due to decreased likelihood of coronary artery laceration. Simultaneous ECG monitoring is advised to detect arrhythmias. Echocardiography is useful to identify the best intercostal space, but if not available, perform pericardiocentesis at the fifth intercostal space just below the costochondral junction. After aseptic skin preparation and local anesthetic block with lidocaine, advance a long (~2 cm), large-bore (~16–18 gauge) catheter into the pericardial sac; may obtain a small amount of clear pleural fluid before advancement of the catheter into the pericardial sac. In dogs,

pericardial effusion is usually hemorrhagic, but some patients have a serous or serosanguinous effusion. Remove as much effusion as possible (unless a left atrial tear is suspected). If arrhythmias develop, reposition the needle or catheter and be prepared to administer IV lidocaine.

- Unless the patient has active hemorrhage into the pericardial sac, the effusion obtained by pericardiocentesis should not clot and should have a packed cell volume that differs from that of peripheral blood. The supernatant of chronic effusions is often xanthochromic.

NURSING CARE

Unless the patient has marked dehydration, fluids are generally not required or recommended for chronic pericardial effusion. Mild volume expansion may be useful in selected animals with acute pericardial effusion. Administer oxygen to dogs with tachypnea or signs of hemodynamic instability.

ACTIVITY

Cage rest, followed by exercise restriction

DIET

N/A

CLIENT EDUCATION

Clients should be informed that pericardial effusions are typically recurrent in nature, though the prognosis may vary greatly depending on the underlying cause. Clients should be educated about the importance for close monitoring for recurrent effusion and warned of the potential for sudden death.

SURGICAL CONSIDERATIONS

- Pericardectomy may be useful in the treatment of pericardial effusion accompanying heart base tumors and prolongs survival; this may also be considered for palliation of right atrial hemangiosarcoma but it is unknown whether it has any impact on survival.
- If idiopathic—may respond to pericardiocentesis; pericardectomy is indicated for recurrent effusion.
- Right auricular appendage masses may be treated surgically but resection alone without adjuvant chemotherapy is unlikely to significantly prolong survival.
- Thoracoscopy allows for partial pericardectomy with reduced risk and reduced postoperative pain.



MEDICATIONS

DRUG(S) OF CHOICE

- Drugs should not be used in place of pericardiocentesis.
- Diuretics—may help reduce ascites but can lead to progressive azotemia and patient weakness; generally not advised.

- Vitamin K—indicated for patients with rodenticide anticoagulant intoxication.
- Appropriate antibiotics are indicated in animals with infectious pericarditis.
- Chemotherapy—may be useful to treat effusion caused by lymphoma; partially effective in the treatment of atrial hemangiosarcoma and generally ineffective for heart-base tumor; adjuvant doxorubicin-based chemotherapy following right atrial mass resection has been shown to increase survival times but dogs rarely survive more than 6 months postoperatively.

CONTRAINdications

Digitalis, vasodilators, and angiotensin-converting enzyme inhibitors—reported to be relatively or absolutely contraindicated.

PRECAUTIONS

Diuretic administration often leads to exacerbation of weakness and azotemia.

ALTERNATIVE DRUG(S)

- Intracavitary chemotherapy may be attempted to treat mesothelioma.
- Anti-inflammatories or colchicine may be useful in selected dogs with idiopathic pericardial effusion.
- Additional immunosuppressives or intracavitary chemotherapy can be considered for recurrent effusions, especially in cases with recurrent pleural effusion after pericardectomy.



FOLLOW-UP

PATIENT MONITORING

- ECG—advised during first 24 hours as pericardiocentesis often leads to ventricular arrhythmias.
- Pericardial effusion may recur at any stage; examination and echocardiography at 10–14 days and every 2–4 months recommended to detect recurrent idiopathic pericardial effusion.

POSSIBLE COMPLICATIONS

- Hypotension or shock.
- Pneumothorax, arrhythmias, and myocardial perforation or coronary laceration secondary to pericardiocentesis.

EXPECTED COURSE AND PROGNOSIS

- Right atrial hemangiosarcoma—poor; tumor is highly malignant, usually not resectable at the time of diagnosis; may respond transiently to adriamycin-based chemotherapy; the benefit of palliative pericardectomy is unproven.
- Chemodectoma—fair; slow-growing tumor, late to metastasize; pericardectomy often resolves clinical signs; may respond to chemotherapy or radiation therapy; survival of up to 3 years has been reported following pericardectomy alone.

(CONTINUED)

- Prognosis is good with idiopathic pericardial effusion; approximately 50% of cases resolve after one or two pericardiocenteses; pericardectomy is often curative in persistent cases.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Hemangiosarcoma of the spleen

AGE-RELATED FACTORS

- Idiopathic pericardial effusion may be more common in middle-aged to elderly dogs.
- Hemangiosarcoma and heart-base tumors are more common in elderly dogs.

ZOONOTIC POTENTIAL

Coccidioidomycosis

SYNOMYS

- Cardiac tamponade
- Pericardial tamponade
- Pericarditis

SEE ALSO

- Anticoagulant Rodenticide Poisoning
- Atrial Wall Tear
- Chemodectoma

- Coccidioidomycosis
- Feline Infectious Peritonitis
- Hemangiosarcoma, Heart
- Myocardial Tumors

ABBREVIATIONS

- CHF = congestive heart failure
- cTnI = cardiac troponin I
- DIC = disseminated intravascular coagulation
- ECG = electrocardiogram
- PPDH = pericardioperitoneal diaphragmatic hernia

Suggested Reading

Chun R, Kelliher HB, Henik RA, et al. Comparison of plasma cardiac troponin I concentrations among dogs with cardiac hemangiosarcoma, noncardiac hemangiosarcoma, other neoplasms, and pericardial effusion of nonhemangiosarcoma origin. *J Am Vet Med Assoc* 2010, 237(7):806–811.

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Client Education Handout available online

PERICARDITIS



BASICS

OVERVIEW

- Pericardial disease accounts for about 5% of cardiovascular disease in dogs (far less in cats), but it is a common cause of emergency presentation, since dogs with pericardial disease often experience serious clinical signs. Clinical signs of pericardial disease are usually caused by cardiac tamponade, which occurs when fluid accumulates in the pericardial space fast enough to increase the intrapericardial pressure above the central venous pressure during part of the respiratory cycle. If the intrapericardial pressure exceeds the central venous pressure continuously for more than a few minutes, death occurs. Pericardial constriction (elevated intrapericardial pressure in the absence of significant effusion) is fortunately rare in both dogs and cats, and occurs most often as a long-term complication of infectious or effusive pericarditis.

- Clinical signs of pericardial disease generally depend on the severity of tamponade (or rarely, constriction), and are independent of the underlying disease (i.e., inflammatory pericardial diseases (pericarditis) cannot usually be distinguished from neoplastic pericardial diseases based on the clinical signs they produce).

SIGNALMENT

- Idiopathic hemorrhagic pericarditis is more common in young to middle-aged, large-breed dogs (e.g., Great Pyrenees, Great Dane, Saint Bernard, golden retriever).
- Infectious pericarditis is relatively rare, but it occurs most often in young, active dogs (occasionally cats), associated with a penetrating injury (e.g., twig, plant awn).
- Pericarditis is rare as an important cause of clinical signs in cats, but the most common cause is feline infectious peritonitis (FIP), which has a "dual peak" age incidence in young and old cats.
- Small amounts of pericardial effusion in the absence of cardiac tamponade occur commonly in cats with hypertrophic cardiomyopathy, most often with other signs of heart failure—this should not be confused with pericarditis.

SIGNS

- Cats—clinical signs are rare, but similar to dogs when they occur.
- Dogs—clinical signs are caused by tamponade, and include signs of low cardiac output (e.g., collapse, weakness, anorexia, prerenal azotemia) as well as those caused by high central venous pressure (e.g., ascites). Diminished arterial pulse strength with noticeable weakening of the pulse on

inspiration is called pulsus paradoxus, a physical finding highly suggestive of tamponade. Dogs with tamponade also commonly have muffled or distant heart sounds, jugular venous distension, and rapid heart rates (tachycardia), but these findings are not pathognomonic.

- Clinical signs of pericardial constriction tend to be more chronic, with ascites prominent among them. Rarely, dogs with chronically elevated central venous pressures develop intestinal lymphangiectasia, with subsequent protein-losing enteropathy.

CAUSES & RISK FACTORS

- The cause of idiopathic hemorrhagic pericarditis is unknown; it may constitute the benign end of a spectrum that on its malignant end may include mesothelioma, when mesothelial cells that line the pericardium (or other body cavity) become malignant.
- Infectious pericarditis can be caused by either bacterial or fungal infection (e.g., tuberculosis, coccidioidomycosis, actinomycosis, nocardiosis, and infection with *Pasteurella* spp.). Infectious pericarditis may result from migrating porcupine quills, plant awns, projectiles, or other objects introduced into the chest.
- Cats—trauma or infection (e.g., FIP, *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus*, *Actinomycetes*, *Cryptococcus*, and possibly *Toxoplasma*).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of pericardial effusion and tamponade (e.g., neoplasia, left atrial rupture, heart failure, peritoneal-pericardial diaphragmatic hernia, and pericardial cysts).
- Other causes of heart failure (e.g., cardiomyopathy, myocarditis, tricuspid or pulmonary valve disease, congenital heart disease, cor pulmonale, and severe left-sided CHF).
- Other causes of abdominal effusion (e.g., neoplasia, hemorrhage, severe hypoalbuminemia).
- Other causes of weak arterial pulse or collapse (e.g., cardiomyopathy, shock, hypoadrenocorticism, arrhythmias).

CBC/BIOCHEMISTRY/URINALYSIS

Most often unhelpful, with nonspecific changes common to many chronic conditions, including mild anemia, relatively nonreactive neutrophilia, and monocytosis.

IMAGING

Thoracic Radiography

Often unhelpful, although a rounded cardiac silhouette may suggest pericardial effusion,

particularly when the slow accumulation of chronic effusion permits significant expansion of the pericardium before the onset of tamponade; absence of this finding does not rule out pericardial effusion or pericarditis.

Echocardiography

The best single test to rule out pericardial effusion. Two-dimensional echocardiography reveals an echo-free space inside the parietal pericardium when effusion is present. Cardiac tamponade is recognized by the diastolic collapse of the right atrium, which is relieved during inspiration. The identification of intracardiac neoplasia is best left to highly trained and experienced echocardiographers.

Hemodynamic Measurements

- In the absence of volume contraction or treatment with diuretics, cardiac tamponade is associated with high central venous pressures (> 10 mmHg), and even if marginally elevated (e.g., 5–10 mmHg), these pressures spike to high levels (> 10 mmHg) and remain elevated on fluid challenge (e.g., 10 mL/kg IV bolus of LRS administered IV in less than 5 minutes).
- Constrictive pericardial physiology is rare and difficult to diagnose even by simultaneous pressure measurements from the right and left ventricles showing pressure equalization at an elevated end-diastolic pressure. Atrial pressure tracings classically show a rapid drop in pressure in early diastole followed by an early rise to a plateau at an elevated end-diastolic pressure.

DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

Potentially, low-voltage QRS complexes (< 0.9 mV in all leads in the dog), electrical alternans, ST segment elevation in the caudal and leftward leads (e.g., II, aVF, V3, I), P-mitrale (even in the absence of left atrial enlargement) and occasionally, arrhythmias. These changes lack sensitivity, and are not pathognomonic even when present.

Fluid Analysis

Cytologic examination of pericardial effusion cannot reliably differentiate among the common neoplastic (e.g., hemangiosarcoma, mesothelioma) and idiopathic causes of effusion. Cytology can identify (and thus rule out if they are not present) some potential causes of effusion (e.g., lymphosarcoma, FIP, sepsis).

Other Procedures

- If an infectious agent is suspected, aerobic and anaerobic cultures of the effusion are indicated.
- Histopathologic examination of the pericardium.
- Significant elevation of serum cardiac troponin I is not typical of benign effusion and suggests hemangiosarcoma.

(CONTINUED)

PERICARDITIS**TREATMENT**

- Pericardiocentesis is the only effective treatment for pericardial effusion causing tamponade. Until pericardiocentesis can be performed, IV fluids are beneficial to support cardiac output; diuretics are contraindicated in the management of cardiac tamponade.
- Effusion caused by idiopathic pericarditis in dogs may spontaneously subside after one or more pericardiocenteses. For chronically recurrent (e.g., more than twice) pericardial effusion in the absence of an echocardiographically identifiable cause, thoracic exploration with partial pericardectomy permits histopathologic examination, removal of foreign material, and evaluation for neoplastic or granulomatous disease. Thoracoscopic pericardectomy may provide similar diagnostic and therapeutic benefits in experienced hands. Surgery may help prevent subsequent constrictive disease. Infectious pericarditis should be treated surgically as soon as the diagnosis is made, in an effort to avoid subsequent pericardial constriction.
- Constrictive pericarditis may require epicardial stripping to relieve the constriction and adhesions between the visceral and parietal layers of the pericardium; this is a difficult and potentially dangerous procedure that should be attempted only by experts.

**MEDICATIONS****DRUG(S)**

- Treat infectious disease with appropriate antibiotics or antifungals based on culture and sensitivity testing.
- While anti-inflammatory, immunosuppressive, or anti-fibrotic strategies have been tried in dogs (e.g., therapy with corticosteroids, azothioprine, or colchicine) the efficacy of these strategies for preventing recurrent effusion is unknown.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Diuretics and preload reducers are contraindicated in tamponade.
- Corticosteroids or other immunosuppressive agents may exacerbate infection.

**FOLLOW-UP**

Pericardial effusion may recur if the pericardium is intact. Pleural effusion may occur months or even years after pericardiocentesis or pericardectomy, often associated with mesothelioma; periodic echocardiographic monitoring following treatment is recommended.

**MISCELLANEOUS****ABBREVIATIONS**

- CHF = congestive heart failure
- FIP = feline infectious peritonitis

Suggested Reading

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PERINEAL HERNIA



BASICS

OVERVIEW

- The term *Perineal hernia* refers to a spectrum of diseases in which the perineal diaphragm is weakened or ruptured, resulting in abnormal function during defecation and progressing to herniation of pelvic and abdominal viscera.
- Weakening of the perineal diaphragm is postulated to result from hormonal influences on the perineal musculature in male dogs, but may also follow from conditions causing chronic and excessive straining, or neuropathic weakness of the perineal muscles.
- Separation of the perineal muscles (levator ani and coccygeus) from the anal sphincter and rectum allows lateral bulging of the rectum when the animal strains, thereby preventing coordinated defecation. Separation of the muscles also allows pelvic and abdominal viscera to migrate caudally.
- Retroflexion of the bladder may occur, and the subsequent incarceration may lead to ureteral or urethral obstruction. Strangulation of herniated viscera may occur in the severest cases.

SIGNALMENT

- This disease is seen most commonly in dogs, but also sporadically in cats.
- Older, intact male dogs are most at risk, however it can occur in females.

SIGNS

- Straining to defecate or urinate.
- Constipation is the main feature, although some patients present for supposed diarrhea, when liquid feces escapes around the firmer stool.
- Unilateral or bilateral perineal bulge due to fecal impaction and/or herniation: this is often the only presenting sign in cats.

CAUSES & RISK FACTORS

- Intact status in older male dogs.
- Underlying pathology leading to excessive straining: prostatomegaly in male dogs, while megacolon and malunion of pelvic fractures can predispose to perineal laxity in cats.
- Caudal neuropathy, malformation or injury such as tail traction.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other conditions leading to obstipation and straining. Perineal neoplasia (adenoma, adenocarcinoma), sub-lumbar lymphadenomegaly secondary to anal sac adenocarcinoma, rectal tumor, perineal lipoma, paraprostatic cyst. Perineal abscess (anal sac abscess, foreign body).

CBC/BIOCHEMISTRY/URINALYSIS

No specific abnormalities on blood work, except azotemia and elevated creatinine if urinary obstruction occurs.

IMAGING

- Abdominal radiography: confirm constipation, prostatomegaly, sublumbar lymphadenomegaly, megacolon in cats.
- Pelvic radiography: confirm pelvic fracture malunion or intrapelvic mass.
- Abdominal ultrasonography: evaluate the size and consistency of the prostate.
- Perineal ultrasonography: evaluate presence of viscera or mass lesions.

DIAGNOSTIC PROCEDURES

- Thorough rectal palpation should confirm accumulation of feces in the dilated rectum, and perineal laxity.
- Insert a finger into the rectum and hook it laterally. If it is possible to pinch the rectal mucosa and skin together between the tip of the forefinger and thumb, without palpating a muscle shelf in between, the integrity of the pelvic diaphragm has been compromised.
- It is important to thoroughly evaluate both sides of the perineum: bilateral perineal laxity is often present even when herniation has only occurred on one side. Also evaluate the position of the anal sphincter in relation to the tuber ischii.
- In a normal patient, the sphincter is held in position dorsal and slightly cranial to the caudal extent of the tuber ischii. When the perineal diaphragm breaks down, the anus migrates caudally.
- Endoscopy or fine-needle aspiration biopsy may be indicated if a mass lesion is present extra or intraluminally.



TREATMENT

- Low residue diet and fecal softeners may ameliorate clinical signs temporarily, but surgical repair of the perineal diaphragm is required for definitive treatment.
- Castration of male dogs should always be performed simultaneously with herniorrhaphy in male dogs, due to the high rate of recurrence in intact dogs.
- Bladder retroflexion is considered an emergency; either due to urinary obstruction or the potential for strangulation and devitalization. In these patients, the urethra should be catheterized and the bladder decompressed if possible.
- In some cases, percutaneous cystocentesis is required to decompress and reposition the bladder before a urethral catheter can be passed.
- A balanced electrolyte solution should be administered intravenously prior to and during surgery in patients suffering from azotemia and hyperkalemia following urinary obstruction.
- Prior to surgical correction, impacted feces should be gently removed from the rectum. Enemas are not recommended as liquid feces may not be completely evacuated, leading to more contamination during surgery.
- Intraoperative antibiotics may be given, but there is no indication to continue antibiotic treatment postoperatively.
- The anal sacs are expressed and flushed, and a purse-string suture placed at the anocutaneous junction. The entire perineum and tail base is clipped, with the clip extending cranially past the greater trochanter of the femur on each side.
- In intact male dogs, the scrotum and surrounding skin is prepped for either a prescrotal or caudal castration approach. Depending on the preferred approach, the dog is castrated in dorsal recumbency and then flipped and placed in a perineal stand for the hernia repair, or placed in the perineal stand and castration performed via a caudal approach to the scrotum.
- A curvilinear incision is made 1–2 cm lateral to the anus, extending from the ventral tail base to the tuber ischium. The subcutaneous tissues are dissected in order to expose the hernia sac. This sac is perforated, at which point a small amount of serosanguinous fluid is usually encountered.
- Omentum is the most common organ within the hernia, and it may contain organizing hematomas or areas of saponification: these can be resected if necessary. The loose connective tissue is dissected to expose the coccygeus muscle (lateral), the anal sphincter (medial) and the internal obturator (ventral).
- Take care to avoid damaging the pudendal nerve and artery as it crosses the dorsal aspect of the internal obturator toward the anus. Most surgeons prefer to elevate the internal obturator from the ischium in order to close the hernia ring with minimal tension.
- Three simple interrupted sutures (nonabsorbable or long-acting absorbable, appropriately spaced) are placed between the following muscles: dorsal anal sphincter and dorsal coccygeus, ventral anal sphincter and medial internal obturator, ventral coccygeus and lateral internal obturator. The surgical wounds are then closed routinely. Ensure that the purse-string suture is removed!
- It may be helpful in large dogs with large bilateral hernias, especially if bladder retroflexion with urinary obstruction has occurred, to initially perform exploratory celiotomy, reposition the bladder and colon, and perform incisional colopexy and cystopexy.
- Staging the procedure, so that herniorrhaphy can be performed a few days later, when the patient's condition has stabilized and the perineal edema has resolved, may facilitate definitive hernia repair.

(CONTINUED)

- This technique has not been shown to affect recurrence rates, but does simplify the definitive herniorrhaphy by allowing local edema to settle, and reducing the tendency of abdominal contents to migrate into the field during surgical correction.
- In patients with very poor perineal muscle development, the repair may be supported by using a flap from the superficial gluteal muscle, incorporating prosthetic mesh into the repair, or in very severe cases, elevating and rotating the semitendinosus muscle. A superficial gluteal muscle flap is recommended in cats and very small dogs.
- The incisions are iced postoperatively to reduce pain and swelling. An Elizabethan collar is placed to prevent self-trauma to the incisions and appropriate analgesia given. A moist, low-residue diet is usually sufficient to maintain sufficiently soft stool to prevent straining or constipation postoperatively. Fecal softeners may be administered, but may lead to diarrhea and fecal soiling in the first days after surgery, especially if a bilateral repair has been performed. The patient's activity should be restricted for at least 3–4 weeks after surgery.

- The main risks of perineal herniorrhaphy are recurrence (greatly reduced by castration and use of internal obturator flap), and temporary dysfunction of the anal sphincter due to stretching following bilateral herniorrhaphy.
- Fecal and urinary incontinence can occur if excessive dissection around the pudendal nerve or peritoneal reflections are performed.



MEDICATIONS

N/A



FOLLOW-UP

PATIENT MONITORING

The patient should be evaluated thoroughly for the first 48 hours following surgery, with particular attention paid to urination and defecation. A rectal examination should be performed at the time of suture removal if feasible.

PREVENTION/AVOIDANCE

The major factor known to reduce the risk of recurrence following surgery is castration.

PERINEAL HERNIA

POSSIBLE COMPLICATIONS

Constipation and bladder retroflexion/obstruction if left untreated.

EXPECTED COURSE AND PROGNOSIS

Recovery and function following surgery is usually excellent. There is a 10–50% risk of recurrence depending on presence of underlying conditions, surgical approach, and intact status of the dog.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Cats should also be evaluated for primary conditions causing excessive straining (e.g., megacolon due to neurologic dysfunction or outflow obstruction).

Suggested Reading

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Author Geraldine Briony Hunt

Consulting Editor Stanley L. Marks

PERIODONTAL DISEASES



BASICS

DEFINITION

Inflammation of some or all of the tooth's support structures (gingiva, cementum, periodontal ligament, and alveolar bone); compared with gingivitis (inflammation of the marginal gingiva), periodontitis indicates some degree of periodontal attachment tissue loss.

PATHOPHYSIOLOGY

• An intact epithelial barrier, high rate of epithelial turnover and surface desquamation prevent bacteria from gaining direct access to underlying tissue. • Normal host defense mechanisms limit the penetration of these products and their damaging effects. • Fluctuations in the host—parasite equilibrium may result in cycles of either diminished or increased intensity of the inflammatory response; it may be possible to think of periodontitis as the outcome of an imperfectly balanced host—parasite interaction. • Caused by bacteria located in the gingival crevice; initially a pellicle forms on the enamel surface of a clean tooth; the pellicle is composed of proteins and glycoproteins deposited from saliva and gingival crevicular fluid; the pellicle attracts aerobic gram-positive bacteria (mostly *Actinomyces* and *Streptococcus*); more bacteria soon adhere, forming plaque; within days the plaque thickens, becomes mineralized, and transforms into calculus. Calculus is rough and can be irritating to the gingiva. In time an anaerobic environment occurs subgingivally, allowing anaerobic motile rods and spirochetes to populate the subgingival area; more plaque builds on top of the calculus; endotoxins released by anaerobic bacteria cause tissue destruction and bone loss (periodontitis).

SYSTEMS AFFECTED

• Gastrointestinal—oral cavity. • Microscopic hepatic, renal, and CNS lesions are found in some animals.

GENETICS

N/A

INCIDENCE/PREVALENCE

Common

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dogs and cats (less common)

Breed Predilections

Toy breeds especially Maltese and Yorkshire terriers are predisposed to developing periodontal disease.

Mean Age and Range

More common in older animals

Predominant Sex

None

SIGNS

Malodor, face rubbing, dropping food, oral bleeding

Examination Findings

- The degree of severity of periodontal disease relates to a single tooth; a patient may have teeth that have different stages of periodontal disease. Attachment loss may involve gingiva and/or alveolar bone loss (as well as periodontal ligament). Either periodontal pockets or recession of tissue with exposure of roots and/or furcation area may occur.
- Normal (PD 0): clinically normal—no gingival inflammation or periodontitis clinically evident.
- Stage 1 (PD 1): gingivitis without attachment loss. The height and architecture of the alveolar margin are normal. Bleeding on probing may be present.
- Stage 2 (PD 2): early periodontitis—less than 25% of attachment loss, or at most, there is a Stage 1 furcation involvement in multirooted teeth. There are early radiologic signs of periodontitis. The loss of periodontal attachment is less than 25% as measured either by probing of the clinical attachment level or radiographic determination of the distance of the alveolar margin from the tooth's cementoenamel junction relative to the length of the root. Stage 1 furcation involvement may be present in multirooted teeth.
- Stage 3 (PD 3): moderate periodontitis—25–50% of attachment loss as measured either by probing of the clinical attachment level, radiographic determination of the distance of the alveolar margin from the cementoenamel junction relative to the length of the root, and/or there is a Stage 2 furcation involvement in multirooted teeth.
- Stage 4 (PD 4): advanced periodontitis—more than 50% of attachment loss as measured either by probing of the clinical attachment level, radiographic determination of the distance of the alveolar margin from the cementoenamel junction relative to the length of the root, or there is a Stage 3 furcation involvement in multirooted teeth.

CAUSES

- Gingivitis—dogs; *Streptococcus* and *Actinomyces* spp.
- Periodontitis—dogs; pigmented and non-pigmented *Bacteroides*, *Porphyromonas denticanis*, *Porphyromonas salivosa*, *Porphyromonas gulae*, *Prevotella* spp., *Fusobacterium* spp.
- Cats—*Peptostreptococcus*, *Actinomyces*, and *Porphyromonas* spp.

RISK FACTORS

- Toy breeds with crowded teeth
- Dogs that groom themselves—causes hair to be embedded in the gingival sulcus
- Other debilitating illnesses
- Poor nutritional state



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pemphigus • Lupus • Oral neoplasia
- Stomatitis

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

DETECTION

- The Visual Awake Exam significantly underestimates the presence and severity of periodontal disease and there is no correlation between the visual awake exam and the presence or absence of periodontal disease.
- OraStrip QuickCheck Canine is a quick, point-of-care test that provides early detection of periodontal disease within 10 seconds and can be used in every wellness exam. • A positive OraStrip test has been shown to correlate with the presence of periodontal disease.

IMAGING

- Radiography—important diagnostic tool; as much as 60% of disease is hidden below the gum line.
- No radiographic changes in Stage 1 disease (gingivitis).
- Early radiographic signs of Stage 2/3 disease include loss of density and sharpness of the alveolar margin; as periodontal disease progresses, loss of lamina dura mineralization apically and furcation involvement in multirooted teeth.
- Advanced periodontal disease appears radiographically as loss of bone support around one or more roots; bone loss may be horizontal (a decrease in bone height around one or more teeth), vertical (infrabony defect), or oblique (a combination of both).

DIAGNOSTIC PROCEDURES

- Exam room—diagnostic strip (OraStrip) measures the amount of thiol levels which correlate to presence of periodontal disease necessitating care.
- Periodontal probing—“probing depth”: distance between free gingival margin and apical extent of pocket; probing depths > 2 mm in the medium-sized dog and 1 mm in the cat are abnormal.
- “Attachment loss” measures between the cementoenamel junction (CEJ) and apical extent of pocket; normally the gingival sulcus is located at the CEJ; any attachment loss is abnormal.



TREATMENT

- The ultimate goal of periodontal therapy is to eliminate periodontal pocket(s) and prevent further attachment loss; a willing patient and a client who can provide

(CONTINUED)

PERIODONTAL DISEASES

homecare are important considerations in creating a therapy plan. • Stages 1 or 2—professional cleaning, hand scaling, polishing, irrigation, application of dental sealant (SANOS). In cases of periodontal pockets locally applied antimicrobials may be helpful in reducing the pocket depth when combined with daily home care to control plaque. After thoroughly cleaning a moderate pocket, placement of a local antibiotic gel Clindoral or Doxirole Gel can help rejuvenate periodontal tissues and may reduce pocket depth. • Stage 3—above plus closed-root planing and subgingival curettage. If client can not provide home care or pet will not accept it consider extraction. • Stage 4—surgery needed to either expose the root for treatment (open-flap curettage) with a guarded prognosis or extract. • If 2–3 mm of healthy, attached gingiva is present—apically reposition flap to decrease pocket depth in areas of alveolar bone loss; if not enough healthy gingiva remains to apically reposition flap; rotated flap (from adjacent gingiva), free gingival flap, or extraction. • Bone replacement procedures—with two-, three-, four-walled infrabony pockets. • Guided tissue regeneration—use tissue barriers to separate gingival tissue and root surface.



MEDICATIONS

DRUG(S) OF CHOICE

Clindamycin and amoxicillin/clavulanic acid are antimicrobials approved for periodontal disease; may be used for a week before periodontal treatment, prior to anesthesia, postoperatively for 7–10 days. Systemic use of antimicrobials is not indicated in the treatment of periodontal diseases without surgical attention to the underlying cause.

HOMECARE

- The Veterinary Oral Health Council was created to accept products that significantly (> 20%) retarded the accumulation of plaque and/or tartar. Those products that are accepted by the VOHC carry the VOHC seal of acceptance. • Fluoride—stannous fluoride preparations (Omni Gel and Gel-Kam) help control periodontal disease by reducing plaque deposition on the surface of enamel and also decrease dental pain; use 0.4% strength in patients with Stage 3 and 4 periodontal disease, especially those with exposed root surfaces. • Chlorhexidine—the most effective product to inhibit plaque

formation in humans; bacteriostatic and bactericidal against bacteria, fungi, and some viruses; once absorbed it continues to be effective for up to 24 hours; in humans, to be maximally effective, it is swished in the mouth for 1 minute twice daily; the contact time of application is important for binding to the tooth and gingival sulcus; 1 minute of oral rinsing is difficult to accomplish in animals; chlorhexidine can be applied with a gauze sponge or cotton-tipped applicators, as a spray, or with finger brushes. Chlorhexidine is incorporated in CEH Hextra Chews (Virbac). • Novadent—chlorhexidine acetate 0.1%. • DentAcetic wipes-(Dechra) contains sodium hexametaphosphate used daily to remove plaque and decrease accumulation of tartar. • OraVet (Merial) plaque prevention gel applied weekly. • Diet—hard biscuit foods are preferable to soft sticky foods. • t/d tartar control diet (Hill's)—specifically indicated to control tartar (calculus) in dogs and cats. • Amount and type of homecare products dispensed depends on dental periodontal pathology. • Stages 1 and 2—daily brushing with dentifrice and VOHC accepted home care products used daily. • Stage 3, established periodontal disease—daily brushing with fluoride-containing toothpaste plus twice-weekly application of stannous fluoride gel. • Stage 4, advanced periodontal disease—zinc ascorbate gel (Maxi/Guard) 3–4 times daily to help regenerate cellular collagen, plus 0.2% chlorhexidine spray twice daily; or CHX-Guard, chlorhexidine gluconate, and zinc.

CONTRAINdications

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

Do not use chlorhexidine and fluoride products concurrently; binding both products may inactivate them; better to wait 30 minutes to 1 hour between use of a dentifrice-containing fluoride and a chlorhexidine rinse or gel.

ALTERNATIVE DRUG(S)

- Tetracycline • Metronidazole



FOLLOW-UP

PATIENT MONITORING

The degree of periodontal pathology dictates recall interval; some patients are checked

monthly, while others can be evaluated every 3–6 months. OraStrip can be used at recall to determine if the periodontal disease has recurred or worsened.

PREVENTION/AVOIDANCE

Good dental homecare

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

Due to the multifactorial aspect of periodontal disease and individual response, the expected course and prognosis can be highly variable, but early assessment, diagnosis, adequate treatment, and therapy can minimize the destructive effects of this disease.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

ABBREVIATIONS

- CEJ = cementoenamel junction • CNS = central nervous system • PD = periodontal disease

INTERNET RESOURCES

<http://www.avdc.org/Nomenclature.html>.

Suggested Reading

Harvey CE. Periodontal disease in dogs. *Vet Clin North Am* 1998, 28:1111–1128.

Wiggs RB, Lobprise HB. *Veterinary Dentistry: Principles and Practice*. Philadelphia: Lippincott-Raven, 1997.

Author Jan Bellows

Consulting Editor Heidi B. Lobprise



Client Education Handout
available online

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PERIPHERAL EDEMA



BASICS

DEFINITION

Edema is focal or diffuse excessive accumulation of tissue fluid within the interstitium; often at gravitational surfaces, whether localized or generalized.

PATHOPHYSIOLOGY

- High capillary hydrostatic pressure
- Increased capillary permeability
- Lymphatic drainage abnormality
- Low plasma colloid osmotic pressure

SYSTEMS AFFECTED

- Musculoskeletal
- Skin/Exocrine

GENETICS

- Dominantly inherited primary lymphedema has been described in poodles.
- Lethal congenital edema has been documented in bulldogs.

INCIDENCE/PREVALENCE

Variable

GEOGRAPHIC DISTRIBUTION

Pertinent when considering infectious disease mechanisms

SIGNALMENT

Species

Dogs and cats

Breed Predilections

Primary or congenital lymphedema has been reported in bulldogs, poodles, Old English sheepdogs, Labradors, and myriad other canine breeds as well as cats.

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SIGNS

Historical Findings

- Allergic or other immune, cardiac, hepatic, or other organic disease.
- Trauma.
- Exposure to toxic (venomous) or infectious agents such as ticks or other arachnids.

Physical Examination Findings

- Unexplained weight gain may be noted initially; otherwise, early detection is unlikely.
- Non-inflammatory subcutaneous edema is often first recognized at the dependent thorax or abdomen or distal limbs.
- Inflammatory edema may be noted in non-dependent foci of the interstitium.

CAUSES

Localized or Single-Limb Edema

- High capillary hydrostatic pressure
- Venous or arterial obstruction, e.g., thrombosis or post-caval syndrome
- Arteriovenous fistula
- Increased capillary permeability
- Focal or multifocal immune, infectious, or toxic (chemical or biologic) insults (e.g., snake bite or bee sting)
- Trauma
- Burns

- Lymphatic obstruction
- Sterile (juvenile pyoderma) or infectious lymphangitis
- Primary or metastatic neoplastic invasion of lymphatic tissue
- Congenital aplasia or dysgenesis of the lymphatic system

Regional or Generalized Edema

- High capillary hydrostatic pressure
- CHF
- Cardiac tamponade
- Cranial or caudal vena caval thrombosis
- Renal failure and hypernatremia (salt retention)
- Paralysis or prolonged recumbency with subsequent failure of the venous pump
- Tourniquet effect of a bandage
- Increased capillary permeability
- Systemic immune, infectious, or toxic insults (e.g., sepsis or vasculitis)
- Lymphatic abnormalities
- Acquired regional traumatic, immune, infectious, or neoplastic process
- Congenital aplasia or other lymphatic dysgenesis
- Low plasma colloid osmotic pressure
- Protein-losing disease (e.g., nephrotic syndrome or intestinal lymphangiectasia)
- Failure to produce protein (e.g., cirrhosis)
- Exudative protein loss (e.g., severe burn)

RISK FACTORS

Variable



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Peripheral edema secondary to myxedema or inflammation is typically non-pitting.
- Bilateral forelimb edema with jugular venous distention implies cranial vena caval syndrome.
- Bilateral rear limb edema with or without ascites implies either hypoalbuminemia or caudal vena caval obstruction.
- Fore and/or rear limb edema with jugular venous distension, hydrothorax, and/or ascites implies cardiac disease.
- Focal edema with bruit and fremitus implies an arteriovenous fistula.
- Focal edema with erythema may be secondary to an insect or other bite.
- Multifocal or diffuse edema with petechiation and/or ecchymosis may be associated with a coagulopathy or vasculitis.
- CBC/BIOCHEMISTRY/URINALYSIS
- Leukocytosis suggests inflammatory or infectious disease.
- Thrombocytopenia may be secondary to vasculitis (e.g., RMSF), SLE, or a coagulopathy (e.g., DIC).
- Panhypoproteinemia is consistent with gastrointestinal disease, but diarrhea is not an obligatory clinical sign.

- Panhypoproteinemia and hypocholesterolemia are seen with intestinal lymphangiectasia.
- Hypoalbuminemia may occur with hepatic failure.
- Hypoalbuminemia with proteinuria suggests glomerular disease.
- Hypoalbuminemia with proteinuria and hypercholesterolemia in an edematous patient defines nephrotic syndrome.

OTHER LABORATORY TESTS

- Antithrombin III assay indicated in conditions with albumin loss.
- Further delineate thrombocytopenia with a bone marrow biopsy, ANA, screen for *Ehrlichia* and RMSF, and a coagulation profile.
- Panhypoproteinemia may dictate a need for intestinal biopsy.
- Hypoalbuminemia may warrant liver function testing (e.g., bile acid test, hepatic biopsy).
- Confirm proteinuria with a urine protein:creatinine ratio.
- Bacterial and fungal cultures of blind fistulae may prove useful.
- Fungal or other assays of infectious disease may be warranted; patient's primary residence and patient's travel history need to be considered.
- Pleural or peritoneal fluid analysis is suggested, if effusion is present.
- Low resting thyroid hormone (T_4) should be elaborated with a TRH stimulation test, free T_4 by equilibrium dialysis, or TSH concentration.

IMAGING

- Suspected heart disease necessitates thoracic radiographs and echocardiogram.
- Angiography (e.g., venacavogram) may help to define a vascular obstruction.
- Diagnostic ultrasound may help to delineate a vascular occlusion.
- Thermography and perfusion scans (e.g., scintigraphy) are esoteric but have been used to diagnose occlusive vascular disease.

DIAGNOSTIC PROCEDURES

- Fine-needle aspiration of an affected area for cytology and culture may be helpful.
- Biopsy and deep culture may help define an underlying cause for edema.

PATHOLOGIC FINDINGS

Depend on cause of the edema



TREATMENT

APPROPRIATE HEALTH CARE

Depends on the cause of the edema

NURSING CARE

- Application of warm compresses is recommended for patients with edema secondary to infection.

(CONTINUED)

- Good nursing care required to prevent decubital ulceration in recumbent patients.

ACTIVITY

Depends on cause of edema—e.g., exercise restriction is recommended in patients with congestive heart failure.

DIET

Depends on the cause of edema—e.g., patients with protein-losing nephropathy require a restricted protein diet.

CLIENT EDUCATION

Depends on the cause of edema

SURGICAL CONSIDERATIONS

- Surgery such as lymphangioplasty, thrombectomy, or lymphaticovenous shunt may be palliative.
- Amputation of the edematous limb is sometimes indicated.
- Arteriovenous fistulae may be treated by various surgical methods.

**MEDICATIONS****DRUG(S)**

- Anaphylaxis—epinephrine (1 mg/mL) at 0.01 mL/kg IM or SC to a maximum of 0.02–0.05 mL; prednisone sodium succinate, 10–30 mg/kg IV; antihistamines are of equivocal benefit once anaphylaxis ensues.
- Lymphedema—benzopyrone use yields variable results in veterinary medicine; rutin, 50 mg/kg PO q8h, has been mixed with food for cats with chylothorax.
- Cardiogenic edema—combinations of positive or negative inotropes, vasodilators, and diuretics commonly used in patients with CHF.
- Immune-mediated edema requires immunosuppressive therapy (e.g., prednisone).
- Vasculitis and edema secondary to rickettsial disease typically respond to tetracycline (22 mg/kg PO q8h) or doxycycline (5 mg/kg PO q12h).
- Edema in association with other infectious agents requires antifungal therapy or antibiotic therapy (ideally dictated by culture and sensitivity).
- Myxedema secondary to hypothyroidism should respond gradually to T₄ supplementation.
- Edema associated with toxic insults may be slowed with antidotes (e.g., antivenom).
- Anticoagulant therapy (e.g., heparin, warfarin, or clopidigrel) may benefit patients with DIC or AT III.
- Vascular volume expanders such as hydroxyethyl starch or plasma often benefit patients with low plasma oncotic pressure; very-low-dose furosemide in a constant-rate infusion of 0.1 mg/kg/hour has been effective in conjunction with a volume expander.

CONTRAINDICATIONS

- Diuretics generally aggravate edema of non-cardiogenic origin.
- Steroids may worsen edema secondary to infectious disease.
- Epinephrine—generally contraindicated in shock except in anaphylaxis.
- Propranolol (beta-blocker)—contraindicated in patients predisposed to bronchospasm.

PRECAUTIONS

- Avoid IM injections in patients with thrombocytopenia.
- Taper patients on long-term steroid therapy so that endogenous steroid production resumes.
- Use epinephrine cautiously in patients predisposed to ventricular fibrillation.
- Use enalapril and other ACE inhibitors cautiously in patients with renal disease.
- Long-term antibiotic therapy may facilitate a superinfection by a fungus (e.g., *Candida*) or resistant bacteria.
- Monitor anticoagulants closely to avoid fatal hemorrhage.

**FOLLOW-UP****PATIENT MONITORING**

- Repeat complete blood counts, chemistries, and urine protein:creatinine ratios for blood dyscrasias and serum and urine protein concentrations.
- Weekly assessment of prothrombin or partial thromboplastin time for patients on warfarin or heparin.
- Serial biopsies of affected tissue such as kidney in glomerulonephritis may help to prognosticate.
- Repeat cultures or acute and convalescing titers for patients suffering from an infectious disease.
- Periodic TSH assay or T₄ assay (4–6 hours post-pill) for patients receiving thyroid supplementation.

PREVENTION/AVOIDANCE

Depends on the cause of the edema

POSSIBLE COMPLICATIONS

- Decubital ulceration
- Fatal hemorrhage
- Fatal thrombosis
- Refractory cardiac, gastrointestinal, hepatic, or renal failure
- Malnutrition
- Cerebral edema and herniation
- Resistant infection and sepsis

EXPECTED COURSE AND PROGNOSIS

Depends on cause of the edema

PERIPHERAL EDEMA**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Pericardial, pleural, or peritoneal effusion

AGE-RELATED FACTORS

Vascular anomalies or primary lymphedema are generally documented in juvenile patients (e.g., anasarca).

ZOONOTIC POTENTIAL

- Recent tick exposure is a common element in pets and their owners who may suffer simultaneously from rickettsial disease.
- Certain protozoal (*Leishmania*), fungal (*Sporothrix*), and bacterial (*Brucella*) organisms may transfer to people via direct contact.

PREGNANCY/FERTILITY/BREEDING

Brucellosis has been associated with vulvar edema, necrotizing vasculitis, and embryonic death or fetal abortion.

SYNONYMS

Anasarca

SEE ALSO

- Ascites
- Chylothorax
- Cirrhosis and Fibrosis of the Liver
- Hyperlipidemia
- Hypoalbuminemia
- Lymphedema
- Proteinuria
- Thrombocytopenia
- Vasculitis, Cutaneous
- Vasculitis, Systemic

ABBREVIATIONS

- ANA = antinuclear antibody
- AT III = antithrombin III
- CHF = congestive heart failure
- DIC = disseminated intravascular coagulation
- RMSF = Rocky Mountain spotted fever
- SLE = systemic lupus erythematosus
- T₄ = thyroxine
- TRH = thyrotropin-releasing hormone
- TSH = thyroid stimulating hormone

Suggested Reading

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Fox PR, Petrie JP, Hohenhaus AE. Peripheral vascular disease. In: Ettinger SJ, Feldman EC, eds., Textbook of Veterinary Internal Medicine, 6th ed. St. Louis: Elsevier, 2005.

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Author Marc Elie

Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

PERIRENAL PSEUDOCYSTS



BASICS

OVERVIEW

- Capsulogenic renal cyst, capsular cyst, pararenal pseudocyst, capsular hydronephrosis, perirenal cyst, and perirenal pseudocyst are terms used to describe renomegaly caused by accumulation of fluid between the kidney and its surrounding capsule. One or both kidneys are affected.
- The tissue adjacent to the fluid accumulation is not lined with secretory epithelium; and thus the name "pseudo"-cyst is appropriate.

SIGNALMENT

- Primarily older male cats (> 8 years).
- When detected in young cats, the disease is usually unilateral.
- Rare in dogs; the difference in prevalence between species may be related to the prominent network of subcapsular veins that characterize feline kidneys.

SIGNS

- May be asymptomatic
- Non-painful, enlarged abdomen is common
- Signs of concomitant renal failure in some patients

CAUSES & RISK FACTORS

- Cause of perirenal accumulation of fluid is not completely understood.
- Accumulation of pseudocyst fluid is a dynamic, not a static, process.
- Cytologic and biochemical evaluation of pseudocyst fluid may aid understanding of pathophysiologic mechanisms.
- Fluid with characteristics of a transudate may accumulate because of high capillary hydrostatic pressure or lymphatic obstruction. Some cats have light microscopic evidence of renal fibrosis. However, it is not known whether progressive renal parenchymal contraction occludes lymphatics and blood vessels, promoting transudation of fluid.
- Perirenal accumulation of transudate can also result from rupture of renal cysts.
- Accumulation of perirenal urine may indicate disruption of the renal pelvis or the proximal ureter.
- Accumulation of blood in pseudocysts can result from external trauma, surgery, neoplastic erosion of blood vessels, rupture of aneurysms, coagulopathies, or paracentesis.

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DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Causes of renomegaly include renal neoplasia, hydronephrosis, polycystic kidney disease (common), feline infectious peritonitis, and mycotic or bacterial nephritis (less common).
- Ascites and enlargement of other abdominal organs can cause non-painful distension of the abdomen.

CBC/BIOCHEMISTRY/URINALYSIS

- Results unremarkable until patient develops renal insufficiency.
- Azotemia and inappropriately low urinary specific gravity (< 1.035) indicate concomitant chronic kidney disease (CKD).

OTHER LABORATORY TESTS

N/A

IMAGING

- Renomegaly is commonly detected by abdominal radiography.
- Excretory urography and ultrasonography can be used to determine whether the underlying renal parenchyma is normal or abnormal. Small kidneys beneath an abnormally wide fluid-filled intracapsular space is a common finding.

DIAGNOSTIC PROCEDURES

Cytologic examination of pseudocyst fluid may provide evidence of the underlying disease process resulting in fluid accumulation (e.g., transudation, hemorrhage, lymphatic obstruction, inflammation, urine, etc.) or secondary complications (e.g., infection). Creatinine concentrations that are higher in pseudocyst fluid compared to serum are consistent with urinary tract rupture.



TREATMENT

- Perirenal pseudocysts are not immediately life-threatening.
- Some patients need no treatment.
- Many patients require further diagnostic evaluation and treatment of concomitant CKD.
- Capsulectomy or pseudocyst fenestration (remove greater than 1-cm × 1-cm section of capsule to minimize spontaneous closure of the fenestration) is generally associated with amelioration of abdominal distention and abdominal organ displacement. Early stages

of CKD may resolve; however, progression of CKD commonly occurs.

- Long-term response is unknown.
- Avoid nephrectomy to maximize kidney function.
- Decompression by paracentesis with a needle and syringe provides temporary relief.
- If pseudocysts refill with fluid (often in 1–2 weeks), paracentesis can then be repeated.



MEDICATIONS

DRUG(S)

Consider appropriate antimicrobial (i.e., lipid-soluble antibiotic chosen on the basis of antimicrobial susceptibility) if pseudocysts become infected.



FOLLOW-UP

- Monitor patients periodically (every 2–6 months) for development and progression of CKD.
- Short-term prognosis appears favorable with or without pseudocyst decompression in patients with no evidence of CKD.
- Long-term prognosis is unknown because it has not been determined whether perirenal pseudocysts are associated with underlying lesions in the renal parenchyma that may be progressive. It is also unknown whether perirenal pseudocysts are associated with hypertension.
- Survival is related to the severity and progression of CKD.



MISCELLANEOUS

Suggested Reading

- Beck JA, Bellenger CR, Lamb WA, et al. Perirenal pseudocysts in 26 cats. Aust Vet J 2000; 78:166–171.
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Ochoa VB, DiBartola SP, Chew DJ, et al. Perinephric pseudocysts in the cat: A retrospective study and review of the literature. J Vet Intern Med 1999; 13:47–55.
- Authors** Jody P. Lulich and Carl A. Osborne
Consulting Editor Carl A. Osborne

PERITONEOPERICARDIAL DIAPHRAGMATIC HERNIA



BASICS

OVERVIEW

- Embryologic malformation of the ventral midline allowing communication between the pericardial and peritoneal cavities.
- May be associated with other congenital malformations including sternal deformities (especially in cats), cranial abdominal hernia, and ventricular septal defects.
- Signs may be due to large amounts of abdominal viscera compressing the heart or lungs and incarceration of abdominal organs (e.g., liver and small bowel).

SIGNALMENT

- Dog and cat.
- Age when clinical signs first occur varies; more than one-third of patients are 4 years of age or older.
- Weimaraners and Persians may be predisposed.
- No evidence that lesions are hereditary, but they have been reported in littermates.

SIGNS

General Comments

- Depend on the nature and amount of abdominal contents that herniated.

Historical Findings

- Vomiting.
- Diarrhea.
- Weight loss.
- Abdominal pain.
- Coughing.
- Dyspnea.

Physical Examination Findings

- Muffled heart sounds.
- Displaced or attenuated apical cardiac impulse.
- Palpable sternal deformity or cranial abdominal hernia.
- Cardiac tamponade and signs of right-sided congestive heart failure (rare).

CAUSES & RISK FACTORS

- Embryologic malformation.
- Prenatal injury of the septum transversum and pleuroperitoneal folds.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Never an acquired traumatic defect because no natural direct communication exists

between the peritoneal and pericardial cavities after birth.

- Pericardial effusion.

CBC/BIOCHEMISTRY/URINALYSIS

No associated hematologic or biochemical alterations

OTHER LABORATORY TESTS

N/A

IMAGING

- Radiographic findings depend on size of defect and amount of herniated abdominal contents; caudal heart border and diaphragm may overlap; thoracic radiographs may show an "empty" abdomen and possible multiple radiographic densities.
- Positive and negative contrast peritoneography have been used to evaluate the diaphragm. Injection of 1–2 mL/kg body weight of water-soluble positive-contrast into the peritoneal cavity followed by right and left lateral, sternal, and dorsal recumbent radiographs allows complete evaluation of the diaphragm. Identification of contrast within the pleural space confirms the diagnosis of diaphragmatic rupture. Air, carbon dioxide, or nitrous oxide may also be used.
- Barium series may demonstrate bowel loops crossing the diaphragm and within the pericardial sac.
- Non-selective angiography outlines the cardiac chambers within the large cardiac silhouette.
- Echocardiography gives a definitive diagnosis.

DIAGNOSTIC PROCEDURES

Electrocardiogram may show small complexes if abdominal contents have herniated or if marked effusion is present.



TREATMENT

Surgical closure of the hernia after returning viable organs to their normal location is usually curative. In asymptomatic adult patients with small hernias, treatment may not be indicated.



MEDICATIONS

DRUG(S)

- Myocardial contractility is unaffected in most patients; drugs for improving cardiac output are not indicated.

- Can give symptomatic treatment based on nature and amount of abdominal contents that are herniated.

CONTRAINDICATIONS/POSSIBLE

INTERACTIONS

Drugs that reduce ventricular afterload (e.g., arteriolar vasodilators) or preload (e.g., venous dilators and diuretics) are not useful and can cause reduction of ventricular filling, hypotension, and low cardiac output.



FOLLOW-UP

Prognosis after surgery is excellent in animals with no other significant congenital anomalies or complicating factors.



MISCELLANEOUS

INTERNET RESOURCES

www.vetgo.com/cardio.

Suggested Reading

- Burns CG, Bergh MS, McLoughlin, MA. Surgical and nonsurgical treatment of peritoneopericardial diaphragmatic hernia in dogs and cats: 58 cases (1999–2008). J Am Vet Med Assoc 2011; 22:643–650.
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Author Larry P. Tilley

Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

PERITONITIS



BASICS

DEFINITION

An inflammatory process involving the serous membrane of the abdominal cavity.

PATHOPHYSIOLOGY

- Insult to the peritoneal cavity, whether localized or generalized, leads to an inflammatory process characterized by vasodilation, cellular infiltration, stimulation of pain fibers, and development of adhesions.
- Extent and severity depend on type and severity of the insult. • Bacterial peritonitis is commonly associated with Gram-negative bacterial endotoxin. The lipopolysaccharide (LPS) binds to macrophages, inducing cytokine release such as interleukin 1 (IL-1) and tumor necrosis factor (TNF). Gram-positive bacteria contain peptidoglycan, teichoic acid, and hyaluronic acid. Resultant cytokine release includes IL-1, TNF, and nitric oxide (NO). NO causes vasodilation and can promote hypotension.
- Release of vasoactive substances (histamine, serotonin, protease, nitric oxide, endotoxin) cause vasodilation and increased vascular permeability. Cytokine release from mast cells, neutrophils, macrophages, and lymphocytes result in chemotaxis, activation of the complement system, and further accumulation of fluid. Activation of the complement system also results in fibrin degradation, damage to the mesothelium in the face of decreased fibrinolysis results in adhesion formation. • Bile damages mesothelial cells and inhibits PMN function. Blood in the peritoneal cavity interferes with chemotaxis and phagocytosis and promotes bacterial growth. The result of significant abdominal inflammation can be systemic inflammatory response syndrome (SIRS) and sepsis. With time, SIRS can progress to multiple organ dysfunction (MODS) and can affect the respiratory system (acute respiratory distress syndrome [ARDS] or pulmonary thromboembolism [PTE]), or cause renal dysfunction, reduced cardiac function, and neurologic signs.

P

SYSTEMS AFFECTED

- Cardiovascular • Gastrointestinal
- Hemic/Lymphatic/Immune
- Renal/Urologic Hepatobiliary

GENETICS

N/A

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat

Breed Predilections

None

Mean Age and Range

None

Predominant Sex

None

SIGNS

General Comments

Signs may be vague and nonspecific and signs depend on the time of evaluation in relation to severity of the inflammation and systemic response present.

Historical Findings

Lethargy, depression, anorexia, vomiting, diarrhea, collapse

Physical Examination Findings

- Abdominal discomfort or pain—localized or generalized; patient usually resents palpation; less common in cats. • A “prayer” position—due to abdominal discomfort.
- Compensatory shock—tachycardia, tachypnea, injected mucus membranes, rapid capillary refill time (CRT). • Early decompensatory shock—tachycardia, poor pulse quality, depressed mentation, pallor, prolonged CRT. Cats often show a normal to decreased heart rate (< 140/min).
- Decompensatory shock—bradycardia, weak or absent pulses, severely depressed mentation, pallor or cyanosis, prolonged CRT. • Vomiting common. • Arrhythmias may be detected. • Fever—not consistent; when noted with other signs of peritonitis strongly suggests bacterial contamination of the abdominal cavity. • Weight loss—reported in one-third of dogs and cats with secondary peritonitis.

CAUSES

Primary Peritonitis

- Uncommon. • Primary peritonitis results from hematogenous or lymphatic spread, or due to translocation from the gastrointestinal tract. Feline infectious peritonitis (FIP) is a form of peritonitis in cats.

Secondary Peritonitis

- Predominant form. • Secondary peritonitis is the most common form of the condition and results due to contamination of the peritoneal cavity originating in one of the abdominal organs. Sources include the gastrointestinal tract (up to 75%), perforation of ulcerations, GI tract tumors, perforation secondary to GDV, leakage following GI surgery, penetrating trauma, biliary tract trauma or rupture due to obstruction or mucocele formation, abscessation of the pancreas, kidney, prostate, spleen or liver, ruptured pyometra, and urine leakage. Uroabdomen and bile peritonitis may or may not be septic; regardless, chemical peritonitis is present.

RISK FACTORS

- Trauma. • Gastrointestinal surgery.
- Undetected abscess of liver, pancreas,

prostate, or uterus. • Prior NSAID use is associated with perforation occurring at the pylorus compared to other sites.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other causes of abdominal pain or distention, sepsis, and shock.

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilic leukocytosis most common finding; may be a left shift; degenerative left shift or development of neutropenia may portend a worsening prognosis.
- Hemoconcentration or anemia.
- Hypoproteinemia—owing to exudation of albumin. • Hypo- or hyperkalemia and hyponatremia. • Azotemia—associated with prerenal, renal, or post-renal causes.
- Metabolic acidosis. • Hypoglycemia—may indicate sepsis; hyperglycemia may be present in cats. • Liver enzyme elevations—associated with hepatic causes of peritonitis or due to MODs. • Hyperlactatemia—due to poor perfusion associated with shock.

OTHER LABORATORY TESTS

- Coagulation abnormalities may develop—prolonged activated partial thromboplastin time (aPTT) and prothrombin time (PT).
- Thromboelastography to evaluate for hyper- or hypoagulability. • DIC may also develop—prolonged aPTT, PT, and thrombocytopenia, elevated D-dimers (> 1,000 U), low protein C levels.

IMAGING

Radiography

- Findings inconsistent and depend on cause.
- Loss of serosal detail (ground-glass appearance suggests fluid in the abdominal cavity)—rule out lack of intra-abdominal fat.
- Generalized ileus may be present.
- Consider making right and left lateral projections of the abdomen.
- Pneumoperitoneum—gas in the abdomen may be slight, closely evaluate the region of the diaphragm; consider making lateral beam images in a sternally recumbent or lateral recumbency. • Can be diagnostic for GDV, GI foreign bodies, mass lesions, enlargement of organs with abscessation. • Contrast procedures—rarely warranted; may complicate management if contrast material enters the abdominal cavity; avoid barium if gastrointestinal perforation is suspected.

Ultrasound

May identify smaller volumes of peritoneal effusion; abscesses of the pancreas, liver, or prostate; rupture of the gallbladder, tumors or mass lesions. Important for aspiration of small volumes of fluid.

DIAGNOSTIC PROCEDURES

- Abdominocentesis and diagnostic peritoneal lavage—safe and reliable and should be

(CONTINUED)

PERITONITIS

performed as soon as possible.

- Abdominocentesis—empty the urinary bladder; aseptically clip and prepare the abdomen. Utilize ultrasound guidance if desired. Use a 22- or 20-gauge needle, butterfly catheter or over-the-needle catheter to penetrate the abdominal cavity. Collect the first few drops of fluid for cytology. Use a 3 mL syringe to apply gentle negative pressure if free flow of fluid does not occur; tap all four quadrants (i.e., four separate needle punctures), with the left side last in an attempt to avoid inadvertent splenic puncture. Ultrasound guidance may be necessary to avoid the falciform fat and spleen and is required when small volumes of fluid are present.
- Diagnostic peritoneal lavage—if abdominal fluid not recovered by abdominocentesis and the index of suspicion is high (e.g., postoperative complication). Empty the urinary bladder and aseptically prepare the abdomen. Infuse 20 mL/kg warm sterile saline through an 18- or 16-gauge over-the-needle catheter using gravity; gently roll patient from side to side to distribute the lavage fluid. Move the infusion bag to a position below the patient to recover fluid. There is no need to recover entire amount of infused fluid.
- Cytology—first collect samples into EDTA tube; note color and clarity of the fluid and presence of fibrin.
- Culture and sensitivity—next, collect sample in a sterile clot tube.
- Suspected chemical peritonitis—finally, analyze abdominal fluid for creatinine (for uroabdomen), amylase (for pancreatitis), and bilirubin (for bile leakage).
- Suspected FIP—submit abdominal fluid for protein electrophoresis and globulin determination.

PATHOLOGIC FINDINGS

- Intra- or extracellular bacteria, degenerative neutrophils, and plant material are diagnostic of septic peritonitis.
- Normal peritoneal fluid contains < 2,500 cells/ μ L; peritoneal fluid glucose levels more than 20 mg/dL below that of the peripheral blood are highly suggestive of septic peritonitis.
- Fluid lactate > 2.5 mmol/L in dogs is suggestive of septic peritonitis, but is not useful in cats.
- Recent surgery results in < 10,000 cells/mL; primary peritonitis usually results in 7,000 cells/ μ L in dogs and 3,000 cells/ μ L in cats.
- Fluid bilirubin or creatinine levels higher than that of peripheral blood indicate bile peritonitis or uroabdomen, respectively.
- Acellular homogenous, laminated, basophilic material on cytology may be mucoid material associated with bile peritonitis.

**TREATMENT****APPROPRIATE HEALTH CARE**

Inpatient—intensive monitoring and supportive care are required.

Intravenous Fluid Therapy

- Critical for correction of hemodynamic disturbances and electrolyte and acid-base abnormalities prior to considering surgery.
- Balanced electrolyte solution—lactated Ringer's solution or Normosol-R for initial treatment; evaluate the response to therapy frequently.
- Potassium and glucose—may need to supplement.
- Replacement rate—may initially be as high as 55 mL/kg (cats) and 90 mL/kg (dogs); adjust rate frequently as patient status changes; if supplemented with potassium, the rate should not exceed 0.5 mEq/kg/h of potassium.
- Colloid administration is highly recommended in acute and/or severe cases (up to 20 mL/kg/d in dogs and 15 mL/kg/d in cats).
- Goals—blood pressure > 90 mmHg, heart rate 80–140/min (dogs) and 140–225/min (cats), CRT < 2 sec, urine output > 1–2 mL/kg/h, serum lactate < 2.5 mmol/L in dogs.
- Inadequate response to therapy prompts vasopressor administration (dopamine, dobutamine, vasopressin, norepinephrine).
- Whole blood or packed red blood cells (PRBC)—as required for anemia.
- DIC—remove the inciting cause, support with plasma; consider heparin therapy.
- Consider canine albumin transfusion in cases of severe hypoalbuminemia.

NURSING CARE

- Significant and dependent upon the severity of systemic signs, SIRS, MODS, ARDS, sepsis.
- Continue intravenous fluid therapy and maintenance of goals per the above.

ACTIVITY

- Will be significantly decreased depending on the severity of systemic illness.
- Depends on the inciting cause and surgery necessary.

DIET

- Dictated by cause, when identified, and any concurrent conditions (e.g., heart disease).
- Feeding tube placement should be considered and placed at the time of surgery for early nutritional support (e.g., esophagostomy, gastrostomy, jejunostomy).
- Adequate nutrition—essential to optimize outcome; may attenuate the hypermetabolic state, preserve hepatic antioxidant defenses, prevent protein-calorie malnutrition, and maintain the gastrointestinal barrier function.

CLIENT EDUCATION

- Advise client of the high rate of morbidity and in most cases of septic peritonitis, mortality.
- Inform client that extensive monitoring and intensive care may be costly.

SURGICAL CONSIDERATIONS

- Decision to treat medically or surgically—dictated by etiology, patient's response to initial treatment, and owner's financial constraints.
- Known bacterial contamination or suspected chemical peritonitis—surgical intervention necessary.
- Perform surgery as soon as the patient is stable.
- Exploratory

laparotomy—prepare for incision extending from xiphoid to pubis; goals of surgery are to remove the source of contamination, debride and clean the abdomen, collect fluid or tissue for Gram stain and aerobic and anaerobic culture, and providing nutritional support; use monofilament absorbable or non-absorbable suture within the abdomen (avoid multifilament, non-absorbable suture and catgut); before closing, thoroughly lavage the abdomen with 200–300 mL/kg sterile saline solution, warmed to body temperature. Do not add antimicrobials or other products (povidone iodine) to the lavage solution; remove all lavage solution from the abdomen.

- Surgeon must be able to assess organ viability and resection. Anastomosis of the GI tract should utilize healthy tissue; consider serosal patching, perform omental patching if serosal patching not done.
- Consider omentectomy of pancreatic abscesses, perform omentectomy for prostatic abscessation. Remove affected organ or part in other cases of abscessation.
- Consider open abdominal drainage—based on degree of contamination, ability to debride the abdomen, severity of the illness, and anticipation of septic complications. Allow continued removal of fluid, bacteria, and toxins. Forms include closed suction drains, vacuum-assisted peritoneal drainage (VAPD), and closure of the caudal abdomen with partial closure of the cranial abdomen. Sterile bandaging is required in each form; less external materials for VAPD, but regulate suction and specialized foam and connections to suction required. Requires anesthesia for abdominal closure unless closed suction drains are used.

P

**MEDICATIONS****DRUG(S) OF CHOICE**

- Antimicrobials—early and aggressive therapy for suspected septic peritonitis; broad-spectrum (against Gram-positive and Gram-negative, aerobic, and anaerobic organisms); final therapy must be based on culture and susceptibility testing.
- Initial therapy—gram negative (enrofloxacin, cefotaxime, amikacin); gram positive (ampicillin, clindamycin); anaerobes (metronidazole).
- Ampicillin 22 mg/kg IV q8h.
- Clindamycin 12 mg/kg IV q12h.
- Cefotaxime 20–80 mg/kg IV q8h.
- Enrofloxacin 10–20 mg/kg IV q12h (5 mg/kg/d IV in cats).
- Amikacin 10–15 mg/kg IV q24h.
- Metronidazole 10 mg/kg IV q8–12h.
- Pain control—depending on the severity of pain; may be intermittent or via continuous rate infusion (CRI). Significant pain is usually present; opioids recommended.
- Multimodal CRI for pain; dogs, morphine—0.05–0.2 mg/kg/h,

PERITONITIS

(CONTINUED)

- ketamine (0.2–0.6 mg/kg/h), lidocaine (2–4 mg/kg/h); cats, fentanyl (2–4 µg/kg/h), ketamine (0.05–0.2 mg/kg/h). • GI protectants—often recommended due to poor perfusion and stress. Required for cases of GI ulceration.
- Famotidine—0.5–1.0 mg/kg IV q12–24h for rapid onset of action.
- Pantoprazole 1 mg/kg IV q24h for more complete decrease in gastric acid.
- Sucralfate: dogs, 0.5–1.0 mg PO q8h; cats, 0.25–0.5 mg PO q8h.

CONTRAINDICATIONS

- Glucocorticoids—use is controversial.
- NSAIDs are not recommended.
- Heparin therapy for the treatment of DIC—less effective in the case of insufficient antithrombin levels.

PRECAUTIONS

- Aminoglycosides—use with caution if renal function is impaired.
- Adequate hydration—essential to enhance safety of these drugs.
- Antiemetic use should be avoided if gastrointestinal foreign body or rupture is at all suspected. Use indicated when GI cause is eliminated.

POSSIBLE INTERACTIONS

Time sucralfate and gastric acid reducer so that sucralfate is given when the pH is lower. Also avoid oral medications at the same time as sucralfate as required.

ALTERNATIVE DRUG(S)

Fluoroquinolone—enrofloxacin or orbifloxacin; substitute for an aminoglycoside, especially with impaired renal function.



FOLLOW-UP

PATIENT MONITORING

- Fluid balance, electrolyte balance, acid-base status—depending on the severity of the condition.. Blood gas, electrolyte, lactate measurements as necessary.
- Frequency of monitoring—varies with severity of the condition and response to treatment. May be frequent (1h).
- Maintain urine output 1–2 mL/kg/h and goals described in fluid therapy section above.
- Replace fluid losses (vomiting, diarrhea) as necessary.
- Change recumbency every 4–6h as necessary.
- Enteral nutrition as soon as possible via oral feeding or nasoesophageal, gastrostomy, or jejunostomy tube feeding promotes enterocyte health and decreases bacterial migration through the intestinal wall.
- Repeat ultrasound and cytologic evaluation depending on index of suspicion for leakage of intestinal surgery sites.
- CBC, chemistry profile, urinalysis—every 1–2 days during

periods of intensive monitoring, even in patients that are responding.

PREVENTION/AVOIDANCE

Prevention—difficult except when specific risk factors are identified (e.g., pyometra).

POSSIBLE COMPLICATIONS

- If underlying cause is not identified and managed, patient is at risk for complications.
- Open peritoneal drainage—increased cost and required intensive care, repeated sedation or anesthesia for aseptic bandage changes, ascending/nosocomial infection, hypoproteinemia, electrolyte imbalances, enterocutaneous fistulation, and abdominal hernia formation.
- Adhesions.

EXPECTED COURSE AND PROGNOSIS

• Prognosis—depends on rapid identification and successful management of the underlying cause and appropriate follow-up care.

- Septic peritonitis—mortality of 30–68%. Prognosis worse in animals with pre-existing septic peritonitis, incorrectable hypotension, low serum albumin and total protein, respiratory dysfunction, DIC, low protein C, low antithrombin, MODS, and better survival in patients with lower pre-operative alanine aminotransferase, gamma-glutamyl transferase, packed cell volume, total solids, thromboelastography consistent with hypercoagulation, and albumin.
- Septic peritonitis—open peritoneal drainage may improve survival.
- Septic bile peritonitis—27% survival compared to 100% with non-septic bile peritonitis.
- Antibiotic treatment within the first hour in cases of suspected septic peritonitis per a specific treatment protocol based on hospital cultures reduced mortality from approximately 80% to 42%.
- Plasma lactate > 2/5 mmol/L or inability to normalize plasma lactate—poorer survival in septic peritonitis.
- Feeding tube complications depend on the site of placement. Esophagostomy (localized infection or abscessation), gastrostomy and jejunostomy (leakage or premature dislodgement associated peritonitis), nasoesophageal (sneezing, epistaxis). Refeeding syndrome—decreased magnesium, phosphorus, potassium. Warrants close monitoring.
- Bradycardia and hypothermia in cats with primary septic peritonitis were associated with mortality.



MISCELLANEOUS ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

Sepsis and Bacteremia

ABBREVIATIONS

- aPTT = activated partial thromboplastin time
- ARDS = acute respiratory distress syndrome
- CRI = continuous rate infusion
- CRT = capillary refill time
- DIC = disseminated intravascular coagulation
- EDTA = ethylene diamine tetraacetic acid
- FIP = feline infectious peritonitis
- GDV = gastric dilatation volvulus
- IL-1 = interleukin 1
- LPS = lipopolysaccharide
- MODS = multiple organ dysfunction
- NO = nitric oxide
- NSAID = nonsteroidal anti-inflammatory drug
- PT = prothrombin time
- PTE = pulmonary thromboembolism
- SIRS = systemic inflammatory response syndrome
- TNF = tumor necrosis factor
- VAPD = vacuum assisted peritoneal drainage

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Client Education Handout
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PETECHIA, ECCHYMOSIS, BRUISING



BASICS

DEFINITION

Pinpoint (petechia) or larger (ecchymosis) hemorrhage in the skin or mucous membranes most often secondary to abnormal primary hemostasis (platelet or vessel-wall mediated); may appear spontaneously or following minimal trauma. Spontaneous development often occurs at sites of increased capillary trauma or increased pressure, e.g., ventrum.

PATHOPHYSIOLOGY

- Thrombocytopenia and/or defective platelet function (i.e., thrombocytopathia) cause impaired primary hemostasis (failure of platelet plug formation). Platelet numbers below $50 \times 10^9/L$ and more often below $25 \times 10^9/L$ are associated with an increased risk of spontaneous hemorrhage.
- Main mechanisms of thrombocytopenia—increased destruction, e.g., immune mediated (ITP); decreased production, e.g., myelophthisis or chemotherapy-induced myelosuppression; increased consumption, e.g., DIC; and sequestration in the spleen or liver, e.g., splenic torsion or neoplasia.
- Main mechanisms of congenital thrombocytopathia—deficient or abnormal von Willebrand factor (most common); defects in platelet membrane glycoproteins, e.g., Glanzmann's thrombasthenia in otter hounds and Great Pyrenees (rare); defects in platelet storage granules, e.g., storage pool disease (Chédiak Higashi) in Persian cats or American cocker spaniels (rare); defects in signal transduction, e.g., in basset hounds or spitzes (rare).
- Main mechanisms of acquired platelet dysfunction are drugs (e.g., NSAIDs) or uremia-induced inhibition of prostaglandin metabolism. Other causes are anti-platelet antibodies, paraproteinemia, liver disease, immune-mediated causes, some snake venoms, and various other drugs/exogenous agents.
- Vascular hemostatic defects—generally caused by increased capillary permeability, e.g., RMSF or FIP-associated vasculitis, or altered dermal vascular support, e.g., hyperadrenocorticism or Ehlers-Danlos syndrome.

SYSTEMS AFFECTED

- Gastrointestinal—melena/hematochezia/hematemesis
- Hemic/Lymphatic/Immune—ITP may be associated with IMHA; concurrent gastrointestinal bleeding can cause significant anemia.
- Neurologic—variable depending on location of bleeding.
- Ophthalmic—scleral/retinal hemorrhage, secondary glaucoma, and uveitis.
- Renal/Urologic—hematuria.
- Respiratory—epistaxis/hemoptysis.
- Skin/Exocrine—petechia/ecchymosis/bruising.

SIGNALMENT

- Doberman pinschers and Scottish terriers are overrepresented for von Willebrand deficiency. Many other breeds have vWD. Note bruising and mucosal hemorrhage is common and petechiation is rare in association with vWD.
- See specific thrombopathias for breed-associated disorders.
- Note: an inherited macrothrombocytopenia (giant platelets) is seen in Cavalier King Charles spaniels and several other breeds; it does not cause bruising. Greyhounds have a lower than normal platelet count causing a mild thrombocytopenia.
- ITP shows a possible genetic predisposition because of the high prevalence in cocker spaniels, toy poodles, and Old English sheepdogs. Middle-aged female dogs also are at increased risk.
- Cats—Primary ITP is rare.

CAUSES

Thrombocytopenia

- Immune mediated—idiopathic, drug induced (e.g., antibiotics), paraneoplastic, and infection induced (e.g., viral, rickettsial, bacterial, protozoal, or fungal).
- Infectious—e.g., *Ehrlichia* spp. (*E. canis*, *E. ewingii*), *Anaplasma platys*, RMSF, babesiosis, leptospirosis, leishmania, *Borrelia*, *Dirofilaria* spp., *Bartonella vinsonii*, *Mycoplasma* spp., *Histoplasma*, *Candida*, FIP, FeLV, Cytauxzoonosis, parvovirus, herpesvirus, or septicemia.
- Bone marrow suppression—e.g., hyperestrogenism or chemotherapy.
- Drug related—procainamide, sulfonamide, azathioprine, methimazole, albendazole, griseofulvin, and chloramphenicol.
- Bone marrow infiltration—myeloproliferative or lymphoproliferative diseases.
- Sequestration in liver and/or spleen secondary to vascular neoplasia, or torsions.
- Consumption—e.g., DIC or recent extensive mucosal and serosal hemorrhage e.g., rodenticide poisoning or splenic tumor rupture.

Thrombocytopathy

- Congenital or acquired disorders affecting platelet adhesion, aggregation; see "Pathophysiology."

Vascular Disease

- Vasculitis secondary to inflammation, neoplasia, drug reactions, infection (e.g., RMSF or FIP); immune-mediated; see specific disease(s).

Coagulation Factor Deficiency

Clinical signs are not usually associated with petechia or ecchymosis but epistaxis is noted. Most commonly hemorrhage occurs within body cavities as well as hemarthrosis and hematomas.

RISK FACTORS

- The occurrence of any of the aforementioned diseases or breed predispositions. Severe vWD is seen in German shorthaired pointers, Shetland

sheepdogs, Scottish terriers, and Chesapeake Bay retrievers.

- History of NSAID use.
- Recent vaccination has not been proven but remains a concern for ITP.
- Geography/travel history, e.g., arthropod-borne diseases.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Petechia are generally not mistaken for anything else. Some inflammatory skin lesions may look like petechia. Diascopy can be used to help distinguish between the two. Vasculitis lesions may have associated edema. Unwitnessed trauma may cause ecchymoses/bruising.

CBC/BIOCHEMISTRY/URINALYSIS

- Platelets are low, either by direct count or by estimation on a well-made blood smear. One platelet per high power field (hpf) represents approximately $15 \times 10^9/L$. An average of 10–30 platelets per hpf corresponds to a normal platelet count. If the platelet count is greater than $100 \times 10^9/L$, consider other causes of primary hemostasis abnormalities.
- RBC fragmentation is associated with DIC or microangiopathies.
- Ehrlichia* morulae or other hemoparasites may be seen on a peripheral blood smear.
- Patients with myeloproliferative or lymphoproliferative disease, myelofibrosis, or a history of chemotherapy or administration of drugs such as estrogens may be concurrently leukemic or have other cytopenias.
- Biochemical analysis—identify renal or liver disease as well as hyperglobulinemia.
- Urinalysis—identify hematuria. Proteinuria—may suggest concurrent immune-mediated disease, such as glomerulonephritis, and increase the suspicion of systemic lupus erythematosus.

OTHER LABORATORY TESTS

- Coagulation studies (APTT, PT, FDP, D-dimer, antithrombin III concentration) help diagnose DIC. Platelet counts less than $10 \times 10^9/L$ will interfere with ACT assay.
- Von Willebrand factor antigen assay—necessary to confirm vWD.
- Platelet function tests—may be necessary to rule out platelet function disorders, e.g., BMBT, thromboelastography, platelet aggregometry, flow cytometry, and DNA testing at Auburn University.
- Antiplatelet antibody tests will not distinguish primary from secondary ITP.
- Serum and urine protein electrophoresis (looking for Bence-Jones proteins)—indicated if hyperglobulinemia noted.
- Protein: creatinine ratio—if proteinuria noted on urine analysis. An elevated ratio > 1 may be suggestive of concurrent glomerulonephritis.
- FeLV/FIV testing—underlying cause of thrombocytopenia.
- Antinuclear antibody titer—helps to diagnose systemic lupus erythematosus if there is evidence of other

PETECHIA, ECCHYMOSIS, BRUISING

(CONTINUED)

immune-mediated disease. • Adrenal function testing may be indicated if hyperadrenocorticism is suspected.

- Serology—aid to diagnose ehrlichiosis, *Anaplasma platys*, *Bartonella vinsonii*, or RMSF. • PCR—for underlying infections such as *Ehrlichia* spp., *Anaplasma platys* or *Babesia* spp., *Mycoplasma* spp.

IMAGING

• Three-view thoracic radiography—look for evidence of metastasis or primary neoplasia/effusion. Identify enlarged lymph nodes or signs suggestive of underlying infectious disease. • Abdominal radiography to assess spleen and liver size/abdominal detail. Identify enlarged sublumbar lymph nodes or an abdominal mass consistent with hemangiosarcoma. • Abdominal ultrasonography to note architectural abnormalities in various organs that suggest underlying neoplasia, infection, or inflammation and to evaluate organ blood flow. Evaluate mesenteric lymph nodes for signs of neoplasia, infection, or inflammation.

DIAGNOSTIC PROCEDURES

• BMBT is indicated if the platelets are above $100 \times 10^9/L$; prolonged BMBT suggests a thrombopathia. Thrombocytopenic patients also have a prolonged BMBT. Normal range is < 4 minutes in dogs and < 2 minutes in cats. • Most invasive procedures are contraindicated in patients with bleeding disorders, except bone marrow aspiration and core biopsy. These procedures are indicated if there are cytopenias, hypergammaglobulinemia, or evidence of leukemia. • Invasive diagnostic procedures may be performed with less risk if platelet concentrate can be administered during the procedure to decrease the risk of hemorrhage.



TREATMENT

• Usually as an inpatient until a definitive diagnosis has been made. • Minimize activity to reduce the risk of even minor trauma. • Discontinue any medications that may alter platelet function, e.g., aspirin and other NSAIDs. • Discontinue medication that is associated with immune-mediated thrombocytopenia, such as methimazole in cats or trimethoprim sulfa in dogs. • Maintain fluid volume with a balanced electrolyte solution. • Avoid subcutaneous and intramuscular injections as well as venipuncture from the jugular vein. • Fresh whole blood or platelet transfusions may be necessary and life saving before a definitive diagnosis is made. Ensure blood samples are collected prior to transfusion for diagnostic

testing such as coagulation tests, serology, or PCR. • No specific treatment is available for congenital thrombopathias, other than DDAVP, which can be used for Type I vWD to help control bleeding and possibly other thrombopathias. It can also be given to blood donors prior to blood collection if the recipient needs surgery. See von Willebrand Disease for additional details. Acquired thrombopathias need to have the underlying disease corrected. The underlying disease needs to be treated when treating vasculitis/vasculopathies. See specific chapters.



MEDICATIONS

DRUG(S)

- Depends on the underlying diagnosis.
- Prednisone ± vincristine for immune-mediated thrombocytopenia.
- Doxycycline ± enrofloxacin/pradofloxacin (cats) for infectious causes or until infectious causes have been ruled out.
- Desmopressin acetate (DDAVP) for mild platelet function defects, e.g., Type 1 VWD.

CONTRAINDICATIONS

Avoid subcutaneous and intramuscular injectable medications whenever possible.

PRECAUTIONS

Avoid NSAIDs and other drugs that inhibit hemostasis, other than heparin in DIC.



FOLLOW-UP

Daily platelet count for patients with thrombocytopenia until an adequate response is seen. See specific diseases for details.

POSSIBLE COMPLICATIONS

- Death or morbidity caused by hemorrhage into brain, gut, lung, or other organs. • Shock caused by hemorrhagic hypovolemia.
- Blindness secondary to hyphema, retinal detachment, and/or glaucoma.



MISCELLANEOUS

SYNOMYS

- Bleeding • Hemorrhagic diatheses

SEE ALSO

- Disseminated Intravascular Coagulation
- Hyperadrenocorticism (Cushing's Syndrome)—Cats • Hyperadrenocorticism (Cushing's Syndrome)—Dogs
- Myeloproliferative Disorders

- Thrombocytopathies • Thrombocytopenia
- Thrombocytopenia, Primary Immune-Mediated • von Willebrand Disease

ABBREVIATIONS

- ACT = activated clotting time • ACTH = adrenocorticotropic hormone • APTT = activated partial thromboplastin time
- BMBT = buccal mucosal bleeding time
- DDAVP = deamino-8-d-arginine vasopressin • DIC = disseminated intravascular coagulation • FDP = fibrinogen degradation product • FeLV = feline leukemia virus • FIP = feline infectious peritonitis • FIV = feline immunodeficiency virus • IMHA = immune-mediated hemolytic anemia • ITP = immune-mediated thrombocytopenia • LDDST = low-dose dexamethasone suppression test • NSAID = nonsteroidal anti-inflammatory drug • PCR = polymerase chain reaction • PT = prothrombin time • RBC = red blood cell • RMSF = Rocky Mountain spotted fever • VWD = von Willebrand disease

INTERNET RESOURCES

- <http://www.cvm.ncsu.edu/vth/ticklab.html>.
- www.diaglab.vet.cornell.edu/service/.
- www.vet.upenn.edu/penngen.

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Client Education Handout
available online

PETROLEUM HYDROCARBON TOXICOSES



BASICS

DEFINITION

• Petroleum hydrocarbons are a diverse group of products derived or synthesized from crude oil. • Certain non-petroleum-origin hydrocarbons, such as turpentine and linseed oil, are toxicologically similar enough to be considered with petroleum-origin products of similar molecular weight. Halogenated hydrocarbons, such as carbon tetrachloride or methylene chloride, are sufficiently unique to warrant separate consideration. • Small animal poisoning most commonly results from exposure to refined commercial products including such disparate mixtures as fuels, solvents, lubricants, and waxes. • Petroleum-based solvents are often used as “inert” carriers for other potential toxicants (e.g., pesticides, paints, medications). • Most petroleum hydrocarbons can be “lumped” into a relatively few broad categories on the basis of volatility, viscosity, and surface tension. Mixtures with high boiling points (low volatility), such as asphalt, mineral oil, and waxes, are relatively non-toxic. Products with relatively low boiling points and low viscosities, such as benzene or turpentine, are more readily aspirated, penetrate further into airways, and are more likely to cause chemical pneumonitis. In general, products that are more volatile also tend to be more lipophilic and more readily absorbed, systemically. Products with high aromatic content are also predisposed to cause systemic toxicity.

PATHOPHYSIOLOGY

• In general, the most acutely life-threatening effects of hydrocarbon ingestion result from aspiration-induced pneumonitis. • Viscosity and surface tension are reliable determinants of pneumotoxic potential. Low viscosity permits hydrocarbons to penetrate further into smaller airways. Low surface tension increases their tendency to “wet” pulmonary surfaces. For example, aspiration of as little as 0.1 mL of a low-viscosity hydrocarbon (e.g., hexane) may produce severe pneumonitis, whereas a high-viscosity product (e.g., motor oil) would not penetrate past the major airways. • Inhalation of hydrocarbon vapors (as opposed to aspirating liquid) may compromise pulmonary immune function and displace oxygen. • Topical exposure to hydrocarbon-based solvents (e.g., petroleum distillates, turpentine) may result in irritation and necrosis of skin and cornea. • Systemic toxicity is possible after oral or topical exposure. Although there are no quantitative data readily applicable to small animals, systemic toxicity should be considered when evaluating pets that have received a heavy topical exposure, or if the hydrocarbon is aromatic (e.g. benzene) or of a low molecular weight (e.g. hexane). Topical exposure is

especially important in very small animals (e.g., puppies, kittens, rodents), which have a relatively high body surface area to mass ratio. Systemic uptake and thus toxicity are also enhanced by factors such as a long hair coat, which traps the product against the skin.

SYSTEMS AFFECTED

- Cardiac
- Gastrointestinal
- Nervous
- Respiratory
- Skin
- Hematopoietic

INCIDENCE/PREVALENCE

In the author's experience, the incidence of small animal poisonings has decreased in recent years

SIGNALMENT

Species

Dogs and cats

SIGNS

General Comments

• Pneumonitis is the most serious complication associated with ingesting the more volatile (e.g., gasoline) hydrocarbons. Respiratory signs usually occur within a few minutes to 1–2 hours post-ingestion. The central nervous and gastrointestinal systems may also be affected, but death usually results from respiratory failure. • If aspiration occurs simultaneously with ingestion, there will be choking, coughing, gagging, and varying degrees of dyspnea. Direct damage of airway components and bronchospasm may result in hypoxia. Cyanosis may also develop immediately as alveolar oxygen is displaced by hydrocarbon vapor. • There is some evidence that *some* hydrocarbons sensitize the myocardium to both endogenous and exogenous catecholamines, precipitating arrhythmias; hemolytic anemia has been occasionally reported in children.

Historical Findings

• A history of (possible) exposure is essential to the diagnosis of hydrocarbon intoxication. Signs of hydrocarbon poisoning are seldom sufficiently characteristic to permit diagnosis. • Respiratory involvement, when present, is usually progressive over the first 24–48 hours, then gradually resolves 3–10 days following exposure. Animals that remain completely asymptomatic for 6–12 hours after ingestion are unlikely to develop respiratory illness.

Physical Examination Findings

• Astute observers may note a characteristic hydrocarbon odor on the animal's breath or coat. • Animals appear to experience a burning sensation in the mouth and pharynx after ingesting hydrocarbons, evidenced by slobbering, champing the jaws, shaking the head, and pawing at the muzzle. • Fever usually occurs in 3–4 hours following aspiration, but may occur in less than an hour or as much as 24 hours. • Vomiting, colic, and diarrhea after oral exposure. The severity and presence of such signs are a function of the dose and the individual hydrocarbon. Heavy aliphatic hydrocarbons (e.g., mineral

oil) may produce mild diarrhea but little else. Lighter hydrocarbons (e.g., gasoline) are more likely to produce colic and vomiting.

• Intoxicated animals may exhibit vertigo, ataxia, and mental confusion. Hydrocarbons produce depression and narcosis in most cases, but tremors and convulsions have also been reported in a few. If the dose is very high, the animal may become comatose and die prior to exhibiting signs of pneumonitis, although this is very rare. • Arrhythmias and syncope may occur as a result of myocardial sensitization to endogenous catecholamines. Myocardial sensitization may persist for as much as 24–48 hours after apparent recovery from the neurologic effects of intoxication.

CAUSES

- Storage in inappropriate containers and failure to clean up spills are common causes of exposure in pets. • Folk remedies using gasoline, kerosene, and other solvents as tonics or vermicifuges have poisoned pets.
- Using gasoline or other solvents in an attempt to remove sticky material from an animal's coat may also result in poisoning. Cats may ingest significant amounts of gasoline or other hydrocarbons by grooming themselves after topical contamination.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Infectious diseases, toxins, and/or injuries may result in respiratory signs similar to hydrocarbon aspiration, but only very acute processes (e.g., trauma, chylothorax) exhibit a similar rapidity of onset. • The diverse spectrum of neurologic effects may be confused with those of acute ethylene glycol, ethanol, or drug intoxication.

CBC/BIOCHEMISTRY/URINALYSIS

• Urine and serum will be negative for ethylene glycol; serum osmolality will be normal. • CBC may indicate stress, but this usually does not occur early in the course.

OTHER LABORATORY TESTS

- A simple spot test involves mixing vomitus or gastric contents vigorously with warm water. If gasoline or other petroleum distillates are present, they will float to the surface. Care must be taken to distinguish between petroleum products and dietary lipids. The former usually have a characteristic odor. • Most petroleum products lighter than kerosene, if isolated and absorbed onto a paper towel, evaporate relatively quickly with little residue and have a characteristic odor.
- Chemical analysis of ingestants or post-mortem tissues is useful forensically but is not practical for clinical evaluation. If chemical analysis is conducted, samples must be taken quickly and frozen in airtight containers to prevent loss due to volatilization.

PETROLEUM HYDROCARBON TOXICOSES

(CONTINUED)

IMAGING

Radiographic findings are typical of aspiration pneumonia and consist of fine, perihilar densities and extensive infiltrates in ventral portions of the lungs. These are worst at 3–4 days, then gradually improve. Not all animals with radiographic signs of hydrocarbon aspiration develop respiratory signs, and radiographic changes usually persist past the resolution of clinical signs.

PATHOLOGIC FINDINGS

- If aspiration has occurred, the principal lesions will be in the respiratory tract. Pulmonary lesions are bilateral and typically involve caudoventral portions of the lung. The earliest lesions include hyperemia, edema, and hemorrhage into the airways. Foreign matter may be grossly visible in the smaller airways. Later, there is bronchospasm, emphysema, and atelectasis. Pneumatoceles, pneumothorax, and subcutaneous emphysema result from airway collapse. There may be ulcerations in the mucosa of the trachea and larger airways.
- Bacterial pneumonia occasionally supervenes and may result in abscesses.
- Systemic toxicity very occasionally results in hepatic, myocardial, and/or renal tubular necrosis if the animal survives > 24 hours.



TREATMENT

APPROPRIATE HEALTH CARE

P In all cases of uncomplicated (i.e., not contaminated with some other, more toxic substance) petroleum hydrocarbon ingestion, the primary goal is to minimize the risk of aspiration. • If the amount ingested was small and the hydrocarbon ingested was one of the less volatile, more viscous products (e.g., motor oil, grease), cage rest and observation may be all that is required. • If the volume ingested was substantial and the product involved known to cause systemic toxicity (e.g., gasoline), activated charcoal is indicated within the first 4–6 hours post-exposure. Retrospective studies indicate that lavage is not beneficial after 60 min post-ingestion. • If the product contains other, highly toxic substances (e.g., pesticide), gastric decontamination may be indicated, despite

the risk of aspiration. It is essential that precautions (e.g., tracheal intubation) be taken to prevent possible aspiration of stomach contents. Emetics are contraindicated unless a last resort.

- Respiratory effects should be treated symptomatically. Supplemental oxygen and mechanical ventilation should be used as needed. Pneumomediastinum, pneumatoceles, and pneumothorax are common complications so positive pressure systems must be used with caution. High frequency jet ventilation reportedly results in fewer adverse sequelae than conventional mechanical ventilation. Since the lungs are the major route of systemic elimination for volatile hydrocarbons, closed or semiclosed systems should be purged frequently.
- Topical exposure may be treated by gently bathing with warm water and a mild detergent shampoo. If the hair coat is heavy or matted, it may be necessary to clip the contaminated areas.
- Symptomatic treatment of petroleum burns may involve topical antibacterials or other agents.
- Very viscous hydrocarbons (e.g., tar, waxes) may also be removed with mild detergents. They are not readily absorbed, pose only a cosmetic and skin irritation problem, and removal is not critical. Lipophilic materials (e.g., butter, lard, mechanic's hand cleaner) may also be useful, but the use of solvents is not recommended.

NURSING CARE

Cage rest is indicated, both for promotion of healing and to minimize the effects of excitement-induced catecholamines on a potentially sensitized myocardium.

CLIENT EDUCATION

Pet owners should be educated about proper storage and use of petroleum products.



MEDICATIONS

DRUG(S)

• Historically, oral mineral or vegetable oil was recommended to increase the viscosity of petroleum hydrocarbons and decrease the risk of aspiration. Retrospective studies suggest that such treatment increases the likelihood of aspiration pneumonia, and the use of such oils is no longer recommended.

- The routine use of antibiotics is of questionable value. Hydrocarbon pneumonitis is largely non-bacterial in origin; however, given the potentially severe consequences of bacterial complications and the relatively small downside to antibiotic use, it may be prudent to use antimicrobial prophylaxis if vomiting has occurred.

- Corticosteroids have been associated with increased numbers of positive lung cultures and are contraindicated.
- Bronchospasm may be treated with a beta adrenergic agonist such as albuterol.

PRECAUTIONS

Emesis should only be used when there is a high degree of certainty that leaving the foreign material in the gut poses a greater hazard than aspiration.



FOLLOW-UP

PATIENT MONITORING

Monitor patients for 3–4 days to ensure that ingested hydrocarbons have cleared the gastrointestinal tract and no pulmonary sequelae will occur.

EXPECTED COURSE AND PROGNOSIS

The diversity of this class of products precludes absolute prediction, but most hydrocarbon exposures respond well to conservative, supportive therapy.



MISCELLANEOUS

Suggested Reading

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PHEOCHROMOCYTOMA



BASICS

DEFINITION

APUDomas are tumors of the cells known as amine precursor uptake and decarboxylation (APUD) cells. APUDomas are peptide-secreting cells that synthesize and metabolize biogenic amines; they are located throughout the body (thyroid, adrenal medulla) and the gastrointestinal tract. Pheochromocytomas consist of chromaffin cells that originate from neural crest cells within the adrenal medulla or sympathetic ganglia (paragangliomas).

PATHOPHYSIOLOGY

Clinical signs develop as a result of the space-occupying nature of the tumor and its metastases or from excessive secretion of catecholamines (e.g., hypertension, tachycardia). Signs of hypertension and tachycardia may be constant or paroxysmal.

SYSTEMS AFFECTED

- Cardiovascular
- Neurologic
- Renal
- Respiratory

INCIDENCE/PREVALENCE

Uncommon disease in dogs; rare in cats

SIGNALMENT

Species

Dog and rarely cat

Breed Predilections

Boxer, miniature poodle, and German shepherd dog

Mean Age and Range

- Median age in dogs is 11 years; range is 1–16 years
- Older cats

SIGNS

General Comments

- The predominant signs result from alpha-mediated vasoconstriction and beta-mediated cardiac effects that cause systemic hypertension or tachyarrhythmias.
- Signs of hypertension may be constant or paroxysmal. Signs may be present for more than a year or develop suddenly resulting in death.
- Thirty percent of cases are asymptomatic and only identified at necropsy.

Historical Findings

- Clinical signs are often episodic or acute
- Generalized weakness and lethargy are common
- Anorexia
- Vomiting
- Weight loss
- Panting, dyspnea
- Diarrhea
- Whining, pacing
- Ascites, edema

- PU/PD
- Shakes/shivers
- Epistaxis
- Adypsia

Physical Examination Findings

- May be normal
- Lethargy, depression
- Tachypnea, dyspnea
- Thin, emaciated
- Weakness
- Peripheral edema
- Ascites
- Cardiac arrhythmias
- Systolic murmur
- Rales
- Pale or hyperemic mucous membranes
- Abdominal mass
- Dehydration
- Blindness
- Abdominal pain

CAUSES

Chromaffin cell tumor



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hyperadrenocorticism
- Hyperaldosteronism
- Essential hypertension (cats)
- Renal disease with secondary hypertension

CBC/BIOCHEMISTRY/URINALYSIS

- Nonregenerative anemia
- Hemoconcentration
- Leukocytosis
- Mild hyperglycemia
- Mild uremia
- Increased liver enzymes
- Hypoalbuminemia
- Hypocalcemia
- Proteinuria

OTHER LABORATORY TESTS

Arterial Blood Pressure

Systolic > 180 or diastolic > 95 mmHg is diagnostic for hypertension. Only 50% of animals with pheochromocytoma are hypertensive when blood pressure is measured because of the episodic nature of secretion of some tumors.

Electrocardiography

Sinus tachycardia is the most common arrhythmia; ventricular premature contractions less common.

IMAGING

Abdominal Radiography

- Abdominal mass (30%)
- Calcification of the adrenal mass (10%)
- Hepatomegaly
- Renal displacement
- Abnormal renal contour
- Ascites
- Enlargement of the caudal venal cava

Thoracic Radiography

- Generalized cardiomegaly
- Pulmonary congestion or edema

Abdominal Ultrasonography

- Unilateral adrenal mass
- Tumor invasion of the caudal vena cava and other adjacent structures
- Intra-abdominal and liver metastasis

Other Imaging Modalities

- CT scan and MRI
- Scintigraphy using ^{123}I -metaiodobenzylguanidine scan

DIAGNOSTIC PROCEDURES

- Plasma catecholamines:
 - > 2,000 pg/mL supports diagnosis of pheochromocytoma.
- Urinary catecholamine and catecholamine metabolites:
 - Total excretion over 24 hours is required or catecholamine/metanephrine to creatinine ratio.
 - No vanilla ingestion, drugs, or radiographic contrast agents prior to obtaining the urine sample.
 - 10–15% false positives.
 - Urine must be acidified ($\text{pH} < 3$).
 - Low sensitivity (0.42) compared with plasma catecholamines (0.97).
 - Metanephrine/normetanephrine—normal < 1.3 $\mu\text{g}/\text{day}$.
 - Catecholamine/metanephrine to creatinine ratio: normal = 53–323.
 - Total urinary catecholamines—normal < 250 $\mu\text{g}/\text{day}$.
- Phentolamine test:
 - Used in hypertensive patients to evaluate the dependence of catecholamines on maintaining hypertension.
 - After a stable arterial blood pressure is obtained, an IV bolus of phentolamine (0.5–1.5 mg) is given.
 - Blood pressure is recorded every 30 seconds for the first 3 minutes and every minute thereafter for an additional 7 minutes.
 - Test is positive if the fall in blood pressure is > 35 mmHg systolic or 25 mmHg diastolic and the decline lasts at least 5 minutes.
 - High incidence of false-positives and hypotension.
- Provocative tests:
 - Histamine, tyramine, glucagon may cause hypertensive crisis.

P

PATHOLOGIC FINDINGS

Immunohistochemical staining of tumor tissues with chromogranin A or synaptophysin allows differentiation of pheochromocytomas from other tumor types.

PHEOCHROMOCYTOMA

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

- Surgical removal of the tumor is the treatment of choice.
- Medical therapy is most commonly used to stabilize patients prior to surgery.

CLIENT EDUCATION

Survival times may be as long as 3 years following successful resection of tumor. In cats, removal of tumor is often curative; these are often benign as opposed to the malignant tumors seen in dogs.

SURGICAL CONSIDERATIONS

Preoperative Care

- Phenoxybenzamine (0.2–1.5 mg/kg PO q12h) 1–2 weeks prior to surgery.
- Atenolol, a β -1 selective antagonist (0.2–1 mg/kg PO q12–24h), can be used to control clinically significant supraventricular tachycardia.

Complications and Patient Monitoring

Common complications—hypertension, severe tachycardia, other cardiac arrhythmias, and hypovolemia/hypotension.

Anesthesia

- Induce anesthesia with a narcotic agent or propofol.
- Maintain anesthesia with isoflurane.

Surgery

Unilateral adrenalectomy and often thrombectomy. Manipulation of the tumor may cause severe hypertension if patient is not properly premedicated.

- Cardiac arrhythmias and severe tachycardia—common problems; usually respond to β -blocking agents such as esmolol (0.5 mg/kg slow IV bolus followed by 0.05–0.2 mg/kg/minute IV infusion).

CONTRAINdications

- Anesthetic agents—morphine, meperidine, xylazine, and ketamine.
- Severe hypertension can develop if a nonselective β -blocker (e.g., propranolol) is used without prior alpha-adrenergic blockade (e.g., phentolamine, phenoxybenzamine).

PRECAUTIONS

Nonselective beta blockade can lead to fatal hypertension.

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

Blood pressure, central venous pressure, and ECG are closely monitored in the immediate postoperative period (24–72 hours).

POSSIBLE COMPLICATIONS

Postoperative— intra-abdominal hemorrhage, hypotension, peritonitis, sepsis.

EXPECTED COURSE AND PROGNOSIS

Prognosis is guarded to fair.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Multiple endocrine neoplasia types II and III

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

Hypertension, Systemic

ABBREVIATIONS

- APUD = amine precursor uptake and decarboxylation
- CT = computed tomography
- ECG = electrocardiogram
- MRI = magnetic resonance imaging
- PU/PD = polyuria/polydipsia
- VMA = vanillylmandelic acid

Suggested Reading

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Author Deborah S. Greco

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MEDICATIONS

DRUG(S) OF CHOICE

- Pre- and intraoperative hypertension can be treated with phentolamine (0.02–0.1 mg/kg IV to effect).



BASICS

DEFINITION

- An inflammatory process involving the tunica intima of the vascular endothelial wall, usually associated with and considered a complication of peripheral IV therapy.
- Thrombophlebitis implies formation of fibrin clot, can involve superficial vasculature or deep tissues.

PATHOPHYSIOLOGY

- Sensitization of vascular endothelium causes release of vasoactive substances that cause vasoconstriction, increase vascular permeability, activate coagulation systems, and promote leukocyte chemotaxis.
- Extravasation of proteins and plasma leads to swelling and edema. • Thrombotic formation obstructs blood flow and may cause palpable thickening or vascular cord, which may progress to irreversible vascular sclerosis.
- Leukocyte pyrogens may cause systemic inflammation and fever. Exudates may be present at venipuncture site, especially with bacterial colonization.

SYSTEMS AFFECTED

- Skin—local inflammation/infection.
- Cardiovascular—altered vascular permeability and blood flow. • Hemic/Lymphatic/Immune—bacteria, inflammatory mediators and emboli can cause systemic inflammatory response and organ dysfunction.
- Respiratory—deep venous thrombophlebitis may cause pulmonary embolism.

INCIDENCE/PREVALENCE

- 20–80% of hospitalized patients receiving peripheral IV therapy. • Superficial thrombophlebitis most common, 10–12% may progress to deep venous thrombosis.

SIGNALMENT

- Dog and cat. • No known specific age, breed, or gender predisposition in veterinary medicine. • Neonatal and geriatric patients may be predisposed due to poor immune function.

SIGNS

- At least two of the following indicators of local inflammation—erythema, pain, heat, swelling, and vessel hardness. • Drainage or exudates may be present with concurrent lymphedema, infection or abscess. • Fever may be present with associated systemic inflammation or infection.

CAUSES

- Mechanical injury—IV catheter size/stiffness/integrity/duration, traumatic placement, previous venipuncture, high fluid infusion rates. • Chemical injury—IV catheter material, drugs, fluids of extreme osmolality or pH, parenteral nutrition, other vesicant solutions. • Bacterial

colonization—improper aseptic technique during placement, poor catheter care after placement, sepsis or immunosuppression. Common sources of bacteria are break points in the infusion system, skin microbes, and circulating organisms. • Obstructed blood flow—large-bore catheter, vasoconstriction, hypotension, thrombus formation.

RISK FACTORS

- Duration of catheterization—higher incidence with catheters in place for longer than 72 hours.
- Types of infusate—caustic, hyperosmolar, immunogenic and/or large-volume bolus.
- Virchow's triad—hypercoagulable state, blood flow abnormalities, and vessel wall damage predispose to thrombosis.
- Patient characteristics—obesity, immobility, poor vein quality, immunodeficiency, thrombophilia, polycythemia or hemoconcentration, chronic cardiac or renal disease, pregnancy.
- Disease characteristics—malignancy, infection, trauma, respiratory or circulatory failure.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cutaneous hypersensitivity, vasculitis, or other immune-mediated reaction.
- Subcutaneous tissue or interstitial infection or inflammation. • Previous unrelated injury or infection over vessel or IV catheter site.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC changes consistent with degree of systemic inflammatory response and platelet consumption.
- Biochemistry and urinalysis changes may be applicable with organ damage secondary to embolism (e.g., hepatic, renal, portal, caval, cerebral, cardiac, pulmonary).

OTHER LABORATORY TESTS

Coagulation—may see alterations in PT, PTT, D-dimer, antithrombin, Protein C, thromboelastography.

IMAGING

- Angiography/phlebography—gold standard for diagnosis of embolism, but invasive; requires contrast and may increase patient risk factors.
- CT or MRI—diagnosis of deep tissue embolism when suspected based on organ damage or dysfunction.
- B-mode ultrasonography, duplex ultrasonography or plethysmography—newer, less invasive methods of assessing venous patency, character, and blood flow, but limited availability.

DIAGNOSTIC PROCEDURES

- Doppler—inexpensive test of venous patency and blood flow.
- Culture intravenous cannula and site drainage (if present)—blood cultures may also be indicated with signs of systemic inflammation.

PATHOLOGIC FINDINGS

- Gross findings—vascular narrowing and thickening, focal or locally extensive with surrounding tissue swelling and discoloration. Thrombi may be present.
- Histopathology—swelling of endothelial cells, leukocytic infiltration of vascular wall with fibrin deposition and thrombus formation.



TREATMENT

APPROPRIATE HEALTH CARE

- Remove IV catheter(s) from affected sites as soon as possible. Initiate appropriate antibiotic, topical therapy, and wound care.
- Monitor for anaphylactic and other reactions when infusing blood products or any new medications. Pain during injection or at the insertion site is often first indicator of phlebitis, infiltration or extravasation.
- Avoid infusing hyperosmolar medications or solutions with pH less than 5 or greater than 9 through peripheral cannulas. With central venous access, always assess for blood return before starting the infusion.
- If caustic infiltration suspected, terminate infusion and leave cannula in place temporarily to aspirate any fluid remaining in the catheter and for instillation of specific antidote into affected tissue when applicable.
- Intermittent warm moist compress or hydrotherapy; some extravasated substances may require cold therapy.
- Photobiomodulation (low-level light therapy or LLLT) can be used directly over affected areas to reduce inflammation, activate stem cells, and promote blood flow and tissue repair.
- To avoid stagnant blood flow and thromboembolism, ensure adequate blood volume resuscitation and promote mobility; consider physical therapy and/or compression therapy.

NURSING CARE

- IV catheter placement—use strict aseptic technique and sterile dressing. With gauze dressing, check site every 48 hours to minimize manipulation during bandage change; transparent semi-permeable dressings are preferable to allow more frequent evaluation of catheter sites. Topical antimicrobial ointments or gels do not reduce the incidence of catheter-related infections, can promote development of antibiotic-resistant organisms, and are not recommended. Avoid lower extremities, joints and nerves when choosing catheter sites. Use smaller bore, longer catheters when possible; polyurethane is preferable to Teflon.
- IV catheter maintenance—IV cannulas should be checked for patency, line integrity and associated swelling every 1–2 hours with continuous infusions. Incidence increases significantly with peripheral catheters left in longer than 72 hours, but does not change from 72 to 96 hours. Change peripheral

PHLEBITIS

(CONTINUED)

catheters every 3–4 days, or within 24 hours if placed under emergency situation. Routine replacement of central venous catheters is not recommended.

ACTIVITY

- Moderate regular activity is recommended to reduce risk of thrombosis.
- Perform regular physical therapy, focused on the affected limb, especially in non-ambulatory patients.

DIET

- Nutritional support appropriate to treatment of underlying illness(es).
- Consider glycemic control if sepsis or risk of sepsis.

CLIENT EDUCATION

- Advise clients of IV catheter risks and complications, especially in patients with predisposing factors.
- Clients should be trained in and continue physical therapy and basic nursing care at home.

SURGICAL CONSIDERATIONS

- Infected catheter sites and/or extensive tissue damage may require surgical debridement and delayed closure.
- Surgical ligation or stripping of the corded vessels may be indicated to avoid deep vein thrombosis.



MEDICATIONS

DRUG(S) OF CHOICE

- Antibiotics (if infection suspected)—use empirical therapy, based on location (e.g., cephalaxin 20 mg/kg PO or IV q8h for skin) and potential contaminants if no culture and sensitivity available.
- NSAIDs—e.g., meloxicam 0.1–0.2 mg/kg PO or SC can significantly improve morbidity and patient comfort.
- Heparin—consider low molecular weight heparin therapy to prevent embolism. Use of heparin (100 U/mL) intravenous catheter flushes may reduce incidence and prolong IV catheter use.
- Topical therapy—heparinoid substances, such as polysulfate of mucopolysaccharide (e.g., Hirudoid) have anticoagulant action, inhibit thrombus formation, stimulate fibrinolysis and can activate local blood flow. Heparinoids may be more effective for treatment of pre-existing phlebitis than for prevention. Notoginseng cream, derived from the root of the ginseng plant, has been shown to be effective in reducing pain, erythema, edema and fibrous cord formation. Nitroglycerine patches, creams or gels (sprays not effective) promote local vasodilation within 10 minutes, last 3–6 hours and are effective for prevention as well as for treating first stages of phlebitis.
- Topical NSAIDs, such as piroxicam or

diclofenac gel, can help alleviate clinical signs and speed resolution.

CONTRAINDICATIONS

- Caustic, irritating, or immunogenic topicals or infusions.
- Use of NSAIDs with concurrent anti-inflammatory or immunosuppressive dose corticosteroid therapy.

PRECAUTIONS

- Avoid use of systemic NSAIDs if renal, hepatic or gastrointestinal dysfunction.
- Corticosteroids, unless used as an appropriate pre-treatment for chemotherapy, are associated with delayed wound healing and may predispose to infection.

POSSIBLE INTERACTIONS

- Systemic NSAIDs with significant inhibition of thromboxane (e.g., salicylate) used in combination with heparin may predispose to coagulopathy.
- Concurrent vasopressor therapy may predispose to thrombophlebitis; use of a topical vasodilator is recommended.

ALTERNATIVE DRUG(S)

- Topical dermatitis creams, such as silver-sulfadiazene may help reduce irritation and prevent infection.
- With excessive moisture or transdermal fluid leakage, keeping the skin dry using medicated powder (e.g., Gold Bond) may be helpful. Do not use on broken skin.



FOLLOW-UP

PATIENT MONITORING

- Persistent or progressive redness, swelling, pain, or heat—adjust antibiotic therapy based on most current culture and sensitivity results.
- Hardness, skin pallor, black discoloration, or eschar formation occur with tissue necrosis.

PREVENTION/AVOIDANCE

- Avoid use of phlebotic veins for IV therapy or blood collection until completely healed.
- Consider using submicron IV catheter filters, which may reduce incidence by removing particulates, endotoxin, and other soluble mediators of morbidity.

POSSIBLE COMPLICATIONS

- Tissue necrosis
- Neuritis or loss of function
- Lymphangitis
- Septicemia
- Extension to deep venous system

EXPECTED COURSE AND PROGNOSIS

- Most cases mild and self-limiting after 1–3 days with removal of catheter. Prognosis good but vascular patency commonly compromised.
- Severe local lesions can take 3–4 weeks to resolve and may result in loss of

function or permanent tissue damage.

- Prognosis guarded when associated with pulmonary thromboembolism and/or sepsis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Pulmonary thromboembolism
- Infection/cellulitis/sepsis

AGE-RELATED FACTORS

- Neonatal and geriatric patients may be predisposed to infection.
- Geriatric patients may have delayed wound healing.

PREGNANCY/FERTILITY/BREEDING

- Pregnancy may predispose to thromboembolism.
- Incidence of fetal complications with phlebitis is unknown.

SYNONYMS

- Thrombophlebitis
- Extravasation/infiltration
- Vasculitis

SEE ALSO

- Pulmonary Thromboembolism
- Sepsis and Bacteremia

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug
- PT = prothrombin time
- PTT = partial thromboplastin time

INTERNET RESOURCES

- www.emedicinehealth.com/phlebitis/article_em.htm
- www.patient.co.uk/health/Phlebitis.htm

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Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

PHOSPHOFRUCTOKINASE DEFICIENCY



BASICS

OVERVIEW

- Phosphofructokinase is the most important rate-controlling enzyme in glycolysis, and RBCs and intensely exercising skeletal muscles depend heavily on anaerobic glycolysis for energy. • Affected dogs have compensated hemolytic anemia and generally mild myopathy caused by markedly reduced total phosphofructokinase activity in both tissues. • Anemia develops because of insufficient generation of ATP to maintain normal RBC shape, ionic composition, and deformability and because RBCs from affected dogs are alkaline fragile and lyse when blood pH is slightly high.

SIGNALMENT

- English springer spaniel, American cocker spaniel, mixed breed, whippet, and wachtelhund dogs. • Transmitted as an autosomal recessive trait. • Affected homozygous animals generally not recognized as abnormal before 1 year of age.

SIGNS

- Some animals exhibit mild clinical signs that go unrecognized for years; others regularly exhibit episodes of severe illness. • Depression or weakness concomitant with episodes of red to brown pigmenturia; hemoglobinuria less likely to be recognized in female dogs, because of the sex difference in urination pattern.
- Mild lethargy with slight fever during mild hemolytic episodes. • Marked lethargy, weakness, pale or icteric mucous membranes, mild hepatosplenomegaly, muscle wasting, and fever as high as 41°C (106°F) possible during severe hemolytic crises. • Intravascular hemolysis can be caused by hyperventilation-induced alkalemia associated with exercise or excitement. • Signs of muscle dysfunction—usually limited to exercise intolerance and slightly diminished muscle mass, but muscle cramping and severe progressive myopathy can occur. • Two affected whippets had progressive cardiac disease in addition to muscle cramping after exercise.
- Heterozygous carrier animals appear clinically normal.

CAUSES & RISK FACTORS

Deficiency of the muscle-type subunit of phosphofructokinase—markedly reduced total activity in RBCs and skeletal muscle.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of hemolytic anemia—immune-mediated hemolytic anemia,

hemotropic mycoplasmosis, babesiosis, Heinz body hemolytic anemia, microangiopathic hemolytic anemia, and pyruvate kinase deficiency. • Affected dogs—negative Coombs' test, no parasites or Heinz bodies in stained blood films, seronegative for *Babesia* spp., and no evidence of DIC or heartworm disease. • Differentiated from pyruvate kinase deficiency by specific enzyme assays or DNA test.

CBC/BIOCHEMISTRY/URINALYSIS

- Persistent compensated hemolytic anemia.
- MCV usually 80–90 fL. • Reticulocyte counts generally 10–30%. • HCT values generally 30–40%; during hemolytic crises may decrease to ≤ 15%. • Bilirubinuria—often markedly high in male dogs.
- Hemoglobinuria in association with episodes of intravascular hemolysis.
- Serum—slightly high potassium, magnesium, calcium, urea, AST, total protein, and globulin; slightly to moderately high LDH, ALP, iron, and bilirubin; markedly high bilirubin in association with a hemolytic crisis; markedly high urea and creatinine if renal failure develops secondary to hemoglobin nephrosis or shock.

OTHER LABORATORY TESTS

- Measure RBC phosphofructokinase activity—easily identify affected animals older than 3 months; heterozygous carrier dogs have approximately one-half normal activity.
- Perform DNA test by PCR technology—clearly differentiate normal and carrier animals of any age. Wachtelhund dogs have a genetic mutation that is different from the defect in the other dog breeds.



TREATMENT

- Bone marrow transplantation is the only cure. • In patients with severe intravascular hemolysis, IV fluid therapy minimizes the chance of acute renal failure. • Blood transfusions usually not needed but should be given if anemia becomes life-threatening.



MEDICATIONS

DRUG(S)

For fever that often accompanies intravascular hemolysis and potentiates hemolytic crisis—aspirin (10 mg/kg PO q12h) or dipyrone (0.055 mL of 50% solution/kg SC q8h).



FOLLOW-UP

- Infrequently, affected dogs may die during a hemolytic crisis because of anemia or renal failure. • Affected animals can have a normal lifespan if properly managed. • Owners should avoid placing affected dogs in stressful situations or subjecting them to strenuous exercise, excitement, or high environmental temperatures.



MISCELLANEOUS

ABBREVIATIONS

- ALP = alkaline phosphatase • AST = aspartate aminotransferase • ATP = adenosine triphosphate • DIC = disseminated intravascular coagulation
- HCT = hematocrit • LDH = lactate dehydrogenase • MCV = mean cell volume
- PCR = polymerase chain reaction • RBC = red blood cell

INTERNET RESOURCES

- <http://research.vet.upenn.edu/penngen>.

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Author John W. Harvey

Consulting Editor Alan H. Rebar

PHYSALOPTEROSIS



BASICS

OVERVIEW

- *Physaloptera* spp. occur in dogs and cats; adults attach to the stomach mucosa; there is no larval migration outside the gastrointestinal tract.
- Infection can be asymptomatic or cause gastritis, vomiting.
- Typically few worms are present; single worm or all-female infections are common.
- Transmitted by ingestion of infective larvae in intermediate hosts (e.g., coprophagous grubs, beetles, cockroaches, crickets) or in paratenic hosts (e.g., birds, rodents, frogs, snakes, lizards).

SIGNALMENT

Dogs and cats; any breed, age, or sex. Infected animals often undergo extensive work-ups for suspected inflammatory bowel disease/ulcers, only to discover the nematodes at the time of endoscopy.

SIGNS

- Vomiting, often chronic and intermittent; occasionally find worms in vomitus.
- Weight loss can occur, especially with chronic infection.
- Signs can occur without egg production during pre-patent period, single worm, or female-only infections.
- Possible melena.

CAUSES & RISK FACTORS

- Outdoor exposure; access to insect intermediate hosts or small vertebrate transport hosts.
- Access to habitat occupied by wildlife species (raccoon, fox, coyote, bobcat, cougar, badger, skunk) infected with *Physaloptera*.

P



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other infectious causes of vomiting including parasite, viral, or bacterial infections.

- *Spirocerca*, the esophageal worm, produces similar smaller eggs ($11\text{--}15 \times 30\text{--}37 \mu\text{m}$).
- *Ollulanus*, a trichostrongylid nematode, can cause chronic vomiting; seen mainly in colony and feral cats; larvae and adults (<1 mm long) but no eggs present in vomitus or feces.
- Roundworms (ascarids) in puppies and kittens; worms can be present in feces and vomitus; larger than *Physaloptera*; characterized by three lips and cervical alae.
- Other non-infectious causes of vomiting including dietary indiscretion, foreign objects in the stomach, noxious substances accidentally ingested, gastrointestinal neoplasia, metabolic diseases.

CBC/BIOCHEMISTRY/URINALYSIS

Mild anemia and eosinophilia can occur.

OTHER LABORATORY TESTS

N/A

IMAGING

Abdominal radiography, including contrast studies, to eliminate other causes of vomiting.

DIAGNOSTIC PROCEDURES

- Endoscopy (gastroscopy) to visualize and remove worms, usually attached to stomach or duodenal mucosa; careful, thorough exam necessary to detect all worms; typically few are present and they can be hidden by mucus, ingesta, stomach rugae; pinpoint hemorrhages from prior attachment sites can be seen.
- *Physaloptera* spp. are small (2.5–5 cm long), stout, white or pink, with an anterior cuticular collar; male and female *P. praeputialis* have a posterior prepuce-like cuticular sheath.
- Direct smear, wet mount, or fecal flotation to detect eggs in vomitus or feces; eggs are dense and can be difficult to detect by fecal flotation using low specific gravity solutions; use flotation solution with s.g. > 1.25 .
- Eggs are small ($42\text{--}58 \times 29\text{--}42 \mu\text{m}$), thick-shelled, larvated, ovoid to ellipsoidal, and colorless.



TREATMENT

- Outpatient treatment; anthelmintic with or without endoscopic removal of worms.

- Anthelmintic use is extra-label and anecdotal.



MEDICATIONS

DRUG(S)

- With no migration beyond the stomach wall, use adulticide anthelmintic released in stomach.
- Fenbendazole (dogs), 50 mg/kg PO q24h for 3–5 days; repeat if signs persist.
- Pyrantel pamoate (dogs/cats), 5 mg/kg twice at 3-week interval or 15–20 mg/kg once; repeat if signs persist.
- Ivermectin (cats), 0.2 mg/kg PO or SC once.
- Medication to reduce gastritis—histamine H₂-antagonists (e.g., famotidine 0.5 mg/kg PO q24h); sucralfate 0.25–1 g PO q8–12h in the dog; 0.25 g PO q8–12h in the cat.



FOLLOW-UP

PATIENT MONITORING

Recheck 1–2 weeks post-treatment and re-treat with anthelmintic if eggs still present on fecal exam and/or if vomiting persists.

PREVENTION/AVOIDANCE

- Prompt removal and disposal of feces to prevent infection of arthropod intermediate hosts.
- Keep pets from roaming freely outdoors; prevent hunting and scavenging.

EXPECTED COURSE AND PROGNOSIS

Clinical signs and/or shedding of eggs in feces should resolve within 2 weeks of treatment.

Suggested Reading

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Author Matt Brewer

Consulting Editor Stephen C. Barr

Acknowledgment The author and editors acknowledge the prior contribution of Julie Ann Jarvinen.



BASICS

OVERVIEW

- *Yersinia pestis*—Gram-negative, bipolar staining rod; reservoir: wild rodents (sylvatic), ground squirrels, prairie dogs, rabbits, bobcats, coyotes. • Occurs worldwide; movement of animals may result in occurrence in non-endemic areas.
- United States—reported cases from western states/Hawaii
- Common: May–October.
- Infected fleas transmit bacterium in bite but cats commonly infected by ingestion of infected rodents, not by bite of fleas.
- Bacteria migrate from skin lymphatics to regional LN; survive phagocytosis/multiply in LN; phagocytic cells rupture.
- Infection—fever and painful lymphadenopathy (bubo); intense local inflammation results in bubonic plague; intermittent bacteremia; LN rupture; may become septicemic with or without LN involvement.
- Cats—highly susceptible; severe fatal disease.
- Dogs—naturally resistant to infection.
- *Y. pestis* is potential bioterrorist agent (beware of clusters of pneumonia cases).

SIGNALMENT

Cat and rarely dog

SIGNS

- Dogs—may exhibit mild febrile signs/depression
- Cats—unique among carnivores in exhibiting bubonic/pneumonic/septicemic forms of plague.

Bubonic (Cats)

- Most common form
- Incubation period 2–7 days after flea bite or after eating infected rodent
- Duration of illness variable
- Bubo—head and neck; marked lymphadenopathy (hemorrhagic/necrotic/edematous); if patient survives long enough, LN abscess, rupture, drain through fistula tracts to skin
- Fever: 39.5–40.5°C (103–105°F)
- Depression
- Vomiting/diarrhea
- Dehydration
- Enlarged tonsils
- Anorexia
- Ocular discharge
- Weight loss
- Ataxia
- Coma
- Oral ulcers

Septicemic (Cats)

- Rare
- Septicemia without lymphadenopathy or abscess formation
- Other signs same as bubonic.

Pneumonic (Cats)

Severe disease; greatest risk for zoonotic spread to in-contact humans.

CAUSES & RISK FACTORS

- Hunter cats—greater exposure to wild rodents/fleas
- Travel to endemic areas
- Environment—homes/pets with heavy flea infestation; homes with large nearby rodent populations (e.g., garbage food source or wood pile)
- Plague becoming more common as homes encroach on wildlife habitats in plague-endemic areas.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Acute disease state manifested by lymphadenopathy, malaise, oral ulceration, and fatal outcome in animals of endemic regions: Infection (feline calicivirus, feline coronavirus, feline immunodeficiency virus, feline leukemia virus, cryptococcosis, histoplasmosis, toxoplasmosis, tularemia, leishmaniasis); neoplasia (lymphoid/myelogenous leukemia; lymphoma in cats, multiple myeloma); drug eruption/skin hypersensitivity; epidermolysis bullosa; pemphigus; systemic lupus erythematosus; oropharyngeal foreign body/plant awn, trauma/injury, gingivitis, stomatitis; osteomyelitis, sequestrum, bone abscess.

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis: left shift/marked toxic changes
- Thrombocytopenia—with DIC
- High liver enzyme activity and hyperbilirubinemia

OTHER LABORATORY TESTS

- Serology—Communicable Disease Center/state health department
- Prolonged clotting times—with DIC.

DIAGNOSTIC PROCEDURES

- Culture by reference lab is definitive; samples from antemortem clinical material (abscess, LN, peripheral blood) **before treatment is given** or from post-mortem tissue (LN, abscess, liver, spleen); seeing large numbers of Gram-negative coccobacilli with bipolar staining on touch preps prior to culture, constitutes presumptive positive diagnosis
- Fluorescent antibody test—presumptive identify infected animals; samples same as for culture
- Molecular testing/PCR of blood/tissues

PATHOLOGIC FINDINGS

- Acutely ill cats—few lesions; enlarged LN (bubo) on head and neck; enlarged liver and spleen.
- LN—destruction of normal architecture; hemorrhagic necrosis; extracellular bacteria.



TREATMENT

- Inpatient
- High mortality if not treated early
- Treat aggressively with intravenous fluids to counteract septicemia
- Treat DIC, if indicated
- Treat patient for fleas.



MEDICATIONS

DRUG(S)

- Treat all suspect cases empirically until confirmed by lab
- Systemic antimicrobials—use in all patients except those with lung

involvement (such patients should be euthanized—high zoonotic potential)

- Tetracyclines—oxytetracyclines, tetracycline, chlortetracycline; 25 mg/kg PO q8h for 10 days; parenteral, 7.5 mg/kg q12h
- Doxycycline (5 mg/kg PO q12h)—effectiveness not established but probably effective
- Chloramphenicol 30–50 mg/kg PO q8h
- Gentamicin (2–3 mg/kg PO or SC q8h); trimethoprim-sulfamethoxazole, and kanamycin—use if the other listed drugs cannot be used
- Coordination with public health officials is necessary if threat of bioterrorism established (bioengineered strains of *Y. pestis* may be drug resistant).



FOLLOW-UP

PATIENT MONITORING

DIC—common later in infection, if disease not treated early.

PREVENTION/AVOIDANCE

- Limit travel with pet to avoid endemic areas
- Endemic areas—keep pet on a leash to control contact to wild rodents/fleas; spray/dust pet and home for flea control
- Neuter cats—limit hunting behavior/rodent exposure
- Eliminate rodents/habitats near houses/outbuildings (wood piles/garbage piles); store food in rodent-proof containers.

EXPECTED COURSE AND PROGNOSIS

- Prognosis—poor if not treated early
- Pneumonic plague has greatest risk of death.



MISCELLANEOUS

ZOONOTIC POTENTIAL

High

CDC Recommendations

- Avoid contact with infectious materials from patient/fleas.
- Any material used in examination of patients—disinfect/autoclave/incinerate.
- Wear mask/gloves when handling patients.
- Use respirator/protective eye equipment during necropsies.
- Monitor staff health for 2 weeks after exposure; discuss post-exposure prophylaxis/fever watch with healthcare provider.

ABBREVIATIONS

- DIC = disseminated intravascular coagulation
- LN = lymph node

INTERNET RESOURCES

- <http://www.cfsph.iastate.edu/DiseaseInfo/disease.php?name=plague&lang=en>

Suggested Reading

Pennisi MG, Egberink H, et al. *Yersinia pestis* infection in cats: ABCD guidelines on prevention and management. J Feline Med Surg 2013, 15:582–584.

Author Patrick L. McDonough

Consulting Editor Stephen C. Barr

PLASMACYTOMA, MUCOCUTANEOUS



BASICS

OVERVIEW

- Tumor of plasma cell origin.
- Typically benign and local therapy can be curative.
- Rarely (< 1%) part of multiple myeloma process.
- Gastrointestinal extramedullary plasmacytoma (GI EMP) may be more aggressive.

SIGNALMENT

- Dog, rarely cat
- Cocker spaniel, West Highland white terrier, boxer, German shepherd, Airedale
- Median age 9–10 years

SIGNS

- 86% are cutaneous, 9% affect mucous membranes, 4% colorectal, 1% non-cutaneous/non-oral.
- Solitary, smooth, raised pink nodules, typically 1–2 cm in diameter.
- Bleeding, hematochezia, tenesmus, rectal prolapse if colorectal form.
- Vague, nonspecific signs if gastrointestinal EMP.

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other round cell tumor types including lymphoma, mast cell tumor, histiocytoma, transmissible venereal tumor.
- Poorly differentiated carcinoma.
- Amelanotic melanoma.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal for EMP

OTHER LABORATORY TESTS

Bone marrow aspirate cytology and serum electrophoresis may be indicated for GI EMP.

IMAGING

- Colonoscopy recommended for colorectal EMP.

- Thoracic radiographs and abdominal ultrasound may be indicated for GI EMP.

DIAGNOSTIC PROCEDURES

- Cytologic examination of fine-needle aspirate reveals moderate to marked cellularity with round to polyhedral individual tumor cells with discrete margins, abundant royal blue cytoplasm, paranuclear clear zone, eccentric round nucleus, and clumped chromatin. Multinuclearity is common.
- Histologic evaluation identify—tumors to be densely cellular with single or multiple variably sized nuclei with many mitoses present, and amyloid deposition may be present. Histologically classified into mature, hyaline, cleaved, asynchronous, monomorphic blastic, and polymorphous blastic cell types. However, no prognostic significance has been associated with this classification.
- Immunohistochemistry may be necessary to distinguish from other neoplasms.



TREATMENT

- Conservative surgery for the majority of EMP types
- Radiation therapy if nonresectable



MEDICATIONS

DRUG(S)

Melphalan and prednisone may be indicated in GI EMP.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

Reevaluation every 3 months to monitor for local tumor control and metastases.

EXPECTED COURSE AND PROGNOSIS

- Excellent in most patients.
- Long-term survival expected for GI EMP treated with surgery ± chemotherapy.
- Reported 15-month median survival time for colorectal form with surgery alone.
- 5% local recurrence rate with conservative surgery for the majority of EMP.
- Metastasis reported in 2% of patients with EMP.
- 2% of patients will develop *de novo* EMP.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Multiple myeloma
- Lymphoma—dogs
- Cats—may note systemic amyloidosis

SEE ALSO

- Amyloidosis
- Lymphoma—Dogs
- Multiple Myeloma

ABBREVIATIONS

- EMP = extramedullary plasmacytoma
- GI = gastrointestinal

Suggested Reading

Cangul IT, Wijnen M, Van Garderen E, et al. Clinico-pathological aspects of canine cutaneous and mucocutaneous plasmacytomas. J Vet Med A Physiol Pathol Clin Med 2002, 49(6):307–312.

Morrison WB. Plasma cell neoplasms. In: Morrison WB, ed., Cancer in Dogs and Cats: Medical and Surgical Management. Jackson, WY: Teton NewMedia, 2002, pp. 671–677.

Vail D. Myeloma-Related Disorders. In: Withrow SJ, Vail DM, Page RL, eds., Small Animal Clinical Oncology, 5th ed. St Louis, MO: Elsevier Saunders, 2013, pp. 665–678.

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Consulting Editor Timothy M. Fan

Acknowledgment The author and editors acknowledge the prior contribution of Wallace B. Morrison.

PLEURAL EFFUSION



BASICS

DEFINITION

Abnormal accumulation of fluid within the pleural cavity

PATHOPHYSIOLOGY

- More than normal production or less than normal resorption of fluid.
- Alterations in hydrostatic and oncotic pressures or vascular permeability and lymphatic function may contribute to fluid accumulation.

SYSTEMS AFFECTED

- Cardiovascular
- Respiratory

SIGNALMENT

Species

Dog and cat

Breed Predilections

Varies with underlying cause

Mean Age and Range

Varies with underlying cause

Predominant Sex

Varies with underlying cause

SIGNS

General Comments

Depend on the fluid volume, rapidity of fluid accumulation, and the underlying cause.

Historical Findings

- Dyspnea
- Tachypnea
- Orthopnea
- Open-mouth breathing
- Cyanosis
- Exercise intolerance
- Lethargy
- Inappetence
- Cough

Physical Examination Findings

- Dyspnea—respirations often shallow and rapid
- Muffled or inaudible heart and lung sounds ventrally
- Preservation of breath sounds dorsally
- Dullness ventrally on thoracic percussion

CAUSES

High Hydrostatic Pressure

- CHF
- Overhydration.
- Intrathoracic neoplasia.

Low Oncotic Pressure

Hypoalbuminemia—occurs in protein-losing enteropathy, protein-losing nephropathy, and liver disease.

Vascular or Lymphatic Abnormality

- Infectious—bacterial, viral, or fungal.
- Neoplasia (e.g., mediastinal lymphoma, thymoma, mesothelioma, primary lung tumor, and metastatic disease).
- Chylothorax (e.g., from lymphangiectasia, CHF, cranial vena caval obstruction

[sometimes associated with transvenous pacemaker implantation], neoplasia, fungal infections, heartworms, diaphragmatic hernia, lung lobe torsion, trauma).

- Diaphragmatic hernia.
- Hemothorax (e.g., from trauma, neoplasia, coagulopathy, *Angiostrongylus vasorum*).
- Lung lobe torsion.
- Pulmonary thromboembolism.
- Pancreatitis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Historical or physical evidence of external trauma—consider hemothorax or diaphragmatic hernia.
- Fever suggests an inflammatory, infectious, or neoplastic cause.
- Murmurs, gallops, or arrhythmias combined with jugular venous distension or pulsation suggest an underlying cardiac cause.
- Concurrent ascites suggests FIP, CHF (mainly dogs), severe hypoalbuminemia, diaphragmatic hernia, disseminated neoplasia, or pancreatitis.
- In cats, decreased compressibility of the cranial thorax suggests a cranial mediastinal mass.
- Concurrent ocular changes (e.g., chorioretinitis and uveitis) suggest FIP or fungal disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram results may be abnormal in patients with pyothorax, FIP, neoplasia, or lung lobe torsion.
- Severe hypoalbuminemia (generally $< 1 \text{ g/dL}$ to cause effusion) suggests protein-losing enteropathy, protein-losing nephropathy, or liver disease.
- Hyperglobulinemia (polyclonal) suggests FIP.

OTHER LABORATORY TESTS

- Fluid analysis should include physical characteristics (i.e., color, clarity, odor, clots), pH, glucose, total protein, total nucleated cell count, and cytologic examination; Table 1 provides characteristics of various pleural fluid types and their disease associations.
- In cats the LDH concentration in transudates is $< 200 \text{ IU/L}$ and in exudates it is $> 200 \text{ IU/L}$.
- Pleural fluid pH < 6.9 suggests pyothorax in cats.
- Glucose concentration in pleural fluid usually parallels levels in serum. In cats, pyothorax and malignancy lower pleural fluid glucose concentration relative to serum glucose concentration; thus, pleural fluid with a normal pH and low glucose concentration suggests malignancy in cats.
- Serologic tests for feline leukemia virus (if patient has mediastinal lymphoma), feline immunodeficiency virus (if patient has

pyothorax), and coronavirus (if FIP is suspected) are available.

- Cardiac disease suspected—consider a heartworm test in dogs and cats and a thyroid evaluation in cats.
- Infection suspected—do aerobic and anaerobic bacterial culture and sensitivity tests and consider special stains (e.g., gram and acid-fast stains) of the fluid.
- FIP suspected—consider protein electrophoresis of the fluid; γ -globulin level $> 32\%$ of total protein strongly suggests a diagnosis of FIP.
- Chyle suspected—do an ether clearance test or Sudan stain of the pleural fluid, and triglyceride and cholesterol evaluations of the fluid and serum.

IMAGING

Radiographic Findings

- Used to confirm pleural effusion; should not be performed until after thoracocentesis in dyspneic patients with evidence of pleural effusion on physical examination.
- Evidence of pleural effusion includes separation of lung borders away from the thoracic wall and sternum by fluid density in the pleural space, fluid-filled interlobar fissure lines, loss or blurring of the cardiac and diaphragmatic borders, blunting of the lung margins at the costophrenic angles (ventrodorsal view), and widening of the mediastinum (ventrodorsal view).
- Rounding of the caudal lung lobe borders (lateral view)—most common in patients with fibrosing pleuritis caused by chylothorax, pyothorax, or FIP.
- Unilateral effusion—most common in patients with chylothorax and pyothorax; hemothorax, pulmonary neoplasia, diaphragmatic hernia, and lung lobe torsion.
- Evaluate post-thoracocentesis radiographs carefully for cardiomegaly, intrapulmonary lesions, mediastinal masses, diaphragmatic hernia, lung lobe torsion, and evidence of trauma (e.g., rib fractures).
- Can diagnose a diaphragmatic hernia with positive-contrast peritoneography.
- Can evaluate the thoracic duct by positive contrast lymphangiography.

Echocardiographic Findings

- Ultrasonographic evaluation of the thorax is recommended whenever cardiac disease, diaphragmatic hernia, or cranial mediastinal mass is suspected.
- Echocardiography is easiest to perform before thoracocentesis, provided the patient is stable.

DIAGNOSTIC PROCEDURES

- Thoracocentesis—allows characterization of the fluid type and determination of potential underlying cause.
- Exploratory thoracotomy or thoracoscopy—to obtain biopsy specimens of lung, lymph nodes, or pleura, if indicated.

PLEURAL EFFUSION

(CONTINUED)

Table 1

Characterization of pleural fluid.						
	<i>Transudate</i>	<i>Modified Transudate</i>	<i>Non-septic Exudate</i>	<i>Septic Exudate</i>	<i>Chyle</i>	<i>Hemorrhage</i>
Color	Colorless to pale yellow	Yellow or pink	Yellow or pink	Yellow to red-brown	Milky white	Red
Turbidity	Clear	Clear to cloudy	Clear to cloudy; fibrin	Cloudy to opaque; fibrin	Opaque	Opaque
Protein (g/dL)	< 1.5	2.5–5.0	3.0–8.0	3.0–7.0	2.5–6.0	3.0
Nucleated cells/ μ L	< 1,000	1,000–7,000 (LSA up to 100,000)	5,000–20,000 (LSA up to 100,000)	5,000–300,000	1,000–20,000	Similar to peripheral blood
Cytology	Mostly mesothelial cells and macrophages	Mostly macrophages and mesothelial cells; few nondegenerate PMNs; neoplastic cells in some cases	Mostly nondegenerate PMNs and macrophages; neoplastic cells in some cases	Mostly degenerate PMNs; also macrophages; bacteria	Small lymphocytes, PMNs, and macrophages	Mostly RBCs; with erytrophagocytosis
Disease associations	Hypoalbuminemia (protein-losing nephropathy, protein-losing enteropathy, or liver disease); early CHF	CHF; neoplasia; diaphragmatic hernia; pancreatitis	FIP; neoplasia; diaphragmatic hernia; lung lobe torsion	Pyothorax	Lymphangiectasia, CHF, cranial vena cava obstruction, neoplasia, fungal, dirofilariasis, diaphragmatic hernia, lung lobe torsion, trauma	Trauma, coagulopathy, neoplasia, lung lobe torsion

Modified from Sherding RG. Diseases of the pleural cavity. In: Sherding RG, ed. The Cat: Diseases and Clinical Management, 2nd ed. New York: Churchill Livingstone, 1994, p. 1061.



TREATMENT

- First, thoracocentesis to relieve respiratory distress; if the patient is stable after thoracocentesis, outpatient treatment may be possible for some diseases. Most patients are hospitalized because they require intensive management such as indwelling chest tubes (e.g., patients with pyothorax) or thoracic surgery.
- Preventing fluid reaccumulation requires treatment based on a definitive diagnosis.
- Surgery is indicated for management of some neoplasias, diaphragmatic hernia repair, lymphangiectasia (i.e., thoracic duct ligation), foreign body removal, and lung lobe torsion (i.e., lung lobectomy).
- Pleuroperitoneal shunts may relieve clinical signs in animals with intractable pleural effusion.
- Vascular access ports attached to intrathoracic Jackson-Pratt drains can be tried for chronic effusions that are not responsive to the therapy of the underlying disorder.



MEDICATIONS

DRUG(S) OF CHOICE

- Treatment varies with specific disease.
- Diuretics generally reserved for patients with diseases causing fluid retention and volume overload (e.g., CHF).

PRECAUTIONS

- Avoid drugs that depress respiration or decrease blood pressure.
- Inappropriate use of diuretics predisposes the patient to dehydration and electrolyte disturbances without eliminating the effusion.



FOLLOW-UP

PATIENT MONITORING

Radiographic evaluation is key to assessment of treatment in most patients.

POSSIBLE COMPLICATIONS

- Death due to respiratory compromise.
- Reexpansion pulmonary edema may develop after pleural effusion is manually removed.

EXPECTED COURSE AND PROGNOSIS

Vary with underlying cause, but usually guarded to poor. In a study of 81 cases of pleural effusion in dogs, 25% recovered completely and 33% died during or were euthanized immediately after completing diagnostic evaluation.



MISCELLANEOUS

SYNOMYS

- Hydrothorax = transudates and modified transudates
- Pyothorax = empyema, septic pleuritis

SEE ALSO

See "Causes"

ABBREVIATIONS

- CHF = congestive heart failure
- FIP = feline infectious peritonitis
- LDH = lactate dehydrogenase
- LSA = lymphoma
- PMN = polymorphonuclear cell
- RBC = red blood cell

Suggested Reading

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Author Francis W.K. Smith, Jr.

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Client Education Handout available online

PNEUMOCYSTOSIS



BASICS

OVERVIEW

- *Pneumocystis carinii (jirovecii)*—saprophyte of low virulence, infects virtually all mammals worldwide.
- Primary habitat is the lung
- Classified as an atypical fungal organism, based on analysis of nucleic acids
- Subclinical infections in cats and dogs. Clinical infections in dogs are linked with immunodeficiency. FIV and FeLV does not predispose cats.

SIGNALMENT

- Young dogs.
- Not reported in cats.
- Miniature dachshunds and Cavalier King Charles spaniels predisposed due to congenital immunodeficiency.

SIGNS

- Respiratory difficulty and weight loss progressing over weeks to months
- Dyspnea without fever
- Exercise intolerance
- Coughing
- Vomiting, and diarrhea
- Cachexia

CAUSES & RISK FACTORS

- *Pneumocystis carinii*. • Primary role of spread is by airborne droplet transmission between hosts. Neonates may be infected through aspiration of contaminated amniotic fluid
- Immunodeficiency or pre-existing pulmonary disease predisposes.
- Higher prevalence in dogs infected with canine distemper.
- Severe immunosuppression—deficiency of IgA, IgG, and IgM in dachshunds. CKCS—immunoglobulin deficiency and decreased lymphocyte function.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Inflammatory (chronic pulmonary fibrosis, eosinophilic bronchopneumopathy, inhalational irritants).
- Infectious agents (systemic mycosis, toxoplasmosis, parasitic [including *Dirofilaria immitis*], bacterial pneumonia, viral).
- Cardiovascular (congestive heart failure, thromboemboli).
- Foreign body.
- Neoplasia.
- Noncardiogenic pulmonary edema.

CBC/BIOCHEMISTRY/URINALYSIS

- Changes usually nonspecific.
- Leukocytosis with neutrophilia and a left shift.
- Eosinophilia and monocytosis.
- Erythrocytosis—secondary to chronic hypoxia.
- Thrombocytopenia (CKCS) or thrombocytosis (dachshunds).
- Hypoglobulinemia.

OTHER LABORATORY TESTS

- Arterial blood gas—hypoxemia; hypocapnia; alkalosis and increased alveolar-arterial oxygen tension difference.

- Immunoglobulin fraction quantification—hypogammaglobulinemia.
- Indirect or direct fluorescent antibody test effective in specifically detecting organisms in sputum, washes, and pulmonary tissues.
- PCR of bronchoalveolar fluid and tissues.

IMAGING

Thoracic Radiography

- Changes not specific for *P. carinii*.
- Diffuse milary-interstitial to alveolar pattern with peribronchial opacification..
- Middle lung lobes more severely affected than the cranioventral lung lobes.
- Cavitary lesions and spontaneous pneumothorax may develop.
- Right-sided cardiomegaly, tracheal deviation, and pulmonary arterial enlargement. Cor pulmonale may develop as a result of increased pulmonary vascular resistance.

DIAGNOSTIC PROCEDURES

- Definitive diagnosis made by direct visualization of *P. carinii* in respiratory fluids, sputum, or biopsy specimens.
- Transtracheal aspiration, bronchoalveolar lavage, transbronchoscopic and endobronchial brushing shown to be reliable methods for obtaining samples.
- Cytology not as reliable or as definitive as histopathology. Biopsy for histopathology is invasive and has potential complications (hemorrhage, pneumothorax).
- Immunohistochemical kits available—positive result is specific and highly diagnostic; may be used on cytologic, formalin-fixed, and paraffin-embedded material; note: host species-specific antigenic variation has been demonstrated and may cause false-negative results.

PATHOLOGIC FINDINGS

- Lungs—firm, consolidated, and pale brown or gray; fluid not expressed from cut surfaces; do not collapse when the chest cavity is opened; small amounts of pleural fluid may be noted.
- Alveolar spaces—may be filled with amorphous, foamy, eosinophilic material with a honeycombed appearance; trophozoites and cyst stages may be identified.
- Pulmonary and mediastinal lymphadenopathy.
- Right-sided cardiomegaly.
- H&E only weakly stains internal structures of organism. Methenamine silver, Toluidine blue, Gram and Periodic acid-Schiff will stain cyst walls.



TREATMENT

- Inpatient—supportive care for patients with pneumonia. Oxygen administration, nebulization and coupage, bronchodilators, and intravenous fluids as required.
- Decrease exposure to other pathogens, discontinue any immunosuppressant agents.
- Anti-inflammatory doses of glucocorticoids improves pulmonary function and survival in humans.
- Cage rest or restricted exercise.



MEDICATIONS

DRUG(S)

- Trimethoprim sulphonamides 15 mg/kg q8h or 30 mg/kg q12h for 3 weeks—preferred therapy (in humans IV shown to be more effective than PO).
- Pentamidine isethionate 4 mg/kg IM q24h for 3 weeks (not as effective as trimethoprim sulphonamides but less toxic).
- Drug combinations—clindamycin and primaquine, dapsone and trimethoprim.
- Potential new drug options—caspofungin (no veterinary cases reported) and trimetrexate.
- Treatment may be started 24–48h before specimen collection without masking diagnosis.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Give folic acid supplementation if side effects of trimethoprim sulphonamides are observed or if long-term therapy required.
- Complications to pentamidine isethionate include renal and hepatic dysfunction, hypoglycemia, hypotension, hypocalcemia, urticarial, and hematologic disorders.



FOLLOW-UP

PATIENT MONITORING

- Pentamidine isethionate—check BUN and glucose daily
- Monitor clinical signs, vitals, radiographs. May need extended (months) course of treatment.

P



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Ubiquitous in environment with humans and animals being exposed to same sources.
- Potential risk if immunocompromised person is in close contact with clinically ill pet.

ABBREVIATIONS

- AIDS = acquired immunodeficiency syndrome
- CKCS = Cavalier King Charles spaniel
- HIV = human immunodeficiency virus

Suggested Reading

Lobetti RG. Pneumocystosis. In: Greene CE, ed., *Infectious Diseases of the Dog and Cat*, 3rd ed. St. Louis: Saunders Elsevier, 2011, pp. 704–709.

Sykes, JE. Canine and Feline Infectious Diseases. St Louis, MO: Saunders, 2014, pp. 685–692.

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PNEUMONIA, ASPIRATION



BASICS

OVERVIEW

• Inflammation of the lungs caused by inhalation of oral ingestants, regurgitated material, and vomitus with subsequent pulmonary dysfunction; develops when laryngeal reflexes function improperly or are overwhelmed. • Pulmonary dysfunction—caused by (1) direct obstruction of small airways and indirect obstruction from bronchospasm and production of mucus and exudate; (2) aspiration of gastric acid—damages respiratory epithelium; can cause bronchospasm and ALI/ARDS; (3) bacterial pneumonia—bacteria in aspirated material can initiate an immediate infection; or later infections occur secondary to lung damage.

SIGNALMENT

Dogs; less commonly cats

SIGNS

• Paroxysmal, acute, or chronic. • Cough, tachypnea, nasal discharge, or exercise intolerance. • Respiratory distress or cyanosis when severe. • Depending on underlying cause—regurgitation; vomiting; dysphagia; altered consciousness; stertor or stridor.

CAUSES & RISK FACTORS

• Pharyngeal abnormalities—local paralysis; generalized neuromuscular disease; cricopharyngeal motor dysfunction; anatomic malformations. • Esophageal abnormalities—megaeosophagus; reflux esophagitis; esophageal dysmotility; esophageal obstruction; bronchoesophageal fistula. • Laryngeal paralysis, webbing, or obstruction; post-laryngeal surgery. • Altered consciousness—sedation, anesthesia; post-ictus; forebrain disease; metabolic disturbance. • Iatrogenic—force feeding; tube feeding, mineral oil administration.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Bacterial pneumonia • Lung abscess

CBC/BIOCHEMISTRY/URINALYSIS

Neutrophilic leukocytosis, left-shift, although WBCs may be normal.

OTHER LABORATORY TESTS

• Arterial blood gas analysis—hypoxemia; PaCO₂ generally low. • Consider tests for predisposing problems—acetylcholine receptor antibodies, resting cortisol or ACTH stimulation, creatine kinase.

IMAGING

• Thoracic radiography—bronchoalveolar pattern usually most severe in the gravity-dependent lobes (right cranial and

middle, left cranial); can take up to 24 hours for pattern to develop after aspiration; scrutinize for evidence of esophageal or mediastinal disease. • Videofluoroscopic swallowing study—provides evidence of swallowing or esophageal dysfunction that can predispose to aspiration. Caution: could result in aspiration of contrast medium.

DIAGNOSTIC PROCEDURES

- Tracheal wash—for bacterial culture and sensitivity testing before administering antibiotics; infection often caused by multiple organisms with unpredictable susceptibility.
- Bronchoscopy—rarely indicated.
- Laryngeal function examination—always perform if patient anesthetized for other purposes; otherwise, after resolution of pneumonia if supportive clinical signs.



TREATMENT

- Oxygen and cage rest—respiratory distress.
- Ventilatory support—if not oxygen responsive. • Intravenous fluids—avoid overhydration, which can exacerbate secondary edema. • Oral intake—withhold until primary problem identified and managed. • Do not allow patient to remain laterally recumbent on one side for more than 2 hours. • Mild exercise and saline nebulization with coupage can facilitate airway clearance. • Airway suction—only if performed immediately following aspiration (such as during recovery from anesthesia).
- Airway lavage—contraindicated.



MEDICATIONS

DRUG(S)

- Antibiotic therapy—if signs of sepsis or severe compromise, ampicillin with sulbactam (20 mg/kg IV q8h) plus a fluoroquinolone IV. Adjust antibiotic selection based on results of airway cytology, C/S, and clinical response; continue for 10 days after resolution of clinical and radiographic signs. • Beta agonist bronchodilators—sometimes cause dramatic improvement but have the potential to worsen ventilation:perfusion mismatch; most often helpful in acute aspiration or with auscultable wheezes. • Short-acting corticosteroids—consider for up to 48 hours to combat inflammation associated with life-threatening aspiration.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Diuretics—generally contraindicated; drying of airways reduces mucociliary clearance. • Corticosteroids—contraindicated beyond initial stabilization; predispose patient to infection. • Fluoroquinolones and

chloramphenicol—can prolong clearance of theophylline-derivative bronchodilators; decrease theophylline dosage by 30–50% or prolong dosing interval.



FOLLOW-UP

PATIENT MONITORING

- Radiographs—evaluate every 2–7 days initially to determine appropriateness of treatment; then every 1–2 weeks. • If signs do not resolve or suddenly worsen—possible recurrence of aspiration or a secondary infection; repeat diagnostic evaluation, including tracheal wash or bronchoscopy.

PREVENTION/AVOIDANCE

- Predisposed patients undergoing anesthesia—cisapride (slow infusion, 1 mL/kg over 30 min) 1–2 hours pre-induction may decrease esophageal reflux. • Suction esophagus prior to extubation. • Antacids could decrease acid related lung injury in predisposed patients; may also increase risk of infection.

POSSIBLE COMPLICATIONS

- Secondary infection common.
- ALI/ARDS. • Abscessation or granuloma formation rare.

EXPECTED COURSE AND PROGNOSIS

- Prognosis—depends on severity of signs and ability to correct underlying disease. • Severe aspiration—can be fatal. • Recurrence—likely if underlying cause not addressed.



MISCELLANEOUS

SEE ALSO

- Acute Respiratory Distress Syndrome
- Megaeosphagus • Pneumonia, Bacterial

ABBREVIATIONS

- ALI/ARDS = acute lung injury/acute respiratory distress syndrome • C/S = culture and sensitivity • WBC = white blood cell

Suggested Reading

Tart KM, Babski DM, Lee JA. Potential risks, prognostic indicators, and diagnostic and treatment modalities affecting survival in dogs with presumptive aspiration pneumonia: 125 cases (2005–2008). J Vet Emerg Crit Care 2010, 20:319–329.

Zacuto AC, Marks SL, Osborn J, et al. The influence of esomeprazole and cisapride on gastroesophageal reflux during anesthesia in dogs. J Vet Intern Med 2012, 26:518–525.

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PNEUMONIA, BACTERIAL



BASICS

DEFINITION

Acquired inflammatory response to virulent bacteria in lung parenchyma characterized by exudation of cells and fluid into conducting airways and alveolar spaces.

PATHOPHYSIOLOGY

- Bacteria—enter the lower respiratory tract primarily by inhalation or aspiration; less commonly by the hematogenous route. Infection incites an overt inflammatory reaction.
- Tracheobronchial tree and carina—normally not sterile.
- Oropharyngeal bacteria—frequently aspirated; may be present for an unknown time period in the normal tracheobronchial tree and lung; can cause or complicate respiratory infection; presence complicates interpretation of airway and lung cultures.
- Respiratory infection—development depends on the complex interplay of many factors: inoculation site, number of organisms and their virulence, and age and resistance of the host.
- Bacteria produce extracellular proteins called invasins that impair host defenses and assist in the spread of bacteria.
- Viral infections—alter bacterial colonization patterns; increase bacterial adherence to respiratory epithelium; reduce mucociliary clearance and phagocytosis; thus allow resident bacteria to invade the lower respiratory tract.
- Foreign body—inoculates bacteria into a focal lung region and leads to obstructive pneumonia.
- Exudative phase—*Inflammatory hyperemia*; extravasation of high-protein fluid into interstitial and alveolar spaces.
- Leukocytic migration phase—leukocytes infiltrate the airways and alveoli; consolidation, ischemia, tissue necrosis, and atelectasis owing to bronchial occlusion, obstructive bronchiolitis, and impaired collateral ventilation.

SYSTEMS AFFECTED

Respiratory—primary or secondary infection

GENETICS

Heritable rhinitis/bronchopneumonia syndrome of Irish wolfhounds, unknown pathogenesis.

INCIDENCE/PREVALENCE

Common in both young and old dogs, less common in cats.

GEOGRAPHIC DISTRIBUTION

Widespread

SIGNALMENT

Species

Dog and cat

Breed Predilections

Dogs—sporting breeds, hounds, working breeds, and mixed breeds > 12 kg

Mean Age and Range

Dogs—range, 1 month–15 years; many cases in dogs < 1 year old

Predominant Sex

Dogs—60% males

SIGNS

Historical Findings

- Cough
- Labored breathing
- Exercise intolerance
- Anorexia and weight loss
- Lethargy
- Nasal discharge

Physical Examination Findings

- Cough
- Fever
- Difficult or rapid breathing
- Abnormal breath sounds on auscultation—increased intensity or bronchial breath sounds, crackles, and wheezes
- Weight loss
- Nasal discharge
- Lethargy
- Dehydration

CAUSES

Dogs

- Most common primary respiratory pathogens—*Bordetella bronchiseptica* and *Mycoplasma* spp.
- Most common gram-positive bacteria—*Staphylococcus*, *Streptococcus*, and *Enterococcus* spp.
- Most common gram-negative bacteria—*Escherichia coli*, *Klebsiella* spp., *Pseudomonas* spp., *Pasturella* spp.
- Anaerobic bacteria—found in pulmonary abscesses and various types of pneumonia (particularly with aspiration or foreign bodies); reported in ~ 20% of cases.

Cats

- Bacterial pathogens—poorly documented; *B. bronchiseptica*, *Pasteurella* spp., and *Moraxella* spp. most frequently reported.
- *Mycoplasma* spp. may be a primary pathogen in the lower respiratory tract.
- Carrier state—may exist; periods of shedding *B. bronchiseptica* after stress; infected queens may not shed organism prepartum but begin shedding post-partum, serving as a source of infection for kittens.

RISK FACTORS

- Preexisting viral infection.
- Regurgitation, dysphagia, or vomiting.
- Functional or anatomic defects—laryngeal paralysis, megaesophagus, cleft palate, primary ciliary dyskinesia.
- Reduced level of consciousness—stupor, coma, and anesthesia.
- Bronchial foreign body.
- Bronchiectasis.
- Immunosuppressive therapy—chemotherapy, glucocorticoids, immunosuppressives.
- Severe metabolic disorders—uremia, diabetes mellitus, hyperadrenocorticism.
- Sepsis.
- Age—very young more susceptible to fatal infections.
- Immunization status.
- Environment—housing, sanitation, ventilation.
- Phagocyte dysfunction—FeLV and diabetes mellitus.
- Complement deficiency—rare.
- Selective IgA deficiency—rare.
- Combined T-cell and B-cell dysfunction—rare.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Viral pneumonia—canine distemper virus, adenovirus, influenza virus, herpesvirus
- Protozoal pneumonia—toxoplasmosis
- Parasitic pneumonia—capillariasis, filarioidiasis
- Fungal pneumonia—histoplasmosis, blastomycosis, coccidioidomycosis, and cryptococcosis
- Eosinophilic pneumonia • Feline bronchial disease (asthma)
- Pulmonary abscess
- Pleural infection—pyothorax
- Bronchial foreign body

CBC/BIOCHEMISTRY/URINALYSIS

Inflammatory leukogram—neutrophilic leukocytosis with or without a left shift; absence does not rule out the diagnosis.

OTHER LABORATORY TESTS

- Arterial blood gas analysis—values correlate well with the degree of physiologic disruption; sensitive monitor of progress during treatment; $\text{PaO}_2 < 80 \text{ mmHg}$ on room air = mild or moderate hypoxemia; $\text{PaO}_2 < 60 \text{ mmHg}$ on room air = severe hypoxemia.
- Consider serology for canine influenza virus.
- Molecular diagnostics also available for viral and bacterial presence.

IMAGING

Thoracic Radiography

- Variable—diffuse, bronchointerstitial pattern to partial or complete alveolar infiltrates to consolidation.
- Most common—alveolar pattern characterized by increased pulmonary densities (margins indistinct; air bronchograms or lobar consolidation).
- More variable lung patterns in cats such as multifocal, patchy interstitial and alveolar changes and/or a diffuse nodular pattern.

P

DIAGNOSTIC PROCEDURES

- Microbiologic (aerobic, anaerobic bacterial, and mycoplasmal culture) and cytologic examinations for definitive diagnosis.
- Samples—transtracheal or endotracheal washing, bronchoscopy, bronchoalveolar lavage (with or without bronchoscope), or fine-needle lung aspiration.
- Degenerate neutrophils with septic inflammation (intracellular bacteria) predominating.
- Recent antibiotic administration—non-septic inflammation likely.
- Bacteria—not always obvious microscopically; always culture specimens, even if no bacteria are seen on cytology.

PATHOLOGIC FINDINGS

- Irregular consolidation in cranoventral regions.
- Consolidated lung—varies from dark red to gray-pink to more gray, depending on age of patient and nature of the process.
- Palpable firmness of the tissue.
- Nidus of inflammation—bronchiolar-alveolar junction.

PNEUMONIA, BACTERIAL

(CONTINUED)

- Early—bronchioles and adjacent alveoli filled with neutrophils and an admixture of cell debris, fibrin, and macrophages; necrotic to hyperplastic epithelium.
- Later—neutrophilic, fibrinous, hemorrhagic, or necrotizing inflammation, depending on virulence of bacteria and host response.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient—recommended with multisystemic signs (e.g., anorexia, high fever, weight loss, and lethargy).

NURSING CARE

- Maintain normal systemic hydration—important to aid mucociliary clearance and secretion mobilization; use a balanced multielectrolyte solution.
- Saline nebulization—results in more rapid resolution if used with physical therapy and systemic antibacterials.
- Physical therapy—chest wall coupage, tracheal manipulation to stimulate mild cough and postural drainage; may enhance clearance of secretions; always do immediately after nebulization; avoid allowing the patient to lie in one position for a prolonged time.
- Oxygen therapy—as warranted for patients with hypoxemia, signs of respiratory distress.

ACTIVITY

Restrict during treatment (inpatient or outpatient), except as part of physical therapy after aerosolization.

DIET

- P**
- Ensure normal intake with food high in protein and energy density.
 - Enteral or parenteral nutritional support—indicated in severely ill patients.
 - Use caution in feeding animals with megaesophagus, laryngeal dysfunction or surgery, pharyngeal disease, or recumbent patients.

CLIENT EDUCATION

Warn client that high morbidity and mortality are associated with severe hypoxemia and sepsis.

SURGICAL CONSIDERATIONS

Surgery (lung lobectomy)—can be required with pulmonary abscessation or broncho-pulmonary foreign body with secondary pneumonia; may be indicated if patient is unresponsive to conventional treatment and disease is limited to one or two lobes.



MEDICATIONS

DRUG(S) OF CHOICE

Antimicrobials

- Antimicrobials are best selected based on results of culture and susceptibility testing from tracheal wash or other pulmonary

specimens.

- Empiric antimicrobial therapy is justified when there is significant risk in obtaining adequate samples or if the time required to culture causes a life-threatening delay in treatment.
- Reasonable initial antimicrobial choices pending culture results include amoxicillin-clavulanic acid (15 mg/kg PO q12h) or cephalaxin (22–30 mg/kg PO q12h) with enrofloxacin (dogs, 5–10 mg/kg q12h or 10–20 mg/kg q24h; cats, maximum 5 mg/kg q24h), or trimethoprim-sulfonamide (15 mg/kg PO q12h).
- Gram-positive cocci—ampicillin (22 mg/kg PO q12h), ampicillin-sulbactam; amoxicillin; amoxicillin-clavulanic acid; azithromycin; chloramphenicol, erythromycin; gentamicin; trimethoprim-sulfonamide; first-generation cephalosporins.
- Gram-negative rods—enrofloxacin, chloramphenicol; gentamicin; trimethoprim-sulfonamide; amikacin; marbofloxacin; carboxypenicillins.
- *Bordetella*—doxycycline (5 mg/kg PO q12h); chloramphenicol; enrofloxacin; azithromycin.
- *Mycoplasma*—doxycycline, enrofloxacin, marbofloxacin, chloramphenicol.
- Anaerobes—amoxicillin-clavulanic acid; chloramphenicol; metronidazole; clindamycin; ticarcillin-clavulanic acid.
- Antimicrobial nebulization for *Bordetella*—gentamicin nebulization 5 mg/kg q24h for 5–7 days, typically adjunctive with systemic antimicrobials.
- Continue treatment for at least 10 days beyond clinical resolution and/or 1–2 weeks following radiographic resolution.

CONTRAINdications

- Anticholinergics and antihistamines—may thicken secretions and inhibit mucokinesis and exudate removal from airways.
- Antitussives—potent, centrally acting agents inhibit mucokinesis and exudate removal from airways, can potentiate pulmonary infection and inflammation.

POSSIBLE INTERACTIONS

Avoid use of theophylline and fluoroquinolones concurrently.

ALTERNATIVE DRUG(S)

- Expectorants—recommended by some clinicians; no objective evidence that they increase mucokinesis or mobilization of secretions.
- Bronchodilators—recommended by some clinicians to alleviate bronchospasm.



FOLLOW-UP

PATIENT MONITORING

- Monitor respiratory rate and effort.
- Complete blood count will normalize.
- Arterial blood gases—most sensitive monitor of progress, pulse oximetry can be helpful.
- Frequent thoracic auscultation.
- Thoracic radiographs—improve more slowly than the clinical appearance.

PREVENTION/AVOIDANCE

- Vaccination—against upper respiratory viruses; against *B. bronchiseptica* if a dog is boarded or exposed to large numbers of other animals.
- Catteries—environmental strategies to lower population density and improve hygiene help control outbreaks of bordetellosis.

POSSIBLE COMPLICATIONS

Sepsis can develop.

EXPECTED COURSE AND PROGNOSIS

- Prognosis—good with aggressive antibacterial and supportive therapy; more guarded in young animals, patients with immunodeficiency, and patients that are debilitated or have severe underlying disease.
- Prolonged infection—potential for chronic bronchitis or bronchiectasis in any patient.
- Mortality—associated with severe hypoxemia (low arterial oxygen concentration) and sepsis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Frequently develops secondary to underlying functional or anatomic abnormalities—cleft palate; tracheal hypoplasia; primary ciliary dyskinesia; laryngeal paralysis; megaesophagus or other esophageal dysmotility disorder.
- Bronchiectasis—both predisposing factor and potential complication.

AGE-RELATED FACTORS

- Young puppies and kittens—may have a poorer prognosis.
- Underlying functional and anatomic problems and immunodeficiencies—suspect in young patients.

PREGNANCY/FERTILITY/BREEDING

Bitches or queens infected with *B. bronchiseptica*—may transmit infection to neonates.

ABBREVIATION

- FeLV = feline leukemia virus

Suggested Reading

Dear JD. Bacterial pneumonia in dogs and cats. Vet Clin North Am Small Anim Pract 2014, 44(1):143–159.

Jameson PH, King LA, Lappin MR, et al. Comparison of clinical signs, diagnostic findings, organisms isolated, and clinical outcome in dogs with bacterial pneumonia: 93 cases (1986–1991). J Am Vet Med Assoc 1995, 206:206–209.

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Client Education Handout
available online

PNEUMONIA, EOSINOPHILIC



BASICS

DEFINITION

The fully developed inflammatory response to antigens in lung parenchyma characterized by exudation of eosinophils and fluid into lung interstitium, conducting airways, and alveolar spaces.

PATOPHYSIOLOGY

- Immunologic basis—supporting evidence generally accepted; mechanisms involved not yet clarified. • Eosinophilic infiltration and a predominance of CD4+ T cells in bronchoalveolar lavage fluid support the role of a dominant TH2 immune response in the lower airways. • Evolution of disease—likely determined by characteristics of antigens, host response, and regulation of that response.
- Antigens enter the lower respiratory tract by inhalation or hematogenous routes.
- Chronic exposure to antigens—elicits a humoral and cellular immune response.
- Allergic or hypersensitivity pulmonary disorders—associated with an abnormal humoral antibody response and a cell-mediated immunoregulatory defect.
- Immunoglobulin classes involved—IgE, IgG, and others. • High numbers of activated macrophages and T-lymphocytes and depressed suppressor T-cell activity—alter cell-mediated immunity. • Collagenolytic enzyme activity—increased. • Generally referred to as eosinophilic bronchopneumopathy although at least three disease patterns appear to exist: eosinophilic pneumonitis, eosinophilic bronchitis, and pulmonary eosinophilic granulomatosis.
- Severely affected dogs appear to develop marked granulomatous disease. • Heartworm disease with pneumonitis—microfilaria may become entrapped in the pulmonary circulation and trigger an immune response.
- Mortality—associated with severe hypoxemia (e.g., low arterial oxygen concentration) and (rarely) severe hemoptysis.

SYSTEMS AFFECTED

- Respiratory—lower respiratory tract primarily but nasal cavity can also be involved. • Cardiovascular—can develop cor pulmonale.

GENETICS

N/A

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

Widespread

SIGNALMENT

Species

Dog

Breed Predilections

Siberian husky, possibly

Mean Age and Range

All ages but more often young adults (4–6 years of age)

Predominant Sex

None

SIGNS

General Comments

Extremely variable, depending on the severity

Historical Findings

- Cough—unresponsive to antibacterial therapy
- Labored breathing
- Exercise intolerance.
- Anorexia
- Lethargy
- Weight loss
- Nasal discharge
- Fever (uncommon)

Physical Examination Findings

- Harsh, moist cough.
- Tachypnea or respiratory distress.
- Abnormal breath sounds on auscultation—increased-intensity breath sounds; crackles; wheezes; decreased sounds can occur.
- Weight loss.
- Yellow-green or mucopurulent nasal discharge.
- Fever (uncommon).

CAUSES

- Purported aeroallergens—spores or hyphae from fungi and actinomycetes; pollen; insect antigens; dust or storage mites, unidentified triggers of the immune response.
- Parasitic antigens—heartworm microfilaria, respiratory parasites.

RISK FACTORS

- Living in a heartworm-endemic area without receiving preventive medication.
- Dusty or moldy environment.
- Air pollution.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Parasitic pneumonia—capillariasis; paragonimiasis; dirofilariasis.
- Fungal pneumonia—histoplasmosis; blastomycosis; coccidioidomycosis; cryptococcosis.
- For eosinophilic pneumonitis—bacterial pneumonia; viral pneumonia (e.g., canine distemper virus and canine adenovirus); rickettsial pneumonia (e.g., ehrlichiosis and Rocky Mountain spotted fever); protozoal pneumonia (e.g., toxoplasmosis); congestive heart failure; bartonellosis.
- For eosinophilic bronchitis—infectious tracheobronchitis; chronic bronchitis.
- For pulmonary eosinophilic granulomatosis—neoplasia (including lymphomatoid granulomatosis); pulmonary abscess; bronchial foreign body.

CBC/BIOCHEMISTRY/URINALYSIS

- Inflammatory leukogram—neutrophilic leukocytosis with or without a left-shift, eosinophilia, basophilia, or monocytosis.
- Absence of eosinophilia does not exclude diagnosis.
- Hyperglobulinemia—suggests chronic antigenic stimulus; rule out occult dirofilariasis.

OTHER LABORATORY TESTS

Arterial Blood Gas Analysis

- Values correlate well with the degree of physiologic disruption; sensitive monitor of patient's progress during treatment.
- Hypoxemia—mild or moderate, $\text{PaO}_2 < 80 \text{ mmHg}$ on room air; severe, $\text{PaO}_2 < 60 \text{ mmHg}$ on room air.

Other

- Heartworm microfilaria and antigen tests—positive results suggest dirofilariasis or eosinophilic pneumonitis associated with microfilaria trapped in the lung. Multiple tests can be required to rule out disease.
- Fecal flotation and Baermann sedimentation.
- Protein electrophoresis— β -globulin spike (hyperbeta-globulinemia) often found with occult dirofilariasis.

IMAGING

- Radiographic findings depend on extent and severity of disease.
- Thoracic radiographs—help document the severity of pulmonary artery disease; reveal interstitial pneumonitis in dogs with dirofilariasis.
- Eosinophilic pneumonitis—linear or miliary interstitial pattern that resembles changes seen with early pulmonary edema or fungal pneumonia; alveolar pattern characterized by increased pulmonary densities with indistinct margins in severely affected patients; tortuous, large pulmonary arteries and right-sided cardiomegaly in patients with dirofilariasis.
- Eosinophilic bronchitis—bronchial pattern with thickened bronchi extending into the periphery of the lung (tram/railroad track and donut signs); bronchiectasis in chronic cases.
- Eosinophilic granuloma—multiple nodular lesions of variable sizes in different lung lobes; patchy, focal alveolar densities; tracheo-bronchial lymphadenopathy possible.

P

DIAGNOSTIC PROCEDURES

- Transtracheal or endotracheal wash appropriate for sample collection.
- Bronchoscopy; yellow-green mucus, polypoid mucosal proliferation, partial airway collapse. Occlusive eosinophilic plaques or granulomas sometimes visible within airways.
- Bronchoalveolar lavage—with or without bronchoscope.
- Bacterial and mycoplasmal culture of bronchoalveolar lavage fluid is recommended to rule-out bacterial infection. Occasionally, concurrent bacterial infection can be identified in dogs with eosinophilic lung disease.
- Fine-needle lung aspiration and examination.
- Cytologic examination of aspirates, washings, or brushings—definitive diagnosis: eosinophilic inflammation predominates; may note other types of inflammatory cells; carefully examine specimens for antigenic sources (e.g., parasites, fungi, or neoplasia).
- Consider intradermal skin or serologic allergen testing—rarely may identify allergens.
- Fecal examinations—routine flotation, direct

PNEUMONIA, EOSINOPHILIC

(CONTINUED)

smear, sediment examination, and Baermann technique to rule out parasitic pneumonia; negative test can occur due to intermittent shedding and empirical therapy warranted in some cases.

PATHOLOGIC FINDINGS

- Gross—diffuse, patchy, or nodular firm lesions; usually pale or mottled.
- Histopathologic—eosinophilic, lymphocytic, and macrophagic infiltration of alveolar walls and alveolar spaces; as disease progresses, interstitial infiltrative process becomes fibrotic with obliteration of alveolar spaces, and granulomas can be dispersed within the interstitial fibrosis. Upper respiratory tract epithelium can also be involved with eosinophilic infiltration.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient—recommended with multisystemic signs (e.g., anorexia, weight loss, or lethargy).

NURSING CARE

- Dehydration—hinders mucociliary clearance and secretion mobilization; maintain normal systemic hydration with a balanced multielectrolyte solution.
- Supplemental oxygen—for respiratory distress.

ACTIVITY

Restricted during treatment (inpatient or outpatient).

DIET

Ensure normal intake.

P

CLIENT EDUCATION

Warn client that morbidity and mortality are associated with severe hypoxemia.

SURGICAL CONSIDERATIONS

Lung lobectomy can be required with large granulomas.



MEDICATIONS

DRUG(S) OF CHOICE

- Corticosteroids—prednisolone or prednisone at 2 mg/kg/day until clinical signs begin to resolve (typically 2–3 weeks); then taper slowly (over months). Maintenance dosages of prednisone are often required long-term (0.125–0.5 mg/kg q48h or every 3 or 4 days for 4–6 months or longer).
- Following adequate control of disease and/or due to side effects of systemic glucocorticoids, inhaled corticosteroids (e.g.,

fluticasone propionate) can be used in conjunction with a spacing chamber and facemask. • Antibiotic therapy indicated only if active infection documented on airway culture. Prophylactic therapy could lead to development of antimicrobial resistance.

- Heartworm adulticidal therapy—for heartworm-positive patient; initiate after the patient has been stabilized with corticosteroids and rest. • Itraconazole or ketoconazole—use antifungal drugs only if the fungal infection is confirmed by cytologic examination or culture. • Hypo sensitization—allergy shots based on results of intradermal skin or serologic testing can be attempted but is not the treatment of choice in most patients. Most dogs will still require steroid therapy.

CONTRAINdications

N/A

PRECAUTIONS

N/A

ALTERNATIVE DRUG(S)

- Other immunosuppressive drugs (e.g., cyclosporine)—can use when corticosteroids are contraindicated or have been ineffective, although inhaled steroids are preferred. No trial results are available to date.
- Bronchodilators—can be helpful, particularly if wheezes are auscultated or labored respiratory effort is observed; see Bronchitis, Chronic.



FOLLOW-UP

PATIENT MONITORING

- Complete blood count will show resolution of peripheral eosinophilia or neutrophilia.
- Arterial blood gases—most sensitive monitor of progress. Can remain abnormal even with successful management of disease.
- Auscultate patient thoroughly several times daily. • Thoracic radiographs—improve more slowly than the clinical appearance.

PREVENTION/AVOIDANCE

- Routine heartworm-prevention medication.
- Consider changing patient's environment if an Aeroallergen is suspected.

POSSIBLE COMPLICATIONS

Pulmonary embolization—dogs treated with adulticidal therapy for dirofilariasis.

EXPECTED COURSE AND PROGNOSIS

- Prognosis good for mild-to-moderate cases; many patients require long-term treatment with steroids. • If allergen can be identified and eliminated—suspect improved prognosis.

- Heartworm infection—prognosis depends on severity of pulmonary hypertension, cor pulmonale, and embolization. • Eosinophilic granulomatosis—prognosis guarded; often disease is progressive.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Dirofilariasis • Bronchopulmonary fungal infection

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Corticosteroids and other immunosuppressive drugs are contraindicated in pregnant animals.

SYNOMYMS

- Allergic alveolitis • Allergic bronchitis
- Bronchitic pulmonary eosinophilia
- Eosinophilic bronchitis or bronchopneumopathy • Eosinophilic pneumonia/pneumonitis • Eosinophilic pulmonary granulomatosis • Extrinsic allergic alveolitis • Hypersensitivity pneumonitis
- Occult heartworm pneumonia • Parasitic pulmonary eosinophilia • Pulmonary infiltrates with eosinophilia (PIE)

SEE ALSO

- Cough • Dyspnea and Respiratory Distress
- Heartworm Disease—Dogs
- Lymphomatoid Granulomatosis • Panting and Tachypnea • Respiratory Parasites

Suggested Reading

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PNEUMONIA, FUNGAL



BASICS

DEFINITION

Inflammation of the pulmonary interstitial, lymphatic, and peribronchial tissues caused by deep mycotic infection.

PATHOPHYSIOLOGY

- Mycelial fungal elements—inhaled from contaminated soil or plant debris; organisms then colonize the lungs.
- Dimorphic fungi such as *Blastomyces dermatitidis*, *Histoplasma capsulatum*, *Coccidioides immitis*—yeast phase at body temperature. Invasive fungal infections with *Aspergillus* spp. follow inhalation of airborne spores with growth as mycelia within tissue.
- Systemic dissemination of yeast from the lungs common in dogs and cats.
- Pulmonary interstitial and alveolar involvement—can cause hypoxia.
- Airway involvement—causes cough.
- Cell-mediated immune response leads to pyogranulomatous inflammation.
- Pulmonary complications include interstitial and/or bronchial pneumonia, pleural effusion, mediastinal granuloma formation, ARDS, and pulmonary thromboembolism.

SYSTEMS AFFECTED

- Depend on the specific fungal disease.
- Blastomycosis**—respiratory involvement in ~85% of cases; diffuse interstitial, alveolar, or bronchial pneumonia most common; solitary mass lesions can be seen, especially in cats; tracheobronchial lymphadenopathy can contribute to cough; nasal infection rare. Multisystemic involvement of skin, lymph nodes, eyes, bone, reproductive tract, and CNS often seen.
- Histoplasmosis**—diffuse interstitial pneumonia common, especially in cats; perihilar or mediastinal lymphadenopathy contributes to cough. Multisystemic involvement of gastrointestinal tract, liver, lymph nodes, spleen, bone marrow, eyes, bone, and CNS often seen.
- Coccidioidomycosis**—diffuse interstitial or bronchial pneumonia common in dogs but less common in cats; perihilar or mediastinal lymphadenopathy common. Multisystemic involvement of bone, skin, eyes, lymph nodes, and CNS often seen.
- Cryptococcosis**—nasal cavity involvement most common in cats, neurologic system in dogs. Skin and other organs also affected.
- Systemic aspergillosis—*Aspergillus terreus***: pneumonia, renal and bone involvement common.

GENETICS

Breed susceptibilities may be related to defects in cell-mediated immunity.

INCIDENCE/PREVALENCE

Depends on geographic distribution.

GEOGRAPHIC DISTRIBUTION

- Blastomycosis**—endemic in US Southeast and Midwest along the Mississippi, Ohio, Missouri, and Tennessee rivers and southern Great Lakes; also in southern Mid-Atlantic States, Pacific Northwest, and southern Canada from east coast to prairie regions of southern Saskatchewan and Manitoba.
- Histoplasmosis**—similar to but more widely distributed than blastomycosis; pockets of disease in Texas, Oklahoma, and California.
- Coccidioidomycosis**—US Southwest from Texas to California. Northern Mexico and parts of South America.
- Cryptococcosis** and aspergillosis—worldwide.

SIGNALMENT

Species

Dog and less commonly cat (except cryptococcosis)

Breed Predilection

- Systemic mycosis**—large-breed, hunting or field trial dogs; Doberman pinschers and rottweilers appear predisposed to disseminated disease.
- Systemic aspergillosis**—German shepherds over-represented. **Cryptococcosis**—cocker spaniels over-represented.

Mean Age and Range

- Young animals (< 4 years) predisposed.
- Any age can be affected.

Predominant Sex

Males affected two to four times more often than females.

SIGNS

General Comments

Multisystemic illness depends on organ systems involved.

Historical Findings

- Chronic weight loss and inappetence.
- Oculonasal discharge.
- Coughing—can be prominent but seen inconsistently even with marked pulmonary disease.
- Tachypnea or exercise intolerance common.
- Labored breathing—more common in cats; sign of severe disease in both dogs and cats.
- Acute blindness or blepharospasm—if eyes are affected.
- Papules and cutaneous nodules—common but often missed until draining tracts appear.
- Lameness—if bones affected or if osteomyelitis develops.
- Seizures, ataxia, behavior change—if CNS affected.

Physical Examination Findings

- Emaciation—in chronically affected patients.
- Fever—about 50% of patients.
- Harsh, loud breath sounds, crackles in cats, cough on tracheal palpation.
- Dyspnea—at rest with severe disease.
- Lymphadenopathy—common in dogs with dimorphic fungal infections.
- Blastomycosis (dogs)**—cutaneous and subcutaneous nodules with draining tracts; chorioretinitis; granulomatous retinal detachment common.
- Coccidioidomycosis (dogs)**—lameness and pain from osteomyelitis, pericardial disease;

cats—skin lesions.

- Histoplasmosis (dogs)**—emaciation and bloody diarrhea; cats—skin lesions.
- Cryptococcosis**—nasal cavity and soft tissue infection common in cats; chorioretinitis in dogs and cats.

CAUSES

- Primary route of infection: *Blastomyces dermatitidis*—lungs, *Histoplasma capsulatum*—lungs and possibly gastrointestinal tract, *Coccidioides immitis*—lungs.
- Cryptococcus neoformans* and *gattii*—nasal cavity, with direct extension into the eyes or CNS, lungs less important.
- Aspergillus* spp.—nasal cavity and lungs.

RISK FACTORS

- Blastomycosis**, histoplasmosis, and cryptococcosis—environmental exposure to soils rich in organic matter; blastomycosis and cryptococcosis—exposure to bird droppings or other fecal matter; blastomycosis—living near water.
- Coccidioidomycosis**—environmental exposure to sandy, alkaline soil after periods of rainfall; outdoor activities (hunting and field trials).
- FeLV** does not appear to be a risk factor and **FIV** may be minor risk factor.
- Prednisone**—may worsen the disease.
- Antineoplastic chemotherapy**.
- Lymphoreticular neoplasia**.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Metastatic neoplasia
- Eosinophilic lung disease
- Lymphomatoid granulomatosis
- Lymphoreticular and histiocytic neoplasia
- Idiopathic pyogranulomatous disease
- FIP or other vasculitic disease
- Parasitic pneumonia
- Bacterial pneumonia
- Chronic bronchial disease
- Pulmonary edema
- Pulmonary thromboembolism

P

CBC/BIOCHEMISTRY/URINALYSIS

- Moderate leukocytosis with or without a left-shift.
- Lymphopenia common.
- Leukopenia, thrombocytopenia, non-regenerative anemia—with histoplasmosis.
- Hyperglobulinemia and hypoalbuminemia common.
- Hypercalcemia—occasionally.
- Liver enzyme activities—more likely to be increased with histoplasmosis.
- Urinalysis usually normal; proteinuria—occasionally seen.
- Organisms—can be seen in urine (rarely, except for *Aspergillus*) if kidneys or lower urinary tract are affected.

OTHER LABORATORY TESTS

- Antigen can be detected in serum or urine by enzyme immunoassay for diagnosis of *Blastomyces* or *Histoplasma*—sensitivity and specificity high. Cross-reaction occurs between *Blastomyces* and *Histoplasma*. Antigen testing for *Coccidioides* is insensitive.
- Serologic (antibody) testing for blastomycosis and histoplasmosis—false-

PNEUMONIA, FUNGAL

(CONTINUED)

positive and false-negative results common. Positive titer for *Coccidioides* using heat-precipitated AGID consistent with infection with relevant clinical history and signs. • Latex agglutination test—for capsular antigen; highly reliable for cryptococcosis. • Cytologic or histologic identification of the organism—definitive diagnosis. • Culture—not usually necessary; can be difficult to isolate and risky due to zoonosis.

IMAGING

- Thoracic radiography—diffuse nodular interstitial and peribronchial infiltrates; nodular densities can coalesce to granulomatous masses with indistinct edges; tracheobronchial lymphadenopathy common; large focal granulomas more likely in cats.
- Appendicular or axial skeleton radiography—osteolysis with periosteal proliferation; soft tissue swelling.
- Abdominal ultrasonography—granulomas or large lymph nodes. • Ocular ultrasonography—retrobulbar mass, posterior uveitis.

DIAGNOSTIC PROCEDURES

- Impression smear or aspirate of a skin nodule—most likely to yield organisms.
- Fine-needle lung aspirate—possibly more diagnostic than tracheal aspirate or bronchoalveolar lavage specimen. • Lymph node aspirate or biopsy. • CSF tap—with cryptococcosis. • Bone marrow or liver/splenic aspirate—with histoplasmosis.
- Biopsy—may be needed.

PATHOLOGIC FINDINGS

- Pyogranulomatous inflammation.
- Organisms—usually seen with blastomycosis, histoplasmosis, cryptococcosis, and aspergillosis; difficult to find with coccidioidomycosis.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—if patient is stable. • Inpatient evaluation and treatment—dehydration, anorexia, and severe hypoxia.

NURSING CARE

Administration of fluids, oxygen, and antibiotics as needed.

DIET

- Feed high-quality protein, calorically dense food. • Histoplasmosis accompanied by marked gastrointestinal involvement—feed highly digestible food.

CLIENT EDUCATION

- Complete response to treatment in <70% of dogs and a smaller percentage of cats.
- Treatment is expensive and will be long term (> 2 months). • Clean environmental areas of highly organic matter or feces.

SURGICAL CONSIDERATIONS

Focal granulomas or glaucomatous; painful eyes can require removal.



MEDICATIONS

DRUG(S) OF CHOICE

- Itraconazole 5–10 mg/kg PO daily; must be given with food. Liquid suspension more bioavailable in cats (dose 1–1.5 mg/kg/day PO). • Fluconazole 10 mg/kg PO q12h; drug of choice for cryptococcosis and patients with CNS or urinary tract involvement. Usually requires longer treatment. • Lipid-complex amphotericin B 1–2 mg/kg IV q48h for 12 treatments; nephrotoxicity low; diuresis not required. • Posaconazole 5 mg/kg PO q24h with food may be more effective for aspergillosis.

CONTRAINDICATIONS

Corticosteroids are relatively contraindicated but may be required to reduce inflammation during initial treatment in severely dyspneic patients.

PRECAUTIONS

- Azole drugs—do not use with severe liver disease. • Amphotericin B—do not use in azotemic or dehydrated patients; stop use if BUN > 50 mg/dL or creatinine > 3 mg/dL.
- Itraconazole and the other azole drugs—anorexia; increase in liver enzymes; cutaneous vasculitis.

POSSIBLE INTERACTIONS

Antacids and anticonvulsants—can lower blood concentration of itraconazole.

ALTERNATIVE DRUG(S)

- Ketoconazole 10–30 mg/kg PO q12h; can be effective; higher incidence of side effects; longer treatment is necessary; relapse common. • Amphotericin B 0.5 mg/kg (dogs) or 0.25 mg/kg (cats) IV three times/week to a total dose of 8 mg/kg if used alone or 4 mg/kg if used with an azole drug; administer in 200–500 mL of D₅W after saline diuresis; best used with itraconazole or ketoconazole for severely affected patients. • Amphotericin B—alternative; 0.5–0.8 mg/kg 2–3 times per week; to reduce nephrotoxicity, can give subcutaneously diluted in 0.45% saline/2.5% dextrose solution (400 mL for cats, 500 mL for dogs < 20 kg, 1,000 mL for dogs > 20 kg). • Voriconazole 3–4 mg/kg PO q12h for invasive aspergillosis. • Terbinafine 30–40 mg/kg PO q12h can be added to azole treatment regimens in resistant infections.



FOLLOW-UP

PATIENT MONITORING

- Liver enzymes—evaluated monthly during azole therapy • BUN and creatinine—

measure before each dose of amphotericin B.

- Thoracic radiographs—reevaluate before discontinuing treatment. • Urine antigen testing for *Blastomyces/Histoplasma*—use to monitor therapy.

PREVENTION/AVOIDANCE

Reduce possible exposure.

POSSIBLE COMPLICATIONS

- Blindness is usually permanent. • Renal failure from amphotericin B.

EXPECTED COURSE AND PROGNOSIS

- Blastomycosis—requires a minimum of 2 months of treatment, 60–70% of dogs cured by itraconazole. Dogs with dyspnea or hypoxemia have poorer prognosis. • Others—continue until 1 month past remission.
- Systemic aspergillosis—poor prognosis.
- Relapse—can occur up to 1 year after treatment.



MISCELLANEOUS

AGE-RELATED FACTORS

Young animals predisposed

ZOONOTIC POTENTIAL

Infections in people—primarily from a common environmental source; no direct transmission from animals to humans, except by penetrating wounds contaminated by the organism; needle stick injury.

PREGNANCY/FERTILITY/BREEDING

- Fungal abortion possible. • Azole antifungals—teratogenic; do not use in pregnant animals.

SEE ALSO

- Aspergillosis • Blastomycosis
- Coccidioidomycosis • Cryptococcosis
- Histoplasmosis

ABBREVIATIONS

- AGID = agar gel immunodiffusion • ARDS = acute respiratory distress syndrome • CNS = central nervous system • CSF = cerebrospinal fluid • FeLV = feline leukemia virus • FIP = feline infectious peritonitis • FIV = feline immunodeficiency virus

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Consulting Editor Lynelle R. Johnson



Client Education Handout available online

PNEUMONIA, INTERSTITIAL



BASICS

DEFINITION

A form of pneumonia in which the inflammatory process occurs in alveolar walls and interstitial space.

PATHOPHYSIOLOGY

- Results from either aerogenous injury to the alveolar epithelium (type I or II pneumocytes) or hematogenous injury to the alveolar capillaries; may be triggered by infectious agents.
- Alveolar wall damage often occurs secondary to inflammation and antigen-antibody complex deposition.
- Progression from acute to chronic interstitial pneumonia can occur leading to alveolar fibrosis ± interstitial mononuclear cell accumulation and persistent type II pneumocyte hyperplasia.

SYSTEMS AFFECTED

- Respiratory.
- Cardiovascular (if cor pulmonale develops).

GENETICS

- IPF is breed associated (West Highland white terriers/terrier breeds); a definitive genetic defect is not known.

INCIDENCE/PREVALENCE

Incompletely understood

GEOGRAPHIC DISTRIBUTION

- Infectious organisms: *Aelurostrongylus abstrusus*—Europe, United States, Australia
- *Angiostrongylus vasorum*—Europe, Africa, South America, North America.
- *Leishmania chagasi*—South and Central America.
- H3N2—China, Chicago (USA).
- Pneumocystis and toxoplasmosis—worldwide.

SIGNALMENT

- Canine distemper virus—dogs 3–6 months of age. Greyhounds, Siberian huskies, Weimaraners, Samoyeds, and Alaskan malamutes overrepresented.
- Endogenous lipid pneumonia (EnLP)—older cats of either sex.
- Pulmonary interstitial lung disease—middle- to old-aged West Highland white terrier, ± cairn terriers and bull terriers.
- Feline idiopathic pulmonary fibrosis-like disease—middle-aged to older cats.
- *Pneumocystis jirovecii*—miniature dachshunds <1 year of age at risk, Cavalier King Charles Spaniels.
- Toxoplasmosis—middle-aged male cats.

SIGNS

General Comments

Depends on severity of disease.

Historical Findings

Tachypnea, coughing, respiratory difficulty, exercise intolerance.

Physical Examination Findings

- Open-mouth breathing, end-inspiratory and early expiratory crackles, orthopnea,

cyanosis, ± hemoptysis.

- Animals with paraquat toxicity often display vomiting, oliguria, diarrhea, and oropharyngeal ulcers (± hyperexcitability and neurologic signs in the early phase).
- Retinitis, uveitis, neurologic signs, and/or gastrointestinal signs can be seen with toxoplasmosis.

CAUSES & RISK FACTORS

Congenital

BOOP secondary to primary ciliary dyskinesia.

Metabolic

Uremic pneumonitis ± BOOP, hepatic disease, or pancreatitis in cats.

Neoplastic

Bronchiectasis or BOOP, pulmonary carcinoma associated with pulmonary fibrosis in cats.

Idiopathic

Pulmonary interstitial fibrosis and DIP, some cases of EnLP, BOOP, primary pulmonary alveolar proteinosis.

Inflammatory

EnLP most common in cats with bronchitis, bronchiectasis or necrotizing bronchiolitis.

Infectious

- Dogs—canine distemper virus, canine adenovirus-2, H3N2 or H3N8 influenza virus, *Leishmania chagasi*, *Pneumocystis jirovecii*, *Angiostrongylus vasorum*, *Toxoplasma*.
- Cats—*Aelurostrongylus abstrusus*, *Toxoplasma*, FIV, influenza virus (anthropozotic transmission described).

Toxic

Inhalation of dusts, gases, or vapors, thiacetarsemide, aspiration of petroleum-based products in cats, secondary PAP, paraquat toxicity, silicosis, asbestosis.

Vascular

Thromboembolism, circulating larval migrants

RISK FACTORS

- Immunosuppression, inadequate vaccination or preventative, and exposure to other animals can predispose to viral or parasitic pulmonary disease.
- Inhalation of toxic material or gases may predispose to pulmonary fibrosis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Airway disease
- Bronchopneumonia
- Heartworm disease
- Embolic pneumonia
- Granulomatous pneumonia
- Neoplasia
- Cardiac disease

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilia, eosinophilia, lymphocytosis, hyperglobulinemia possible; polycythemia if chronically hypoxic.
- Thrombocytopenia with *Angiostrongylus vasorum*.
- Neutropenia or high liver enzymes and hyperbilirubinemia

possible with *Toxoplasma*.

- High liver enzymes and hyperbilirubinemia (dogs only)
- possible with hepatotoxicity due to thiacetarsemide therapy ± paraquat toxicity.
- Severe azotemia and isosthenuria with uremic pneumonitis.

OTHER LABORATORY TESTS

- Arterial blood gas measurement and calculation of alveolar-arterial (A-a) gradient to assess degree of respiratory impairment; $\text{PaO}_2 < 80 \text{ mmHg}$ indicates hypoxemia, A-a gradient > 15 is abnormal.
- Serologic and other tests for infectious causes.
- Fecal Baermann examination for *Aelurostrongylus abstrusus* or *Angiostrongylus vasorum*.
- Toxicologic analysis of the urine or serum to diagnose paraquat toxicity in live animals.
- Coagulation testing with *Angiostrongylus*.
- Immunodiagnostic testing for exposure to *Leishmania*.

IMAGING

Thoracic Radiographic Findings

- A focal or diffuse, mild to severe interstitial to bronchial to alveolar pattern can be present, dilated bronchi with bronchiectasis or BOOP.
- Right heart ± PA enlargement and hepatosplenomegaly if secondary pulmonary hypertension.
- Pleural effusion occasionally seen.

Computed Tomography

CT characteristics include ground-glass opacification, peribronchovascular thickening, and parenchymal banding.

DIAGNOSTIC PROCEDURES

- Electrocardiography—arrhythmias can occur with severe hypoxia or systemic disease.
- Open lung biopsy required for definitive diagnostic test.
- Endotracheal or transtracheal wash, bronchoscopy with bronchoalveolar lavage, and/or fine-needle aspirate of lungs might be useful (e.g., may visualize trophozoite or cysts of *Pneumocystis jirovecii* or *Toxoplasma* or see L1 larvae with *Aelurostrongylus abstrusus* or *Angiostrongylus vasorum*); cultures can reveal secondary bacterial infections. With pulmonary alveolar proteinosis, an opaque white material is retrieved from airway wash.
- Echocardiogram can document pulmonary hypertension.

PATHOLOGIC FINDINGS

- *Aelurostrongylus abstrusus*—greenish nodules in lungs, eggs and larvae in the alveolar spaces with foreign body type reaction (surrounded by mononuclear cells and giant cells), submucosal gland hypertrophy, and smooth muscle hypertrophy in airway and vessel walls.
- *Angiostrongylus vasorum*—thrombosing arteritis and fibrotic peribronchitis, parasites in arterioles.
- BOOP—polypoid plugs of loose, fibrous tissue fill bronchioles and alveoli, foamy macrophages within alveoli, variable inflammatory infiltrate with type II pneumocyte reactivity.
- Interstitial lung

PNEUMONIA, INTERSTITIAL

(CONTINUED)

disease in the West Highland white terrier—diffuse, mature pulmonary fibrosis (most common in caudal lung lobes), multifocal areas of accentuated subpleural and peribronchiolar fibrosis, thickening of the alveolar septum due to excess collagen in the extracellular matrix. • IPF-like disease in the cat lacks inflammation and may be associated with pulmonary carcinoma. Typical changes include multifocal distribution of interstitial fibrosis with foci of fibroblast/myofibroblasts, alveolar epithelial metaplasia, and interstitial smooth muscle metaplasia/hyperplasia.

- *Leishmania chagasi* is characterized by chronic and diffuse interstitial pneumonitis and thickened inter-alveolar septae in some cases.
- Lipid pneumonias—macroscopic lesions can include subpleural, parenchymal, or perivascular white, firm nodules. Mixed pattern of inflammation with accumulation of lipid-laden macrophages, cholesterol clefts, and multinucleated giant cells.
- Paraquat toxicity—lungs are heavy, edematous, and hemorrhagic. Emphysematous bullae and pneumomediastinum are commonly present.
- PAP—alveolar spaces are distended with a PAS staining eosinophilic proteinaceous material. Intra-alveolar cholesterol clefts and mucus-laden macrophages with mild mixed-inflammatory infiltrates are common.
- Uremic pneumonitis—pulmonary edema and calcification of smooth muscle and/or alveolar walls.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient care and monitoring for animals with evidence of respiratory distress.

NURSING CARE

- Oxygen therapy.
- Minimize exposure to house dust, vapors, chemical fumes, or tobacco smoke.
- Humidification of inspired air.
- PAP—therapeutic bronchoalveolar lavage.
- Antimicrobial therapy—as indicated by results of culture and susceptibility.

ACTIVITY

- Exercise restriction as needed.
- Harness preferred to collar.

DIET

Weight loss if obese.

CLIENT EDUCATION

Palliative care employed.

SURGICAL CONSIDERATIONS

Definitive diagnosis of interstitial lung disease requires histopathology; it is best preceded by CT to determine an appropriate site for biopsy.



MEDICATIONS

DRUG(S) OF CHOICE

- Inhaled corticosteroids (e.g., fluticasone, 1 puff q12h) using a spacing chamber and facemask.
- Bronchodilators can be helpful in reducing respiratory effort: extended-release theophylline (dog, 10 mg/kg PO q12h; cat, 15–19 mg/kg q24h in the evening), terbutaline sulfate (dog or cat, 0.01 mg/kg SC, IM, or IV q8–12h). Inhaled bronchodilators can also be used.
- Aeluropromys abstrusus*—fenbendazole 50 mg/kg PO q24h for 14 days (off label), ivermectin (400 µg/kg, SC, twice at a 3-week interval), or spot-on selamectin 45 mg (once).
- Angiostrongylus vasorum*—levamisole, 20–40 mg/kg PO q48h for 5 treatments ± aspirin ± corticosteroids. Alternative therapies include fenbendazole, mebendazole, and ivermectin.
- BOOP—corticosteroid use has been reported.
- Idiopathic pulmonary fibrosis—no effective therapy.
- Anti-inflammatory steroid therapy with prednisolone (0.5–1 mg/kg PO q24–48h often used) and bronchodilators, antitussives, or antibiotics if indicated. Pirfenidone not yet investigated.
- Leishmania chagasi*—meglumine antimonate 100 mg/kg IV or SC q24h for 3–4 weeks or sodium stibogluconate 30–50 mg/kg IV or SC q24h for 3–4 weeks.
- Paraquat toxicity—vomition and activated charcoal therapy is indicated if recent ingestion is known. Supportive care, diuresis using furosemide (most effective in the first 3 days following ingestion), ± immunosuppressive dexamethasone, cyclophosphamide, nicotinamide, superoxide dismutase, and vitamin A.

CONTRAINDICATIONS/PRECAUTIONS

Immunosuppressive therapy can exacerbate secondary infections.



FOLLOW-UP

PATIENT MONITORING

- Have owners observe clinical response to therapy, monitor respiratory rate and effort.
- Repeat physical examination/chest auscultation, chest radiographs, lab test, and arterial blood gas analysis as indicated.

PREVENTION/AVOIDANCE

- Avoid proximity to toxic fumes or paraquat.
- Vaccinate and deworm animals.
- Appropriate insect and rodent control.
- Avoid ingestion by pets of frogs, lizards, rodents, and birds.

POSSIBLE COMPLICATIONS

- Secondary pulmonary infections possible.
- Pulmonary hypertension can develop.

EXPECTED COURSE AND PROGNOSIS

- Guarded to poor with interstitial pneumonia caused by infectious agents or uremic pneumonitis.
- Poor long-term prognosis with idiopathic pulmonary fibrosis (mean survival time is 17 months in dogs and 5.5 months in cats).
- Paraquat toxicity—commonly fatal in dogs.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Pulmonary carcinoma—associated with IPF in cats.

AGE-RELATED FACTORS

Young, free-roaming animals are more likely to succumb to infectious diseases.

ZOONOTIC POTENTIAL

Toxoplasmosis, if animal is shedding oocysts.

PREGNANCY/FERTILITY/BREEDING

Transplacental infection with *Toxoplasma* and canine distemper virus is possible.

SEE ALSO

- Bronchiectasis
- Canine Distemper
- Canine Infectious Respiratory Disease
- Feline Immunodeficiency Virus Infection
- Leishmaniasis
- Primary Ciliary Dyskinesia
- Toxoplasmosis

ABBREVIATIONS

- BOOP = bronchiolitis obliterans with organizing pneumonia
- CT = computed tomography
- DIP = desquamative interstitial pneumonitis
- EnLP = endogenous lipid pneumonia
- FIV = feline immunodeficiency virus
- IPF = idiopathic pulmonary fibrosis
- PAP = pulmonary alveolar proteinosis
- PAS = periodic acid-Schiff

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Client Education Handout
available online

PNEUMOTHORAX



BASICS

DEFINITION

- Air accumulation in the pleural space; categorized as traumatic or spontaneous.
- Closed pneumothorax—no defects in the thoracic wall.
- Open pneumothorax—defect in the thoracic wall resulting in communication of the pleural space with the atmosphere.
- Tension pneumothorax—where pleural pressure in a closed pneumothorax exceeds atmospheric pressure; created by unidirectional transfer of air into the pleural space.

PATHOPHYSIOLOGY

- The pleural space is normally a potential space between visceral and parietal pleura containing a thin layer of fluid that contributes to “tethering” of the lungs to the thoracic wall. Air accumulation in the pleural space causes the lungs to collapse away from the thoracic wall.
- Closed pneumothorax—air leakage from the pulmonary parenchyma, large airway, or esophagus.
- Tension pneumothorax—typically due to a pleural or pulmonary flap-like defect that opens on inspiration to allow leakage of air into the pleural space and closes during expiration. Development of high intrathoracic pressure can reduce venous return to the heart.
- Open pneumothorax—may or may not have associated pulmonary pathology; pleural pressure equals atmospheric pressure, leading to lung collapse.
- Spontaneous pneumothorax associated with underlying pulmonary disease that ruptures, allowing air leakage.
- Pneumothorax is usually bilateral disease due to mediastinal fenestrations.

SYSTEMS AFFECTED

- Respiratory • Cardiovascular

INCIDENCE/PREVALENCE

Traumatic pneumothorax occurs in > 40% of cases with chest trauma and 11–18% of dogs and cats presented for vehicular trauma. Pneumothorax has been reported in ~ 25% of cases with intrathoracic grass awns and 70% of dogs with thoracic bite wounds.

SIGNALMENT

Species

Dog and cat

Breed Predilections

Spontaneous pneumothorax—more common in large, deep-chested dogs. Siberian huskies may be overrepresented.

SIGNS

Historical Findings

- Traumatic—recent trauma, thoracocentesis, jugular venipuncture, lung aspirate, thoracotomy, mechanical ventilation, neck surgery. Recent anesthesia and intubation raises the possibility of tracheal trauma or

pulmonary barotrauma.

- Spontaneous—may or may not have previous history of pulmonary disease; usually acute, but can have a slowly progressive onset.

Physical Examination Findings

- Respiratory distress (tachypnea, increased respiratory effort, +/- orthopnea).
- Shallow, rapid abdominal breathing common.
- Decreased to absent breath sounds dorsally (difficult to appreciate with severe distress).
- Cyanosis.
- Tachycardia.

Traumatic Pneumothorax

- Signs of trauma (blunt or penetrating thoracic wall injury) or hypovolemic shock (pale mucous membranes, prolonged capillary refill time, altered mentation, poor pulse quality, tachycardia, decreased extremity compared to core temperature).
- Subcutaneous emphysema in some cases with pneumomediastinum and/or tracheal trauma.

CAUSES

- Traumatic: blunt trauma, penetrating thoracic or cervical injuries, post-thoracocentesis or thoracotomy, esophageal perforation, endotracheal tube—associated tracheal trauma, mechanical ventilation, pulmonary aspirate.
- Spontaneous: bullous emphysema (most common in dogs), pulmonary bullae or bleb.
- Migrating pulmonary foreign body, pulmonary neoplasia, pulmonary abscess, feline asthma, bronchopneumonia, mycotic pulmonary granuloma, parasitic pulmonary disease (*Paragonimus*, *Dirofilaria immitis*—pulmonary bullae rupture), congenital pulmonary cyst, congenital lobar emphysema, secondary to lung lobe torsion.
- Extension of pneumomediastinum.

RISK FACTORS

- Trauma
- Thoracocentesis
- Thoracotomy
- Overinflation of endotracheal cuff
- Excessive airway pressure during ventilation
- Pulmonary disease/pathology
- Migrating grass awns



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pleural effusion
- Diaphragmatic hernia
- Pulmonary parenchymal disease (i.e., pulmonary contusions, pneumonia)

CBC/BIOCHEMISTRY/URINALYSIS

Neutrophilia with a left-shift if pulmonary infection or inflammation.

OTHER LABORATORY TESTS

- Arterial blood gases—hypoxemia; hypocapnia or hypercapnia can occur.
- Fecal sedimentation or zinc sulfate centrifugation-flotation for *Paragonimus*.

IMAGING

Thoracic Radiography

- Delay until patient is stable; may not be able to get more than one view.
- Air in pleural space, pulmonary vascular pattern does not extend to the chest wall, cardiac silhouette elevated off the sternum.
- Pulmonary pathology can be obscured by lung lobe collapse; often need to repeat radiographs following thoracocentesis.
- Traumatic pneumothorax—evaluate for other traumatic injury such as contusions, rib fractures, diaphragmatic hernia, hemothorax, foreign bodies.
- Spontaneous pneumothorax—evaluate for any sign of parenchymal pathology.
- Right lateral horizontal beam results in the highest rate of detection and severity gradation while VD/DV views have the lowest rate.

Thoracic Ultrasound

- Pneumothorax evidenced by loss of the “glide sign.”
- Sensitivity of 78% and specificity of 93% compared to thoracic radiographs in identification of traumatic pneumothorax in dogs.

Thoracic Computed Tomography

- Used preoperatively to improve localization of pulmonary pathology in cases with spontaneous pneumothorax.
- CT can fail to detect pulmonary bullae prior to surgical exploration; larger pulmonary bullae more readily identified than smaller bullae.

DIAGNOSTIC PROCEDURES

- Thoracocentesis—confirms diagnosis; remove maximal amount of air from pleural space.
- Bronchoscopy—consider if evidence of tracheal or large airway trauma.

P

PATHOLOGIC FINDINGS

- Will vary depending on underlying disease.
- Gross evaluation—may be able to visualize pulmonary blebs, pulmonary or airway tears, pulmonary parenchymal disease or masses.
- Histopathology—blebs are most commonly found at the apex and are contained entirely within the pleura; bullae are lined by pleura, fibrous pulmonary tissue, and emphysematous lung.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient care until air accumulation has stopped or has stabilized.
- Animals in respiratory distress must have thoracocentesis and a maximal amount of air removed.
- Thoracocentesis can be performed with an intravenous catheter attached to an extension set and stopcock or via a butterfly needle.
- ALWAYS provide oxygen therapy until patient is stabilized.
- If large open chest wound—cover as cleanly as possible with airtight bandage (use of sterile lubricant/ointment around periphery of wound). Must

PNEUMOTHORAX

(CONTINUED)

be accompanied by chest tube placement; will require surgical closure once animal is stable.

- Tube thoracostomy—use if unable to stabilize with thoracocentesis or repeated thoracocentesis required for continued pneumothorax; chest tube placement (under local or general anesthesia)—skin entrance site aseptically prepared in dorsal caudal quadrant of lateral thorax; skin incision similar in size to the tube is made over rib space 11–12 or 12–13; skin is then pulled cranially by an assistant so that the incision now lies over rib spaces 7–8 or 8–9. Chest tube is passed into pleural space, aiming cranoventrally; skin can then be released and a subcutaneous tunnel is formed. Purse string suture around insertion site and secure tube with finger trap suture pattern; thoracic radiographs should be performed after chest tube placement to ensure proper positioning.
- If pneumothorax is rapidly accumulating—use continuous chest tube suction via one-, two- or three-bottle drainage system with an underwater seal. If pneumothorax is not severe or is resolving—use intermittent tube aspiration. • In emergency situation of life-threatening tension pneumothorax—consider emergency thoracotomy to convert problem to an open pneumothorax; animal can then be intubated and ventilated with positive pressure until stabilized.
- Open traumatic pneumothorax—surgery as soon as patient is stable.
- Closed traumatic pneumothorax—rarely requires surgical intervention.
- Spontaneous pneumothorax—early surgical intervention recommended in dogs; exploratory thoracotomy often performed via median sternotomy if location of lesion is unknown. Pleural access port placed for medical management.

NURSING CARE

• Intravenous fluids required in most cases of trauma.

- Appropriate pain control.
- Chest tube maintenance—ensure all connections are airtight (cable ties are excellent for securing connections); ensure that tube is attached to animal at two points to reduce chance of inadvertent tube removal. Clean tube site and change dressing once daily. Do not allow animal to chew at chest tube.

ACTIVITY

Strict rest for at least a week following resolution of pneumothorax in an effort to minimize the chance of recurrence.

CLIENT EDUCATION

- Traumatic pneumothorax—discuss possibility of a chest tube and need for hospitalization; some animals require surgery.
- Spontaneous pneumothorax—recommend early surgical intervention in most canine cases. Discuss possibility of underlying pulmonary disease that can make resolution challenging and recurrence possible. Warn owner that even with thoracotomy, the source

of the pneumothorax may not be found and recurrent disease is possible.

SURGICAL CONSIDERATIONS

- Do not use positive-pressure ventilation for closed pneumothorax. Place chest tube prior to ventilation or await thoracotomy prior to ventilation.
- Thoracoscopy—may allow visualization of local lesion; allows instillation of substances for pleurodesis.
- Thoracotomy—if lesion is not evident, can fill thorax with saline and look for bubbles as sign of a leak. Greater than one lesion is not uncommon. Partial or full lung lobectomy for localized lesions. Traumatic lacerations can be sutured. In some cases the location of the leak may not be evident at surgery. Thoracostomy tube should be placed at time of surgery in all patients.
- Pleurodesis with mechanical abrasion of the pleura or instillation of an inflammatory substance, such as talc, into the pleural space (success rate is believed to be poor).
- Autologous blood-patch treatment for persistent pneumothorax is a simple and relatively safe procedure that can be considered in patients that have failed conservative or surgical management.



MEDICATIONS

DRUG(S)

Judicious use of pain control.

PRECAUTIONS

Beware excess respiratory depression with opiates.



FOLLOW-UP

PATIENT MONITORING

- Respiratory rate—increased rate suggests recurrence of pneumothorax.
- Serial thoracic radiographs to quantitate accumulation of air.
- Pulse oximetry if breathing room air can help determine oxygenation status. Arterial blood gases give the best evaluation of oxygenation status if lung disease is present.
- Central venous (jugular) blood gases can be used to evaluate ventilation status via PvCO₂.
- Rate of air production from chest tube—on continuous drainage with a three-bottle suction system need to count bubbles/minute produced in middle chamber; if intermittent aspiration, can quantitate with syringe.

PREVENTION/AVOIDANCE

Keep pets confined—less likely to be injured.

POSSIBLE COMPLICATIONS

- Death from hypoxemia and cardiovascular compromise.
- Incorrect placement of chest tube or trauma associated with thoracocentesis—lung lobe laceration, cardiac puncture, diaphragmatic laceration, liver

trauma.

- Pleural infection from thoracocentesis or chest drain.

EXPECTED COURSE AND PROGNOSIS

- Traumatic pneumothorax—if thoracic trauma is not severe, the prognosis is good with thoracocentesis ± chest drain placement. With severe thoracic trauma, patient can deteriorate despite all efforts to stabilize it—usually because of severe pulmonary contusions.
- Spontaneous pneumothorax—prognosis depends on underlying cause. If a single, focal lesion can be surgically resected, prognosis is good. If unable to locate lesion or diffuse or neoplastic pulmonary disease is present—prognosis is poor.



MISCELLANEOUS

SYNOMYMS

Punctured lung

SEE ALSO

- Dyspnea and Respiratory Distress • Panting and Tachypnea

Suggested Reading

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Client Education Handout
available online

PODODERMATITIS



BASICS

DEFINITION

An inflammatory, multifaceted complex of diseases that involves the feet of dogs and cats.

PATOPHYSIOLOGY

- Depends on the underlying cause including infection, allergy, auto-immune dermatoses, endocrine or metabolic disease, neoplasia, and environmental disease.
- Psychogenic dermatosis (rare cause).

SYSTEMS AFFECTED

Skin/Exocrine

INCIDENCE/PREVALENCE

- Dogs—common
- Cats—uncommon

SIGNALMENT

Species

Dogs and cats

Breed Predilections

- Dogs: short-coated breeds—most commonly affected; English bulldog, Great Dane, basset hound, mastiff, bull terrier, boxer, dachshund, Dalmatian, German shorthaired pointer, and Weimaraner.
- Dogs: long-coated breeds—German shepherd dog, Labrador retriever, golden retriever, Irish setter, and Pekingese.
- Cats—none.

Mean Age and Range

- Any age.
- Young dogs—hypersensitivity, demodicosis, infection, follicular cysts, auto-immune dermatoses.
- Old dogs—also neoplasia or systemic diseases.

Predominant Sex

- Dogs—male
- Cats—none

SIGNS

General Comments

History and physical findings vary considerably depending on the underlying cause.

Historical Findings

- Environment and general husbandry—indoor vs. outdoor, working dog vs. pet, unsanitary conditions, other pets affected, trauma, contact irritants, hookworms.
- Age of onset.
- Seasonality—atopic dermatitis, allergic contact dermatitis, or irritant contact dermatitis.
- Lesions elsewhere on the body.
- Lesions confined to just the feet; note which feet are affected and what parts of the feet are affected (entire foot, one area, or one toe).
- Response to previous therapy—antibiotics, antifungals, and corticosteroids.
- Diet, travel history, and other medical problems.

Physical Examination Findings

Infectious (Dogs)

- Erythema and edema, nodules, inflammatory plaques (fungal “kerions”), ulcers, fistulae, hemorrhagic bullae, or serosanguineous or seropurulent discharge.
- Feet—may be grossly swollen; may have

pitting edema of the metacarpal and metatarsal areas.

- Skin—may be alopecic and moist from constant licking; patient may have some degree of pain, pruritus, and paronychia.
- Regional lymph nodes may be enlarged.

Infectious (Cats)

- Painful paronychia, involving one or more claws.
- Higher incidence of nodular, often ulcerated lesions, compared to dog.
- Footpads and periungual areas—commonly involved.
- Interdigital spaces—seldom affected.
- Scaly and crusted lesions—occasionally seen.

Allergic (Dogs)

- Erythema and alopecia (dorsal or ventral or both) secondary to pruritus; dorsal surfaces may be more severely affected than ventral surfaces.
- Interdigital erythema.
- Salivary staining.
- Allergic contact dermatitis—an uncommon cause; dermatitis of the ventral interdigital surfaces is usually worse.

Allergic (Cats)

- Single or multiple, exudative or ulcerated, pruritic plaques of the digits, periungual, and interdigital spaces.
- Eosinophilic granuloma complex lesions.

Immune-Mediated (Dogs)

- Crusts and ulcerations—most common lesions; occasional vesicles or bullae.
- All feet may be affected, especially the nailbeds and footpads.
- Hyperkeratotic and erosive dermatitis of the footpad margins—common finding in pemphigus foliaceus.

Immune-Mediated (Cats)

- Lesions—generally involve the footpad, including hyperkeratosis and ulceration.
- Lameness and paronychia with ungual fold exudate.

Endocrine/Metabolic (Dogs)

- Lesions—usually consistent with secondary infection.
- Hepatocutaneous syndrome (superficial necrolytic dermatitis)—rare condition; skin disease precedes the onset of signs of internal disease; hyperkeratosis (with adherent crusts), fissures, and ulceration of the footpads.

Endocrine/Metabolic (Cats)

- Cutaneous xanthomatosis—seen with diabetes mellitus; whitish nodules resembling candle wax.

Neoplastic

- Dogs—nodules, variably ulcerated, scale, erythema, depigmentation of the footpads; may have only one digit involved (nailbed carcinoma, ungual keratoacanthoma); multiple feet involvement with nailbed squamous cell carcinoma, epitheliotrophic lymphoma; pruritus variable.
- Cats—nodules; variably ulcerated and painful; localized destruction variable, depends on tumor type; foot pad tumors may develop *de novo* or be metastatic carcinoma.

Environmental (Dogs and Cats)

- Depends on underlying cause.
- Lesions—involve one digit or foot (foreign body, trauma) or multiple digits (irritant

contact dermatitis, thallium toxicity, housing on rough surface or in moist environment).

- Chronic interdigital inflammation, ulceration, pyogranulomatous abscesses, draining tracts, or swelling, with or without pruritus.

Miscellaneous

- Hyperkeratosis of the footpads (dogs)—associated with several diseases (e.g., zinc-responsive dermatosis, generic dog food dermatosis), and idiopathic digital hyperkeratosis.
- Interdigital follicular cysts—interdigital nodules, fistulae and draining tracts dorsally; most often only the front feet; affects the lateral interdigital space; history of recurrence and poor to no response to antibiotics, with an area of alopecic, thickened skin with comedones ventrally.
- Nodules without draining tracts (dogs)—associated with sterile pyogranuloma in several breeds and nodular dermatofibrosis of German shepherd dogs and golden retrievers.
- Hypomelanosis of the footpads (cats)—associated with vitiligo.
- Hypermelanosis of the footpads (cats)—associated with lentigo simplex.
- Acral mutilation and analgesia—seen in pointers (English and German shorthaired) and spaniels (English springer and French)—cause unknown; often runts of the litter; no known treatment; dogs are usually euthanized within days to months of diagnosis.

CAUSES

Infectious (Dogs)

- Bacterial—*Staphylococcus pseudintermedius*, *Pseudomonas* spp., *Proteus* spp., *Mycobacterium* spp., *Nocardia* spp., *Actinomyces* spp.
- Fungal—dermatophytes, intermediate mycoses (sporotrichosis, mycetoma), deep mycoses (blastomycosis, cryptococcosis).
- Parasitic—*Demodex canis*, *Pelodera strongyloides*, hookworms.
- Protozoal—leishmaniasis.

Infectious (Cats)

- Bacterial—same as dog; *Pasteurella* spp.
- Fungal—same as dog, excluding blastomycosis.
- Parasitic—*Neotrombicula autumnalis*, *Notoedres cati*, *Demodex* spp.
- Protozoal—*Anatrichosoma cutaneum*.

Allergic

- Dogs—atopy; food hypersensitivity; allergic contact dermatitis.
- Cats—atopy; rare for flea allergic dermatitis, food hypersensitivity, or contact dermatitis to involve paws (except lesions of eosinophilic granuloma complex).

Immune-Mediated

- Dogs—pemphigus foliaceus; systemic lupus erythematosus; erythema multiforme; cold agglutinin disease; pemphigus vulgaris; bullous pemphigoid; epidermolysis bullosa acquisita, symmetrical lupoid onychodystrophy.
- Cats—pemphigus foliaceus; systemic lupus erythematosus; erythema multiforme; vasculitis; cold agglutinin disease; plasma cell pododermatitis.

P

PODODERMATITIS

(CONTINUED)

Endocrine/Metabolic

- Dogs—hypothyroidism; hyperadrenocorticism; hepatocutaneous syndrome (superficial necrolytic dermatitis).
- Cats—hyperthyroidism; hyperadrenocorticism; cutaneous xanthomatosis (secondary to diabetes mellitus); endocrine pododermatitis rare.

Neoplastic

- Higher incidence in cats than in dogs.
- Dogs—squamous cell carcinoma; epitheliotrophic lymphoma, melanoma; mast cell tumor; keratoacanthoma; inverted papilloma; eccrine adenocarcinoma.
- Cats—papilloma; spinocellular epithelioma; trichoepithelioma; fibrosarcoma; malignant fibrous histiocytoma; metastatic primary adenocarcinoma of the lung; other metastatic carcinoma.

Environmental

- Dogs—irritant contact dermatitis; trauma; concrete and gravel dog runs; excessive exercise; clipper burn; foreign bodies (grass awns, bristle-like hairs of short-coated dogs); thallium toxicity.
- Cats—irritant contact dermatitis; foreign bodies; thallium toxicity.

Miscellaneous

- Dogs—sterile interdigital granuloma; interdigital follicular cyst; see “Physical Examination Findings.”
- Cats—see “Physical Examination Findings.”

RISK FACTORS

- Lifestyle and general husbandry conditions—fluence development.
- Excess exercise, abrasive or moist housing, poor grooming, and/or lack of preventive medical care may predispose an animal or exacerbate condition.
- Body size, foot conformation, and breed influence the development of interdigital follicular cysts.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

See “Signs” and “Causes”

CBC/BIOCHEMISTRY/URINALYSIS

- Depends on the underlying cause
- Rarely significant

OTHER LABORATORY TESTS

- Depends on the underlying cause
- Endocrine tests, serology, or immune studies

IMAGING

Depends on the underlying cause

DIAGNOSTIC PROCEDURES

- Skin scrapings or hair plucks—demodicosis.
- Fungal culture—dermatophytosis.
- Exudate or pustule smear—bacterial or yeast infection.
- Culture and sensitivity from exudates and/or biopsy tissues.
- Dogs—biopsies indicated if skin scrapings are negative and lesions (nodules, draining tracts)

are seen; samples from the ventral surface with draining tracts may reveal follicular cysts and pyogranulomatous inflammation leading to the dorsal surface.

- Cats—biopsies may be indicated in all cases; pedal dermatosis is relatively rare.
- Restricted-ingredient food trial—food hypersensitivity.
- Intradermal testing—atopy.
- Endocrine assays—hypothyroidism, hyperadrenocorticism, diabetes mellitus.

PATHOLOGIC FINDINGS

Depends on the underlying cause



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient, unless surgery is indicated.

NURSING CARE

Foot soaking, hot packing, and/or bandaging may be necessary, depending on cause.

ACTIVITY

Depends on severity of the lesions and on the underlying cause.

DIET

Restricted-ingredient food trial if indicated.

CLIENT EDUCATION

- Depends on underlying cause and severity of condition.
- Discuss husbandry and preventive medical practices.
- Allergic, immune-mediated, or endocrine etiologies can be managed but not cured.

SURGICAL CONSIDERATIONS

- Melanoma and squamous cell carcinoma—very poor prognosis; early diagnosis necessitates amputation of the digit(s) or paw.
- Infectious—may benefit from surgical debridement of devitalized tissue before medical therapy.
- Recurrent draining tracts caused by interdigital follicular cysts may be cleared with laser ablation.



MEDICATIONS DRUG(S) OF CHOICE

- Depend on the underlying cause and secondary infections; see related chapters for dosages of appropriate medications
- Antibiotics based on culture and sensitivity; 4–6 weeks minimum
- Antifungal medications
- Anti-inflammatory or immunosuppressive dosage of corticosteroids
- Immunomodulatory medications
- Chemotherapeutic agents
- Hormone-replacement therapy
- Zinc supplementation
- Intravenous amino acids

PRECAUTIONS

Depend on the treatment protocol selected for the underlying cause; see specific drugs and their precautions.

POSSIBLE INTERACTIONS

Depends on the underlying cause and treatment protocol selected.



FOLLOW-UP

PATIENT MONITORING

Depends on the underlying cause and treatment protocol selected.

PREVENTION/AVOIDANCE

- Environmental cause—good husbandry and preventive medical care.
- Allergic cause—avoidance (food) or immunotherapy (atopy), if possible.

POSSIBLE COMPLICATIONS

Depends on the underlying cause and treatment protocol selected.

EXPECTED COURSE AND PROGNOSIS

- Success of therapy depends on finding the underlying cause; often the cause is unknown; even when the cause is known, management can be frustrating owing to relapses or lack of affordable therapeutics.
- Often the disease can only be managed and not cured.
- Referral to dermatologist often appropriate.
- Surgical intervention is sometimes necessary.



MISCELLANEOUS

AGE-RELATED FACTORS

Depends on the underlying cause.

ZOONOTIC POTENTIAL

Depends on the underlying cause; uncommon.

PREGNANCY/FERTILITY/BREEDING

Avoid systemically administered corticosteroids, antifungals, chemotherapeutic agents, azathioprine, and certain antimicrobials (e.g., enrofloxacin) in pregnant animals.

Suggested Reading

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Client Education Handout
available online

POISONING (INTOXICATION) THERAPY



BASICS

DEFINITION

- Acutely ill patients are often diagnosed as poisoned when no other diagnosis is obvious.
- Direct initial efforts toward stabilizing the patient. Remember ABCs (airway, breathing, circulation).
- Make the diagnosis after determining preexisting conditions and controlling clinical signs.
- Goals of treatment—provide emergency intervention; prevent further exposure; prevent additional absorption; apply specific antidotes; hasten elimination; provide supportive measures; offer client education.
- Suspected intoxication—suspected toxic materials and specimens may be valuable from a medical-legal aspect; maintain a proper chain of physical evidence; keep excellent medical records.
- Valuable time can be saved by applying the appropriate treatment for a suspected or known intoxicant.

Initial Instructions to Client

- Transport patient to a veterinarian as soon as possible.
- Delayed transport—keep patient warm; avoid any other stress.
- Warn onlookers about the condition of the patient and danger to themselves.
- May need to muzzle the patient.
- Transport urine (if available), uncontaminated vomitus and suspected toxic materials and their containers to the veterinary facility.
- Use clean plastic containers or clean glass jars for the specimens.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Definitive diagnosis—difficult; animals come in contact with a vast array of toxicants. ASPCA Animal Poison Control Center; Pet Poison Helpline; local poison control center; state diagnostic laboratory. Provide great value for cases of suspected intoxication, especially when labels or containers are available.
- When suspected compound and clinical signs do not concur—treat the signs; disregard the label.
- Confirmation of diagnosis—chemical analysis (often after the fact); accurate diagnosis and detailed records may help with future patients affected by the same toxicant and are invaluable in medico-legal proceedings.



TREATMENT

SUPPORTIVE

- Control body temperature.
- Maintain respiratory and cardiovascular function.
- Control acid-base balance.
- Alleviate pain.
- Control CNS disorders—see specific chapters.

EMERGENCY

- Establish a patent airway.
- Artificial respiration.
- Cardiac massage—external or internal.
- Apply defibrillation techniques.
- After stabilization—may proceed with more specific therapeutic measures.

PREVENT ABSORPTION

- Major treatment factor.
- Remove patient from the affected environment, especially with inhaled toxins.
- Protect caregivers as well from inhaled toxins.
- Other available measures—washing or bathing; judicious use of emetics; gastric lavage; adsorbents and cathartics.

Washing Skin or Bathing

- External toxicants.
- Wash patient's skin or bathe to remove the noxious agent.
- CAUTION: avoid contamination of the people handling the patient.

Emetics

- Of little value beyond 1–2 hours after ingestion of most toxicants; material will have passed into the duodenum.
- Do not induce in unconscious or severely depressed patients or after ingestion of strong acids, alkalis, petroleum distillates, tranquilizers, or other antiemetics.
- Apomorphine—most effective and reliable for use in dogs; availability at any given time unknown; 0.03–0.04 mg/kg IV or IM; emesis occurs in 4–6 minutes; control adverse clinical signs caused by apomorphine with an appropriate intravenous narcotic antagonist (e.g., naloxone at 0.01–0.04 mg/kg).
- 3% Hydrogen peroxide—emetic of choice for home use; 2.2 mL/kg PO, do not exceed 45 mL in dogs; ineffective in cats, not always effective in dogs.
- Ipecac—little efficacy and no longer recommended; never use when activated charcoal is part of the therapeutic regimen.
- Xylazine—most successful in cats (0.44–1 mg/kg IM or SQ). Can be reversed with an alpha₂-adrenergic antagonist such as atipamezole or yohimbine.
- Salt or salt solution is NOT recommended. Salt can be toxic.

Activated Charcoal

- Does not detoxify but prevents absorption if properly used.
- Highly absorptive of many toxicants—organophosphate insecticides; other insecticides; rodenticides; mercuric chloride; strychnine; other alkaloids (e.g., morphine and atropine); barbiturates; ethylene glycol.
- Ineffective against alcohols, chlorate, cyanide, heavy metals, petroleum distillates, sodium chloride, and xylitol.
- Administered after emetic—increases efficacy of toxicant elimination.
- Use easily cleansed area when administering.
- Dosage 1–5 g/kg body weight; generally a single dose administration but some situations require multidose administration (1–2 g/kg PO q4–6h for 24 hours).
- Generally administered with a cathartic such as sorbitol or sodium sulfate; only the first dose should contain a cathartic.
- Hypernatremia has been reported after administration of activated charcoal, especially when a cathartic (sorbitol) is used in a dehydrated patient.

Gastric Lavage

- Effective means of emptying the stomach, but must be used in the first 1–2 hours.
- An appropriate size, cuffed endotracheal tube must be in place prior to starting the lavage procedure.
- Orogastic (stomach) tube size—use the largest possible; a good rule: use the same size as the cuffed endotracheal tube (1 mm = 3 Fr).
- Volume of water or lavage solution for each washing—5–10 mL/kg body weight.
- Infusion cycle—repeated more than 5–10 times.
- After the last cycle and prior to the removal of the orogastric tube, activated charcoal with a cathartic should be instilled.
- Precautions: (1) use low pressure to prevent forcing the toxicant into the duodenum; (2) reduce the infused volume in obviously weakened stomachs (e.g., in a patient that has ingested a caustic or corrosive toxicant); (3) do not force the stomach tube through either the esophagus or the stomach wall.

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Oils

- Mineral or vegetable oil—valuable for lipid-soluble toxicants.
- Mineral oil (liquid petrolatum)—inert; less likely to be absorbed.
- Use as a cathartic.

Enemas

- Colonic lavage or high enema—may hasten the elimination of toxicants from the gastrointestinal tract.
- Warm water with Castile soap—excellent solution.
- Commercially available preparations that act as osmotic agents are available.

Poisoning (Intoxication) Therapy

(Continued)

- Take care to avoid the induction of dehydration and electrolyte imbalances with overzealous treatment.
- Do not use hexachlorophene soaps or phosphate-based enemas in cats.

ENHANCE ELIMINATION

- Absorbed toxicants—generally excreted by the kidneys; may be excreted by other routes (e.g., bile, feces, lungs, and other body secretions).
- Renal excretion—may be manipulated in many animals.
- Urinary excretion—may be enhanced by the use of diuretics or by altering the pH of the urine.

Diuretics

- Enhance urinary excretion of some toxicants—requires maintenance of adequate renal function.
- If minimum urine flow cannot be established—must use peritoneal dialysis (normal urine output is 1–2 mL/kg/hour).
- Agents of choice—furosemide (2 mg/kg IV q6–8h, if no response increase dose to 4–6 mg/kg IV q6–8h) or mannitol (1–2 g/kg IV slowly over 20–30 minutes q6h).

Manipulating Urine pH

- Classic pharmacologic technique
- Acidic compounds remain ionized in alkaline urine; alkaline compounds remain ionized in acidic urine.
- Intravenous 0.9% sodium chloride—rapid, urinary acidifying agent.
- Intravenous sodium bicarbonate may be used as an alkalinizing agent.
- Ammonium chloride (200 mg/kg PO divided 4 times a day) and ethylenediamine dihydrochloride (1–2 tablets q8h for the average-sized dog)—long-term urinary acidification.

Peritoneal Dialysis

- Indicated for patients with oliguria or anuria.
- Indicated for simple removal of absorbed toxicants in patient with normal renal function.

- pH of the solution—may be altered to maintain the ionized state of the offending compound.

FLUID THERAPY

Consider volume replacement with crystalloids and colloids if necessary.

Lipid Emulsion Therapy (ILE or IFE)

- Promising use as antidote for toxicosis from many fat soluble drugs.
- Useful for complications associated with local anesthetic medications. Successfully resuscitated human patients with cardiac collapse related to local anesthetics in particular, but also clomipramine and verapamil.
- Has been used successfully in veterinary medicine to treat toxicity from baclofen, beta antagonists, calcium channel antagonists, ivermectin, moxidectin, and other fat-soluble medications.
- Exact mechanism of action remains unknown, but may act as a lipid sink.
- Potential adverse effects include hyperlipidemia, hepatosplenomegaly, jaundice, seizures, hemolytic anemia, prolonged clotting time, thrombocytopenia, and fat embolism.
- Dosage extrapolated from humans using the 20% commercially available fat emulsion product. Standard Protocol: 1.5 mL/kg IV over 5–15 minutes followed by 0.25 mL/kg/minute CRI over 1–2 hours. Repeat in several hours if signs return and serum in not lipemic. See Appendix V on Antidotes and Other Useful Drugs.



MEDICATIONS

Specific antidotes or procedures are available for the more common toxicants; see specific chapter and Appendix V.



FOLLOW-UP

Specific monitoring depends on the toxicant and the patient's signs and laboratory abnormalities.



MISCELLANEOUS

ABBREVIATIONS

- CNS = central nervous system
- ILE = intravenous lipid emulsion
- IFE = intravenous fat emulsion

INTERNET RESOURCES

- ASPCA Poison Control Center: <http://www.aspca.org/pet-care/poison-control/>.
- Pet Poison Helpline: <http://www.petpoisonhelpline.com/>
- ToxiBan: <http://www.lloydinc.com/pdfs/ToxiBan.pdf>.

Suggested Reading

Lee JA. Decontamination and detoxification of the poisoned patient. In: Osweiler GD et al., eds. Blackwell's Five-Minute Veterinary Consult Small Animal Toxicology. Ames, IA: Blackwell, 2011, pp. 5–19.

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Authors Tam Garland and E. Murl Bailey

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POLIOENCEPHALOMYELITIS—CATS



BASICS

OVERVIEW

- Subacute to chronic nonsuppurative encephalomyelitis with a predominance of pathologic changes in the gray matter, mainly affecting the medulla oblongata and the spinal cord.
- This disease is considered rare with a prevalence of less than 1% in cats presented with spinal cord diseases.

SIGNALMENT

- There is no breed or sex predilection.
- Cats of any age can be affected.
- The disease is sporadic but has been observed worldwide, especially in northern Europe.

SIGNS

- Ataxia, paresis, and decreased postural reactions of pelvic or all four limbs.
- Lower motor neuron signs may be also possible (muscle atrophy and decreased to absent segmental spinal reflexes).
- Intracranial signs (seizures, cerebellar signs, and cranial nerve deficits) are uncommon.
- The progression is subacute to chronic (over weeks to months) but may also stabilize.

CAUSES & RISK FACTORS

The underlying cause remains still unknown but pathologic findings are highly suggestive of a viral agent.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- FIP
- Toxoplasmosis
- Fungal infection
- Bacterial infection

CBC/BIOCHEMISTRY/URINALYSIS

- Laboratory changes not well characterized
- Nonspecific changes (e.g., leukopenia and non-regenerative anemia) rare

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- The presumptive diagnosis is based on history, clinical signs, and possibly CSF changes (mononuclear pleocytosis with or without moderate increased total protein levels).
- The final diagnosis is based on histopathology (disseminated inflammatory lesions in the brain and spinal cord and, as the disease progresses, there is extensive neuronal loss and astrogliosis with little inflammation).



TREATMENT

No curative treatment has been found.



MEDICATIONS

DRUG(S)

- No drug therapy used in reported cases.
- Because lesions are nonsuppurative, steroid therapy may palliate clinical signs, at least temporarily.
- Supportive treatment with antiepileptic medication to control seizures if indicated.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

Prognosis can be good if the neurologic signs are mild and nonprogressive.



MISCELLANEOUS

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- FIP = feline infectious peritonitis

Suggested Reading

Gunn-Moore D. Infectious diseases of the central nervous system. *Vet Clin North Am Small Anim Pract.* 2005, 35:103–128.

Hoff EJ, Vandevelde M. Non-suppurative encephalomyelitis in cats suggestive of a viral origin. *Vet Pathol* 1981, 18:170–180.

Tipold A. Inflammatory diseases of the spine in small animals. *Vet Clin North Am Small Anim Pract* 2010, 40:871–879.

Tipold A, Vandevelde M. Neurological diseases of suspected infectious origin and prion disease. In: Greene CE (eds.), *Infectious Diseases of the Dog and Cat*, 4th ed. St. Louis, MO: Elsevier, 2012, p. 860.

Author Elsa Beltran

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POLYARTHRITIS, IMMUNE-MEDIATED



BASICS

DEFINITION

An immune-mediated inflammatory disease of joints resulting in progressive destruction of articular tissues and subsequent pain and lameness. The disease may be erosive in nature (including rheumatoid arthritis, idiopathic, erosive polyarthropathy of greyhounds or feline chronic progressive polyarthropathy) or nonerosive (including idiopathic polyarthritides, SLE, polyarthritides associated with chronic disease, polyarthritides-polymyositis syndrome, polymyositis syndrome, polyarthritides-meningitis syndrome, polyarthritides nodosa, familial renal amyloidosis in Chinese shar-pei dogs, lymphocytic-plasmacytic synovitis, juvenile-onset polyarthritides of Akitas).

PATHOPHYSIOLOGY

- Pathogenesis—inciting cause unknown as extrapolated from human arthritis research; likely perpetuated by cell-mediated immunity; predominance of CD4+ helper T-lymphocytes and immune complex depositions found in synovium of affected joints; leukocytes, leukocyte enzymes, cell-mediated immunity, immune complexes, and auto-allergic reactions are directed against cartilage components; leads to an inflammatory response and complement activation.
- SLE—nuclear material from various cells becomes antigenic, leading to formation of auto-antibodies (antinuclear antibody).
- IEP—associated with an abnormal antigenic response to host immunoglobulin, similar to human rheumatoid arthritis.
- EPG and FCPP—offending antigens unknown.

SYSTEMS AFFECTED

Musculoskeletal—diarthrodial joints

GENETICS

Not known to be hereditary

INCIDENCE/PREVALENCE

- Overall, uncommon
- Idiopathic—most common in dogs
- Chronic infection related form may be misdiagnosed as idiopathic
- Other forms uncommon

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Idiopathic nonerosive—large- (more common) and small-breed dogs; uncommon in cats; German shepherd, Doberman pinscher, retriever, spaniel, pointer, toy poodle, Lhasa apso, Yorkshire terrier, and Chihuahua overrepresented.
- Idiopathic erosive—small or toy breeds.
- SLE—tendency to affect large-breed dogs; collie, German shepherd, poodle, terrier, beagle, and Shetland sheepdog.
- Secondary to

administration of sulfa drugs—increased sensitivity in Doberman pinscher.

- Polyarthritis-meningitis syndrome—reported in Weimaraner, German shorthaired pointer, boxer, Bernese mountain dog, beagle, rottweiler, and Japanese Akita.
- Amyloidosis and synovitis—prominent features of a syndrome affecting young Shar-Pei dogs.
- Greyhound specific version.
- Juvenile onset polyarthritides reported in Akitas.
- Lymphocytic-plasmacytic synovitis in German shepherds and other large-breed dogs.

Mean Age and Range

Dogs—young to middle-aged. Cats—FCPP: onset at 1.5–4.5 years of age.

Predominant Sex

FCPP—male cats only

SIGNS

General Comments

Non-erosive and erosive forms of immune-mediated inflammatory disease initially appear similar.

Historical Findings

- Dogs and cats—acute or insidious onset; single- or multiple-limb (more common in most syndromes) lameness.
- Lameness—may shift from leg to leg.
- Usually no history of trauma.
- May also note vomiting, diarrhea, anorexia, pyrexia, polyuria, or polydypsia.
- May also note signs associated with systemic disease or infections (pyometra, prostatitis, or discospondylitis), or neoplastic disease.
- Often cyclic—may appear to respond to antibiotic therapy, but may be undergoing spontaneous remission.
- Disease may develop when patient is being treated with antibiotics.

Physical Examination Findings

- Stiffness of gait, lameness, decreased range of motion, crepitus, and joint swelling and pain in one or more joints.
- Joint instability, subluxation, and luxation—depend on duration of disease.
- Lameness—mild weight-bearing to more severe non-weight-bearing.
- Diarthrodial joints—all may be affected; small distal joints more common.
- Chronic localized focus of infection (pyometra, prostatitis).

CAUSES

- Unknown for most.
- Immunologic mechanism likely.
- Chronic—associated with antigenic stimulation along with concurrent meningitis, gastrointestinal disease, neoplasia, urinary tract infection, periodontitis, bacterial endocarditis, heartworm disease, pyometra, chronic otitis media or externa, fungal infections, and chronic *Actinomyces* or *Salmonella* infections.
- May occur secondary to a hypersensitivity reaction involving the deposition of drug antibody complexes in the blood vessels of the synovium; suspected antibiotics include sulfas, cephalosporins, lincomycin, erythromycin, and penicillins.
- FeLV and FeSFV—linked to FCPP.

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infectious arthritis
- Joint trauma
- Polymyositis
- Osteoarthritis—primary or secondary

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal.
- Hemogram—may show leukocytosis, neutrophilia, and hyperfibrinogenemia.
- Hematologic abnormalities (e.g., thrombocytopenia and hemolytic anemia)—rare.

OTHER LABORATORY TESTS

- Positive lupus erythematosus preparation or positive antinuclear antibody test—dogs with SLE (both false-positive and false-negative results are common).
- Rheumatoid factor—positive in only about 25% of IEP patients.
- Coombs' test and antinuclear antibody titer—normal.
- Serum titers (*Borrelia*, *Ehrlichia*, and *Rickettsia*)—should be normal.
- Serologic evidence of FeSFV—found in all FCPP patients.
- Serologic evidence of FeLV exposure—found in 50% or fewer of cats with FCPP.

IMAGING

- Earliest finding is periarticular soft tissue swelling.
- Severe disease—joint capsular distention; osteophytosis; soft tissue thickening; narrowed joint spaces; subchondral sclerosis; decreased trabecular bone density; bony ankylosis in severely affected joints.
- Cyst-like lucencies—occasionally seen in subchondral bone in erosive forms.
- Chronic disease—subluxation, luxation, and obvious joint deformity.

DIAGNOSTIC PROCEDURES

- Arthrocentesis and synovial fluid analysis—essential for diagnosis.
- Synovial fluid—typically appears cloudy with normal viscosity; large increase in non-degenerate neutrophils (20,000–200,000 cells/mL); submit for bacterial culture and sensitivity.
- Synovial biopsy—may help diagnosis.
- Look for a source of chronic infection.

PATHOLOGIC FINDINGS

- Joint capsule—may be thickened; synovial effusion.
- Synovial hypertrophy and hyperplasia—associated with a mononuclear cell infiltrate.
- Neutrophils—seen in the synovial tissues owing to chemotaxis.
- Erosion of articular cartilage—particularly near the periphery at synovial attachments (erosive forms).
- Eburnation and sclerosis of subchondral bone with full-thickness cartilage loss—chronic disease.
- Granulation tissue (pannus)—may invade the margins of articular cartilage, and arise from the marrow

(CONTINUED)

POLYARTHRITIS, IMMUNE-MEDIATED

cavity to destroy cartilage at central regions of the joint. • Enthesiophytes—at joint capsular attachments and adjacent to the joint.

- Histopathology of the synovial membrane—typically reveals villous synovial hyperplasia, hypertrophy, and lymphoplasmacytic inflammatory infiltrate.
- Synovial fluid—cloudy; increased volume.

**TREATMENT****APPROPRIATE HEALTH CARE**

Usually outpatient

NURSING CARE

- Physical therapy—range-of-motion exercises and swimming; may be indicated for severe disease.
- Bandages and/or splints—to prevent further breakdown of the joint; may be indicated for severe disease with compromised ambulation.

ACTIVITY

Limited to minimize aggravation of clinical signs

DIET

Weight reduction—to decrease stress placed on affected joints

CLIENT EDUCATION

Warn client of poor prognosis for cure and complete resolution if a primary cause is not found.

SURGICAL CONSIDERATIONS

Remove source of infection where applicable (e.g., pyometra); no other therapy needed in these cases.

- Healing rates—may be long and protracted; range of recovery levels.
- Surgery—generally not a good treatment option.
- Arthroplasty—total hip replacement, femoral head ostectomy; may consider if the hip is the primary clinical problem.
- Arthrodesis—in selective cases of joint pain and joint instability; carpus; generally yields the best results and is a good salvage option; shoulder, elbow, stifle, or hock: less predictable results.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Eliminate underlying causes if possible—chronic disease; offending antibiotic.
- Typical therapy—initial trial of glucocorticoids; if poor response, then combination chemotherapy (glucocorticoids and cytotoxic drugs). • Complete remission—usually achieved in 2–16 weeks; determined by resolution of clinical signs and confirmation of normal synovial fluid analysis.
- Recurrence rate—30–50% once therapy is discontinued.
- Prednisone

1.5–2 mg/kg PO q12h for 10–14 days as initial treatment; synovial fluid cell counts <4,000 cells/mL and mononuclear cells predominate: If positive response is achieved, slowly taper by reducing doses every 3–4 weeks to 1 mg/kg PO q48h; clinical signs persist or abnormal synovial fluid analysis: add cytotoxic agents; no clinical signs after 2–3 months of alternate-day therapy: discontinue. • Combination of glucocorticoids and cytotoxic drug—recommend for synergistic effect; may try cyclophosphamide or a thiopurine (azathioprine or 6-mercaptopurine).

- Cyclophosphamide—patient <10 kg: 2.5 mg/kg; patient 10–50 kg: 2 mg/kg; patient >50 kg: 1.75 mg/kg; agent given PO q24h for 4 consecutive days of each week; given concurrently with prednisone (as described above; some clinicians reduce the total steroid dose by half).
- Azathioprine or 6-mercaptopurine 2 mg/kg PO q24h for 14–21 days, then q48h; given concurrently with prednisone as for cyclophosphamide, but on alternating days.
- Leflunomide—may be used synergistically with azathioprine, prednisone, and cyclophosphamide (4 mg/kg q24h for dogs). After several days, adjust dose to plasma trough levels of 20 µg/mL.
- Discontinue cytotoxic drugs 1–3 months after remission is achieved.
- Maintaining remission—alternate-day glucocorticoid therapy (prednisone 1 mg/kg PO) is generally successful; clinical signs or synovial neutrophilia recur: long-term cytotoxic drug therapy may be necessary; clinical signs do not recur after 2–3 months: may stop the glucocorticoid; clinical signs recur after glucocorticoid is stopped: continue treatment.
- Aurothiomalate (chrysotherapy) 1 mg/kg IM weekly; successfully alleviates symptoms in some reports.

FCPP

- Treatment may slow progression.
- Prednisone (2 mg/kg PO q12h) and cyclophosphamide (2.5 mg/kg PO)—typically as described above.

EPG

- Treatment is unrewarding.
- Antibiotics, NSAIDs, glucocorticoids, cytotoxic drugs, and polysulfated glycosaminoglycan (Adequan)—fail to induce remission.

CONTRAINDICATIONS

- Do not use cytotoxic drugs with chronic infections or bone marrow suppression (cats with FCPP).
- Avoid using glucocorticoids with NSAIDs such as aspirin, carprofen, etodolac, and deracoxib, as gastric ulceration may result.
- Chrysotherapy—do not use with renal disease owing to nephrotoxicity.

PRECAUTIONS

- Glucocorticoids—long-term use may lead to iatrogenic Cushing's disease.
- Cytotoxic drugs—frequently induce bone marrow

suppression; monitor CBC weekly (see Polyarthritis, Immune Mediated).

- Leflunomide may cause intestinal necrosis with overdosing.

POSSIBLE INTERACTIONS

None known

**FOLLOW-UP****PATIENT MONITORING**

- Treatment is often frustrating and requires frequent reevaluation.
- Clinical deterioration—requires a change in drug selection or dosage, or surgical intervention.
- Important to try to induce remission; allowing the disease to smolder uncontrolled will increase risk of secondary degenerative joint disease.

EXPECTED COURSE AND PROGNOSIS

- Recurrence—seen with moderate frequency
- Erosive forms—progression likely; cure is not expected; remission is the goal.
- SLE and FCPP—progression common; guarded prognosis
- Other forms—good prognosis

**MISCELLANEOUS****ABBREVIATIONS**

- FCPP = feline chronic progressive polyarthritis
- FeLV = feline leukemia virus
- FeSFV = feline syncytium-forming virus
- SLE = systemic lupus erythematosus
- EPG = erosive polyarthritis of greyhounds
- IEP = idiopathic erosive polyarthritis
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

Hanna FY. Disease modifying treatment for feline rheumatoid arthritis. Vet Comp Orthop Traumatol 2005, 18(2):94–99.

Hastings D. Suggested treatment for polyarthritis in dogs. J Am Vet Med Assoc 2004, 225(1):29.

Jacques D, Cauzinille L, Bouvy B, Dupre G. A retrospective study of 40 dogs with polyarthritis. Vet Surg 2002, 31(5): 428–434.

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Consulting Editor Walter C. Renberg

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Client Education Handout available online

P

POLYCYSTIC KIDNEY DISEASE



BASICS

OVERVIEW

Disorder in which large portions of normally differentiated renal parenchyma are displaced by multiple cysts; renal cysts develop in preexisting nephrons and collecting ducts; both kidneys are invariably affected. In most cases the disease is inherited.

SIGNALMENT

- Persian and Persian-related breeds (e.g., Exotic Shorthair, Himalayan, Scottish fold) are affected more commonly than other breeds.
- Dog breeds affected include cairn terriers and beagles.

SIGNS

- Cysts often remain clinically silent until their increasing size and number contribute to renal failure or abdominal enlargement; thus patients typically are clinically normal during initial stages of cyst formation.
- May detect bosselated (lumpy) kidneys by abdominal palpation.
- Most renal cysts are not painful when palpated, but acute secondary infection of cysts may be associated with rapid distension of the renal capsule and pain.

CAUSES & RISK FACTORS

- Autosomal-dominant inheritance in Persian cats. A nucleotide transversion (cytosine to adenine) causing a premature stop codon has been strongly associated with the phenotype.
- The stimuli for renal cyst formation remains obscure; genetic, endogenous, and environmental factors appear to influence the process.
- Cystogenic chemicals include diphenylthiazole, nordihydroguaiaretic acid, diphenylamine, trichlorophenoxyacetic acid, and long-acting corticosteroids.

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DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other multicystic diseases of the kidneys.
- Glomerulocystic disease of collies.
- Renal cystadenocarcinoma associated with nodular fibrosis in German shepherd dogs.
- Renal cysts associated with chronic renal failure or renal dysplasia.
- Non-cystic causes of renomegaly.
- Renal neoplasia.
- Hydronephrosis.
- Perirenal pseudocysts.
- Feline infectious peritonitis.
- Mycotic or bacterial nephritis.

CBC/BIOCHEMISTRY/URINALYSIS

- Results usually unremarkable unless patient has renal insufficiency.
- Hematuria is rare.

OTHER LABORATORY TESTS

- Genetic tests are available to identify the autosomal dominant-polycystic kidney

disease (AD-PKD) type 1 mutation in cats. This test is especially useful to screen kittens less than 3–4 months old when ultrasonography may be less sensitive. The test is also useful to confirm inherited AD-PKD type 1 in breeding cats, once renal cysts are detected ultrasonographically. Other mutations may also cause inherited kidney cysts.

- Cyst fluid can be clear, cloudy, or hemorrhagic, and the fluid from different cysts in the same kidney can differ.
- Bacterial culture of cyst fluid helps in diagnosing concomitant infection.
- Hypertension is uncommon without renal failure.

IMAGING

Radiography

Survey radiography and intravenous contrast urography are insensitive methods of confirming cystic disease.

Ultrasonography

- Reveals anechoic cavitating lesions characterized by sharply marginated smooth walls and distal enhancement, which are diagnostic.
- Cysts have been detected in cats as young as 7 weeks; screening cats younger than 6 months is associated with higher false-negative test result rate.
- Used to detect cysts in other organs (e.g., liver, pancreas), which helps to differentiate AD-PKD from other inherited or acquired multicystic disorders of the kidneys.

DIAGNOSTIC PROCEDURES

Evaluation of fine-needle aspirates of the kidney may allow differentiation of cystic disease from other diseases that cause renomegaly.



TREATMENT

- Usually not immediately life-threatening, but bacterial nephritis and cyst involvement warrant immediate measures to prevent sepsis and mortality. In our experience, bacterial infection of cysts is rare.
- Spontaneous resolution of cysts has not been documented in dogs and cats; most cysts increase in size and number, often compressing adjacent normal functioning renal parenchyma.
- Elimination of renal cysts and associated renal parenchymal lesions is not yet feasible; treatment is often limited to minimizing the pathophysiologic consequences of renal cyst formation (i.e., chronic kidney disease [CKD], renal infection, hematuria, and pain).
- Removing fluid (cystocentesis, fenestration) from large renal cysts may minimize pain and compression of adjacent normal renal parenchyma. However, this procedure is impractical for kidneys with multiple large

- Some patients may require treatment for concomitant CKD.
- Consider nephrectomy only if infected cysts are associated with uncontrollable sepsis.

- Disease eradication by selective breeding of unaffected cats may be impossible because almost 40% of Persians are affected. Selective breeding may reduce genetic diversity, increasing the frequency of other unwanted inherited traits.



MEDICATIONS

DRUG(S)

- Bacterial infection of cysts has been observed in cats but is rare. Unless infection is accompanied by pyelonephritis, bacteria may not be observed in urine. Consider parenchymal infection when renal cysts are associated with renal pain and fever, even in absence of bacteriuria.
- Treatment of infected cysts requires special consideration. The acidic nature of cyst fluid and its containment by an epithelial barrier might reduce bactericidal concentrations of commonly used acidic antibiotics (e.g., cephalosporins and penicillins) within cystic lumens. Alkaline, lipid-soluble antibiotics (e.g., trimethoprim-sulfonamide combinations, fluoroquinolones, chloramphenicol, tetracycline, and clindamycin), which penetrate epithelial barriers and become ionized and trapped in cyst lumens, have been recommended.



FOLLOW-UP

- Monitor patients every 2–6 months for associated disease (e.g., CKD, renal infection, and pain).
- In the absence of sepsis, the short-term prognosis appears to be favorable without treatment.



MISCELLANEOUS

ABBREVIATIONS

AD-PKD = autosomal dominant-polycystic kidney disease

Suggested Reading

Bonazzi M, Volta A, Gnudi G, et al. Comparison between ultrasound and genetic testing for early diagnosis of polycystic kidney disease in Persian and Exotic Shorthair cats. J Feline Med Surg 2009;11:430–434.

Authors Jody P. Lulich and Carl A. Osborne

Consulting Editor Carl A. Osborne



BASICS

DEFINITION

An increase in PCV, hemoglobin concentration, and RBC count above the reference intervals because of a relative, transient, or absolute increase in the number of circulating RBCs.

PATHOPHYSIOLOGY

- Number of circulating RBCs affected by changes in plasma volume, rate of RBC destruction or loss, splenic contraction, EPO secretion, and rate of bone marrow production.
- Erythropoiesis also affected by hormones from the adrenal cortex, thyroid gland, ovary, testis, and anterior pituitary gland; normal PCV maintained by an endocrine loop.
- Polycythemia is classified as relative, transient, or absolute.
- Relative—develops when a decrease in plasma volume, usually caused by dehydration, produces a relative increase in circulating RBCs.
- Transient—caused by splenic contraction, which injects concentrated RBCs into the circulation; because splenic contraction is a momentary response to epinephrine; this type is usually not a major diagnostic consideration.
- Absolute—characterized by an absolute increase in the circulating RBC mass as a result of an increase in bone marrow production; either primary or secondary to an increase in the production of EPO.
- Primary absolute (polycythemia rubra vera)—a myeloproliferative disorder characterized by the uncontrolled but orderly production of excessive numbers of mature RBCs.
- Secondary absolute—caused by a physiologically appropriate release of EPO resulting from chronic hypoxemia or by an inappropriate and excessive production of EPO or an EPO-like substance in an animal with normal SaO₂.

SYSTEMS AFFECTED

- Cardiovascular, respiratory, nervous, renal/urologic—hyperviscosity and poor perfusion and oxygenation of tissues, which are related directly to the high PCV, especially values > 60–70%.

GEOGRAPHIC DISTRIBUTION

- Reference intervals for PCV, hemoglobin, and RBC count vary with geographic location and breed.
- Animals living at altitudes > 6,000 feet have higher values than those at sea level.

SIGNALMENT

Species

Dogs and cats

Breed Predilections

- Brachycephalic breeds have higher PCV values than do normocephalic breeds.
- Large, excitable breeds are prone to splenic contraction.
- Greyhounds typically have

high PCV values; normal range is 50–65%.

Mean Age and Range

Primary and absolute polycythemia—cats 6–7; dogs 7 years or older.

Predominant Sex

Cats males, dogs females

SIGNS

General Comments

Vary with the degree of polycythemia

Historical Findings

- Transient—excitement or vigorous exercise.
- Absolute—lethargy, anorexia, epistaxis, seizures, hyperemia of mucous membranes.

Physical Examination Findings

- Relative—dehydration caused by vomiting, diarrhea, or lack of water intake and oliguria.
- Absolute—lethargy, low exercise tolerance, behavioral change, brick red or cyanotic mucous membranes, sneezing, bilateral epistaxis, large size and tortuosity of retinal and sublingual vessels, and cardiopulmonary impairment.
- Primary absolute—variable degrees of splenomegaly, hepatomegaly, thrombosis, and hemorrhage; occasional seizure.
- Secondary absolute caused by tissue hypoxia—clinical signs of hypoxemia caused by chronic pulmonary disease, cardiac disease or anomaly with right-to-left shunting, or hemoglobinopathy.
- Secondary absolute caused by inappropriate EPO secretion—signs associated with neoplasia, space-occupying renal lesion, or endocrine disorder.

CAUSES

- Relative (common)—hemoconcentration/dehydration.
- Transient—excitement, anxiety, seizures, and restraint.
- Primary absolute—rare myeloproliferative disorder.
- Secondary absolute caused by tissue hypoxia—chronic pulmonary disease, cardiac disease or anomaly with right-to-left shunting, high altitude, brachycephalic breed conformation, methemoglobinemia, and impairment of renal blood supply.
- Secondary absolute caused by inappropriate EPO secretion (rare)—renal cyst or tumor, hydronephrosis, hyperadrenocorticism, hyperthyroidism, pheochromocytoma, nasal fibrosarcoma, hepatic neoplasia, extradural schwannoma, cecal leiomyosarcoma, hyperandrogenism, therapeutic administration of recombinant EPO.

RISK FACTORS

None



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Moderately high PCV and total plasma protein with concurrent dehydration—suggest relative polycythemia.
- Secondary absolute—caused by diseases that produce chronic hypoxemia or by space-occupying

lesions of the kidney, endocrine disorders, neoplasms that produce EPO or an EPO-like substance independent of hypoxia, history of EPO administration.

• Polycythemia vera—diagnosed by elimination of other causes.

CBC/BIOCHEMISTRY/URINALYSIS

Assessment begins with CBC and total plasma protein measurement. Concurrent anemia, hypoproteinemia, dehydration, and dilutional effects of fluid therapy can affect interpretation of PCV and total plasma protein values; additional tests selected as indicated and noted in following table (Inc = Increase, Dec = Decrease):

OTHER LABORATORY TESTS

- SaO₂ and EPO determinations—diagnose absolute polycythemia.
- Hormone assays—assessment of endocrine dysfunction; EPO samples can be sent to a human testing laboratory; control sample from a normal animal (not a blood donor) should also be submitted.
- Extensive overlap in EPO values exists between normal and affected animals; in some animals with secondary absolute polycythemia, low or normal EPO values have been reported. Laboratories at the University of Pennsylvania and Tennessee have established reference intervals for EPO in dogs and cats.

IMAGING

Radiography and ultrasonography to detect cardiopulmonary disease and space-occupying lesions of the kidneys or other neoplasms.

DIAGNOSTIC PROCEDURES

Pulse oximetry to determine oxygen saturation of the blood.

PATHOLOGIC FINDINGS

- Polycythemia vera—generalized vascular congestion, arterial thrombosis, variable splenomegaly, and diffusely red bone marrow with reduced fat gross findings.
- Microscopic findings include a hyperplastic marrow with a normal or reduced myeloid/erythroid ration and reduced iron content.



TREATMENT

APPROPRIATE HEALTH CARE

- Relative—rehydration with IV fluids appropriate for the primary cause; assessment of renal function, gastrointestinal system, acid-base status, and electrolyte balance important to the selection of the fluid.
- Absolute—phlebotomy recommended (20 mL/kg over 1 to several days) to reduce the RBC mass to a PCV of 55%; blood volume should be replaced concurrently with isotonic fluids to prevent hypotension, cardiovascular collapse, and thrombosis.
- Secondary caused by inappropriate EPO production—phlebotomy combined with identification and removal of the EPO source.
- Secondary caused by hypoxemia—

POLYCYTHEMIA

(CONTINUED)

Table 1

Mechanism	Relative	Absolute		
	Dehydration	Primary Myeloproliferative	Secondary Hypoxemia	Secondary Excess EPO
PCV	Inc	Marked Inc > 60%	Marked Inc > 60%	Marked Inc > 60%
TPP	Inc	N	N	N
SaO ₂		N > 90%	Dec << 90%	N > 90%
EPO		N/Dec	Inc	Inc
Bone marrow		Erythroid Hyperplasia	Erythroid Hyperplasia	Erythroid Hyperplasia
Other	Prerenal Azotemia	Inc WBC Inc Platelets		

phlebotomy and hydroxyurea. The high PCV is an appropriate compensatory response; thus phlebotomy may be dangerous; if indicated, remove blood at a slower rate (5 mL/kg); a higher PCV (60–65%) may be necessary to sustain life until the cause of hypoxemia can be corrected. • Polycythemia vera—phlebotomy (20 mL/kg) and hydroxyurea; frequency of bleeding and dosage adjusted to maintain a PCV of 55% in dogs and 45% in cats.

NURSING CARE

Oxygen therapy may be indicated for patients with cyanosis, low arterial oxygen saturation, severe cardiopulmonary disease, or weakness following phlebotomy.

ACTIVITY

Excessive exercise should be avoided during phlebotomy.

DIET

Normal diet with free-choice water.

P

CLIENT EDUCATION

- Patients need to be observed for change in activity such as weakness, difficult breathing, bleeding episodes, or evidence of systemic infections.
- If chemotherapy drugs are dispensed, personal safety handling and administration of these drugs should be discussed. These drugs can cause changes in skin pigmentation and sloughing of toenails.

SURGICAL CONSIDERATIONS

If surgery is necessary, monitoring oxygen saturation with pulse oximetry is necessary to avoid hypoxemia.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Polycythemia vera—hydroxyurea (40–50 mg/kg PO divided twice daily, dogs; 30 mg/kg q24h, cats).
- Polycythemia secondary to hypoxemia—hydroxyurea (40–50 mg/kg PO q48h).

CONTRAINDICATIONS

Phlebotomy may be contraindicated in patients with hypoxemia.

PRECAUTIONS

- Removal of blood at a rapid rate can cause hypotension and cardiovascular collapse.
- Adverse effects of hydroxyurea include marrow hypoplasia with thrombocytopenia, anemia, and neutropenia, alopecia, changes in skin pigmentation, and sloughing of toenails.
- Methemoglobinemia and hemolytic anemia are reported in cats treated with hydroxyurea.

ALTERNATIVE DRUG(S)

Polycythemia vera—chlorambucil (0.2 mg/kg PO q24h, dogs and cats) or busulfan (2–4 mg/m² PO q24h, dogs).

**FOLLOW-UP****PATIENT MONITORING**

- PCV, total plasma protein, urine output, and body weight 2–3 times daily in severely dehydrated animals until normal hydration is maintained.
- Patients being treated for polycythemia vera by chemotherapy—monitor weekly for changes in PCV, leukocytes, and platelets during the initial treatment; then monthly for adjustment of chemotherapy and periodic phlebotomy.
- Periodic assessment of marrow iron store or serum iron levels is indicated to detect iron deficiency.

POSSIBLE COMPLICATIONS

- Hyperviscosity in patients with absolute polycythemia, especially polycythemia vera, may lead to thrombosis, infarction, or hemorrhage.
- Chemotherapy may cause bone marrow suppression.
- Patients with absolute polycythemias can develop iron deficiency as a result of phlebotomy and active erythropoiesis.

EXPECTED COURSE AND PROGNOSIS

- Relative polycythemia: identification and correction of the primary cause with appropriate fluid therapy result in recovery with a fair to good prognosis depending on primary cause.
- Secondary absolute polycythemia due to hypoxemia: clinical course and prognosis are determined by the severity of the lesion causing hypoxemia. Improvement of cardiac

function or inflammatory lung disease and a reduction in PCV with improved oxygen saturation improves quality of life. Prognosis would remain guarded.

- Secondary absolute polycythemia due to inappropriate EPO secretion: if the tissue source of excessive EPO secretion can be identified (tumor, renal cyst, endocrine disease) and removed or corrected, the polycythemia will resolve with a good to fair prognosis depending on cause.
- Primary absolute polycythemia: this myeloproliferative disorder does respond to treatment but requires monitoring for changes in CBC values and clinical evidence of hemorrhage, thrombosis, or decreased activity. Prognosis is guarded.

**MISCELLANEOUS****PREGNANCY/FERTILITY/BREEDING**

Hydroxyurea may arrest or inhibit spermatogenesis.

SYNOMYS

Erythrocytosis

SEE ALSO

- Hyperviscosity Syndrome
- Polycythemia Vera

ABBREVIATIONS

- EPO = erythropoietin
- PCV = packed cell volume
- RBC = red blood cell
- SaO₂ = arterial oxygen saturation

Suggested Reading

Cook SM, Lothrop CD. Serum erythropoietin concentrations measured by radioimmunoassay in normal, polycythemic, and anemic dogs and cats. J Vet Intern Med 1994; 8:18–25.

Author Alan H. Rebar

Consulting Editor Alan H. Rebar

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Client Education Handout
available online

POLYCYTHEMIA VERA



BASICS

OVERVIEW

Myeloproliferative disorder of the chronic myelogenous leukemia spectrum (CML), resulting in high blood viscosity secondary to an increased RBC mass.

SIGNALMENT

- Dog and cat
- Primarily old animals

SIGNS

- Gradual in onset; may be incidental diagnosis
- Depression
- Anorexia
- Weakness
- Polydipsia and polyuria
- Erythema of skin and mucous membranes
- Dilated and tortuous retinal blood vessels
- Uveitis
- Acute blindness
- Splenomegaly and hepatomegaly uncommon

CAUSES & RISK FACTORS

A *JAK2* mutation has been implicated in the disease pathogenesis.



DIAGNOSIS

Diagnostic tests should exclude all other conditions that may lead to increased packed cell volume (PCV) and red blood cell mass.

DIFFERENTIAL DIAGNOSIS

- Severe dehydration
- Renal neoplasia
- Chronic pyelonephritis
- Hyperadrenocorticism
- Androgen stimulation
- Chronic pulmonary disease
- Cardiac disease with right-to-left shunts

CBC/BIOCHEMISTRY/URINALYSIS

- High PCV
- Absolute increase in RBC mass

- Prerenal azotemia possible
- Leukocytosis in 50% of dogs

OTHER LABORATORY TESTS

- PaO₂—normal.
- Serum erythropoietin concentrations are usually low to zero and often overlap with those reported for other causes of polycythemia.
- Cytologic examination of bone marrow and core biopsy, in parallel with peripheral blood count analysis.

IMAGING

- Radiography—assess kidneys and cardiopulmonary system.
- Abdominal ultrasonography—assess kidneys and adrenal glands.
- Echocardiography—evaluate for right-to-left cardiac shunts.

DIAGNOSTIC PROCEDURES

- Bone marrow biopsy
- Electrocardiography—assess heart disease
- Retinal examination/ophthalmologic consult
- Blood pressure measurement



TREATMENT

- Phlebotomy and concurrent replacement with intravenous isotonic fluids—to provide relief of signs during clinical crisis.
- Hydroxyurea—may temporarily decrease the RBCs and provide disease control.
- Consult a veterinary medical oncologist for most current recommendations and disease management.



MEDICATIONS

DRUG(S)

Hydroxyurea—40–50 mg/kg PO divided twice daily; titrate to response and toxicity (dog and cat).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

Periodic reexaminations with serial CBCs, retinal examinations, and serum biochemical profiles to monitor disease control and hydroxyurea side effects on bone marrow and other organs.



MISCELLANEOUS

SEE ALSO

Polycythemia

ABBREVIATIONS

- CML = chronic myelogenous leukemia
- PCV = packed cell volume
- RBC = red blood cell

Suggested Reading

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Weiss DJ, Aird B. Cytologic evaluation of primary and secondary myelodysplastic syndromes in the dog. *Vet Clin Pathol* 2001, 30:67–75.

Author Nick Dervisis

Consulting Editor Timothy M. Fan

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POLYNEUROPATHIES (PERIPHERAL NEUROPATHIES)



BASICS

DEFINITION

Diseases affecting peripheral motor, sensory, autonomic, and/or cranial nerves, in any combination.

PATHOPHYSIOLOGY

- Inherited or acquired (degenerative, idiopathic, metabolic/endocrine, neoplastic, paraneoplastic, immune-mediated inflammatory, infectious, drugs/toxic).
- Primary pathologic process—(1) *axonal neuropathies*, caused by either destruction or degeneration of neuronal cell bodies in dorsal root ganglia, ventral horn cells, or autonomic ganglia (neuronopathies) or axonal degeneration with secondary demyelination (axonopathies), or (2) *demyelinating neuropathies* with primary demyelination due to disease of the Schwann cells or myelin sheath.

SYSTEMS AFFECTED

- Nervous—peripheral nervous system (occasionally also affecting CNS); possible involvement of the cranial nerves.
- Other organ systems may be involved in the primary disease process.

GENETICS

- Most inherited—autosomal recessive disorders.
- Spinal muscular atrophy in Brittany spaniels, laryngeal paralysis in Bouvier des Flandres—autosomal dominant.

INCIDENCE/PREVALENCE

- Inherited—rare.
- Peripheral nerve involvement in metabolic and neoplastic diseases—incidence unknown.
- Inflammatory—uncommon; CHP most frequent.

GEOGRAPHIC DISTRIBUTION

- CHP—North and Central America, parts of South America.
- Distal denervating disease—dogs in UK; not reported elsewhere.
- Dysautonomia—mostly dogs (occasionally cats) in Missouri, Oklahoma, and Kansas; cats in Scandinavia and UK.

SIGNALMENT

Species

Dog and cat

Breed Predilections

Inherited

Spinal Muscular Atrophy

- Brittany spaniel, Swedish Lapland dog, English pointer, German shepherd, Doberman, rottweiler, Griffon Briquet, Saluki, Maine Coon cats
- Progressive neuronopathy—cairn terrier

Axonopathies

- Giant axonal neuropathy—German shepherd
- Progressive axonopathy—Boxer
- Laryngeal paralysis—Bouvier des Flandres
- Laryngeal paralysis/polyneuropathy complex—Dalmatian, rottweiler, Pyrenean

mountains dog • Distal sensorimotor polyneuropathy—rottweiler, Alaskan Malamute, Great Dane, Leonberger dog, Bouvier des Flandres • Progressive central and peripheral sensorimotor axonopathy—golden retriever • Central-peripheral distal axonopathy—Birman cat • Axonal neuropathy—Snowshoe cat • Primary hyperoxaluria—domestic shorthair cats

Demyelination

- Hypertrophic neuropathy—Tibetan mastiff
- Congenital hypomyelination neuropathy—golden retriever • Demyelinating polyneuropathy—miniature schnauzers
- Recurrent demyelinating-remyelinating polyneuropathy—Bengal cat

Lysosomal Storage Diseases

- Globoid cell leukodystrophy—West Highland white terrier, cairn terrier, domestic shorthair cats • Alpha-L-fucosidosis—English Springer spaniel • Mannosidosis—Persian and domestic shorthair cats • G_{M1} gangliosidosis type II—Siamese and Korat cats • Sphingomyelinosis (Niemann-Pick disease type A)—Siamese and Balinese cats
- Glycogenosis type IV—Norwegian forest cat

Sensory Neuropathy

- Longhaired dachshund, English pointer, German shorthaired pointer, English springer spaniels, French spaniels, Jack Russell terrier, border collies • Ganglionic radiculitis—Siberian husky

Acquired

- CHP—higher incidence in coonhounds
- Clinical diabetic polyneuropathy—more common in cat than dog • Insulinomas—German shepherd, boxer, Irish setter, standard poodle, collie

Mean Age and Range

Inherited

- Often begin at < 6 months of age.
- Feline hyperchylomicronemia—1–8 months.
- Feline hyperoxaluria—5–9 months.
- Rottweiler, Bouvier, Leonberger distal polyneuropathies—> 1 year.
- Giant axonal neuropathy in German shepherd—14–16 months.
- Intermediate and chronic forms of spinal muscular atrophy in heterozygote Brittany spaniel—6–12 months.

Acquired

- Secondary to neoplasia and insulinoma-associated hypoglycemia—middle-aged to older animals.
- Neospora caninum* polyradiculoneuritis—usually dogs < 6 months of age.
- Ganglionic radiculitis—> 1 year.

SIGNS

Historical Findings

Inherited

- Most—progressive LMN tetraparesis; generalized weakness, muscle tremors and atrophy, plantigrade/palmigrade stance; stridor/voice change if laryngeal paralysis.
- Sensory neuropathies—self-mutilation (nociceptive deficits), mild to severe ataxia.

- Lysosomal storage diseases—slowly progressive CNS involvement (head tremors, ataxia, dysmetria, seizures, blindness, dementia) occur in conjunction with the LMN signs.
- Sphingomyelinosis in cats—often present only with progressive motor and sensory neuropathy.
- Giant axonal neuropathy of German shepherds—rapidly progressive generalized weakness (< 3 weeks). **Acquired**

- Rapid or slow progression.
- Rapidly progressive course—initial stiff, stilted gait, leading to generalized LMN paresis or paralysis (CHP, distal denervating disease).
- Slowly progressive course—generalized weakness and muscle atrophy; in distal polyneuropathies (diabetic neuropathy especially in cats), plantigrade/palmigrade stance.
- Dysautonomia—primarily acute onset (< 48 hours) of depression, anorexia, regurgitation, vomiting, paralytic ileus, xerostomia, KCS, third eyelid protrusion, urinary incontinence.
- Metabolic—owner reports non-neurologic clinical signs associated with weakness.
- Paraneoplastic—primary tumor may be clinically silent at time of presentation or revealed on thoracic radiographs or abdominal ultrasound.

Physical Examination Findings

- Motor and sensorimotor—tetraparesis to tetraplegia, hyporeflexia to areflexia, hypotonia to atonia, and muscle atrophy classic; muscle tremors common.
- Sensory—proprioceptive deficits, hypoesthesia to anesthesia, without muscle atrophy or hyporeflexia (except in boxers); sensory ataxia.
- Paraesthesia—feline diabetic neuropathy, sensory neuropathies.
- Hypothyroidism—may be associated with generalized polyneuropathy, laryngeal and/or facial nerve paralysis, megaesophagus, and vestibular signs.
- Lysosomal storage diseases—hepatosplenomegaly common.
- Paraneoplastic—may find evidence of neoplasia.
- Dysautonomia—dry nose, KCS, bradycardia, anal areflexia.
- Primary hyperchylomicronemia (cats)—lipid granulomata, which can be palpated under the skin and abdomen.
- Primary hyperoxaluria (cats)—enlarged, painful kidneys on palpation.
- Cranial nerve abnormalities (including dysphonia/aphonia)—variable.

CAUSES

Acquired

- Immune-mediated—primary or secondary; may be seen with SLE, glomerulonephritis, polyarthritis.
- Metabolic/endocrine—diabetes mellitus (cats), hypothyroidism, hyperadrenocorticism.
- Neoplastic/Paraneoplastic—insulinoma, carcinomas, malignant melanoma, mast cell tumor, osteosarcoma, multiple myeloma, lymphosarcoma.
- Infectious—*N. caninum*, FeLV, FIV.
- Chemotherapy drugs—vincristine, vinblastine, cisplatin.
- Toxic—

(CONTINUED)

POLYNEUROPATHIES (PERIPHERAL NEUROPATHIES)

thallium, organophosphates, salinomycin (cats), lasalocid (dogs). • Idiopathic.

RISK FACTORS

Development of specific diseases (metabolic, immune, neoplastic) or exposure to specific drugs/toxins or causal factors (raccoon saliva).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute—botulism; tick paralysis; fulminant myasthenia gravis; acute multifocal myelopathies. • Chronic—polymyopathy; chronic multifocal myelopathies.

CBC/Biochemistry/Urinalysis

- Standard laboratory tests—often normal; may indicate underlying metabolic or neoplastic disease. • High serum creatine kinase—indicates an accompanying myopathy or diagnosis of polymyopathy.

OTHER LABORATORY TESTS

- Antinuclear antibody, Coombs' test—if immune disease suspected. • Low total T₄, low free T₄, and high endogenous TSH—hypothyroidism. • Amended insulin: glucose ratio > 30—supports the diagnosis of insulinoma. • Serology—assists in the diagnosis of *N. caninum*, FIV, FeLV infection.
- Diminished lysosomal enzyme activity in leukocytes, cultured fibroblasts—lysosomal storage diseases. • Pharmacologic testing (pilocarpine ophthalmic drops, bethanechol challenge)—dysautonomia. • High serum cholesterol and triglycerides, low lipoprotein lipase—hyperchylomicronemia. • Oxalate and/or l-glyceric acid in urine—primary hyperoxaluria. • Monoclonal gammopathy—multiple myeloma.

IMAGING

Thoracic and abdominal radiographs—search for a neoplastic cause; megaesophagus, ileus, bladder atony, constipation, and delayed gastric emptying in dysautonomia.

DIAGNOSTIC PROCEDURES

- Electrophysiology (EMG, motor and sensory nerve conduction studies ventral and dorsal nerve root studies)—cornerstone for diagnosis. • Lumbar CSF analysis—valuable in diagnosing nerve root involvement.
- Muscle biopsy—confirms denervation.
- Peripheral nerve biopsy (distal)—further characterizes disease process.

PATHOLOGIC FINDINGS

Lesion distribution along peripheral nerves (proximal, distal, widespread) and degree of axonal degeneration, demyelination, and/or neuronal cell body degeneration depends on the specific condition present.



TREATMENT

APPROPRIATE HEALTH CARE

- Usually outpatient. • Inpatient—observe dogs with CHP closely for respiratory failure in early progressive phase of disease.

NURSING CARE

- Dysautonomia—may require IV fluid therapy and/or parenteral feeding. • Physical therapy.

DIET

- Generally no special management, unless megaesophagus or dysphagia occurs.
- Hyperchylomicronemia—low-fat diet alone can resolve the polyneuropathy in 2–3 months. • Paralysis—ensure patient can reach food and water. • Regurgitation and/or vomiting—temporarily halt oral intake; consider gastrostomy tube. • Diabetes mellitus—monitor food intake; in cats, feed a low-carbohydrate, high-protein diet; diabetic neuropathy often reversible with treatment.

CLIENT EDUCATION

- Treatment of primary cause may not lead to reversal of signs; in some cases, deterioration will continue. • Canine axonal degeneration—progressive deterioration.



MEDICATIONS

DRUG(S) OF CHOICE

- Inherited—most untreatable. • Acquired—treat primary cause with the hope that the secondary polyneuropathy improves or resolves; not always successful. • Chronic relapsing demyelinating neuropathy—most likely of immune origin; may improve with long-term immunosuppressive therapy (prednisone, azathioprine, cyclophosphamide); response of individual patient variable.
- SLE-related—treat as for chronic relapsing polyneuropathy. • Neoplasia—treat primary neoplasia. • *Neospora*-associated polyradiculoneuritis—clindamycin combined with pyrimethamine. • Dysautonomia—treat symptomatically with IV fluids, artificial tears, metoclopramide, bethanechol (cats, 0.5–2.5 mg SC q12h or 2.5–10 mg PO q6–8h; dogs, 0.5–15 mg SC q12h or 2.5–30 mg PO q6–8h), and pilocarpine eye drops.

CONTRAINdicATIONS

- Corticosteroids—contraindicated in *Neospora*-associated polyradiculoneuritis, hyperadrenocorticism, and CHP.



FOLLOW-UP

PATIENT MONITORING

Repeat neurologic examinations.

PREVENTION/AVOIDANCE

- Avoid breeding patients with *Neospora* (placental transfer of the organism from the bitch). • Avoid contact with raccoons.
- Avoid future vaccinations if suspected associated with vaccines.

POSSIBLE COMPLICATIONS

Continued neurologic deterioration leading to inability to ambulate, severe muscle atrophy, pressure sores, urinary tract infection, muscle fibrosis, aspiration pneumonia.

EXPECTED COURSE AND PROGNOSIS

- Demyelinating conditions—more rapid improvement than axonal neuropathies (majority), which can take months for partial or complete recovery, if at all. • Inherited—most have a poor prognosis (except hyperchylomicronemia in cats). • Acute polyradiculoneuritis (CHP)—good long-term prognosis; may take weeks to months to recover. • Metabolic—fair-to-good prognosis with successful treatment of primary metabolic abnormality; insulinomas have high recurrence rate. • Other acquired—most show continued deterioration despite treatment.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Immunosuppressive agents—contraindicated.

ABBREVIATIONS

- CHP = coonhound paralysis • CNS = central nervous system • CSF = cerebrospinal fluid • EMG = electromyography • FeLV = feline leukemia virus • FIV = feline immunodeficiency virus • LMN = lower motor neuron • SLE = systemic lupus erythematosus • T4 = thyroxine • TSH = thyroid stimulating hormone

INTERNET RESOURCES

vetneuromuscular.ucsd.edu

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Client Education Handout
available online

POLYPHAGIA



BASICS

OVERVIEW

Increased food intake

PATHOPHYSIOLOGY

- Failure to assimilate or loss of nutrients (e.g., maldigestion/malabsorption syndromes such as exocrine pancreatic insufficiency).
- Inability to use nutrients (e.g., diabetes mellitus, poor-quality diets, gastrointestinal parasites).
- Hypoglycemia (e.g., insulinoma, insulin overdose).
- Increased metabolic rate or demand (e.g., hyperthyroidism, cold environments, pregnancy, lactation).
- Psychologic or learned behaviors (e.g., palatable diets, competition, drugs such as anticonvulsants or glucocorticoids).

SYSTEMS AFFECTED

- Cardiovascular—obesity can worsen clinical cardiac disease.
- Central nervous system—tumors of the brain, especially of the hypothalamus, can cause polyphagia.
- Integument—obese animals, especially cats, are susceptible to dermatitis.
- Musculoskeletal—overweight patients are susceptible to arthritis and other orthopedic problems.
- Respiratory—obesity exacerbates dyspnea in patients with respiratory disease.

SIGNALMENT

Dogs and cats

P SIGNS

Historical Findings

- Eating more frequently and/or a greater quantity than normal.
- Excessive food-seeking and food-stealing behaviors possible.
- Weight loss may occur with certain disease states (e.g., exocrine pancreatic insufficiency, diabetes mellitus, hyperthyroidism).
- PU/PD occurs in some patients (diabetes mellitus, hyperthyroidism, hyperadrenocorticism).

Physical Examination Findings

Patients may have excessive body fat, but those with an underlying medical problem (e.g., exocrine pancreatic insufficiency, diabetes mellitus, hyperthyroidism) may be thin.

CAUSES & RISK FACTORS

Physiologic

- Pregnancy
- Lactation
- Growth
- Response to a cold environment
- Increased exercise

Pathologic

- Diabetes mellitus

- Hyperthyroidism—cats
- Hyperadrenocorticism—dogs
- Exocrine pancreatic insufficiency
- Gastrointestinal parasites
- Insulinoma
- Insulin overdose
- Lymphangiectasia
- Growth hormone–secreting pituitary tumor
- Megaesophagus
- Lymphocytic plasmacytic enteritis—cats—uncommon
- Neoplasms of the brain—rare
- Gastrointestinal neoplasms—rare

Iatrogenic

- Corticosteroids
- Progestins
- Benzodiazepines
- Anticonvulsants
- Palatable food/overfeeding
- Poor diet
- Competition for food



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

PU/PD (excessive trips to food/water area)—differentiate by observation.

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilia, monocytosis, lymphopenia, and eosinopenia with hyperadrenocorticism, and in patients receiving corticosteroids.
- Hyperglycemia with diabetes mellitus, growth hormone–secreting pituitary tumors (cats, insulin-resistant diabetes mellitus), and hyperadrenocorticism (mild).
- Hypercholesterolemia with recent food intake, hyperadrenocorticism, and diabetes mellitus, and in patients receiving corticosteroids.
- High ALP and ALT activity with hyperadrenocorticism (dogs), hyperthyroidism (cats), and diabetes mellitus, and in patients receiving corticosteroids.
- Hypoproteinemia with protein-losing enteropathies (e.g., lymphangiectasia, inflammatory bowel disease).
- Hypoglycemia in patients with insulinoma or insulin overdose.
- Low urine specific gravity with diabetes mellitus, diabetes insipidus, hyperthyroidism, and hyperadrenocorticism, and in patients receiving corticosteroids.
- Glucosuria, possibly ketonuria, with diabetes mellitus.

OTHER LABORATORY TESTS

- Fecal examination to rule out gastrointestinal parasites.
- Serum trypsin-like immunoreactivity to diagnose exocrine pancreatic insufficiency.
- Total serum T_4 to rule out hyperthyroidism (cats); T_3 suppression testing if hyperthyroidism is suspected but serum total T_4 is normal.

- Low-dose dexamethasone suppression or ACTH stimulation test to diagnose hyperadrenocorticism; plasma ACTH level or high-dose dexamethasone suppression testing to differentiate pituitary-dependent hyperadrenocorticism from adrenal tumor if hyperadrenocorticism is confirmed with the low-dose dexamethasone suppression test or ACTH stimulation test.
- Serum insulin levels in hypoglycemic patients to rule out insulinoma.

IMAGING

- Abdominal radiology may demonstrate hepatomegaly associated with hyperadrenocorticism, diabetes mellitus, and corticosteroid administration.
- Abdominal ultrasonography may demonstrate an adrenal mass or bilateral adrenomegaly (hyperadrenocorticism), hepatomegaly (hyperadrenocorticism, diabetes mellitus, and corticosteroid administration), bowel wall thickening or bowel wall layering disruption (inflammatory bowel disease, lymphoma, lymphangiectasia), and pancreatic masses (insulinoma).
- Magnetic resonance imaging could be used to visualize a neoplasm of the hypothalamus.

DIAGNOSTIC PROCEDURES

Endoscopy with biopsy of the upper gastrointestinal tract to rule out gastrointestinal diseases.



TREATMENT

- Usually outpatient medical management.
- Polyphagia without weight gain or with weight loss is more likely due to a medical problem; evaluate the animal prior to food restriction or manipulation.
 - Once pathologic causes of polyphagia have been excluded, limit the amount of food available, feed a reduced-calorie diet, and/or increase exercise if obesity or weight gain is present.
 - Owners must measure food to accurately assess intake.
 - Some dogs may benefit by the addition of low-calorie bulky foods such as canned green beans.
 - Feeding smaller meals two to three times daily may be beneficial for some patients, provided the total food provided remains the same as required by life stage and activity to promote weight loss or prevent weight gain.
 - Removing the pet during human meal preparation and consumption to reduce begging behavior and the pet obtaining additional food.
 - Slowing down the rate of eating may be beneficial in some dogs, using food-dispensing toys that require manipulation to obtain daily ration.

(CONTINUED)

POLYPHAGIA

- If social issues within the home influence intake these must be addressed:
 - Feed all dogs in separate locations, preferably without visual contact.
 - Have multiple feeding stations available in a multiple-cat home.
- The average animal's daily caloric need can be estimated by the formula $30 \times \text{weight (kg)} + 70$.
- Chew toys can be used as a substitute for food.

**MEDICATIONS****DRUG(S)**

- See specific diseases for detailed therapy.
- Drug-induced—attempt to taper or discontinue drug.
- If a compulsive eating disorder is suspected in dogs, clomipramine (1–3 mg/kg PO q12h) or fluoxetine 1–2 mg/kg q24h may be used or in cats clomipramine 0.25–1.0 mg/kg q24h or fluoxetine 0.5–1.0 mg/kg q24h.
- Dirlotapide is a selective microsomal triglyceride transfer protein inhibitor that blocks the assembly and release of lipoprotein chylomicrons into the bloodstream, thus triggering peptide YY release and a decreased

appetite. This could be used in obese dogs at a dose of 0.01–0.02 mL/kg PO q24h (see package insert for dose adjustment protocol).

**FOLLOW-UP****PATIENT MONITORING**

- Monitor body weight in patients with non-pathologic causes of polyphagia.
- Assess compliance with feeding regime and food measurement to decrease intake and promote weight loss.

POSSIBLE COMPLICATIONS

- Obesity in non-pathologic polyphagia.
- Owner responds to begging behavior and caloric intake is not decreased.
- Weight loss/emaciation in pathologic causes of polyphagia.
- Worsening of respiratory or cardiovascular disease processes in obese patient.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Obesity

PREGNANCY/FERTILITY/BREEDING

A normal physiologic response to pregnancy.

SYNONYMS

- Eating disorder
- Hyperphagia

SEE ALSO

- Compulsive Disorders—Cats
- Compulsive Disorders—Dogs
- Coprophagia and Pica
- Obesity

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- PU/PD = polyuria/polydipsia
- T₃ = triiodothyronine
- T₄ = thyroxine

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POLYPOID CYSTITIS



BASICS

OVERVIEW

Polyloid cystitis is a chronic inflammatory condition of the urinary bladder characterized by villous or polyloid protrusions from the mucosa. Polyloid projections are diffusely located over the bladder surface and may be present in the urethra. If they become eroded and ulcerated, varying degrees of hematuria and dysuria occur. The gross appearance of polyps cannot be distinguished from that of bladder neoplasms such as transitional cell carcinomas. Polyloid cystitis in dogs appears to be associated with chronic irritation of the mucosa from either infectious or non-infectious inflammation.

SIGNALMENT

- Dogs with chronic urinary tract infections or urolithiasis.
- No cases reported in cats.

SIGNS

- Initially, may be asymptomatic.
- Hematuria is the most common sign.
- Gross hematuria often occurs at the end of the micturition stream.
- Pollakiuria and dysuria may also be present and are associated with irritation of the polyps.
- Urethral obstruction could occur if a sufficient number of bladder polyps are located in the trigone area of the bladder. Polyps originating or in the urethra may also cause partial or total obstruction.
- Ureteral obstruction may occur if polyps surround the ureteral orifice.
- Urinary tract infection may be present concurrently, which can predispose to upper UTI.

P

CAUSES & RISK FACTORS

- Causes of polyloid cystitis in dogs have not been well documented, but this disorder is commonly associated with UTI or urolithiasis.
- Chronic infection and inflammation secondary to indwelling transurethral urinary catheters have been related to cases of polyloid cystitis in humans.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Polyloid cystitis should be ruled-out in cases of hematuria, pollakiuria, dysuria, and recurrent UTI.
- Bladder neoplasms (such as TCC), UTI, and urolithiasis are the most common rule-outs.

CBC/BIOCHEMISTRY/URINALYSIS

- Serum biochemistry profiles should be normal in most cases of polyloid cystitis unless azotemia occurs as a result of obstruction to urine outflow and/or concurrent pyelonephritis.
- Urinalysis will reveal hematuria, pyuria, and transitional epithelial cells.

OTHER LABORATORY TESTS

- Urine should be cultured by sterile catheterization or at the time of cystoscopy, but not by cystocentesis until TCC has been ruled-out. This will prevent potential abdominal spread of TCC along the needle track.
- Representative polyps removed via cystoscopy or cystotomy should be placed in formalin for light microscopic examination.
- An adequate sample of bladder tissue should be placed in culture media suitable for growth of microbes. Treatment with antimicrobics should be discontinued to minimize inhibition of growth of pathogens in the bladder tissue.

IMAGING

- Survey radiographs may reveal a normal bladder, an irregular thickening of the surface contour of the bladder, and/or concurrent urolithiasis.
- Double-contrast cystography or positive-contrast cystography may reveal irregular polyloid masses in the bladder lumen and/or a thickened bladder wall. The most common location of involvement is the cranioventral bladder wall. Single large polyps with a narrow or broad base may be observed scattered throughout the contrast puddle. Uroliths will migrate to the most dependant portion of the contrast puddle.
- Ultrasonography may show polyps scattered along the mucosal surface of the bladder, especially in the cranioventral aspect.

DIAGNOSTIC PROCEDURES

- Cystoscopic or ultrasound-guided biopsy may be used to obtain representative portions of the polyps for light microscopic examination of stained sections of the lesions.
- More invasive, full-thickness biopsy of the wall of the bladder via cystotomy may be required to include the base of the polyps with an adequate margin of healthy tissue.

PATHOLOGIC FINDINGS

- Gross changes involving the mucosal surface of the urinary bladder include single or multiple small masses ranging from 1 to 10 mm in size. The masses may be nodular with a broad base or attached to the bladder wall by a thin stalk.
- Light microscopic changes include polyloid projections of hyperplastic epithelium that surround a core of proliferative connective tissue mixed with acute and chronic

inflammation (congestion, edema, and acute and chronic inflammatory cells). Findings characteristic of malignancy (e.g., disproportionate enlargement of nuclei in relation to the cytoplasm; increase in chromatin content causing hyperchromasia; structural changes such as aberrant chromatin patterns, lack of distinct cell boundaries, irregularity in cell outlines; enlargement and/or increase in number of nuclei; multinucleated cells with atypical nuclei; abnormal number of mitotic figures; cytoplasmic inclusions and vacuolization; invasion of basement membranes) are conspicuously absent. In some patients, changes typical of granulomatous inflammation predominate.



TREATMENT

- Elimination of bacteria that are a source of chronic irritation is a rational therapeutic goal.
- Non-surgical removal of urocystoliths (voiding urohydropropulsion, lithotripsy, dietary management) that are causing chronic irritation may result in elimination of inflammatory polyps.
- The polyps may also be removed either by cystoscopy or cystotomy.
- Partial cystectomy may be required to remove polyps affecting large portions of the bladder. The remaining portion of the urinary bladder may compensate by increasing its capacity to contain urine in 3–6 months.



MEDICATIONS

DRUG(S)

- Select an antibiotic based on culture of urine and polyp tissue. The patient should receive antibiotic therapy for a minimum of 4–6 weeks.
- Piroxicam and immunosuppressive drugs are of unproven value.



FOLLOW-UP

PATIENT MONITORING

- A urine culture should be performed 7–10 days after antimicrobial therapy is initiated, to confirm urine sterility. Follow-up urinalysis and urine cultures should also be performed by cystocentesis 7 days after antimicrobial therapy has ceased and 1 month post-therapy.

(CONTINUED)

- Ultrasonographic reevaluation of the urinary tract is recommended at 1, 3, and 6 months.

PREVENTION/AVOIDANCE

Control of predisposing factors such as UTI and urolithiasis.

POSSIBLE COMPLICATIONS

- Chronic UTIs
- Upper UTI
- Complete obstruction of ureters or urethra

EXPECTED COURSE AND PROGNOSIS

- The expected course is favorable and the prognosis good if the underlying cause is treated and eradicated.
- Rarely patients with polypoid cystitis develop TCC several years after initial diagnosis. It is unknown if some of these cases represent early carcinoma in situ.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Urinary tract infection
- Urolithiasis

AGE-RELATED FACTORS

No age-related factors have been reported

SEE ALSO

- Hematuria
- Transitional Cell Carcinoma
- Urinary Tract Obstruction
- Urolithiasis chapters

ABBREVIATIONS

- TCC = transitional cell carcinoma
- UTI = urinary tract infection

POLYPOID CYSTITIS*Suggested Reading*

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POLYURIA AND POLYDIPSIA



BASICS

DEFINITION

- PU—greater than normal urine production (dogs, > 45 mL/kg/day; cats, > 40 mL/kg/day).
- PD—greater than normal water consumption (dogs, > 90 mL/kg/day; cats, > 45 mL/kg/day).

PATHOPHYSIOLOGY

The volumes of urine produced and water consumed are controlled by interactions between the kidneys, pituitary gland, and hypothalamus. Plasma osmolality (normally determined primarily by serum sodium concentration) is the primary parameter monitored by this control system. Volume receptors within the cardiac atria and aortic arch also influence thirst and urine production. PU may occur when the quantity of functional antidiuretic hormone synthesized in the hypothalamus or released from the posterior pituitary is limited, or when the kidneys fail to respond normally to ADH. PD occurs when the thirst center in the anterior hypothalamus is stimulated. • In most patients, PD maintains hydration (as normal tonicity) as a compensatory response to PU. Patients' plasma becomes relatively hypertonic and activates thirst mechanisms. Occasionally PD is the primary process and PU is the compensatory response. In this case, the patient's plasma becomes relatively hypotonic because of excessive water intake, ADH secretion is reduced, resulting in PU.

SYSTEMS AFFECTED

- Urologic—full bladder
- Cardiovascular—circulating volume
- Endocrine/Metabolic—pituitary gland, hypothalamus play a role in compensation to PU or PD

SIGNALMENT

- Dog and cat. • Congenital diseases in many breeds (e.g., central diabetes insipidus, nephrogenic diabetes insipidus, portal-vascular anomalies, certain renal diseases).
- Hypoadrenocorticism, some causes of primary PD predominantly affect young dogs.
- Renal failure, hyperadrenocorticism, hyperthyroidism, neoplastic disorders affecting the pituitary and hypothalamus predominantly affect middle-aged and older dogs and cats.

CAUSES

- Primary PU due to impaired renal response to ADH—renal failure, HAC (dogs), hyperthyroidism (cats), pyelonephritis, leptospirosis, pyometra, hepatic failure, hypercalcemia, hypokalemia, renal medullary solute washout, dietary protein restriction, drugs, congenital NDI. • Primary PU caused by osmotic diuresis—diabetes mellitus, primary renal glucosuria, post-obstructive

diuresis, some diuretics (e.g., mannitol and furosemide), ingestion or administration of large quantities of solute (e.g., sodium chloride or glucose), and

hypersomatotropism. • Primary PU due to ADH deficiency—idiopathic, traumatic, neoplastic, or congenital CDI; some drugs (e.g., alcohol and phenytoin). • Primary PD—behavioral, pyrexia, pain, organic disease of the anterior hypothalamic thirst center of neoplastic, traumatic, or inflammatory origin.

RISK FACTORS

- Renal, liver and/or endocrine disease
- Administration of diuretics, corticosteroids, anticonvulsants
- Low-protein diets
- Low purine u/d?



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiating Similar Signs

• Differentiate PU from abnormal increase frequency of urination (pollakiuria). Pollakiuria: often associated with dysuria, stranguria, hematuria. Patients with PU void large quantities of urine; patients with pollakiuria frequently void small quantities of urine. Confirm PU/PD by measuring 24-hour water intake and urine output (3- to 5-day collection period preferred). • Alternatively, urinary specific gravity measurement may provide evidence of adequate urine concentrating ability (dogs, > 1.030; cats, > 1.035), ruling-out persistent PU/PD.

Differentiating Causes

- Renal failure, HAC, and DM (dogs). Renal failure, hyperthyroidism, DM: (cats). • If associated with progressive weight loss—consider renal failure, DM, hyperthyroidism, hepatic failure, pyometra, pyelonephritis, hypoadrenocorticism, malignancy-induced hypercalcemia. • If associated with decreased appetite—consider kidney disease, pyelonephritis, malignancy-induced hypercalcemia, hepatic disease, hypoadrenocorticism. • If associated with polyphagia—consider DM, hyperthyroidism, HAC, acromegaly. • If associated with bilateral alopecia or other cutaneous problems—consider HAC, endocrinologic disorders. • If associated with uremic breath and stomatitis—consider advanced kidney disease. • If associated with vomiting—consider kidney disease, hypoadrenocorticism, pyelonephritis, hepatic failure, hypercalcemia, hypokalemia, hyperthyroidism, DM. • If associated with malaise and/or weakness—kidney disease, hypoadrenocorticism, pyometra, hypercalcemia, DM, hepatic disease, hypokalemia, HAC. • If associated with

palpable thyroid nodule—consider hyperthyroidism. • If associated with hypertensive retinopathy—consider renal failure, hyperthyroidism, DM, HAC. • If associated with recent estrus (previous 2 months) in a middle-aged intact female—consider pyometra. • If associated with abdominal distention—consider hepatic failure, HAC, pyometra, nephrotic syndrome. • If associated with lymphadenopathy, anal sac mass or other neoplastic process—consider hypercalcemia of malignancy. • If associated with behavioral or neurologic disorder—consider hepatic failure, primary PD, CDI. • If associated with marked PD (patients almost continuously seek and consume water)—consider primary PD, CDI, NDI. • If patient is on medication, consider drug induced (steroids, diuretics, anticonvulsants) PU/PD. • If patient is consuming a urolith prevention/dissolution or high salt diet, consider diet-induced PU/PD. • **Key point:** PU/PD may be the first sign of disease with many conditions.

CBC/BIOCHEMISTRY/URINALYSIS

- Urinalysis is useful to confirm PU, discriminate water diuresis from solute diuresis, and identify UTI. • Serum sodium concentration or osmolality may help differentiate primary PU from primary PD. Measuring serum osmolality is preferred; calculated serum osmolality is not an acceptable alternative. • Relative hypernatremia or high serum osmolarity suggests primary PU (values typically at or exceed the high end of normal range).
- Hyponatremia or low serum osmolarity suggests primary PD (values typically at or below normal range), except in animals with hypoadrenocorticism, which have hyponatremia and primary PU. • Azotemia is typical of renal causes for PU/PD, but may also indicate dehydration resulting from inadequate compensatory PD.
- Unexpectedly low BUN concentrations suggest hepatic failure. • With high hepatic enzymes, consider HAC (especially when value for ALP exceeds ALT), hyperthyroidism, hepatic failure, pyometra, DM. Administration of some drugs that promote PU/PD (e.g., anticonvulsants and corticosteroids) also may elevate hepatic enzymes. • Persistent hyperglycemia is consistent with DM. • Hyperkalemia, particularly if associated with hyponatremia, suggests hypoadrenocorticism or therapy with potassium-sparing diuretics. • Hypercalcemia induces PU only when it results from increased ionized calcium (not protein-bound calcium) concentration. • Hypercalcemia and hypokalemia can cause, or occur in association with, other diseases that cause PU/PD. • Hypoalbuminemia supports renal or hepatic causes of PU/PD. • Neutrophilia is

(CONTINUED)

consistent with pyelonephritis, pyometra, HAC, corticosteroid administration. • USG values 1.001- 1.003 suggest primary PD, CDI, congenital NDI. • Glucosuria supports a diagnosis of DM or renal glucosuria. • Pyuria, white blood cell casts, and/or bacteriuria should prompt consideration of pyelonephritis.

OTHER LABORATORY TESTS

- ACTH stimulation or dexamethasone suppression tests rule out HAC in middle-aged to older dogs. • Thyroxine concentration to rule out hyperthyroidism in middle-aged to old cats. • Bile acids (fasting and postprandial) to rule out portosystemic shunt or hepatic failure. • Urine culture—chronic pyelonephritis cannot be conclusively ruled-out by absence of pyuria or bacteriuria.
- Cytologic examination of lymph node aspirate may provide evidence of lymphoma, which induces PU by hypercalcemic nephrotoxicity or direct infiltration of renal tissues. • Paired *Leptospira* titer to rule out leptospirosis. • ADH response test to rule-out CDI. • Water deprivation testing (to assess ability to make and respond to ADH) is controversial due to humane considerations; use selectively.

IMAGING

Abdominal survey radiography, ultrasonography: may provide evidence of renal (e.g., primary renal diseases, urinary obstruction), hepatic (e.g., microhepatica, portal vascular anomalies, hepatic infiltrate), adrenal (e.g., adrenal mass or bilateral adrenal hypertrophy suggesting HAC), or uterine (e.g., pyometra) disorders that can contribute to PU/PD.

DIAGNOSTIC PROCEDURES

Modified Water Deprivation with ADH Response Test (see Appendix II)

- Differentiates CDI from primary PD and NDI. Rule out other causes for PU/PD before performing this test. Controversial, some suggest omitting water deprivation and proceeding directly to ADH administration to rule in CDI. Administration of ADH to patients with primary PD may be dangerous.
- Useful for patients with marked PU/PD and hyposthenuria. • Contraindicated in dehydrated and azotemic patients, but ADH response testing may be performed safely in these patients. • Patients that concentrate urine adequately in response to water deprivation have adequate ADH production and renal response to ADH. If other causes have been ruled out, primary PD is presumed to be present. • Failure to concentrate urine adequately in response to properly designed

water deprivation tests, but further concentrate their urine in response to administration of exogenous ADH = CDI.

- Failure to concentrate urine adequately in response to water deprivation and also failure to further concentrate urine in response to administration of exogenous ADH = NDI.



TREATMENT

• Serious medical consequences are rare if patient has free access to water and is able to drink. Until the mechanism of PU is understood, discourage owners from limiting access to water. Direct treatment at the underlying cause. • Provide PU patients with free access to water unless they are vomiting. If vomiting, give replacement maintenance fluids parenterally after appropriate samples have been collected for initial diagnostics. Provide fluids parenterally when other conditions limit oral intake or dehydration persists despite PD. • Base fluid selection on knowledge of the underlying cause for fluid loss. In most patients, lactated Ringer's solution is acceptable. • When dehydration has resulted from withholding water, or when urine is hyposthenuric, providing oral water or parenteral administration of dextrose 5% in water may be preferred to lactated Ringer's solution. • Primary PD—treat by gradually limiting water intake to a normal daily volume. May be necessary to reduce water intake over days–weeks to avoid undesirable behavior such as barking, urine consumption, or other bizarre behavior. Monitor patient closely to avoid iatrogenic dehydration. Salt (1 g/30 kg q12h) or sodium bicarbonate (0.6 g/30 kg q12h) may be given orally to help reestablish renal medullary solute gradient. Consider behavior modification if water restriction alone is unsuccessful.

CLIENT EDUCATION

Do not withhold water from patients with PU because potentially dangerous dehydration may result.



MEDICATIONS

DRUG(S) OF CHOICE

Varies with underlying cause

CONTRAINDICATIONS

Do not administer ADH (or any of its synthetic analogs, such as DDAVP) to patients with primary PD because of the risk of inducing water intoxication.

PRECAUTIONS

Until renal and hepatic failure have been excluded as potential causes for PU/PD, use caution in administering any drug eliminated via these pathways.



FOLLOW-UP

PATIENT MONITORING

- Hydration status—clinical assessment of hydration, serial evaluation of body weight.
- Fluid intake and urine output provide a useful baseline for assessing adequacy of hydration therapy.

POSSIBLE COMPLICATIONS

Dehydration, hypovolemic shock, hypernatremia



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Bacterial UTI. • Urinary incontinence may develop in dogs with concurrent urethral sphincter dysfunction, presumably because of increased bladder filling associated with PD.

SEE ALSO

- Congenital and Developmental Renal Diseases • Diabetes Insipidus • Diabetes Mellitus chapters • Fanconi Syndrome
- Hepatic Failure, Acute
- Hyperadrenocorticism (Cushing's Syndrome) • Hypercalcemia
- Hyperthyroidism • Hypoadrenocorticism (Addison's Disease) • Hypokalemia
- Leptospirosis • Pyelonephritis • Pyometra
- Renal Failure, Acute • Renal Failure, Chronic • Urinary Tract Obstruction

P

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- ADH = antidiuretic hormone • CDI = central diabetes insipidus • CRF = chronic renal failure • DDAVP = trademark for preparation of vasopressin • DM = diabetes mellitus • HAC = hyperadrenocorticism
- NDI = nephrogenic diabetes insipidus
- PU/PD = polyuria/polydipsia • UTI = urinary tract infection

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Client Education Handout
available online

PORTOSYSTEMIC SHUNTING, ACQUIRED



BASICS

OVERVIEW

- Acquired portosystemic shunts (APSS): develop subsequent to portal hypertension (PH).
- Prehepatic PH: abdominal portion of portal vein causes.
- Intrahepatic PH: presinusoidal, sinusoidal, postsinusoidal causes.
- Posthepatic PH: rostral to hepatic vein causes (includes cardiac, pericardial, major veins).

SIGNALMENT

- Most common—dogs with chronic necroinflammatory liver disease.
- Less common—dogs with ductal plate malformations (congenital hepatic fibrosis phenotype), non-cirrhotic portal hypertension, recovery from panlobular necrosis, dogs with PSVA intolerant to ligation (portal atresia).
- Cats—ductal plate malformations (DPM), congenital hepatic fibrosis [CHF] phenotype), severe CCHS (rare), or PSVA intolerant to ligation (portal atresia).
- Extrahepatic bile duct obstruction (EHBD) > 6 weeks.
- Certain disorders—have age or breed incidence (see Ductal Plate Malformations (Congenital Hepatic Fibrosis); Cirrhosis and Fibrosis of the Liver; Chronic Hepatitis).
- Breeds: DPM more common in Persians and Himalayan cat, and Boxer dogs.

SIGNS

- P**
- Clinical signs represent sequelae of impaired hepatic perfusion; or reduced hepatic function in chronic liver disease.
 - Episodic HE—major sign, may include neurobehavioral abnormalities, blindness, PU/PD, anorexia, lethargy, vomiting; neurologic signs may localize to cerebrum, brainstem, or suggest transverse myelopathy; signs often improve with fluid therapy (e.g., dextrose and potassium supplements), broad-spectrum antibiotics, lactulose, and dietary protein restriction (see Hepatic Encephalopathy).
 - Ascites—common but variable; may fluctuate.

- Hypertensive splanchnic vasculopathy—causes gastroduodenal bleeding/ulceration; may progress to perforation and septic peritonitis, life-endangering blood loss if coexistent coagulopathy; can provoke severe HE due to potent encephalogenic effect of enteric blood; causes anorexia, vomiting, diarrhea, abdominal pain, anemia, and sometimes iron deficiency.
- Urogenital—obstructive uropathy due to ammonium biurate urolithiasis: gross or microscopic hematuria; pollakiuria; dysuria.

CAUSES & RISK FACTORS

- Multiple tortuous vessels—represent vasculature interconnecting portal splanchnic and systemic venous circulations.
- Lack of valves in the portal vein—allows blood to follow “a path of least resistance.”
- Portal hypertension—results from many disease processes: importantly, diffuse hepatic fibrosis with or without cirrhosis; chronic unresolved EHBD (> 6 weeks); other causes, include portal venous thromboembolism (TE), idiopathic portal hypertension, non-cirrhotic PH (obliteration of tertiary portal venules), and hepatic sinusoidal occlusion syndrome (zone 3, level of hepatic venules, veins, or vena cava); less common, disorders impair abdominal portal venous (splanchnic segment): TE, stricture, strangulation, rare portal vein atresia (congenital malformation) and congenital or acquired hepatic AV malformation (arterialized portal circulation); see Hypertension, Portal).
- Episodic HE coincidental with meal ingestion (high protein), enteric hemorrhage (bleeding tendencies, portal vasculopathy), azotemia, alkalemia, electrolyte disturbances, blood transfusion or hemolysis, infections, and administration of certain drugs.
- Hyperammonemia and impaired metabolism of uric acid to water-soluble allantoic causes ammonium urate urolithiasis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- CNS signs—*infectious* disorders (e.g., FIP, canine distemper, toxoplasmosis, FeLV- or FIV-related infections); toxicities (e.g., lead,

mushrooms, drugs, acute hepatic failure); hydrocephalus; idiopathic epilepsy; metabolic disorders (e.g., severe hypoglycemia, hypo- or hyperkalemia, hypocalcemia, severe hypophosphatemia).

- Gastrointestinal signs—bowel obstruction; dietary indiscretion; foreign body ingestion; inflammatory bowel disease.
- Urinary tract signs—bacterial urinary tract infection; urolithiasis.
- PU/PD—disorders of urine concentration (e.g., diabetes insipidus, abnormal adrenal function, hypercalcemia, primary polydipsia, congenital or acquired renal disease).
- Causes of abdominal effusion—cardiopulmonary disorders causing right-sided heart failure; pericardial disease; primary inflammatory hepatopathies; infiltrative hepatic disease (e.g., neoplasia, amyloid); non-hepatic abdominal disorders associated with effusions (e.g., splenic torsion, visceral neoplasia, carcinomatosis); or peritonitis: chemical (e.g., bile, urine, chyle) or sepsis.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—microcytosis (reflects PSS or iron deficiency); mild nonregenerative anemia common; poikilocytes (cats); target cells (dogs).
- Biochemistry—low BUN, low to low normal creatinine, glucose, albumin, and cholesterol are common; variable liver enzyme activity (ALP usually high in young animals [bone isoenzyme]) and bilirubin variable; findings depend on underlying cause.
- Urinalysis—variable urine concentration; ammonium biurate crystalluria, hematuria, pyuria, and proteinuria reflect urolithiasis (mechanical trauma, inflammation or infection).

OTHER LABORATORY TESTS

- TSBA—sensitive indicator of PSS; variable pre-meal and markedly increased postprandial values (> 100 µmol/L) = “shunting pattern.”
- Blood ammonia values—sensitive but inconsistent indicator of HE; samples cannot be frozen or mailed for later analysis (ammonia lability); ammonium biurate crystalluria infers high blood ammonia (evaluate 3 urine specimens, 4–8 h after eating); ammonia tolerance testing—(ammonium chloride solution) most reliable test for ammonia intolerance; **caution:** may induce HE.

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PORTOSYSTEMIC SHUNTING, ACQUIRED

- Coagulation tests—prolonged PT, APTT, and PIVKA reflect severity of liver dysfunction, synthetic failure, DIC, or vitamin K₁ adequacy; PIVKA useful in deciding need for supplemental vitamin K₁ treatment. Low protein C activity reflects PSS (PSVA, APSS).
- Abdominal effusion—usually pure or modified transudate; high serum:effusion albumin ratio (> 1.1) substantiates provocative role of PH in effusion formation.

IMAGING

Abdominal Radiography

- Liver size depends on underlying cause; microhepatia: common in dogs with chronic liver disease or PSVA variant causing ascites (portal atresia) and DPM in dogs, DPM causes variable liver size in cats; severe polycystic liver may cause hepatomegaly.
- Abdominal effusion.
- Ammonium biurate calculi—radiolucent unless radiodense mineral shell (infection).

Radiographic Portovenography

Demonstrates multiple APSS; not recommended due to risks of iatrogenic complications, see alternatives below.

Abdominal Ultrasonography

- Liver size depends on underlying cause.
- May disclose disease related parenchymal or biliary system changes.
- APSS—identify with color-flow Doppler; confirms hepatofugal portal flow; tortuous APSS usually adjacent to kidneys or spleen.
- Abdominal effusion—common.
- Uroliths: renal pelvis, urinary bladder; rare in ureters.
- Intrahepatic AV communication—pulsating arterialized vascular structure within enlarged liver lobe, abdominal effusion and APSS; see Arteriovenous Malformation of Liver.
- Color-flow Doppler may detect portal thrombi.

Colorectal (CRS) or Splenoporttal (SPS) Scintigraphy

- Sensitive noninvasive test confirms PSS.
- Cannot differentiate PSVA from APSS.
- CRS: Administer technetium-99m pertechnetate rectally; gamma camera imaging determines rate of isotope appearance in liver and heart; calculate shunt fraction from time/activity plots (normal ≤ 15%); not quantitative.

- SPS: isotope splenic injection via US guidance under heavy sedation or anesthesia; may not provide superior information vs. CRS.

Multisector CT

Non-invasive imaging method of choice; details vascular anatomy and visceral abnormalities, rapid data collection; requires short-term anesthesia, and IV contrast injection.

DIAGNOSTIC PROCEDURES

Fine-needle Aspiration Cytology

- Hepatic aspiration—22-gauge needle aspirates cannot differentiate disorders causing PSS.
- Liver biopsy—open surgical wedge biopsy or laparoscopic sampling (cup biopsy forceps); obtain tissue from several liver lobes; Tru-Cut samples may not provide adequate tissue for definitive diagnosis.

PATHOLOGIC FINDINGS

- Gross—small, irregularly contoured liver with chronic liver disease (cirrhosis, fibrosis).
- Normal to large size in early venous outflow obstruction (Budd-Chiari, sinusoidal obstruction syndrome).
- Large liver lobe (remainder of liver normal to small) with intrahepatic AV malformation.
- Normal to small—DPM (CHF phenotype), non-cirrhotic PH, portal TE.
- Small liver if congenital portal atresia.
- Normal to large liver in cats with polycystic liver disease: may only have microscopic cystic structures inapparent on US; characterized microscopically as DPM.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient—severe signs of HE; critical care

NURSING CARE

See Hepatic Encephalopathy

DIET

- Nutritional support—essential to maintain body condition for optimal management of HE; balanced, restricted-protein diet important; but diet should be optimized for that patient's tolerance—(see Hepatic Encephalopathy).

- Protein allocation titrated to response in combination with treatments ameliorating HE (see Hepatic Encephalopathy); use commercial diets formulated for liver disease or moderate renal insufficiency as diet baseline.

- Dogs: baseline diet provides 2.2–2.5 g protein/kg body weight when fed to meet energy requirements; titrate protein using 0.5 g/kg allocation additions (dairy protein or soy sources), q5–7 days until optimum level established: dairy and soy protein are best sources.

- Cats being pure carnivores require meat-derived protein.

- Parenteral nutrition—see Hepatic Encephalopathy.

CLIENT EDUCATION

- Depends on underlying cause.
- Educate client about signs of HE and potential for ammonium biurate obstructive uropathy in males; male dogs may require pre-scrotal urethrostomy.
- Educate client how to adjust diuretics (as-needed basis) to mobilize abdominal effusion.
- Educate client how to adjust oral medications and enemas (as-needed basis) to ameliorate HE (see Hepatic Encephalopathy).



MEDICATIONS

DRUG(S)

- Enteric hemorrhage—associated with hypertensive splanchnic vasculopathy (diapedesis and gastroduodenal ulceration) and coagulopathy; some clinicians use prophylactic acid blockers or gastroprotectants to reduce risk; treat symptomatic animal with H₂blocker or HCl pump inhibitor (omeprazole) and sucrlate; may require blood components or DDAVP (see Coagulopathy of Liver Disease).

- *Abdominal effusion*—sequentially measure weight, girth, body condition; initially exercise restrict (improves renal perfusion, sodium and water elimination), dietary sodium restriction.

- *Conventional diuretics*—combine furosemide and spironolactone; furosemide (0.5–2 mg/kg PO q12–24h) and

PORTOSYSTEMIC SHUNTING, ACQUIRED

(CONTINUED)

- spironolactone (0.5–2 mg/kg PO q12h, use a single doubled dose for loading one time); dose titrations based on response q4 days; adjust using incremental 25–50% dose increase. Spironolactone: potassium sparing; less potent than furosemide. Furosemide: potassium wasting, diuresis induces RAAS response. Serum:effusion albumin ratio (> 1.1) may predict response to diuretics.
- *Losartan and telmisartan*—angiotensin receptor blockers (ARB), selectively antagonizing angiotensin-1 receptor, bypassing intermediary activation within RAAS cascade—may improve water and sodium elimination (see Portal Hypertension; Hepatic Fibrosis and Cirrhosis).
 - *Vasopressin V₂ antagonists* (aquaretics) may assist with management of diuretic resistant ascites. Tolvaptan: see Portal Hypertension.
 - *Diuretic-resistant ascites*—see Portal Hypertension.
 - Avoid dehydration as this can lead to HE.
 - Avoid hypokalemia as this can provoke HE.

PRECAUTIONS

- Remain aware of altered drug metabolism related to reduced first-pass extraction (portosystemic shunting), altered hepatic metabolism/biotransformation, and reduced protein binding (if hypoalbuminemic).
- Remain vigilant for diuretic-induced dehydration and electrolyte dysregulation that may provoke HE.

POSSIBLE INTERACTIONS

Avoid metoclopramide if using spironolactone (blocks effect); avoid NSAIDs; these may inhibit furosemide-induced diuresis, potentiates renal injury, may cause sodium accumulation.

P



FOLLOW-UP

PATIENT MONITORING

- Reevaluate patient's at-home demeanor and appetite as a reflection of HE.
- Monitor clinical signs, appetite, body condition, weight, abdominal girth, CBC, serum biochemistry, and urine for ammonium

biurate crystalluria; TSBA not useful for sequential evaluation as these are consistently increased due to PSS and ursodeoxycholic acid (drug measured in assay) administration.

- Adjust medical management to reduce episodic HE, ammonium biurate crystalluria (potential for urolith formation), and abdominal effusion.
- Inspect patient carefully for evidence of clinical bleeding; determine need for intermittent chronic vitamin K₁ administration (parenteral route).

PREVENTION/AVOIDANCE

- Early treatment of acquired liver disease and EHBDO minimizes fibrosis/ remodeling.
- Cautious PSVA attenuation.

POSSIBLE COMPLICATIONS

- Treat underlying disorder(s).
- Enteric hemorrhage associated with hypertensive vasculopathy; may require acute intensive care: to manage hypovolemia, coagulopathy, and ensuing HE; may require surgical resection of involved gut (rare).
- Dehydration, contraction alkalosis, azotemia—complications of diuretics.
- Death—from liver failure, HE complications, lethal enteric hemorrhage, or sepsis.

EXPECTED COURSE AND PROGNOSIS

- Varies with underlying cause.
- Management of chronic liver disease or hepatic fibrosis seemingly extends life.
- Animals with non-cirrhotic PH and DPM (CHF phenotype) may live > 8 years if managed successfully during symptomatic illness.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Ammonium urate urolithiasis
- Ascites
- Coagulopathy
- Hepatic encephalopathy
- Enteric bleeding/ulceration
- Obstructive uropathy

SYNONYM

Portovascular anastomosis

SEE ALSO

- Ascites
- Cirrhosis and Fibrosis of the Liver
- Coagulopathy of Liver Disease
- Ductal Plate Malformation (Congenital Hepatic Fibrosis)
- Hepatic Encephalopathy
- Hepatitis, Chronic
- Portal Hypertension
- Portosystemic Vascular Anomaly, Congenital

ABBREVIATIONS

- APSS = acquired portosystemic shunt
- APTT = activated partial thromboplastin time
- ARB = angiotensin receptor blocker
- AV = arteriovenous
- CCHS = cholangitis/cholangiohepatitis syndrome
- CHF = congenital hepatic fibrosis
- DPM = ductal plate malformation
- EHBDO = extrahepatic bile duct obstruction
- HE = hepatic encephalopathy
- NSAID = nonsteroidal anti-inflammatory drugs
- PD = polydipsia
- PH = portal hypertension
- PIVKA = proteins invoked by vitamin K absence or antagonism
- PSS = portosystemic shunt
- PSVA = portosystemic vascular anomaly
- PT = prothrombin time
- PU = polyuria
- TE = thromboembolism
- TSBA = total serum bile acids

Suggested Reading

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Consulting Editor Sharon A. Center

PORTOSYSTEMIC VASCULAR ANOMALY, CONGENITAL



BASICS

DEFINITION

- Congenital PSVA—are venous malformations connecting the portal and systemic circulations permit portal blood to circumvent the liver (hepatofugal circulation, away from the liver).
- May be extrahepatic (more common in small breed dogs and cats) or intrahepatic (more common in large-breed dogs).
- Most are single vessels.
- Many small-breed dogs with PSVA also have vascular abnormalities involving tiny branches of the intrahepatic microvasculature (see Hepatoportal Microvascular Dysplasia).
- Acquired portosystemic shunts (APSS)—develop subsequent to portal hypertension (PH) and result if the patient is intolerant to shunt attenuation (surgical); see Portosystemic Shunting, Acquired.
- Genetically transmitted in high-risk small breeds; complex polygenic trait.

PATHOPHYSIOLOGY

- Clinical signs—caused by hepatofugal circulation; prohibits hepatic cleansing of enteric toxins and food derived nitrogenous toxins substances from portal blood.
- Microhepatia—deprivation of enteric hepatotrophic factors causes hepatic atrophy.
- Episodic HE—associated with high-protein food, gastrointestinal bleeding, dehydration, azotemia, alkalosis, electrolyte disturbances, blood transfusion, hemolysis, infections, constipation, catabolism, and certain drugs.
- Ammonium biurate crystalluria/ urolithiasis—caused by hyperammonemia and impaired transformation of uric acid to water-soluble allantoin; may be presenting problem.
- Clinical signs reflect the magnitude of shunting through anomalous vasculature.

SYSTEMS AFFECTED

- Nervous—episodic HE in many but not all.
- Gastrointestinal—intermittent inappetence; vomiting; diarrhea; pica; ptalism (cats).
- Urogenital—“plump” kidneys; ammonium urate urolithiasis; 50% of male dogs cryptorchid (one report).
- Asymptomatic—up to 20% of dogs.

GENETICS

- Breeds affected—e.g., most small-breed dogs: esp., Yorkshire terrier, cairn terrier, Maltese, Tibetan spaniel, miniature schnauzer, Norfolk terrier, pugs, Shih Tzu, Havanese, Papillon; large breeds: Irish wolfhound; Labrador retriever, Old English sheepdog.
- Autosomal dominant polygenic complex trait causes PSVA/MVD trait in small breeds; MVD most common phenotype.

INCIDENCE/PREVALENCE

0.2–0.6% of large referral clinic population

GEOGRAPHIC DISTRIBUTION

Reported worldwide

SIGNALMENT

Species

Dog and cat; more common in dog

Breed Predilections

- Higher risk—purebred and mixed small “terrier” dogs; cats—DSH, fewer pure breeds
- See “Generics” (above)

Mean Age and Range

- Usually identified in juveniles; some dogs as old as 13 years at initial diagnosis
- Asymptomatic animals present older; miniature schnauzers; portoazygous shunts
- Serendipitous discovery: if asymptomatic

Predominant Sex

N/A

SIGNS

Historical Findings

- Stunted growth—common.
- Signs often initiate with weaning of puppy or kitten to commercial growth foods.
- Gastrointestinal signs—inappetence; vomiting; diarrhea; pica.
- Cats initially thought to have upper respiratory infection (display ptalism).
- Episodic HE—most dramatic predominate signs, transiently improve with fluids, broad-spectrum antibiotics, and lactulose.
- CNS signs—weakness; pacing; ataxia; disorientation; head pressing; amaurotic blindness; behavioral change: aggression (cats), vocalization, hallucination; seizure; coma.
- Urinary signs—PU/PD; ammonium biurate crystalluria: pollakiuria, dysuria; hematuria; urethral (rarely ureteral) urolith obstruction.
- Asymptomatic—up to 20% of dogs.
- Affected bitches may produce litters.

Physical Examination Findings

- Normal appearance; stunted stature; microhepatia; HE; copper-colored irises in non-blue-eyed cats (note: Persian, Russian blue, some others normally have copper-colored iris; iris color does not change with PSVA ligation).
- Neurologic signs (see above).
- Ascites; rare, implies congenital portal atresia with APSS or erroneous diagnosis.

CAUSES

- Congenital malformations.
- APSS in congenital PSVA—develop subsequent to portal atresia (cats > dogs) or surgically induced PH (from shunt attenuation).

RISK FACTORS

PSVA—purebred dogs, especially small terrier-type breeds; Irish wolfhound have slow ductus venosus closure, early puppy screening in this breed may erroneously identify apparently “affected” dogs.



DIAGNOSIS

DIFFERENTIAL DIAGNOSES

- CNS signs—*infectious disorders* (e.g., FIP, canine distemper, toxoplasmosis, FeLV- or FIV-related infections); *toxicities* (e.g., lead, mushrooms, recreational drugs); hydrocephalus; idiopathic epilepsy; *metabolic disorders* (e.g., severe hypoglycemia, hypokalemia or hyperkalemia, hypocalemia).
- Gastrointestinal signs—bowel obstruction; dietary indiscretion; foreign body ingestion; inflammatory bowel disease.
- Urinary tract signs—bacterial urinary tract infection; urolithiasis.
- PU/PD—*disorders of urine concentration* (e.g., diabetes insipidus, abnormal adrenal function, hypercalcemia, primary polydipsia); associated with high GFR in PSVA.
- Primary liver disease—distinguished by diagnostic imaging and liver biopsy.
- Abnormal liver function (high TSBA) suggests PSVA, without clinical signs or clinicopathologic features or macroscopic shunt—most likely hepatoportal MVD.
- APSS—many differentials; see Portosystemic Shunting, Acquired.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—microcytosis; mild nonregenerative anemia; poikilocytosis (cats); target cells (dogs).
- Biochemistry—low BUN, creatinine, and cholesterol common but inconsistent; hypoglycemia—least common, liver enzyme activity variable (ALP high in young patients [bone isoenzyme]); bilirubin normal, hypoalbuminemia inconsistent and mild.
- Urinalysis—dilute urine (PU/PD); ammonium biurate crystalluria, hematuria, pyuria, and proteinuria: mechanical inflammation and infection secondary to metabolic calculi.

OTHER LABORATORY TESTS

- TSBA—sensitive indicator of PSS; random fasting values may be within reference intervals; 2 h postprandial values usually markedly high (> 100 µmol/L); always use paired samples around meal ingestion, no need to fast.
- Blood ammonia—sensitive indicator of HE and shunting but less reliable than TSBA in practice (analytic/methodologic issues [samples cannot be frozen or mailed for analysis]); ammonia tolerance testing—oral or rectal NHCl₄ administration demonstrates ammonia intolerance. **Note:** may cause transient HE.
- Coagulation tests—prolonged clotting times compared to healthy dogs but not clinically significant; not associated with bleeding.
- Protein C—low values help differentiate PSVA from MVD; protein C < 70% in PSVA, usually > 70% in MVD; reflects shunting magnitude. Protein C may be normal in asymptomatic PSVA dogs; used to estimate improved portal flow postoperatively. TSBA often remains

PORTOSYSTEMIC VASCULAR ANOMALY, CONGENITAL

(CONTINUED)

abnormal due to concurrent MVD. Not similarly used in cats. • Abdominal effusion—as post-surgical complication reflects iatrogenic portal hypertension; cytologic/physicochemical analysis: pure or modified transudate

IMAGING

Abdominal Radiography

- Microhepatia—dogs > cats.
- Renomegaly—coordinates with high GFR.
- Abdominal effusion—may be transient after surgical ligation; if precedes surgery coordinates with APSS and suggests portal atresia, AV malformation, non-cirrhotic PH, ductal plate malformation (congenital hepatic fibrosis phenotype).
- Ammonium urate urolithiasis—radiolucent unless combined with radiodense mineral shell.

Radiographic Portovenography

- Mesenteric portography—old gold standard confirming PSVA; defines portal circulation.
- Verifies shunt location—extrahepatic suggested by caudal extent of PSVA caudal to vertebra T₁₃; intrahepatic if caudal extent of PSVA cranial to vertebra T₁₃.

Abdominal Ultrasonography (US)

- Subjective assessment; may be difficult to identify some PSVA (e.g., portoazygous, splenophrenic); microhepatia; hypovascular liver, may confirm shunting vessel.
- Color-flow Doppler—assists shunt localization; interrogate vena cava cranial to phrenicoadominal vein for turbulence (where PSVA enters).
- Intrahepatic shunts—easily imaged.
- Other features: renomegaly, uroliths common (cystic, renal pelvis, rarely ureteral).
- Microbubble study—used to confirm shunting; splenic injection of heparinized blood with microbubbles with hepatic US observation for hepatopetal delivery.

Colorectal (CRS) or Splenoportal (SPS) Scintigraphy

- Technetium-^{99m} pertechnetate; gamma camera imaging documents isotope appearance in heart before liver; shunt fraction (time activity plot) is not quantitatively reliable; shunt fraction $\leq 15\%$ = normal; PSVA usually $> 60\%$.
- CRS: sensitive noninvasive test—confirms shunting; cannot differentiate PSVA from APSS or intra- from extrahepatic PSVA.
- SPS: involves splenic isotope injection; may miss caudal PSVA malformations.

Multisector CT

- New imaging gold standard demonstrates arterial and portal circulations and PSVA.
- Noninvasive: requires IV iodinated contrast and short-term general anesthesia (20 min.).

DIAGNOSTIC PROCEDURES

- Fine-needle aspiration cytology—cannot differentiate PSVA; binucleate small hepatocytes common.
- Liver biopsy—open surgical wedge or laparoscopic cup samples

necessary, biopsy of several liver lobes (avoid caudate lobe: best perfused lobe receives circulation from first portal vein branch; fewest lesions); needle core samples may be inadequate for definitive diagnosis of portal hypoperfusion.

PATHOLOGIC FINDINGS

- Gross—small, smooth-surfaced liver; PSVA may be difficult to verify at autopsy; young animals with portal atresia may have APSS.
- Portal hypoplasia: invalid microscopic diagnosis; lesion best termed “portal hypoperfusion” as portal thrombi, portal vein ligation, surgically created PSS—have histologic features identical to PSVA.
- Microscopic—small non-perfused or absent portal venules; multiple portal arteriole cross-sections; juvenile portal triads (tiny, too many), lobular atrophy, variable scattered lipogranulomas (coalesced foamy macrophages contain hemosiderin-iron); thick prominent throttling musculature of hepatic venules; unusual longitudinal hepatic venule profiles; engorged lymphatics; some dogs with severe zone 3 lipid vacuolation, lipogranulomas, and nonsuppurative inflammation shrouding hepatic venules, appear intolerant to complete PSVA ligation.
- **Note:** MVD has histologic features identical to PSVA but lack macroscopic shunt. MVD diagnosis requires clinical information (lack of signs, absence of clinicopathologic features typical of PSVA), and scintigraphy or vascular imaging (usually not justified).



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient—severe signs of HE; medical intervention prior to liver biopsy and ligation.

NURSING CARE

See Hepatic Encephalopathy

DIET

- Nutritional support—essential to maintain body condition as muscle functions as a site of temporary ammonia detoxification.
- Balanced protein-restricted diet—use commercial canine liver diet for dogs and feline liver diet for cats as baseline diet. To this diet, additional protein allocations are titrated based on patient response) in combination with treatments ameliorating HE.
- Dogs—as tolerated, add 0.5 g protein/kg body weight using dairy quality protein (e.g., cottage cheese, cheddar cheese, yogurt): observe over 5–7 day intervals to adjust (see Hepatic Encephalopathy).
- Asymptomatic or minimally symptomatic animals can survive well with dietary and medical interventions.
- Explain therapeutic options: medical vs. surgical.
- Surgical ligation—has potential to cure; expect improvement in all symptomatic dogs that tolerate some degree of shunt attenuation.
- Postoperative clinical signs—may persist requiring chronic nutritional and medical management; some dogs can have medical and dietary interventions withdrawn.
- Clinical improvement after surgical ligation despite persistent high TSBA values.
- Surgical/anesthetic risks—5–25% mortality; depending on surgeon, type of PSVA, hepatic microscopic lesions, supportive critical care.
- Monitoring protein C—documents change in hepatic portal perfusion; values increase and may normalize if successful surgery; re-test 2–6 months after surgery.
- If surgery not pursued or ligation not tolerated: remain vigilant for ammonium biurate obstructive uropathies (all levels of urinary system); urethral obstruction (males) may require permanent urethrostomy.

dogs that tolerate some degree of shunt attenuation.

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SURGICAL CONSIDERATIONS

- HE—should be mitigated with medical management before anesthesia and surgery.
- ICU monitoring—recommended postoperatively for 72–96 h.
- Surgical PSVA ligation—optimal goal is total ligation; may not be tolerated leading to APSS (esp. ameroid or cellophane banding).
- Partial ligation: improves patient health.
- Degree of tolerated PSVA closure judged at surgery: physiologic responses to temporary shunt occlusion (change in portal/systemic blood pressure, splanchnic circulation, pulse rate); but intraoperative assessments can be inaccurate.
- Ameroid constrictor—reduces immediate surgical risks of ligation; **caution:** may later result in APSS in some patients.
- Intrahepatic PSVA—most difficult to ligate; coil embolectomy is alternative procedure, may require multiple procedures, expensive.
- Intraoperative portography advised for all patients—verifies correct vascular ligation.
- Postoperative complications—acute severe PH; portal venous thrombi; mesenteric ischemia; endotoxemia; seizures; sepsis; acute pancreatitis; enteric hemorrhage.
- Intra- and postoperative hypothermia—risk for very small patients; prolongs recovery.
- Emergency surgery—rarely required for ligature removal; ameroid constrictors difficult to remove if complications develop.
- Abdominal effusion—transient after shunt ligation; alone, does not indicate intolerable PH if resolves within 7 days; serious PH indicated by signs of mesenteric ischemia (bloody diarrhea, abdominal pain, failure to recover from surgery/anesthesia, unexplained tachycardia, hyper- or hypothermia); monitor girth and body weight postoperatively.
- Hetastarch can increase bleeding risks.
- Blood component therapy containing ACD may provoke hypocalcemia and coagulopathy (hypercalcemia) in patients < 5 kg.
- Intractable seizures in $< 5\%$ dogs post-ligation; cause unclear, treatment for cerebral edema and sedation required; no rigorous clinical evidence that prophylactic

(CONTINUED)

PORTOSYSTEMIC VASCULAR ANOMALY, CONGENITAL

KBr or Keppra is beneficial; CRI propofol unreliable; flumazenil (5–10 µg/kg IV bolus) anecdotally suggested but is unreliable for resolution of neurologic signs.



MEDICATIONS

DRUG(S)

See Hepatic Encephalopathy

PRECAUTIONS

Remain aware of altered drug metabolism related to reduced first-pass extraction (portosystemic shunting), altered hepatic metabolism/biotransformation.



FOLLOW-UP

PATIENT MONITORING

- Reevaluate—patient's at-home behavior; body condition, weight, girth circumference (postoperatively); CBC (resolution of microcytosis), biochemistry (resolution of low cholesterol, BUN, creatinine), urinalysis (resolution of ammonium biurate crystalluria). • TSBA (small-breed dogs)—persistent high values do not substantiate surgical failure because of common coexistent MVD.

POSSIBLE COMPLICATIONS

See "Surgical Considerations"

PREVENTION/AVOIDANCE

Multiple portosystemic shunts—should be detected by US; if identified indicate need for liver biopsy but contraindicates pursuit of shunt ligation; implicates portal atresia or another underlying disorder causing PH; PSVA is not associated with PH and APSS.

EXPECTED COURSE AND PROGNOSIS

- Cannot predict individual response to surgery. • Dogs—ligation improves signs in ~80% symptomatic patients. • Cats—many develop APSS with ligation. • Post-surgery—continue HE management (especially diet) until reevaluation and observation confirm improvement. • Some patients—require indefinite nutritional and medical support after surgical ligation. • Partial ligation—may result in full shunt attenuation (granulation response to ligature). • Ameroid constrictor—may result in full ligation within a few days (twisting after placement, thrombi); may cause APSS. • Increased risk for poor surgical outcome—in small dogs with zone 3 lipogranulomas/lipid vacuolation shrouding hepatic venule; and cats. • Despite initial good response, recrudescence shunting may develop 3 years post-ligation. • Asymptomatic non-ligated PSVA dogs can have a full life expectancy with medical management.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Ammonium urate urolithiasis • Copper-colored iris (cats) • Cryptorchidism (dogs) • Hepatic encephalopathy

AGE-RELATED FACTORS

- PSVA—surgical outcome may be good in young and old patients, especially those with minimal signs of HE. • Dogs with PSVA identified at older ages are usually asymptomatic for HE and may have easily attenuated shunts (portoazygous).

PREGNANCY/FERTILITY/BREEDING

- Asymptomatic bitches can carry litters to term. • Asymptomatic dogs have been used

for stud. • Breeding PSVA dogs not advised (genetic).

SYNONYM

Portacaval shunt

SEE ALSO

- Hepatic Encephalopathy • Hepatoportal Microvascular Dysplasia • Juvenile Fibrosing Liver Disease • Portosystemic Shunting, Acquired

ABBREVIATIONS

- APSS = acquired portosystemic shunt
- CRS = colorectal scintigraphy • HE = hepatic encephalopathy • MVD = microvascular dysplasia • PSVA = portosystemic vascular anomaly • SPS = splenoportal scintigraphy • TSBA = total serum bile acids • US = ultrasound

Suggested Reading

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Client Education Handout
available online

P

Poxvirus Infection—Cats



BASICS

OVERVIEW

- Member of the genus Orthopoxvirus, family Poxviridae.
- Enveloped DNA virus, resistant to drying (viable for years) but readily inactivated by most disinfectants.
- Geographically limited to Eurasia.
- Relatively common.
- Serologic evidence of infection may approach 10% in cats in western Europe.

SIGNALMENT

- Cats—domestic and exotic
- No age, sex, or breed predisposition

SIGNS

- Skin lesions—multiple, circular; dominant feature; usually develop on head, neck, or forelimbs.
- Primary lesions—crusted papules, plaques, nodules, crateriform ulcers, or areas of cellulitis or abscesses.
- Secondary lesions—erythematous nodules that ulcerate and crust; often widespread; develop after 1–3 weeks.
- Oral lesions—erosions, ulcers either concurrently or alone (20% of cases).
- Pruritus variable.
- Systemic—20% of cases; anorexia; lethargy; pyrexia; vomiting; diarrhea; oculonasal discharge; conjunctivitis; pneumonia.

CAUSES & RISK FACTORS

- Reservoir host—wild rodents (voles, mice, gerbils, ground squirrels).
- Infection thought to be acquired during hunting and being wounded by infected rodents; most common in young adults and active hunters, often from rural environment.
- Lesions—often develop at the site of a bite wound (presumably inflicted by the prey animal carrying the virus).
- Most cases occur between August and October, when small wild mammals are at maximum population and most active.
- Severe cutaneous and systemic signs with poor prognosis are frequently associated with immunosuppression (iatrogenic or co-infection with FeLV or FIV).
- Cat-to-cat transmission—rare; causes only subclinical infection.

P



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Bacterial and fungal infections
- Eosinophilic granuloma complex

- Neoplasia—particularly mast cell tumor; lymphoma
- Miliary dermatitis

CBC/BIOCHEMISTRY/URINALYSIS

Non-contributory

OTHER LABORATORY TESTS

Serologic testing—demonstrate rising titers; hemagglutination inhibition, virus neutralizing, complement fixation, or ELISA; titers may remain high for months or years.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Virus isolation from scab material—definitive diagnosis; 90% positive.
- Electron microscopy of extracts of scab, biopsy, or exudate—rapid presumptive diagnosis; 70% positive.
- Skin biopsy—characteristic histologic changes of epidermal hyperplasia and hypertrophy; multilocular vesicle and ulceration; large eosinophilic intracytoplasmic inclusion bodies; immunofluorescence tests.
- PCR.



TREATMENT

- No specific treatment.
- Clean and treat ulcerated areas to prevent secondary infection.
- Supportive (antibiotics, fluids) when necessary.
- Elizabethan collar—to prevent self-induced damage.



MEDICATIONS

DRUG(S)

Antibiotics—prevent secondary infections.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Immunosuppressive agents (e.g., glucocorticoids and megestrol acetate)—absolutely contraindicated because they can induce fatal systemic disease.



FOLLOW-UP

PREVENTION/AVOIDANCE

- Natural reservoir host is possibly small rodents; cats infected incidentally.
- Vaccines—none available; vaccinia virus may be considered for valuable zoo

collections, but its effects in non-domestic cats have not been investigated.

EXPECTED COURSE AND PROGNOSIS

- Most cats recover spontaneously in 1–2 months.
- Healing may be delayed by secondary bacterial skin infection.
- Prognosis is poor with severe respiratory or pulmonary involvement.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Rare human poxvirus infections have been linked to contact with infected cats with skin lesions; use basic hygiene precautions (disposable gloves) when handling infected cats.
- Infection is usually mild and transient in healthy humans, but severe and even lethal infections can occur in immunocompromised individuals.
- May cause painful skin lesion and severe systemic illness, particularly in the very young or elderly, people with a pre-existing skin condition, and the immunodeficient.
- With discontinuation of vaccination against smallpox (with its cross-reactive immune effect) may expect increase in human poxvirus infections.

ABBREVIATIONS

- ELISA = enzyme-linked immunosorbent assay
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- PCR = polymerase chain reaction

Suggested Reading

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PREMATURE LABOR



BASICS

OVERVIEW

Inappropriate myometrial activity preterm, which can lead to abortion.

SIGNALMENT

Gravid female dog or cat, no age or breed predilection.

SIGNS

- Early: no signs, fetal resorption evident ultrasonographically.
- Late: vulvar discharge: hemorrhagic or lochial.
- History of unexplained loss of pregnancy.

CAUSES & RISK FACTORS

- Unknown; genetics can play a role; luteolysis can result; luteal insufficiency suspected but not documented.
- Myometrial activity inappropriate for stage of pregnancy precedes luteolysis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Term gestation, onset of normal labor.
- Pathologic loss of pregnancy (trauma, toxin, developmental disorder, or infectious causes).

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal (typical anemia of pregnancy can be present).
- Blood loss anemia, inflammatory leukogram can occur.

OTHER LABORATORY TESTS

Serum progesterone will be < 2 ng/mL when abortion occurs.

IMAGING

- Ultrasonographic evaluation of fetal heart rate (stress evidenced by rates consistently < 170).
- Change in the normal morphologic appearance of uterus and fetuses when death occurs (See Web Figures 1, 2).

DIAGNOSTIC PROCEDURES

- Tocodynamometry is diagnostic: finding $> 0\text{--}2$ contractions/hour is not normal for preterm (earlier than eighth week) gestation.
- Quantitative (chemiluminescence, fluorescence enzyme immunoassay)

progesterone assay is important to detect levels < 2.0 ng/mL. Rapid in-hospital semi-quantitative assays are least accurate between 2 and 5 ng/mL.



TREATMENT

- In humans, bed and pelvic rest and antibiotics do not contribute to a positive outcome, although frequently prescribed.
- Tocolytic agents are administered (beta-agonists, calcium channel blockers, magnesium sulfate, prostaglandin synthetase inhibitors).



MEDICATIONS

DRUG(S)

- Tocolytics (terbutaline 0.03 mg/kg PO q6–12h PRN); the dose is titrated based on uterine monitoring.
- \pm Progestagen compounds: progesterone in oil dosed at 2 mg/kg IM q72h; altrenogest (Regu-Mate, Hoechst-Roussel), a synthetic progestagen manufactured for use in the mare, is dosed at 0.088 mg/kg PO q24h; oral progesterone (Prometrium® capsules) dosed at 10 mg/kg q24h with monitoring of serum progesterone q24–48h for dosage adjustments. Clients should be informed of potential side effects with exogenous progesterone, and should only be used if the serum progesterone is < 2 ng/mL.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Prolonged gestation if terbutaline or progestagen compounds are not withdrawn 24–48 hours before due date calculated from first progesterone rise, luteinizing hormone peak, or Day 1 cytologic diestrus (see Breeding, Timing) if natural whelping is planned. If elective cesarean section is planned, medications can be continued until day of surgery.
- Poor lactation if progestagen compounds are used (inhibits normal prolactin elevation resulting from declining progesterone level).
- Masculinization of female fetuses if progestagen compounds are used.
- Forced retention of a pathologic pregnancy if idiopathic premature labor is misdiagnosed.



FOLLOW-UP

- Serial abdominal ultrasound
- Serial tocodynamometry
- Fetal heart rate monitoring with Doppler or dual B- and M-mode ultrasonography



MISCELLANEOUS

Usually a diagnosis by exclusion of all other causes of late-term abortion (*Brucella canis*, metritis, placatitis, trauma, metabolic disease, coagulopathy, inborn error of metabolism, genetic defects) prompting midterm tocodynamometry at the next pregnancy.

INTERNET RESOURCES

<http://www.ivis.org>

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PRIMARY CILIARY DYSKINESIA



BASICS

OVERVIEW

- Congenital (autosomal recessive) disorder of ciliary dysfunction in the respiratory tract, auditory tubes, ventricles of the brain, spinal canal, oviducts, efferent ducts of the testes, and sperm flagellum. • In normal animals ciliary beating is coordinated—characteristically dyskinetic or absent in affected dogs.
- Hydrocephalus and/or situs inversus (Kartagener syndrome) can be concurrent.
- Dogs with chronic respiratory disease and situs inversus likely have primary ciliary dyskinesia and do not warrant extensive workup.

SIGNALMENT

- Generally young dogs (< 8 weeks) but some are asymptomatic until older (1/2–10 years).
- Reported predominately in purebred dogs, higher incidence in Bichon frise, Old English sheepdog, but mixed-breed dogs and cats can be affected.

SIGNS

Historical Findings

- Chronic sneezing, nasal discharge, coughing, exercise intolerance, and respiratory distress. Dramatic initial response to antibiotics, but relapse after treatment is stopped. • Family history—large litters can have > 1 affected dog. • Infertility in males.

Physical Examination Findings

- Bilateral mucopurulent nasal discharge.
- Productive cough. • Tachypnea, dyspnea, and cyanosis during exacerbation of infection.
- Diffuse increase in lung sounds of variable intensity. • Heart sounds can be inaudible with severe bronchopneumonia, can be loudest on the right side with situs inversus.

CAUSES & RISK FACTORS

Genetics—recessive mutation identified in the Old English sheepdog, inbreeding.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Congenital (neutrophil dysfunction, immunoglobulin deficiency) or acquired disease (canine distemper) producing chronic rhinosinusitis and bronchopneumonia.
- Recurrent aspiration pneumonia. • Chronic bacterial pneumonia. • Bronchoesophageal fistula. • Exposure to cigarette smoke—can delay mucociliary clearance. • *Mycoplasma* spp. or *Bordetella* infection—can cause acquired ciliary defects.

CBC/BIOCHEMISTRY/URINALYSIS

- Mature neutrophilic leukocytosis—left-shift and toxic neutrophils with severe bronchopneumonia.

- Hyperglobulinemia—older dogs.
- Polycythemia—with chronic hypoxemia.

OTHER LABORATORY TESTS

- Blood gas analysis can reveal hypoxemia with normocapnia or hypocapnia.
- Bronchoalveolar lavage typically yields mucoid to mucopurulent material characterized cytologically as a purulent exudate with one or more bacterial species isolated on culture. *Mycoplasma* culture should be requested. • Normal sperm motility in an intact male rules out ciliary dyskinesia.

IMAGING

Radiography

- Changes consistent with chronic bronchopneumonia. • Situs inversus.
- Bronchiectasis. • Thickened or sclerotic tympanic bullae.

Tracheal Scintigraphy (Mucociliary Clearance)

- First exclude infections or chronic exposure to cigarette smoke. • Affected animals show no movement of radiopharmaceutical from the carina.

DIAGNOSTIC PROCEDURES

Electron Microscopy

- Ultrastructural lesions in the cilia of nasal or bronchial mucosa identified in most patients, including central microtubular disarrangement and loss of dynein arms. • Specific lesions must be found in > 20% of cilia. • Acquired ultrastructural lesions involving < 20% of cilia common with chronic respiratory tract infection. • Dogs with primary ciliary dyskinesia but no ultrastructural ciliary lesions have been described and require in vitro analysis of ciliary beat frequency and synchrony for diagnosis.

PATHOLOGIC FINDINGS

Upper Respiratory Tract

Chronic bacterial rhinitis with mucoid to mucopurulent exudate, and mucosal inflammation, mucous gland hyperplasia, and occasionally hypoplastic nasal turbinates, atresia of the frontal sinuses, frontal sinusitis, and rhinoliths.

Lower Respiratory Tract

Mucoid to mucopurulent material within airways with bronchitis, bronchiectasis, atelectasis, and subpleural emphysema.

Miscellaneous

- Hydrocephalus. • Situs inversus of thoracic viscera or abdominal viscera or both (situs inversus totalis). • Impaction of one or both middle ears with a sterile gelatinous material.



TREATMENT

- Routine exercise enhances mucus clearance by increasing respiration and inducing coughing. • Supplemental oxygen therapy

during episodes of severe bronchopneumonia.

- Airway therapy with saline nebulization and coupage useful for clearing secretions.



MEDICATIONS

DRUG(S)

- Antibiotics based on bacterial culture and sensitivity testing; duration varies with severity of infection. • Continuous antibiotic therapy not advised due to colonization with resistant bacteria.

CONTRAINdications/POSSIBLE INTERACTIONS

Cough suppressants trap secretions and exacerbate airway inflammation.

Anesthesia

- Patients have impaired gas exchange and increased risk of complications. • Minimize respiratory depression and recovery time.



FOLLOW-UP

POSSIBLE COMPLICATIONS

- Pneumothorax—subpleural cysts, bronchiectatic cysts, interstitial cysts, and emphysematous bullae can develop from prolonged infection or inflammation causing air entrapment and rupture. • Pulmonary arterial hypertension, cor pulmonale, and right-sided heart failure can result from chronic hypoxemia. • Systemic reactive amyloidosis secondary to persistent bacterial bronchopneumonia.

EXPECTED COURSE AND PROGNOSIS

- Clinical course of disease and longevity of patients highly variable. • Some dogs will become subclinical with age. • Appropriate antibiotic treatment and pulmonary physical therapy can result in prolonged survival.



MISCELLANEOUS

SEE ALSO

Pneumonia, Bacterial

Suggested Reading

- Edwards DF, Patton CS, Kennedy JR. Primary ciliary dyskinesia in the dog. *Probl Vet Med* 1992, 4:291–319.

Merveille AC, Battaille G, Billen F, et al. Clinical findings and prevalence of the mutation associated with primary ciliary dyskinesia in Old English Sheepdogs. *J Vet Intern Med* 2014, 28(3):771–778.

Author Ned F. Kuehn

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PROLAPSED GLAND OF THE THIRD EYELID (CHERRY EYE)



BASICS

OVERVIEW

- Gland of the third eyelid—normally anchored by a fibrous attachment to the periorbita beneath the third eyelid.
- Weak attachment—several breeds of dogs and cats; predisposes animals to unilateral or bilateral prolapse.

SIGNALMENT

- Dog and cat.
- Dog—usually in young dogs (aged 6 months to 2 years); common breeds: cocker spaniel, bulldog, beagle, bloodhound, Lhasa apso, mastiff, Shih Tzu, other brachycephalic breeds.
- Cat—rare; occurs in Burmese and Persians.

SIGNS

- Oval, hyperemic mass protruding from behind the leading edge of the third eyelid.
- May be unilateral or bilateral.
- May see accompanying epiphora, hyperemic conjunctiva, or blepharospasm.
- Additional swelling and hyperemia caused by environmental irritation and desiccation of the exposed gland.

CAUSES & RISK FACTORS

- Congenital weakness of the attachment of the gland of the third eyelid.
- Inheritance unknown, but considered complex and multigenic.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Scrolled or everted cartilage of the third eyelid—seen in Wiemaraners, Great Danes, German shorthaired pointers, and other breeds in which the T-shaped cartilage of the third eyelid is rolled away from the surface of

the eye instead of conforming to the surface of the cornea.

- Neoplasia of the third eyelid—usually seen in older animals; may see squamous cell carcinoma, lymphoma, or fibrosarcoma; may be origin of adenoma or adenocarcinoma; small incisional biopsy is indicated in older patients (> 7–9 years) to differentiate.
- Orbital fat prolapse—may dissect anteriorly between the conjunctiva and globe; occasionally occurs in the medial canthus and simulates a prolapsed gland of the third eyelid.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Surgical replacement of the gland (imbrication technique)—see “Suggested Reading.”
- Excision of the gland—avoid; gland produces up to 50% of the aqueous tear film; puts patient at substantial risk for developing KCS as the dog ages.
- Elizabethan collar—recommended to prevent self-trauma.



MEDICATIONS

DRUG(S)

Topical anti-inflammatory medications, such as corticosteroids (if no corneal ulceration) or nonsteroidal anti-inflammatory medications—may be used before and after surgery to lessen swelling.

CONTRAINdications/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- Recurrence—5–20%, depending on the breed, with large-breed dogs such as mastiffs having the highest recurrence rates; re-replacement of the gland is encouraged.
- If unilateral, warn client that the other gland may also prolapse and that no preventive procedure or medication exists.



MISCELLANEOUS

SYNONYM

Cherry eye

ABBREVIATION

KCS = keratoconjunctivitis sicca

Suggested Reading

Edelman ML, et al. Investigating the inheritance of prolapsed nictitating membrane glands in a large canine pedigree. *Vet Ophthalmol* 2013, 16: 416–422.

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Maggs DJ. Third eyelid. In: Maggs DJ, Miller PE, Ofri R, Slatter's Fundamentals of Veterinary Ophthalmology, 5th ed. St. Louis, MO: Elsevier, 2013, pp. 159–164.

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P

PROPTOSIS



BASICS

OVERVIEW

- Forward displacement of the globe, with the eyelids trapped behind the globe's equator.
- Frequently acute and due to bite wounds, head trauma. • Vision threatening.
- Immediate repositioning of the globe critical if eye is salvageable.

SIGNALMENT

- More common in the brachycephalic breeds due to a relatively shallow orbit and large palpebral fissure. • May occur in any species or breed if the traumatic force is severe enough.

SIGNS

Possible Accompanying Signs

- Subconjunctival or intraocular hemorrhage.
- Abnormalities in pupil size—dilated or constricted. • Intraocular inflammation (uveitis).
- Globe deviation/strabismus/rupture.
- Corneal ulceration/desiccation.
- Periorbital bite wounds. • Fractures of the bony orbit or skull. • Systemic injuries.
- Trauma to the contralateral eye.

CAUSES & RISK FACTORS

- Trauma—primary cause; relatively minor force (restraint) in brachycephalic breeds; usually severe force in dolichocephalic and mesocephalic breeds. • Space-occupying retrobulbar lesion—secondary cause: rare.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Buphthalmia—globe enlargement; rarely acute. • Exophthalmia—forward displacement of the globe due to a retrobulbar space occupying lesion; may be acute, rarely peracute.

CBC/BIOCHEMISTRY/URINALYSIS

Normal, unless trauma-related abnormalities present.

IMAGING

Skull CT or radiographs—may show fractures due to trauma. Further diagnostic workup indicated if suspect other systemic injuries.



TREATMENT

- Prevent further trauma,—lubricate the cornea, E-collar. • Stabilize patient and do a thorough systemic physical examination before surgery.

Repositioning the Globe

- As soon as safely possible. • Performed under sedation and local anesthesia or, if the

patient is stable, under general anesthesia.

- Lateral canthotomy—may ease tension on the eyelids and allow easier globe repositioning; not always necessary. • Engage the eyelid margins with eyelid forceps (e.g. Von Graefe or Allis forceps) or strabismus/muscle hooks, then pull the eyelids forward and away from the globe while protecting and gently pushing the globe back into the orbit (a lubricated scalpel blade handle can serve this function). • Place two or three temporary tarsorrhaphy mattress sutures (sutures emerge from the eyelid margin in line with the meibomian gland openings) with stents; suture the lateral canthotomy wound.
- Fluorescein—stain the cornea prior to replacing the globe. • If the optic nerve and/or more than two extraocular muscles are severed, if the globe is ruptured, infected, or desiccated, enucleation may be the best option.



MEDICATIONS

DRUG(S)

- Systemic and topical broad-spectrum antibiotics—until sutures are removed.
- Systemic corticosteroids—usually used at least initially; may be continued with marked periorbital and retrobulbar swelling. • Topical corticosteroids—to treat uveitis or hyphema, if cornea is not ulcerated. • Topical atropine—for intraocular inflammation or hemorrhage; relieve ciliary spasm and lower the risk of synechiae.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Topical corticosteroids—do not use with ulcerations. • Systemic corticosteroids—do not use with peri- or retrobulbar infection.



FOLLOW-UP

PATIENT MONITORING

Suture removal—usually done sequentially, rather than all at once, starting 10–14 days after repositioning. Integrity of the globe and vision are reassessed 10–14 days after surgery.

PREVENTION/AVOIDANCE

Bilateral medial and/or lateral canthoplasty to shorten the palpebral fissure and prevent future proptosis in brachycephalic breeds should be discussed with the client.

POSSIBLE COMPLICATIONS

- Blindness. • Most patients retain a dorsolateral strabismus and slight forward displacement of the medial side of the globe due to rupture of the inferior oblique and

medial rectus muscles. This may improve with time due to tissue fibrosis and contraction.

- Decreased tear production—perform Schirmer tear tests after suture removal.
- Corneal denervation causing neurotrophic keratitis with chronic ulceration and decreased corneal sensitivity. • Exposure keratitis due to forward displacement of globe, decreased tear production, facial nerve palsy and/or corneal denervation (decreased blink reflex). • Phthisis bulbi.

EXPECTED COURSE AND PROGNOSIS

- Most affected eyes can be salvaged; majority will be blind (especially if proptosis was caused by significant trauma: more common in dolichocephalic than brachycephalic breeds). • Extensive tissue damage, avulsion of more than two extraocular muscles, facial and/or orbital fractures, and corneal or scleral rupture—grave prognosis for vision and globe salvage for cosmesis. • Normal retinal vessels and optic nerve, normal IOP, and a short time from occurrence to repair—relatively favorable prognosis for maintaining vision.
- Positive menace response, dazzle and/or pupillary light reflexes—good prognosis for maintaining vision (always observe the indirect pupillary light reflex in the healthy eye originating from the injured eye!). • Pupil size at the time of the injury—not necessarily an accurate prognostic indicator; mydriasis may be the result of trauma to the optic nerve (if permanent, results in blindness) or damage to the oculomotor nerve (does not affect vision). Miosis can be caused by uveitis (if the uveitis is severe enough, pupillary constriction occurs even with retinal or optic nerve damage).



MISCELLANEOUS

SEE ALSO

Orbital Diseases (Exophthalmos, Enophthalmos, Strabismus)

ABBREVIATIONS

- CT = computed tomography • IOP = intraocular pressure

Suggested Reading

Miller PE. Ocular Emergencies. In: Maggs DJ, Miller PE, Ofri R, eds. Slatter's Fundamentals of Veterinary Ophthalmology, 5th ed. St. Louis, MO: Saunders, 2013, pp. 372–393.

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PROSTATE DISEASE IN THE BREEDING MALE DOG



BASICS

OVERVIEW

- Prostate is the only accessory sex gland in the dog; easily palpated per rectum as a bilobed oval gland with a median septum.
- 5- α reductase in prostatic epithelial cells metabolizes serum testosterone to DHT; DHT stimulates growth of the prostate gland.

Benign Prostatic Hyperplasia

- Normal hormonally dependent diffuse glandular, stromal hyperplasia and hypertrophy of the prostate. • Cystic hyperplasia may occur later in the disease process. • Pathogenesis unknown; contributing factors include age-associated alteration in the intraprostatic estrogen:androgen ratio, which potentiates the hyperplastic response, and DHT-permissive growth of the prostate.
- Clinical effects minimal or absent in most dogs. • Renders the prostate more susceptible to ascending infection and subsequent development of bacterial prostatitis.

Prostatitis/Prostatic Abscess

- Inflammation/infection of the prostate; abscess of the prostate. • Associated with acute or chronic bacterial infection. • Abscess formation usually secondary to chronic bacterial prostatitis. • May be associated with BPH or retention cysts. • Prostate gland and urinary tract are normally sterile. • Bacterial colonization typically via urinary tract pathogens; hematogenous spread possible.
- Common isolates include *E. coli*, *Proteus vulgaris*, *Streptococci* spp., *Staphylococci* spp.; concurrent bacterial urinary tract infection is not always noted with chronic bacterial prostatitis. • *Brucella canis* may be associated with acute or chronic prostatitis (see Brucellosis). • Fungal prostatitis (*Blastomyces* and *Cryptococcus*).

Prostatic Cysts

- Either within the prostatic parenchyma due to coalescing glandular/cystic hyperplasia and ductular occlusion (retention cysts), or outside the prostate (paraprostatic cysts). • Estrogen exposure induces stratified squamous change to prostatic epithelium; subsequent ductular occlusion contributes to cyst formation (see Sertoli Cell Tumor). • Paraprostatic cysts are attached to the prostate, are lined by secretory epithelium, and variable in size; larger cysts may be transabdominally palpable; almost always sterile.

Prostatic Neoplasia

- Prostatic ACA is most common; other tumor types include fibrosarcoma, leiomyosarcoma, and SCC. • Prostatic TCC arises from prostatic urethra and invades the prostate gland. • BPH is not a risk factor for prostatic neoplasia. • Tumor development is

not androgen dependent; castration is not protective. • Tumors typically detected after metastatic spread as clinical signs occur late and early screening is unavailable. • ACA bone metastasis is common, typically to LS spine or pelvis; intraprostatic fibrosing reaction with some areas of ossification and hyperplasia is typical.

SIGNALMENT

INCIDENCE/PREVALENCE

- BPH: incidence high; 50% of intact dogs exhibit histologic evidence by 5 years of age, > 95% by 9 years of age. • Prostatitis/prostatic abscess: considered common; about 40% of dogs with prostatic cysts have evidence of bacterial infection. • Prostatic cysts: prevalence around 14%, 42% of these had evidence of bacterial infection.
- Neoplasia: low; prevalence range 0.2–0.6% in general population, and 5–7% of dogs with prostatic disease.

Mean Age and Range

- BPH: microscopic onset by 5 years of age.
- Prostatitis/prostatic abscess: any age; more common in the adult (> 6 years). • Prostatic cysts: more common after 8 years of age.
- Neoplasia: mean age 10 years.

SIGNS

General Comments

- Dogs with prostatic disease display overlapping clinical signs:
- Asymptomatic
- Dyschezia, tenesmus, constipation, ribbon-like stool
- Sanguinous urethral/preputial discharge
- Dysuria, hematuria, stranguria
- Hemospermia

Benign Prostatic Hyperplasia

- If mild, generally asymptomatic
- Hematuria and hemospermia are most common signs

Prostatitis—Acute

- Systemic illness (vomiting, fever, inappetance)
- Pyuria
- Stiff-legged gait

Prostatitis—Chronic

- Recurrent/chronic urinary tract infection
- Stiff gait
- Infertility

Prostatic Cyst

- See BPH, above
- If infected see signs associated with prostatitis

Prostatic Neoplasia

- Emaciation
- Dyschezia
- Rear limb locomotory disturbance
- LS pain

Physical Examination Findings

Benign Prostatic Hyperplasia

Large, symmetrically enlarged, nonpainful prostate

Prostatitis—Acute

- Fever
- Dehydration
- Signs of sepsis
- Caudal abdominal pain
- Normal to enlarged, asymmetrical, painful prostate

Prostatitis—Chronic

- Symmetrical, nonpainful, firm, normal size prostate.
- May have fluctuant areas (focal cysts) on palpation.

Prostatic Cyst

- Symmetrical, enlarged prostate with fluctuant areas; large cysts may preclude rectal palpation, enlarged prostate may be transabdominally palpable.
- External signs of feminization if cyst (retention cysts) formation is due to estrogen exposure (e.g., Sertoli cell tumor).

Prostatic Neoplasia

- Large, asymmetrical, irregular painful prostate.
- Rectal, abdominal, LS pain.
- Palpable abdominal mass.
- Lymphadenopathy (sublumbar).

CAUSES & RISK FACTORS

BPH

Age and sexual status

Prostatitis

- BPH and/or prostatic cysts
- Breeding dogs may have higher risk for *Brucella canis*



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Hematuria

- Urinary tract infection
- Thrombocytopenia
- Penile trauma
- Urinary tract neoplasia (TCC)

Tenesmus

Disease of the colon or rectum

Hind Limb Gait/Locomotory Disturbance

- Arthritis
- Degenerative disc disease
- Neuromuscular disease
- Cauda equina syndrome

CBC/BIOCHEMISTRY/URINALYSIS

Benign Prostatic Hyperplasia

Typically normal with the exception of hematuria

Prostatitis—Acute

- Leukocytosis and neutrophilia (+/- immaturity and signs of toxicity)
- Hypoalbuminemia
- Pyuria
- Bacteriuria
- Hematuria

Prostatitis—Chronic

- CBC typically normal; occasionally leukocytosis
- Pyuria
- Bacteriuria
- Hematuria

Prostatic Cyst

- Anemia (if cyst formation due to hyperestrogenism)
- Biochemistry and urinalysis typically normal

Prostatic Neoplasia

- Leukocytosis and neutrophilia
- Elevated alkaline phosphatase
- Pyuria
- Hematuria
- Atypical cells may be noted in urine sediment

OTHER LABORATORY TESTS

- Prostate culture: culture third ejaculate fraction or fine-needle aspirate of prostate; positive growth supports bacterial prostatitis.
- Paired Seminal Fluid and Urethral culture:

PROSTATE DISEASE IN THE BREEDING MALE DOG

(CONTINUED)

prostatitis is confirmed when seminal fluid bacterial growth (in CFU) is ≥ 100 times the corresponding urethral/urine growth.

- Semen evaluation: may be normal or hemospermic with BPH; neutrophils, phagocytized bacteria, variable degree of reduced sperm motility and teratospermia, with bacterial prostatitis. • Prostate specific markers: not of clinical use in the dog.

IMAGING

- Abdominal ultrasound: preferred method for imaging; detects size, and tissue homogeneity; identifies focal parenchymal abnormalities, such as cysts or abscesses; loss of tissue homogeneity (prostatitis or neoplasia); regional lymph nodes and paraprostatic structures (paraprostatic cysts).
- Abdominal radiography: bony metastases; degree of prostatomegaly not correlated with any specific prostatic disease. • Lack of prostatic mineralization in intact dogs with prostatomegaly has a negative predictive value of 96% for neoplasia. • Retrograde cystourethrogram: evaluates urethral compression or identifies contrast leakage.

DIAGNOSTIC PROCEDURES

- Prostatic wash: culture and cytologic evaluation of prostatic fluid. • Ultrasound-guided fine-needle aspirate: cytologic evaluation may distinguish between BPH, prostatitis and neoplasia; aspiration of active infections may seed the periprostatic and subcutaneous tissues; aspiration of cysts rarely provides clinical resolution. • Ultrasound-guided transabdominal biopsy: provides definitive diagnosis for BPH, prostatitis, prostatic neoplasia.

P

TREATMENT

- Temporary indwelling urethral catheter placement may benefit animals with severe pain or urethral obstruction. • Analgesia.
- Stool softeners and low residue diets to ease defecation.

BENIGN PROSTATIC HYPERPLASIA

- Treat symptomatic dogs. • Castration is curative. • Finasteride is the medical treatment of choice in breeding animals; decreases prostatic weight and diameter; prostate returns to pretreatment size 8 weeks after stopping therapy; typically used to reduce clinical signs permitting frozen semen stores to be generated; castrate when desired doses of semen are stored.

PROSTATITIS—ACUTE

Antibiotics based on culture and sensitivity; blood-prostate barrier is not intact with acute prostatitis; administer for a minimum of 3 weeks; document negative prostatic fluid culture prior to, and 1–2 weeks after, stopping antibiotic treatment.

PROSTATITIS—CHRONIC

- Antibiotics based on culture and sensitivity, and ability to penetrate the blood-prostate barrier (enrofloxacin, trimethoprim, chloramphenicol, erythromycin, doxycycline).
- Administer for a minimum of 6 weeks; repeat urine and prostatic fluid culture at 1 week, and prior to discontinuing, to document no growth. • If positive culture is obtained, continue appropriate antibiotic administration 4 weeks after the first negative culture; repeat culture at 1 week and 1 month post-therapy to evaluate for return of infection. • Castration recommended for refractory cases.

PROSTATIC CYST

- Castration treatment of choice.
- Finasteride may be useful if associated with BPH. • Remove source of estrogen if squamous metaplasia. • Large solitary cysts: surgical marsupialization and castration advised. • Paraprostatic cysts: may be surgically excised. • Aspiration and drainage of cysts: not associated with resolution; fluid should be cultured.

PROSTATIC NEOPLASIA

- Metastasis—typical at time of diagnosis.
- Differentiation between adenocarcinoma and transitional cell carcinoma will determine appropriate chemotherapeutic agents (see Adenocarcinoma, Prostate, and Transitional Cell Carcinoma). • Urine should be cultured to evaluate for UTI. • A piroxicam trial should always be offered with or without chemotherapy.

CLIENT EDUCATION

- Regular *Brucella canis* testing for breeding animals. • Proactive semen freezing at young age prior to onset prostatic disease/BPH.



MEDICATIONS

DRUG(S)

- Finasteride (0.1 mg/kg PO q24h to a maximum of 5 mg PO q24h): 5 α reductase inhibitor; inhibits intraprostatic conversion of testosterone to DHT without altering serum testosterone; causes decreased semen volume but no change in semen quality; suitable for use in breeding male dogs. • Antimicrobials: drug used, and duration, will vary with culture results and disease process; e.g., enrofloxacin (2.5–5 mg/kg PO q12h) for 3–6 weeks.

PRECAUTIONS

- Estrogens and progestagens decrease prostatic mass via negative feedback on serum testosterone concentrations; however, toxic side effects are common and their use is not recommended. • NSAIDs may be associated with hepatic and/or renal dysfunction, GI ulcerations; patients should be monitored for

adverse reactions. • Trimethoprim-sulpha use may be associated with KCS, and hepatic necrosis.

ALTERNATIVE DRUG(S)

GnRH agonist—deslorelin (Suprelorin) not approved for this use in the US; not recommended for dogs intended for breeding; dramatically suppresses hypothalamic-pituitary-gonadal axis and testosterone production.



FOLLOW-UP

PATIENT MONITORING

- Repeat prostatic fluid cultures to document antimicrobial efficacy as described above.
- Semen evaluation should be performed 70 days after resolution of illness in any dog being used for breeding. • Repeat abdominal ultrasound to evaluate the prostatic response to treatment. • Dogs testing positive for brucellosis should not be used for breeding.

EXPECTED COURSE AND PROGNOSIS

- BPH generally responsive to finasteride.
- Chronic prostatitis more refractory to medical management; castration may be indicated. • Poor prognosis for prostatic neoplasia.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Sertoli cell tumor • Infertility • Recurrent urinary tract infection

ABBREVIATIONS

- ACA = adenocarcinoma • BPH = benign prostatic hypertrophy • CFU = colony forming units • DHT = dihydrotestosterone • GI = gastrointestinal • KCS = keratoconjunctivitis sicca • LS = lumbosacral • NSAID = nonsteroidal anti-inflammatory drug • SCC = squamous cell carcinoma • TCC = transitional cell carcinoma • UTI = urinary tract infection

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PROSTATIC CYSTS



BASICS

OVERVIEW

- Prostatic cysts in the dog include those associated with diffuse epithelial cystic change from androgen-dependent benign prostatic hypertrophy, retention cysts within the prostatic parenchyma that are cavitating, fluid-filled lesions with a distinct capsule, and paraprostatic cysts that are cavitating, fluid-filled lesions with a distinct capsule located outside of the prostatic parenchyma. Prostatic cysts may range in diameter from a few mm to more than 20 cm.
- Paraprostatic cysts usually arise craniolateral to the prostate, displacing the bladder cranially and ventrally, or caudal to the prostate in the pelvis. Prostatic cysts may represent dilated embryonal remnants of the wolffian ducts.
- Pathogenesis is unknown, but the occurrence of retention cysts in dogs with estrogen-secreting Sertoli cell tumors causes speculation that these cysts are dilations of prostatic acini secondary to estrogen-induced squamous metaplasia.

SIGNALMENT

- Male intact dogs. Rare occurrence in castrated dogs
- Age range—2–12 years, mean age 8 years
- Large dogs are more commonly affected than small dogs

SIGNS

- Asymptomatic
- Lethargy and anorexia
- Abdominal distention
- Tenesmus if the cyst compresses the rectum
- Dysuria if the cyst compresses the urethra
- Sanguineous urethral discharge in the presence of BPH

CAUSES & RISK FACTORS

- Benign prostatic hypertrophy
- Androgenic hormones
- Estrogenic hormones



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- BPH—distinguished by ultrasound.
- Prostatic abscess—distinguished by ultrasound and semen culture.

- Distended urinary bladder—distinguished by cystocentesis, imaging.
- Caudal abdominal mass of undetermined origin—distinguished by imaging.

CBC/BIOCHEMISTRY/URINALYSIS

No abnormalities

OTHER LABORATORY TESTS

- Examination of prostatic fluid collected by ejaculation or prostatic massage confirms absence of infection.
- Culture and cytology of cyst fluid collected by ultrasound-guided fine-needle aspiration or by aspiration at surgical exploration reveals sterile clear or sanguineous fluid consistent with prostatic fluid.

IMAGING

Retrograde contrast urethrocystography followed by prostatic ultrasonography confirms presence, location, echo-texture, and size of prostatic cysts, and differentiates retention cysts from paraprostatic cysts.

DIAGNOSTIC PROCEDURES

Collection of prostatic fluid by ejaculation followed by prostatic imaging is recommended prior to fine-needle aspiration of cystic fluid to rule-out bacterial infection.

PATHOLOGIC FINDINGS

Epithelial cysts within the prostatic parenchyma occur with parenchymal hypertrophy and hyperplasia; squamous metaplasia of the ducts and alveoli may be present. Retention cysts and paraprostatic cysts are lined by a single layer of prostatic epithelium or fibrous connective tissue and contain clear to sanguineous fluid with fibrin.



TREATMENT

- Intraprostatic cysts (epithelial, retention) respond to prostatic involution, which may be induced by castration or by the 5 alpha-reductase inhibitor finasteride. Large cysts may be drained percutaneously with ultrasound guidance prior to initiation of finasteride therapy.
- Large retention cysts and paraprostatic cysts should be partially or completely surgically resected, depending on adherence to surrounding structures, or marsupialized and drained for 1–2 months.
- Simple drainage of the cyst(s) is not recommended, as persistence of the capsule may result in recurrence.



MEDICATIONS

DRUG(S)

Prostatic parenchyma and diffuse epithelial cysts involute following treatment with the 5 alpha-reductase inhibitor finasteride (0.1–1 mg/kg PO q24h for 2–4 months). Finasteride prevents conversion of testosterone to dihydrotestosterone, causing prostatic involution without adversely affecting libido or spermatogenesis. BPH recurs following cessation of finasteride therapy. Paraprostatic cysts do not respond to finasteride treatment.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- Imaging assessment of cyst size at 4-week intervals following treatment.
- Standard postoperative monitoring of marsupialized stoma, if any.



MISCELLANEOUS

ABBREVIATION

- BPH = benign prostatic hypertrophy

Suggested Reading

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Consulting Editor Carl A. Osborne
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PROSTATITIS AND PROSTATIC ABSCESS



BASICS

DEFINITION

Acute Prostatitis

Infection of the canine prostate with bacteria, mycoplasmas, and/or fungi with systemic signs of fever, anorexia, lethargy, pain, and inflammatory exudate in prostatic fluid.

Abscessation is variable, occurring in 15 of 25 dogs with prostatitis in one study. Abscesses occasionally rupture into the peritoneal cavity, causing sepsis, shock, and death.

Chronic Prostatitis

Subclinical (recent or long-term) infection of the canine prostate in absence of prostatic abscessation and polysystemic signs. Affected animals are asymptomatic except for inflammatory exudate in the prostatic fluid, which causes infertility. Chronic prostatitis may occur after or independently of acute prostatitis.

PATHOPHYSIOLOGY

• Predisposing pathology is gross and/or microscopic benign prostatic hypertrophy, which occurs under the influence of dihydrotestosterone in more than 80% of intact male dogs > 5 years of age. • BPH is characterized by large, irregularly shaped, well-vascularized prostatic alveoli and branching infoldings of epithelium with microcysts containing sanguineous prostatic fluid; if infected, these can become abscesses. • Infection of the hypertrophied canine prostate develops most commonly from ascent of normal urethral flora—rarely from blood-borne bacteria and/or from penetrating wounds introducing bacteria or fungi to the scrotum. The prostate of intact male dogs constantly secretes prostatic fluid, which is deposited into the prostatic urethra and then flows both into the urinary bladder and out the tip of the penile urethra. With prostatitis, prostatic fluid containing blood, inflammatory exudate, and bacteria or fungi is deposited into the urinary bladder and discharged intermittently from the tip of the penis.

SYSTEMS AFFECTED

- Gastrointestinal—tenesmus if the enlarged prostate compresses the rectum. • Hemic/Lymphatic/Immune—mature or immature neutrophilia in acute prostatitis.
- Polysystemic—septic shock if prostatic abscesses rupture, tachycardia, poor tissue perfusion, elevated temperature, and focal or generalized peritonitis. • Urinary—dysuria if the enlarged prostate compresses the urethra; deposition of prostatic fluid with inflammatory exudate into the urinary bladder. • Reproductive—pain at copulation

and reduction in libido; infertility from infected prostatic fluid in the ejaculate.

INCIDENCE/PREVALENCE

High in intact male dogs more than 5 years of age. Infection is reported in 40% of dogs with prostatic disease.

SIGNALMENT

Species

Dog

Breed Predilections

All breeds and mixed breeds

Mean Age and Range

Middle-aged; mean age range, 7–11 years

Predominant Sex

Intact male dogs; may occur secondary to prostatic neoplasia in castrated dogs.

SIGNS

Acute Prostatitis

- Lethargy/depression • Anorexia • Tenesmus
- Dysuria • Pyrexia • Pain at prostatic or caudal abdominal palpation • Sanguineous urethral discharge • Stiff hindlimb gait
- Septic shock (rare)

Chronic Prostatitis

- Asymptomatic • Tenesmus • Dysuria
- Sanguineous urethral discharge

CAUSES

- Infection of the hypertrophied prostate with ascending urethral flora, including *Escherichia coli*, *Staphylococcus* spp., *Streptococcus* spp., *Proteus mirabilis*, *Klebsiella* spp., *Enterobacter* spp., *Hemophilus* spp., *Pseudomonas* spp., *Pasteurella* spp., anaerobic bacteria, and *Mycoplasma* (most common). • Infection of the hypertrophied prostate with systemic bacterial infection, including *Brucella canis*.
- Systemic or local puncture wound infection with *Blastomyces dermatitidis*.

RISK FACTORS

- Increasing age • Presence of functional testes in affected dogs • BPH and, less commonly, prostatic neoplasia • Historical androgen or estrogen administration
- Impaired host defense mechanisms



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- BPH without infection, distinguished by semen culture • Prostatic cysts, distinguished by ultrasound and semen culture • Prostatic neoplasia, distinguished by ultrasound and tissue biopsy • Abdominal mass or abscess, distinguished by abdominal imaging

CBC/BIOCHEMISTRY/URINALYSIS

- CBC abnormalities in acute prostatitis and abscessation include immature neutrophilia and toxic neutrophils; immature neutropenia

may occur with sepsis. Most dogs with chronic prostatitis have a normal CBC.

- Serum chemistry abnormalities are variable with acute prostatitis. Most dogs with chronic prostatitis have normal serum chemistries.
- Urinalysis abnormalities include hematuria, purulent exudate, and causative microbes; these abnormalities arise, not from primary UTI, but from deposition of infected prostatic fluid into the urinary bladder.

OTHER LABORATORY TESTS

- Gross examination, cytology, and culture of whole semen or the prostatic fluid (third) fraction of semen or fluid collected at prostatic massage yields inflammatory exudate with aerobic bacteria, anaerobic bacteria, *Mycoplasma*, or fungi. Normal prostatic fluid should contain fewer than 100,000 colony-forming bacterial units per mL, and fewer than 5 leukocytes per high power field following fluid centrifugation.
- Although infection with *Brucella canis* is uncommon, because of the zoonotic potential of this infection, *B. canis* serology is recommended in all dogs with suspected prostatitis, with follow-up culture of semen for *B. canis* if serology is positive.

IMAGING

Survey radiography of the caudal abdomen, retrograde urethrocytography, and prostatic ultrasonography are indicated to evaluate prostatic size, echo-texture, and detection of cavitating prostatic lesions. The prostate is enlarged if its greatest craniocaudal diameter measured on a line parallel to the line connecting the sacral promontory to the anterior aspect of the pubis on a lateral radiograph exceeds 70% of the length of the distance between the sacral promontory and the anterior aspect of the pubis.

DIAGNOSTIC PROCEDURES

- Collection and evaluation of prostatic fluid in seminal plasma and collection of prostatic fluid by prostatic massage in dogs reluctant to ejaculate.
- Ultrasound-directed percutaneous fine-needle aspirate of the prostate.

PATHOLOGIC FINDINGS

- Gross pathology of the infected prostate includes enlargement, variable loss of symmetry of the dorsal median raphe, and variable presence of fluid-filled abscesses within or on the surface of the gland. Enlargement may be focal, multifocal, or diffuse.
- Bacterial or fungal infection causes suppurative (bacterial) or granulomatous (fungal) inflammation of the gland. Inflammatory lesions may be focal, multifocal, or diffuse. Abscesses contain accumulations of purulent fluid exudate.
- Biopsy of the infected prostate is not recommended because biopsy may result in the spread of infection to adjacent tissues.

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

- Acute prostatitis, prostatic abscess, and rupture of prostatic abscesses into the peritoneal cavity are potentially life-threatening emergencies that can lead to septic shock and death. Hospitalize affected patients and collect diagnostic samples (blood, urine, semen, imaging) immediately.
- Chronic prostatitis patients may be seen as outpatients for diagnostic procedures and started on specific therapy when laboratory results are available.

NURSING CARE

- Dogs with acute prostatitis or prostatic abscess should receive antimicrobial drugs intravenously. • If abscess rupture and peritonitis is suspected, administer intravenous fluid therapy for septic shock.

ACTIVITY

Breeding should be avoided until bacteria have been cleared from the prostatic fluid.

CLIENT EDUCATION

- Castration is recommended for dogs with acute prostatitis and/or prostatic abscess, as castration induces permanent prostatic involution. • If maintenance of breeding potential is necessary, long-term or intermittent treatment with finasteride is recommended to induce prostatic involution; routine rechecks at 2- to 3-month intervals for semen culture, semen cytology, and prostatic imaging are recommended. BPH recurs over time in intact male dogs after treatment with finasteride is discontinued, and BPH increases risk of recurrence of prostatitis.

SURGICAL CONSIDERATIONS

- Surgical management of prostatic abscesses should be deferred until after initiation of antimicrobial therapy and prostatic involution; involution is associated with resolution of abscesses, often making surgery unnecessary. • Castration is recommended for induction of prostatic involution in non-breeding dogs with prostatitis; castration should be deferred until after identification and treatment (for at least 1 week) of the causative bacterial/fungal agent; alternatively, medical involution of the prostate may be induced with finasteride. • Placement of Penrose drains, marsupialization, partial prostatectomy, and use of an ultrasonic surgical aspirator have been advocated for treatment of prostatic abscesses in dogs; however, these procedures have been associated with a high percentage of short- and long-term adverse sequelae, including recurrence of abscesses. Surgical drainage with subsequent packing of the cavity with omentum has been associated with the fewest adverse sequelae among surgical treatments.

PROSTATITIS AND PROSTATIC ABSCESS



MEDICATIONS

DRUG(S)

Eradicating Infection

- Choice of antimicrobial agent is based on culture and susceptibility findings in the prostatic fluid, antibiotic lipid solubility (which enhances its ability to diffuse into prostatic tissue in therapeutic concentrations), and assessment of acute or chronic status of the infection. • Antibiotics of choice in chronic prostatitis are those known to diffuse into normal prostatic tissue in therapeutic concentrations including chloramphenicol, erythromycin, fluoroquinolones, and trimethoprim. In acute prostatitis, the blood-prostate barrier is assumed to be disrupted, and almost any antibiotic will penetrate the prostatic parenchyma in therapeutic concentrations. • Emergency antibiotic treatment of choice in dogs with acute prostatitis and/or abscess, administered after collection of prostatic fluid for culture, is amoxicillin/clavulanate (25 mg/kg PO q8h) with enrofloxacin (5 mg/kg PO q12h).

Inducing Prostatic Involution

- Treatment of choice for inducing permanent prostatic involution is castration. • Alternatively, the 5 alpha-reductase inhibitor finasteride (0.1–1 mg/kg PO q24h) for 2–4 months induces involution of the prostatic parenchyma and diffuse epithelial cysts and abscesses. • Finasteride prevents conversion of testosterone to DHT, thereby causing prostatic involution without adversely affecting libido or spermatogenesis. • BPH recurs following cessation of finasteride therapy.

CONTRAINdications

Estrogens and androgens cause squamous metaplasia of the prostate and BPH, respectively.

PRECAUTIONS

Long-term therapy with trimethoprim may lead to keratoconjunctivitis sicca and/or hypothyroidism.



FOLLOW-UP

PATIENT MONITORING

- Repeated evaluation of semen culture, cytology, and prostatic imaging. • Intervals between reevaluations vary with severity of signs, presence of an abscess, selection of castration or finasteride therapy for prostatic involution, and use of the dog in a breeding program. Intervals between evaluations range from 1 to 8 weeks, with recheck recommended prior to breeding. • Continue patient monitoring until the dog has been castrated.

PREVENTION/AVOIDANCE

Castration is recommended to induce prostatic involution, resolution of BPH, and prevention of recurrent infection.

POSSIBLE COMPLICATIONS

- Recurrence of infection if prostatic involution is not induced. • Surgical drainage of abscesses is associated with many complications, including urinary incontinence, recurrent abscessation, hypoproteinemia, scrotal edema, anemia, sepsis, and shock.

EXPECTED COURSE AND PROGNOSIS

- Prognosis is good to excellent except in the case of rupture of prostatic abscesses into the peritoneal cavity, with resulting peritonitis.
- Castration prevents recurrence and improves prognosis. • Surgical management of prostatic abscesses is associated with complications and a poorer prognosis than medical/surgical induction of prostatic involution.



MISCELLANEOUS

ASSOCIATED CONDITIONS

When prostatic fluid is infected, blood, inflammatory exudate, and microbial organisms may reflux into the urinary bladder, which, if detected in a urine sample collected by cystocentesis, may be misinterpreted as primary UTI.

ZOONOTIC POTENTIAL

Rare. *Brucella canis* and *Blastomycoses dermatitidis* have been isolated from the urine of dogs with prostatic infection, but human infection from these sources has not been reported.

P

SEE ALSO

- Benign Prostatic Hyperplasia • Dysuria and Pollakiuria • Hematuria • Peritonitis
- Prostatic Cysts • Shock, Septic

ABBREVIATIONS

- BPH = benign prostatic hypertrophy
- DHT = dihydrotestosterone • UTI = urinary tract infection

Suggested Reading

Root Kustritz MV. Collection of tissue and culture samples from the canine reproductive tract. Theriogenology 2006, 66:567–574.

Smith J. Canine prostatic disease: A review of anatomy, pathology, diagnosis, and treatment. Theriogenology 2008, 70:375–383.

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Client Education Handout
available online

PROSTATOMEGLY



BASICS

DEFINITION

Abnormally large prostate gland determined by rectal or abdominal palpation or by abdominal radiography or prostatic ultrasonography. The enlargement can be symmetrical or asymmetrical, painful or non-painful. Normal prostate size varies with age, body size, castration status, and breed so assessment of enlargement is subjective.

PATOPHYSIOLOGY

Enlargement can result from epithelial cell hyperplasia or hypertrophy (e.g., benign prostatic hyperplasia), neoplasia of prostatic epithelium or stroma, cystic change within the prostatic parenchyma, or inflammatory cell infiltration (e.g., acute and chronic bacterial prostatitis and prostatic abscess).

SYSTEMS AFFECTED

- Urinary
- Reproductive

SIGNALMENT

- Dog
- Typically occurs in middle-aged to older males

SIGNS

- May be none
- Straining to defecate
- Ribbon-like stools
- Dysuria
- Urethral outflow obstruction

CAUSES

- Benign prostatic hyperplasia
- Squamous metaplasia
- Adenocarcinoma
- Transitional cell carcinoma
- Sarcoma
- Metastatic neoplasia
- Acute bacterial prostatitis
- Prostatic abscess
- Chronic bacterial prostatitis
- Prostatic cyst

RISK FACTORS

- Castration lowers the risk of benign prostatic hyperplasia and bacterial prostatitis.
- Risk of adenocarcinoma may be increased three-fold in castrated dogs.

- Primary or metastatic neoplasia—typically causes painful, non-symmetric enlargement of the prostate gland; weight loss, impaired appetite, rear limb weakness observed in some patients; suspect neoplasia in castrated dogs.

- Acute bacterial prostatitis—typically results in slight-to-moderate symmetric or non-symmetric enlargement of the prostate gland with prostatic pain. Fever, impaired appetite, rear limb weakness, and painful abdomen observed in some patients.
- Chronic bacterial prostatitis—signs similar to those seen in dogs with acute prostatitis or those related to recurrent lower urinary tract infection (e.g., dysuria and hematuria). Systemic signs less common than in acute bacterial prostatitis; bacterial prostatitis uncommon in castrated dogs.
- Prostatic abscess—may result in signs similar to those in patients with acute or chronic prostatitis; abscess rupture causes fever and caudal abdominal pain.
- Prostatic cysts—may be associated with palpable caudal abdominal mass, straining to urinate, or straining to defecate; patient may also be asymptomatic.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC normal in patients with benign prostatic hyperplasia.
- Leukocytosis in patients with acute and chronic (occasionally) bacterial prostatitis, prostatic abscess, and prostatic neoplasia (occasionally).
- High bilirubin and alkaline phosphatase in some patients with prostatic abscess.
- Urinalysis—may be normal.
- Hematuria in patients with benign prostatic hyperplasia.
- Pyuria, hematuria, proteinuria, and bacteriuria in patients with bacterial prostatitis.
- Pyuria, hematuria, proteinuria, and, occasionally, neoplastic cells in dogs with prostatic neoplasia.

OTHER LABORATORY TESTS

Serum prostatic esterase concentration may be high in dogs with benign prostatic hyperplasia.

IMAGING

Radiographic Findings

Prostatomegaly

Ultrasonographic Findings

- Abscess or cyst—hypoechoic or anechoic lesions with distal enhancement.
- Acute bacterial prostatitis—uniform prostatic echogenicity.
- Benign prostatic hyperplasia—uniform prostatic echogenicity; small fluid-filled cysts in some patients.
- Chronic bacterial prostatitis—focal or diffuse hyperechogenicity.

- Prostatic neoplasia—focal to multifocal areas of coalescing echogenicity and acoustic shadowing (if dystrophic mineralization occurs).

DIAGNOSTIC PROCEDURES

- Examination of prostatic fluid obtained by ejaculation or prostatic massage may reveal changes similar to those seen on urinalysis.
- Bacterial culture of prostatic fluid typically reveals $> 100,000$ CFU of bacteria/mL in dogs with bacterial prostatitis.
- Needle biopsy of the prostate with ultrasound guidance provides visualization of the area to be sampled and increases the likelihood of obtaining a diagnostic sample; take care to avoid iatrogenic rupture of a prostatic abscess.



TREATMENT

- Varies with the cause of prostatomegaly.
- Surgical castration—indicated in symptomatic dogs with benign prostatic hyperplasia and after acute infection resolves in dogs with bacterial prostatitis.
- Surgical drainage—indicated in dogs with prostatic abscess or large prostatic cysts.



MEDICATIONS

DRUG(S) OF CHOICE

Benign Prostatic Hyperplasia

- If castration is not acceptable, the following drugs may produce a temporary response:
 - Finasteride (0.1–0.5 mg/kg/day PO for up to 4 months)
 - Megestrol acetate (0.11 mg/kg PO daily for 3 weeks)
 - Medroxyprogesterone (3 mg/kg SC).

Bacterial Prostatitis

Choose antibiotics on the basis of antibacterial susceptibility testing of the isolated pathogen and ability of the antibiotic to diffuse into prostatic fluid in therapeutic concentrations. Good choices for the latter include trimethoprim-sulfa, chloramphenicol, and fluoroquinolones.

Prostatic Carcinoma

Chemotherapy has not been proven beneficial.

PRECAUTIONS

Long-term administration of megestrol acetate or medroxyprogesterone can cause diabetes mellitus.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Benign prostatic hyperplasia—typically causes non-painful symmetrical enlargement of the prostate gland; not found in neutered dogs.

(CONTINUED)

PROSTATOMEGLY**FOLLOW-UP****PATIENT MONITORING**

- Abdominal radiographs or prostatic ultrasonography to assess efficacy of treatment in benign prostatic hyperplasia, prostatic carcinoma, or bacterial prostatitis.
- Urine and prostatic fluid culture to access efficacy of treatment in patients with bacterial prostatitis.

POSSIBLE COMPLICATIONS

- Urethral obstruction
- Rectal obstruction

**MISCELLANEOUS****SEE ALSO**

- Adenocarcinoma, Prostate
- Benign Prostatic Hyperplasia
- Prostatic Cysts
- Prostatitis and Prostatic Abscess

Suggested Reading

Smith J. Canine prostatic disease: A review of anatomy, pathology, diagnosis, and treatment. Theriogenology 2008, 70:375–383.

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PROTEIN-LOSING ENTEROPATHY



BASICS

DEFINITION

- Any disease process that is characterized by excessive loss of protein into the gastrointestinal lumen.
- Diseases associated with PLE include primary gastrointestinal diseases such as inflammatory bowel disease, intestinal lymphoma, or intestinal lymphangiectasia and systemic disorders such as congestive heart failure.

PATOPHYSIOLOGY

- Under physiologic conditions, two-thirds of normal protein loss in dogs occurs through the small intestine.
- Plasma proteins that leak into the gastrointestinal lumen are rapidly digested into constituent amino acids that can then be reabsorbed and used for the synthesis of new proteins.
- This normal loss of plasma proteins can be accelerated by gastrointestinal mucosal disease or by increased leakage of lymph into the gastrointestinal lumen.
- Gastrointestinal protein loss is associated with loss of both albumin and globulin.
- In response to increased gastrointestinal protein loss, the liver increases albumin synthesis.
- However, the liver cannot increase albumin synthesis to more than twice the normal output.
- When protein loss exceeds protein synthesis, hypoproteinemia results.
- Severe hypoproteinemia causes decreased plasma oncotic pressure, which may be associated with hemodynamic changes and may lead to effusion into body cavities or, less commonly, peripheral edema.
- Dogs and cats with PLE are not always panhypoproteinemic, and can have low-normal serum globulin concentrations with hypoalbuminemia.

P

SYSTEMS AFFECTED

- Coagulation—patients with PLE also lose antithrombin and may be hypercoagulable.
- Gastrointestinal—primary gastrointestinal disease that may be associated with diarrhea, vomiting, or other clinical signs of GI disease.
- Hemodynamic—ascites or pleural effusion due to decreased oncotic pressure leading to abdominal discomfort or even dyspnea.
- Lymphatic—lymphangiectasia.
- Respiratory—dyspnea due to pleural effusion.
- Skin—subcutaneous edema.

GENETICS

A hereditary nature of PLE due to specific underlying causes is suspected, based on an increased prevalence of such conditions in specific dog breeds.

INCIDENCE/PREVALENCE

- The true incidence and prevalence are unknown.
- Many dogs with subacute or acute gastroenteritis have transient PLE.

SIGNALMENT

Species

Dog and cat

Breed Predilections

Soft-coated Wheaten terrier, Basenji, Yorkshire terrier, and Norwegian Lundehund.

Mean Age and Range

Any age

SIGNS

General Comments

Clinical signs are variable

Historical Findings

- Diarrhea (chronic, continuous or intermittent, watery to semisolid), weight loss, and lethargy are most frequently reported. However, a significant number of dogs with PLE have normal stools.
- Vomiting is uncommon.
- Dogs can be presented for apparent weight gain or abdominal distension as the only clinical sign.

Physical Examination Findings

- Ascites, dependent edema, and dyspnea from pleural effusion may be detected with marked hypoproteinemia.
- Abdominal palpation may reveal thickened bowel loops, although most dogs with intestinal lymphangiectasia do not have thickened bowel loops.

CAUSES

Disorders of Lymphatics

- Intestinal lymphangiectasia
- Gastrointestinal lymphoma
- Granulomatous infiltration of the small bowel
- Congestive heart failure leading to lymphatic hypertension

Diseases Associated with Increased Mucosal Permeability or Mucosal Ulceration

- Viral gastroenteritis—parvovirus and others.
- Bacterial gastroenteritis—salmonellosis and others.
- Fungal gastroenteritis—histoplasmosis and others (note: serum globulin concentrations can be in the normal reference interval range with fungal disorders causing PLE in light of increased globulin production secondary to antigenic stimulation).
- Parasitic enteritis—hookworms, whipworms, and others.
- Inflammatory bowel disease—lymphocytic, lymphocytic-plasmacytic, or eosinophilic gastroenteritis.
- Adverse food reactions—food allergy, food intolerance, and others.
- Mechanical enteropathies—chronic intussusception, chronic foreign body, and others.
- Intestinal neoplasia—lymphoma, adenocarcinoma.
- Gastric or intestinal ulcers.

RISK FACTORS

- Gastrointestinal disease
- Lymphatic disease
- Heart disease



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hypoalbuminemia due to PLE must be differentiated from other causes of

hypoalbuminemia.

- Hypoalbuminemia due to hepatic failure is most often associated with a normal or even increased serum globulin concentration. Hepatic enzyme activities may be increased, serum BUN, cholesterol, and even glucose may be decreased, and serum pre- and postprandial bile acids concentrations may also be increased.

- Hypoalbuminemia due to PLN: mild in patients with fever or hyperadrenocorticism, moderate to severe in patients with glomerulonephritis or amyloidosis; is commonly associated with a normal or even increased serum globulin concentration—ruled out by a normal urine protein:creatinine ratio.
- Hypoalbuminemia due to severe blood loss is associated with hypoglobulinemia—blood loss can be excluded by assessment of erythrocyte count on CBC and a thorough physical examination; in some cases a test for fecal occult blood may be necessary.
- Inadequate protein intake (i.e., starvation) is a rare cause of hypoalbuminemia.
- Hypoalbuminemia due to PLE is often associated with hypoglobulinemia—confirmed by an increased fecal α_1 -protease inhibitor concentration (must be assessed in naturally passed and freshly frozen fecal samples from 3 consecutive days).

CBC/BIOCHEMISTRY/URINALYSIS

- Hypoalbuminemia and frequently hypoglobulinemia (panhypoproteinemia).
- A normal or increased serum globulin concentration in some cases, when the underlying disease is associated with chronic antigenic stimulation (e.g., immunoproliferative enteropathy of the Basenji).
- Hypocalcemia—secondary to hypoalbuminemia.
- Hypocholesterolemia can be seen.
- Lymphopenia may be seen with lymphangiectasia.

OTHER LABORATORY TESTS

- Increased fecal α_1 -protease inhibitor concentration.
- Once PLE has been identified as the cause of the hypoalbuminemia, specific tests may be useful to determine the specific cause of PLE—multiple fecal examinations (smears and centrifugation flotations) to rule-out intestinal parasitism as a cause of PLE; serum cobalamin and folate concentrations to diagnose small intestinal dysbiosis or cobalamin deficiency.

IMAGING

- Thoracic radiographs may show evidence for cardiac or fungal disease.
- Abdominal radiographs may show evidence for a mechanical enteropathy or other causes of PLE.
- Abdominal ultrasound also may show evidence for a mechanical enteropathy or other causes of PLE.
- Abdominal ultrasound is helpful for evaluating the intestinal wall layering pattern associated with a variety of enteropathies. A hyperechoic linear or “tiger stripe” effect associated with distension of

(CONTINUED)

intestinal lacteals with lymph fluid can be seen in many dogs with lymphangiectasia and is characterized by hyperechoic lacteals extending from the lumen of the bowel to the submucosal layer. • Cardiac ultrasound may show evidence for cardiac disease.

DIAGNOSTIC PROCEDURES

- Broad-spectrum anthelmintic agent-to treat for potential parasitism with a variety of gastrointestinal endoparasites.
- Feeding trial of an elimination diet containing an intact protein source or hydrolyzed protein source—to rule out adverse reactions to food.
- Rectal mucosal scraping—to help rule out histoplasmosis in geographic regions where histoplasmosis is endemic.
- Gastroduodenoscopy and colonoscopy—to visualize the gastrointestinal mucosa and to collect endoscopic biopsies for histopathologic evaluation. Visualizing white “plaques” (e.g., chylomicron distended lacteals) along the mucosa suggests lymphangiectasia. Endoscopic biopsies should contain full-thickness mucosa to maximize the diagnostic yield of tissue specimens.
- Abdominal exploratory laparotomy may show dilated intestinal lymphatics and allows for full-thickness biopsies of intestines and lymph nodes.
- Fecal α_1 -protease inhibitor concentration to document excessive gastrointestinal protein loss. α_1 -protease inhibitor is a plasma protein with a similar molecular weight to albumin and is thus lost at a similar rate to albumin. Assays for the measurement of α_1 -protease inhibitor are species-specific for dogs and cats and are only available through the Gastrointestinal Laboratory at Texas A&M University. Samples from 3 consecutive defecations need to be collected in special pre-weighed fecal tubes that can be sourced from the GI Lab.

PATHOLOGIC FINDINGS

PLE is not associated with any specific gross or histopathologic lesions. Lesions identified are those of the specific cause of PLE.



TREATMENT

NURSING CARE

- In cases of severe hypoalbuminemia that are associated with clinical signs due to edema or effusion plasma transfusions or colloids (such as hetastarch or dextran) should be considered to increase plasma oncotic pressure.
- Abdominocentesis to remove ascites or pleurocentesis to remove pleural effusion in cases with compromise from severe effusion.

ACTIVITY

Normal

DIET

- May need to be modified depending on the underlying cause of PLE.
- If lymphangiectasia is diagnosed or highly suspected, a low-fat diet that contains < 25% fat in a ME basis should be used. An elemental diet can also be used in patients with severe disease.

suspected, a low-fat diet that contains < 25% fat in a ME basis should be used. An elemental diet can also be used in patients with severe disease.

CLIENT EDUCATION

Prepare clients for long-term therapy; spontaneous cures are rare.

SURGICAL CONSIDERATIONS

- Hypoalbuminemia increases postoperative morbidity because of slow wound healing.
- Some causes of PLE (e.g., intussusception, chronic foreign body, and some intestinal neoplasias), however, require surgical intervention.



MEDICATIONS

DRUG(S) OF CHOICE

- There is no pharmacologic therapy for PLE itself. Instead, the underlying cause of PLE must be addressed. See “Treatment” for these conditions.
- However, patients with PLE also lose antithrombin and can be hypercoagulable. Thus, patients should be treated with a platelet aggregation inhibitor:
 - In dogs or cats: clopidogrel bisulfate (3–5 mg/kg PO q24h in dogs; 18.75 mg/cat PO q24h, which equals one-fourth of a 75-mg tablet).
 - In dogs: low-dose aspirin (0.5 mg/kg q12h PO; use an 81-mg tablet of aspirin and put into the barrel of a 10-mL syringe, add 8.1 mL of water and shake until completely dissolved to make a 10-mg/mL solution; discard unused portion immediately).

CONTRAINdicATIONS

- Aspirin and clopidogrel should not be used concurrently.
- Clopidogrel should not be used with other NSAIDs, phenytoin, torsemide, or warfarin.

PRECAUTIONS

Bleeding may be enhanced in patients treated with platelet aggregation inhibitors that have to undergo surgery.

ALTERNATIVE DRUG(S)

- Diuretics such as furosemide (1 mg/kg PO q12h) in combination with spironolactone (1 mg/kg PO q12h) have been used by some clinicians to control edema, pleural effusion, and ascites. However, they do not work consistently in patients with PLE because of decreased plasma oncotic pressure and may be associated with side effects.
- There are anecdotal reports about the use of the long-acting somatostatin analogue octreotide in dogs with PLE, but no clinical trials have been completed to date.

PROTEIN-LOSING ENTEROPATHY



FOLLOW-UP

PATIENT MONITORING

Check body weight, serum albumin concentration, and evidence of recurrent clinical signs (i.e., pleural effusion, ascites, and/or edema). Frequency depends on the severity of the condition. Monitor serum cobalamin concentrations after initial 6-week induction phase of weekly administrations.

POSSIBLE COMPLICATIONS

- Respiratory difficulty from pleural effusion
- Severe protein-calorie malnutrition
- Intractable diarrhea

EXPECTED COURSE AND PROGNOSIS

- Prognosis is guarded and depends on the underlying cause. Smaller breed dogs carry a more favorable prognosis because nutritional support is easier to perform.
- The primary disease cannot be treated in many cases.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Soft-coated Wheaten terriers may have PLN in conjunction with PLE and should be evaluated accordingly.

ZOONOTIC POTENTIAL

Histoplasmosis, hookworms, and coccidia have zoonotic potential to humans.

ABBREVIATIONS

- GI = gastrointestinal
- NSAID = nonsteroidal anti-inflammatory drug
- PCV = packed cell volume
- PLE = protein-losing enteropathy
- PLN = protein-losing nephropathy

INTERNET RESOURCES

<http://vetmed.tamu.edu/gilab/>

Suggested Reading

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PROTEINURIA



BASICS

DEFINITION

- Urinary protein detected by dipstick analysis, urinary protein:creatinine ratio (UP:C ≥ 0.4 in cats or ≥ 0.5 in dogs), urinary albumin:creatinine ratio (UA:C probably $> 30 \text{ mg/g}$), or 24-hour urine protein content ($> 20 \text{ mg/kg}$). UP:C of 0.2–0.4 in cats and 0.2–0.5 in dogs is borderline.
- Microalbuminuria is the abnormal presence of low concentrations of albumin in the urine (1–30 mg/dL) below the limit of detection of standard urine dipsticks.

PATHOPHYSIOLOGY

- Prerenal: greater than normal delivery of low molecular weight plasma proteins to glomeruli.
- Renal, glomerular: excessive loss of larger molecular weight proteins (e.g., albumin) across the GBM secondary to altered permselectivity of glomeruli.
- Renal, tubular: reduced tubular reabsorption of proteins.
- Post-reenal: exudation of blood or plasma into lower urinary tract.

SYSTEMS AFFECTED

- Renal/Urologic—chronic glomerular proteinuria causes progressive tubular damage resulting in advanced chronic kidney disease (CKD).
- Cardiovascular—systemic hypertension is common with glomerular disease.
- Hemic/Lymphatic/Immune—severe glomerular proteinuria can lead to edema and/or hypercoagulability. Hypercoagulability is brought about by vascular stasis, hyperfibrinogenemia, platelet abnormalities, loss of antithrombic substances, and an increase in procoagulant factors. The pathogenesis of edema involves both inappropriate renal sodium retention and decreased plasma oncotic pressure.

GENETICS

Familial nephropathies associated with glomerular proteinuria have been described in several breeds of dogs; in only a few has the mode of inheritance been established: Samoyed (X-linked), English cocker spaniel (autosomal recessive), bull terrier (autosomal dominant), Dalmatian (autosomal dominant), Bernese mountain dog (suspect autosomal recessive), Brittany spaniel (autosomal recessive), Chinese Shar-Pei (suspect autosomal recessive). Doberman pinscher, bullmastiff, Newfoundland, rottweiler, Pembroke Welsh corgi, beagle, English foxhound, soft-coated Wheaten terrier, and others.

INCIDENCE/PREVALENCE

- In a study of urinalysis data from 500 dogs, the prevalence of proteinuria was approximately 19%.

- The prevalence of microalbuminuria was 25% in 3,041 dogs and 25% 1,243 cats. Prevalence increased with advancing age.

SIGNALMENT

Species

Dog and less commonly cat

Breed Predilections

Glomerular proteinuria may be the initial manifestation of several familial renal diseases (see "Genetics").

Mean Age and Range

Proteinuria can occur in animals of any age. Familial renal diseases tend to occur in younger animals; acquired glomerular proteinuria more likely in middle-aged or older animals.

Predominant Sex

Probably varies with different diseases.

SIGNS

- Vary with underlying cause and severity of proteinuria.
- Patients with glomerular proteinuria are frequently asymptomatic or have signs attributable to underlying diseases.

Historical Findings

- Many have weight loss and lethargy; animals with pulmonary thromboembolism may have acute dyspnea.
- Patients with LUT disorders may have dysuria, pollakiuria, inappropriate urination, and/or hematuria.

Physical Examination Findings

- May have edema or abdominal distention.
- May have oral ulceration (if uremic), edema or cavity effusion, or changes in pulse quality (if thromboembolic).

CAUSES

Prerenal Proteinuria

Overload proteinuria—tubular resorptive capacity exceeded by large amounts of low molecular weight plasma proteins in glomerular filtrate (e.g., excessive hemolysis or rhabdomyolysis, neoplastic production of paraproteins or Bence-Jones proteins).

Renal Proteinuria

- Functional proteinuria—strenuous exercise, fever, hypothermia, seizures, or venous congestion; poorly documented causes of proteinuria in dogs and cats.
- Glomerulonephritis (e.g., membranoproliferative, proliferative), glomerulonephropathy (e.g., membranous nephropathy), minimal change disease, hereditary nephritis, amyloidosis, focal segmental glomerulosclerosis, glomerulosclerosis.
- All glomerular diseases can be associated with severe proteinuria but those that are immune-complex mediated (particularly membranoproliferative and membranous) may be associated with higher magnitude proteinuria than those that are not immune-complex mediated.
- Tubular dysfunction resulting in failure of tubular protein reabsorption is associated with mild-to-moderate proteinuria.

Post-reenal Proteinuria

Hemorrhage or inflammation of the urogenital tract.

RISK FACTORS

- Chronic inflammatory (e.g., infectious and immune-mediated) and neoplastic diseases can lead to development of glomerulonephritis or amyloidosis. Examples include dirofilariasis, ehrlichiosis, borreliosis, babesiosis, chronic bacterial infections (e.g., endocarditis, pyoderma), pyometra, bartonellosis, FIV, mast cell tumor, lymphosarcoma, hyperadrenocorticism, and systemic lupus erythematosus.
- Systemic hypertension.
- Chronic hyperlipidemia (e.g., miniature schnauzer).
- Multiple myelomas can produce paraproteins resulting in Bence-Jones proteinuria.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiate prerenal, post-reenal, and renal tubular from glomerular causes.

CBC/BIOCHEMISTRY/URINALYSIS

- Urine dipstick and sulfosalicylic acid tests allow qualitative and semiquantitative assessment of urine protein content. Results of both are affected by urine concentration and must be interpreted in context of urine specific gravity. Low urine protein (trace or 1+) may be normal in a concentrated urine sample.
 - The dipstick lacks specificity (dog, 69%; cat, 31%) and sensitivity (dog, 54%; cat, 60%).
 - Contamination with quaternary ammonium compounds causes false-positive urine dipstick colorimetric (tetrabromphenol blue) test results. False-positive test results also occur when urine is highly alkaline (pH > 8–9) or when the dipstick is immersed in the urine for a prolonged time.
 - Low concentrations of Bence-Jones proteins or gamma globulins may not be detected by urine dipsticks.
 - SSA turbidometric test results are falsely increased by radiographic contrast media, penicillins, sulfisoxazole, or the urine preservative thymol.
 - SSA test results are falsely decreased by very alkaline urine and increased by uncentrifuged urine.
 - If proteinuria is detected by these methods, the urine sediment should be evaluated for hematuria, pyuria, and/or bacteriuria. Hematuria alone typically does not increase urine albumin content above the negligible range (i.e., > 1 mg/dL) or the UP:C above

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0.4 until there is a visible color change in the urine. In a study of the effects of inflammation on urine protein determination, 67% of dogs with varying degrees of pyuria had negligible urine albumin concentrations ($< 1 \text{ mg/dL}$) and 81% had normal UP:C (< 0.4).

- To determine if proteinuria is persistent repeat the urine protein screening test in proteinuric patients that initially have a normal urine sediment or have been treated for urinary tract inflammation or hemorrhage. If proteinuria is transient and the urine sediment is normal, consider functional proteinuria or false-positive test results.
- Although not all animals with glomerular disease are hypoalbuminemic, glomerular proteinuria should be suspected when proteinuria and hypoalbuminemia are concurrent. As disease progresses, clinicopathologic changes consistent with glomerular disease may develop.

OTHER LABORATORY TESTS

- Urine protein should be quantified in dogs and cats that have hypoalbuminemia and/or repeatedly positive urine dipstick or SSA tests in absence of LUT hemorrhage or inflammation. In theory, the UP:C, UA:C or 24-hour urine collections can be used for quantification. The UP:C is the preferred for quantification because more is known about use of this test and it is technically easier to perform than 24-hour urine collections.
- Microalbuminuria is detected in dogs using a point of care immunoassay or quantitation using an immunoassay. Microalbuminuria is an early predictor of proteinuria. If microalbuminuria is detected via one of these tests, the test should be repeated in 2–4 weeks. If repeatedly positive, and if the concentration is increasing, the patient may be at risk for glomerular disease.
- Appropriate diagnostic testing should be performed to thoroughly evaluate an animal for an underlying disease when persistent proteinuria is believed to be of glomerular origin.

IMAGING

Ultrasound and radiographs may reveal an underlying infectious, inflammatory, or neoplastic disease process or evidence of LUT disease. Ultrasound may provide information about structural changes suggesting primary renal disease (e.g., loss of corticomedullary distinction, hyperechogenicity, and irregular surface margin) or evidence in support of LUT disease.

DIAGNOSTIC PROCEDURES

- Blood pressure should be monitored in patients with persistent renal proteinuria.
- Renal biopsy is needed to specifically diagnose the glomerular disease when an underlying disease cannot be identified or proteinuria has persisted for several months following treatment of an underlying disease.



TREATMENT

APPROPRIATE HEALTH CARE

Most patients with proteinuria can be managed as outpatients. Inpatient care may be required during select diagnostic evaluation (renal biopsy) or when there are complications associated with uremia, thromboembolism or edema in patients with glomerular proteinuria.

NURSING CARE

Physical therapy and exercise may limit formation of edema in patients with glomerular proteinuria and hypoalbuminemia. For these patients, cage confinement should be avoided.

ACTIVITY

Activity should not be restricted in animals with proteinuria.

DIET

If glomerular disease is suspected, feed a diet formulated for kidney diseases.

CLIENT EDUCATION

It is important to determine the cause of persistent proteinuria, which may indicate the presence of kidney disease. Renal proteinuria is a risk factor for progressive kidney disease, thromboembolism, and edema. It is important that all medications are given and the animal is evaluated as prescribed by a veterinarian.

SURGICAL CONSIDERATIONS

Animals with severe hypoalbuminemia (i.e., $< 2 \text{ g/dL}$) present unique challenges to anesthesia. Consideration should be given to referral of these patients to a secondary or tertiary care facility if anesthesia and/or surgery are indicated.



MEDICATIONS

DRUG(S) OF CHOICE

An angiotensin-converting enzyme inhibitor should be given to dogs and cats with glomerular proteinuria. Animals that do not have a meaningful reduction in proteinuria (see "Patient Monitoring") when given a maximal dose of an ACEi can also be given an angiotensin receptor blocker (ARB). An ARB can also be given to those animals that have adverse effects from an ACEi. Use of aldosterone antagonists in management of proteinuria needs further investigation but may be indicated for patients that have increased aldosterone concentrations following treatment with an ACEi or ARB. Animals with concurrent hypertension often require addition of a calcium channel blocker (e.g., amlodipine) or another antihypertensive agent to control both hypertension and

proteinuria. Supplementation with n-3 polyunsaturated fatty acid (PUFA) should be considered in dogs, and possibly cats, with glomerular proteinuria when the diet being fed does not have a reduced n-6/n-3 PUFA ratio that approximates 5:1. Dogs with glomerular disease should also be given low-dose aspirin or clopidogrel as thromboprophylaxis.

CONTRAINDICATIONS

There are no known contraindications in animals with proteinuria.

PRECAUTIONS

Drugs highly bound to albumin may have an altered effect if hypoalbuminemia is present. The use of warfarin as an anticoagulant should be avoided. With hypoalbuminemia or azotemia, higher doses of furosemide may be required to mobilize edema effectively; however, they should be used with extreme caution.

POSSIBLE INTERACTIONS

There are no known important drug interactions in dogs with proteinuria other than the previously mentioned concern with highly protein-bound drugs.

ALTERNATIVE DRUGS

An ARB is an alternative to an ACEi.



FOLLOW-UP

PATIENT MONITORING

- The UP:C, urinalysis, systemic arterial blood pressure and serum albumin, creatinine and potassium concentrations should be monitored at least quarterly in all dogs and cats being treated for glomerular disease.
- Use the UP:C to assess progression of glomerular disease. Response to treatment should be evaluated for several months after resolution of any underlying disease. In general, a reduction of a UP:C to < 0.5 (dog) or < 0.2 (cat) without inappropriate worsening of renal function is considered a therapeutic success. However, this ideal target is often not achieved and a reduction in UP:C of 50% or greater is the recommended alternate target.
- Monitor serum creatinine concurrently. Reduced proteinuria or reduced albuminuria that is concurrent to a rising serum creatinine may reflect deteriorating renal function.
- Because UP:Cs may vary, two to five serial assessments may be needed to evaluate response to treatment or progression in patients with glomerular proteinuria. Alternatively, the UP:C can be measured in a sample that has been pooled by adding equal aliquots of 2 to 3 samples that have been collected and refrigerated over a 48-hour time period.
- When given an ACEi or an ARB, dogs with stage 1 or 2 CKD can have an increase in

PROTEINURIA

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serum creatinine of up to 30% without warranting a change in treatment. Worsening of renal function in dogs with stage 3 or 4 CKD should be avoided. During therapy the serum potassium concentration should not be allowed to exceed 6 mmol/L and the systolic blood pressure should not be < 120 mmHg.

PREVENTION/AVOIDANCE

Adult dogs and cats should have annual urinalyses including determination of urine protein. Repeat the tests in 2–4 weeks if proteinuria is detected. Patients with persistent proteinuria or microalbuminuria of glomerular origin should be evaluated more thoroughly for underlying causes of glomerular injury. Potential underlying causes should be eliminated or managed. If proteinuria persists, potential underlying causes have been managed appropriately or underlying causes were not identified, and the patient is in CKD stage 1, 2, or 3, the dog or cat should be evaluated via renal biopsy and managed appropriately.

POSSIBLE COMPLICATIONS

- Edema
- Thromboembolism
- Systemic hypertension
- Progressive kidney disease
- Poor wound healing

EXPECTED COURSE AND PROGNOSIS

- Vary with the cause of proteinuria.
 - Post-renal and prerenal proteinuria should resolve following resolution of inciting causes.
 - Most diseases associated with renal tubular proteinuria are progressive.
 - Although glomerular diseases are often progressive, the rate of progression varies and spontaneous remissions have been reported.
- Animals with persistent glomerular proteinuria may develop renal tubular damage

resulting in advanced CKD and eventual uremia and death. Some dogs die shortly after the initial detection of proteinuria, while others remain alive for years. Dogs with nephrotic syndrome and/or azotemia may have a shorter survival.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Heavy proteinuria can be associated with hypoalbuminemia, hypoglobulinemia (rare), hypercholesterolemia, low antithrombin III, thrombocytosis, hyperfibrinogenemia, edema, thromboembolism, and systemic hypertension.

AGE-RELATED FACTORS

Familial glomerular diseases should be considered in young animals with glomerular range proteinuria.

ZOONOTIC POTENTIAL

Proteinuria does not have a zoonotic potential. However, glomerular proteinuria can occur with a variety of infectious diseases, some of which could have a zoonotic potential.

PREGNANCY/FERTILITY/BREEDING

Some drugs used in the treatment of diseases associated with proteinuria may be contraindicated in pregnancy.

SYNONYMS

None

SEE ALSO

- Amyloidosis
- Azotemia and Uremia
- Glomerulonephritis
- Hematuria
- Hypoalbuminemia

- Nephrotic Syndrome
- Pyuria

ABBREVIATIONS

- ACEI = angiotensin converting enzyme inhibitor
- ARB = antiotensin receptor blocker
- CKD = chronic kidney disease
- FIV = feline immunodeficiency virus
- GBM = glomerular basement membrane
- LUT = lower urinary tract
- PUFA = polyunsaturated fatty acid
- SSA = sulfosalicylic acid
- UA:C = urinary albumin:creatinine ratio
- UP:C = urine protein:creatinine ratio

Suggested Reading

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PROTOTHECOSIS



BASICS

OVERVIEW

- *Prototheca wickerhamii* and *P. zopfii*—single-celled achlorophylous blue-green algae (Chlorophyta) that can cause disease in warm-blooded animals.
- Humans and cats—usually localized infection of the skin or gastrointestinal tract.
- Dogs—usually colitis.

SYSTEMS AFFECTED

- Skin/Exocrine
- Gastrointestinal
- Nervous
- Ophthalmic

SIGNALMENT

- Dogs—young, female adult, medium- to large-breed dogs, boxer and collie are overrepresented.
- Cats—uncommon, usually cutaneous form.

SIGNS

Historical Findings

Dogs

- Intermittent and chronic large bowel diarrhea with fresh blood.
- Chronic weight loss.
- Acute onset blindness.
- Neurologic disease; deafness, seizures, ataxia.
- Cutaneous lesions.

Cats

Chronic cutaneous or mucous membrane ulceration with few systemic signs.

Physical Examination Findings

Dogs

- Gastrointestinal, ocular, or neurologic disease most common.
- Severe weight loss and debilitation.
- Hemorrhagic colitis, vomiting, anorexia.
- Blindness due to chorioretinitis and/or detached retinas.
- CNS—depression, ataxia, vestibular signs, seizures and/or paresis.
- Cutaneous—ulcers and crusts on the extremities and mucosal surfaces.

Cats

Large cutaneous nodules on the face or limbs.

CAUSES & RISK FACTORS

- Dogs—usually *P. zopfii*; *P. wickerhamii* infection may also occur.
- Cats—usually *P. wickerhamii*.
- Basis for the pathogenicity of *Prototheca* sp. unknown, likely traumatic inoculation.
- Organism—ecologic niche is raw and treated sewage; contaminants of water, soil, and food; occasionally isolated from fecal samples from healthy individuals.
- Dogs and humans—depressed cell-mediated immunity may predispose to gastrointestinal and disseminated infections with *P. zopfii*.
- Cats—no known predisposing factors.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Systemic—histoplasmosis, blastomycosis, cryptococcosis, pythiosis.
- Cutaneous—

systemic and subcutaneous mycoses; mycobacterioses, neoplasia, L-form bacterial infection, actinomycosis.

CBC/BIOCHEMISTRY/URINALYSIS

- Dogs—often normal; depends on organ system affected; organism occasionally seen in urine sediment.
- Cats—almost always normal.

OTHER LABORATORY TESTS

CSF tap—pleocytosis with mononuclear cells; increased protein; organisms.

DIAGNOSTIC PROCEDURES

Cytology

- Definitive diagnostic test; gram's iodine solution.
- Rectal or colonic mucosa, vitreous humor, CSF, cutaneous aspirations.
- Organisms—unicellular, non-pigmented, oval or round cell walls often appear folded; diagnostic characteristic is endospore formation with internal septation in two planes.

Culture

- Blood agar or Sabouraud's dextrose agar (without cycloheximide) at 25–37°C (77–97°F) white or creamy, smooth colonies within 48 hours.
- Specific identification by selective agars or biochemical tests in culture (susceptibility to clotrimazole, sugar and alcohol assimilation tests) or immunohistochemistry.

Polymerase Chain Reaction (PCR) Assays

PCR and DNA to determine species; specimens can be taken from biopsies, CSF or urine.

PATHOLOGIC FINDINGS

Dogs

- Small granulomatous foci or hemorrhagic ulcers—found in many organs, especially kidneys; identification of organisms is diagnosed.
- Nodular thickening of the gastrointestinal mucosa with ulceration.
- Nonspecific inflammatory foci surrounding organisms or pyogranulomas—poorly organized; mixed with other inflammatory cells.

Cats

Cutaneous masses—localized; extend deep into subcutaneous tissues; consist of granulomatous inflammation and mixed-cell inflammation; made up primarily by organisms.



TREATMENT

- Dogs—surgical excision and combination drug therapy.
- Cats—excision of localized cutaneous masses is primary therapeutic modality.



MEDICATIONS

DRUG(S)

- Amphotericin B—use for localized disease after surgical excision; 0.25–0.5 mg/kg IV three times weekly or until a total dose of 8 mg/kg; lipid formulation 1 mg/kg every other day until 12 mg/kg cumulative; concurrent administration of tetracycline or amikacin may provide synergistic effect; lipid formulations may be more efficacious and less toxic for cutaneous disease; reported effective for ocular disease.
- Ketoconazole, fluconazole, and itraconazole (5–10 mg/kg PO q12h)—may use with amphotericin B, or as sole agents for less life-threatening disease.
- Alternative treatments—clotrimazole (locally for *P. wickerhamii*); potassium iodide.
- Amphotericin B cream or clotrimazole enemas for colitis.



FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS

- Difficult to eradicate with drug therapy.
- No definitive therapeutic protocol.
- Dogs—prognosis guarded to grave (median survival 4 months).
- Cats—prognosis fair to good for cutaneous disease if lesions completely excised.



MISCELLANEOUS

ZOONOTIC POTENTIAL

None

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid

INTERNET RESOURCES

- <http://aem.asm.org/cgi/reprint/25/6/981>
- <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1865593>

Suggested Reading

- Lane LV, Meinkoth JH, Bunker J, et al. Disseminated protothecosis diagnosed by evaluation of CSF in a dog. *Vet Clin Pathol* 2012; 41(1):147–152.

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PRURITUS



BASICS

DEFINITION

- Pruritus—a sensation that triggers itch.
- Acute pruritus—a component of the innate immune response.
- Identification and treatment of the cause is required for long-term control and to reduce the need for long-term medical therapy.
- Chronic cases should be referred to a dermatologist.

PATHOPHYSIOLOGY

- Activation of neuronal cells by cytokine, neurotrophin and neuropeptide release from keratinocytes, mast cells, eosinophils and lymphocytes.
- Many factors modify the perception of pruritus peripherally and centrally.

SYSTEMS AFFECTED

- Skin/Exocrine
- Behavioral

SIGNALMENT

Variable depending on the underlying cause

SIGNS

- Scratching, licking, biting, rubbing, or chewing
- Self-trauma and cutaneous inflammation
- Alopecia without evident inflammation (cats)

CAUSES

- Parasitic—fleas, *Sarcoptes*, *Demodex*, *Otodectes*, *Notoedres*, *Cheyletiella*, *Trombicula*, lice, *Pelodera*, endoparasite migration.
- Allergic—parasite allergy, atopy, cutaneous adverse reaction to food, contact allergy, drug hypersensitivity, bacterial hypersensitivity, *Malassezia* hypersensitivity.
- Infectious—*Staphylococci* and *Malassezia*; rarely dermatophyte.
- Primary or secondary seborrhea.
- Calcinosis cutis.
- Cutaneous neoplasia.
- Immune-mediated dermatoses.
- Psychogenic.

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DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pruritus often causes alopecia.
- Demodicosis, dermatophytosis, bacterial pyoderma, immune-mediated dermatoses, seborrhea, some cutaneous neoplasms, and unusual diseases such as leishmaniasis may be pruritic.
- Severe pruritus is common with scabies; flea bite dermatitis or hypersensitivity, cutaneous adverse reaction to food, and *Malassezia* dermatitis can be highly pruritic.
- Uncomplicated atopy—initially steroid-responsive, possibly seasonal,

progressive pruritus of the face, feet, ears, forelimbs, axillae, and caudal body; inadequate management encourages tachyphylaxis; allergen-specific immunotherapy is the only treatment that permits control without chronic medical therapy; flea-allergic and food-hypersensitive animals may be predisposed to atopy.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Miscellaneous Procedures

- Identification and treatment of the underlying cause of pruritus is paramount; multiple concurrent causes possible.
- History and physical examination required for diagnostic workup.
- Skin scrapes—demodicosis, scabies.
- Epidermal cytology—bacterial or yeast infection.
- Dermatophyte culture—dermatophytosis.
- Skin biopsy useful if lesions associated with pruritus are unusual or appear to be primary.

Allergy Testing

- Positive test result does not diagnose allergy as the cause of pruritus; used to select allergens for immunotherapy; results must be carefully correlated with history and physical examination; combined intradermal and serum testing for allergen selection associated with most successful immunotherapy.
- Skin testing—gold standard; allows for identification of individual allergens by physiologically-appropriate mechanism; preferred over serum testing whenever possible.
- Serum tests—measure serum IgE; not a physiological test; repeatability and inter-laboratory consistency (as well as quality control) highly variable; acceptable only when referral for intradermal testing not possible.
- Immunotherapy—selection of allergens based on patient history and environmental exposure; administration produces immunotolerance and/or downregulation of reaction to native allergens; see chapter, Atopic Dermatitis.

Trial Courses of Treatment

- Useful diagnostic tool—empirical therapy for scabies or restricted-ingredient diet trial.
- Canine scabies—difficult to diagnose; skin scrapes are often negative.
- Cutaneous adverse reaction to food—restricted-ingredient food trial using a novel or hydrolyzed protein; commercial tests are available; multiple studies have documented neither demonstrated efficacy nor accuracy, and are not recommended; see chapter, Food Reactions, Dermatologic.



TREATMENT

- More than one disease can contribute to pruritis.
- Numerous palliative therapeutic options exist but identification and treatment or removal of the causative agent permits long-term control.
- Avoidance or reduction of long-term medical therapy should be pursued when possible.
- Chronic cases should be referred to a dermatologist for diagnosis and management.

Topical Therapy

- Topical therapy—helpful for most pruritic patients.
- Localized areas—sprays, lotions, and creams/ointments.
- Large regions/generalized symptoms—shampoos and conditioners/rinses.
- Colloidal oatmeal—common in all forms of topical therapy; short duration of effect.
- Topical corticosteroids—very useful to reduce need for systemic therapy; can cause localized and systemic side effects with overuse; preferred over systemic corticosteroids when effective; low-potency products useful for long-term management (Genesis spray: Virbac).

Systemic Therapy

- Therapy is complex and depends on the etiology—identification of the underlying cause is required for successful outcome; see specific chapters for treatment.
- Scabies—scabicidal therapy.
- Food hypersensitivity—diet trial.
- Atopy—allergen-specific immunotherapy based on testing.
- Flea bite/hypersensitivity dermatitis—adequate flea control.
- Secondary infections should be identified and treated; if the underlying cause is not properly addressed, infections will recur.

DRUG(S)

Chronic therapy without evaluation or management by a dermatologist not recommended.

Glucocorticosteroids

- Affect many biologic responses associated with pruritus; rapid onset of action and easily adjusted dose (oral administration) allow intermittent or pulse treatment; can be a safe adjunct therapy in some patients; best for acute relief.
- Acute relief—subcutaneous injection of dexamethasone (0.15–0.2 mg/kg); results in significant benefit for 2–5 days; rarely causes significant polyuria.
- Chronic control—oral prednisolone (or prednisone—dogs) (0.5 mg/kg tapering to twice-weekly maintenance). A prednisolone or prednisone dose of 0.15–0.2 mg/kg/Q48 hours and initiated the day after a

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PRURITUS

dexamethasone injection often provides adequate intermediate to long term relief with minimal side effects; dose is approximatively one half of the equivalent physiological replacement dose for glucocorticoids and typically well tolerated while waiting for allergen specific immunotherapy to become effective for atopic dermatitis.

Cyclosporine, modified

- Atopica (Novartis) 5 mg/kg/day—effective to control pruritus associated with chronic atopic dermatitis.
- Success rate is similar to that of glucocorticosteroids.
- Slow onset of activity (1–4 weeks).
- Many patients can be adequately controlled with less frequent dosing (every 2–4 days).
- Patient monitoring (CBC/serum chemistry) recommended.
- Serum/plasma drug concentration should be monitored in cats.

Oclacitinib

Janus Kinase (JAK) inhibitor (0.4–0.6 mg/kg q12h for 14 days then 0.4–0.6 mg/kg q24h); new category of drug.

Antihistamines

- Dogs: hydroxyzine (1–2 mg/kg PO q12h), chlorpheniramine (0.2–0.4 mg/kg PO q12h), diphenhydramine (2.2 mg/kg PO q12h), fexofenadine (2–5 mg/kg PO q12–24h), and clemastine (0.04–0.10 mg/kg PO q12h).
- Cats: chlorpheniramine (0.5 mg/kg PO q12h); efficacy estimated at 10–50%.

Fatty acids

Modulate formation of inflammatory mediators and improve the epidermal barrier function (eicosapentaenoic acid 66 mg/kg/day); ω -3 may be more effective than ω -6 (linoleic acid 130 mg/kg/day) fatty acids; may require 6–8 weeks of use for maximum effect.

Behavior-modifiers

- Dogs: amitriptyline (1–2 mg/kg q12h); doxepin 1–2 mg/kg PO q12h; potent antihistaminic effects; side effects similar to antihistamines.

- Fluoxetine (1 mg/kg q24h).
- Gabapentin—pain modifier; dogs, 10–30 mg/kg q6–12h; cats, 3–8 mg/kg q6–8h.

CONTRAINDICATIONS

Palliative medical therapy should be avoided in cases of pruritus caused by an infectious etiology; evaluate to determine the underlying cause; referral to a dermatologist is advisable.

PRECAUTIONS

- Client frustration is common; client education is extremely important.
- Cyclosporine—gastrointestinal upset; not recommended in patients with history of malignancy; papillomatosis; gingival hyperplasia; hirsutism.
- Oclacitinib—should not be used in dogs < 12 months of age; may increase susceptibility to infection, including demodicosis and exacerbate neoplastic conditions; humans should wash hands immediately after handling the tablets; long term effects and safety currently unknown; most appropriate for temporary relief of pruritus.

POSSIBLE INTERACTIONS

- Concurrent use of cyclosporine and ketoconazole requires a 50% dose reduction of each drug.
- Safety of concurrent use of oclacitinib and other medications unknown.

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

- Patient monitoring as well as client communication are imperative.
- Several different unrelated diseases may contribute to pruritus and the control of more than one disease may be necessary until the “itch threshold” is reduced; one or more may have a seasonal incidence.

- Patients receiving chronic medication should be evaluated regularly for potential side effects as well as for the occurrence of new contributing factors.

POSSIBLE COMPLICATIONS

- Due to the chronic nature of pruritus, client frustration is common.
- Skin scrapes and other tests that may have been negative or normal during the original workup should be repeated if symptoms return.
- Complications are also common with chronic corticosteroid use.

**MISCELLANEOUS****Suggested Reading**

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Client Education Handout
available online

P

PSEUDOEPHEDRINE/PHENYLEPHRINE TOXICOSIS



BASICS

OVERVIEW

- Syndrome resulting from exposure to excessive levels of pseudoephedrine or phenylephrine.
- Present in a variety of concentrations in a variety of OTC cold and allergy products.

SIGNALMENT

Any species may be affected, but dogs are most commonly involved in accidental overdoses.

SIGNS

- Mydriasis, panting, hyperthermia, agitation/hyperactivity, tachycardia, hypertension are common. Other signs include vomiting, vocalization, tremors, disorientation, or lethargy.
- Head-bobbing, sinus arrhythmias, scleral hemorrhage, or seizure-like activity are possible. Acute collapse may follow.
- Signs of acute intoxication may persist 1–3 days, depending on dose ingested.
- Severe cases may progress to DIC, myoglobinuria/uria with secondary renal injury, or permanent CNS dysfunction.

CAUSES & RISK FACTORS

- Pseudoephedrine is a synthetic salt of ephedrine and is an indirect sympathomimetic amine.
- Phenylephrine is a synthetic sympathomimetic amine chemically related to ephedrine and pseudoephedrine. Phenylephrine has poor oral bioavailability and generally will have less severe cardiovascular effects than pseudoephedrine.
- Pseudoephedrine indirectly stimulates alpha and, to a lesser degree, beta-adrenergic receptors.
- Pseudoephedrine dosages > 1 mg/kg can result in agitation, hyperactivity, and panting.
- Phenylephrine dosages > 3–4 mg/kg may cause vomiting, lethargy or hyperactivity, hypertension, and tachycardia.
- Head-bobbing, DIC, or myoglobinuria indicate serious intoxication and a more guarded prognosis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other CNS stimulants and sympathomimetics: amphetamines, cocaine, serotonergic antidepressants, phenylpropanolamine, methylxanthines, ephedra.

CBC/BIOCHEMISTRY/URINALYSIS

- No specific clinical pathology alterations are expected in most cases.
- In severe cases DIC, myoglobinemia, myoglobinuria, or azotemia may occur.

OTHER LABORATORY TESTS

Urine or serum from patients with pseudoephedrine toxicosis may give a positive test for amphetamine in over-the-counter drug test kits or human hospital drug screens.



TREATMENT

- Manage severe or life-threatening signs first.
- Control CNS stimulation, then manage CV stimulation, as blood pressure and heart rate may decrease significantly once CNS signs are managed.
- For seizures, use propofol, pentobarbital, or phenobarbital; consider gas anesthetic for refractory cases.
- For agitation, hyperactivity, or other CNS stimulation, use acepromazine or chlorpromazine.
- Cyproheptadine has been used with some success to manage dysphoria, vocalization, and hyperthermia.
- Propranolol (or other beta blocker) may be considered in patients with sustained tachycardia.
- External cooling measures may be required for hyperthermic patients.
- Intravenous fluid administration assists in stabilization of cardiovascular effects, support of kidney function, and excretion of pseudoephedrine and its metabolites.
- Monitor heart rate/rhythm, body temperature, and blood pressure. In severely affected patients, monitor renal function, coagulation parameters, hydration, and electrolytes.
- Gastrointestinal decontamination (induction of emesis, administration of activated charcoal) may be considered in patients that have ingested > 1 mg/kg of pseudoephedrine and are not displaying significant clinical signs.



MEDICATIONS

DRUG(S)

- Propofol 0.1–0.6 mg/kg/min IV.
- Pentobarbital 30 mg/kg IV to effect.
- Phenobarbital 3–4 mg/kg IV.
- Acepromazine 0.05–1.0 mg/kg IM or IV; start low and titrate up as needed.

- Chlorpromazine 0.5–1.0 mg/kg IV or IM; start low and titrate up as needed.
- Cyproheptadine 1.1 mg/kg PO or per rectum q6h (dogs); 2–4 mg PO or per rectum (cats).
- Propranolol 0.02–0.06 mg/kg IV q6–8h PRN.
- Emetics—3% hydrogen peroxide 2.2 mL/kg PO, maximum 45 mL, may repeat once if first dose unsuccessful; apomorphine crushed and diluted with sterile saline and instilled in conjunctival sac, rinse eye after emesis, or 0.03 mg/kg IV.
- Activated charcoal 1–3 g/kg suspended in 50–200 mL of water.

CONTRAINdications/POSSIBLE INTERACTIONS

The use of diazepam to control CNS stimulation should be avoided, as diazepam may induce a dysphoric effect in these patients and worsen the CNS excitation.



FOLLOW-UP

Renal insufficiency resulting from myoglobinuria may require long-term follow-up and care.



MISCELLANEOUS

Ma huang (ephedrine) and amphetamine exposures in animals are managed similarly to pseudoephedrine toxicosis.

ABBREVIATIONS

- CNS = central nervous system
- CV = cardiovascular
- DIC = disseminated intravascular coagulation

Suggested Reading

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Author Sharon Gwaltney-Brant
Consulting Editor Lynn R. Hovda

PSEUDORABIES VIRUS INFECTION



BASICS

OVERVIEW

- Uncommon but highly fatal disease of dogs and cats, usually occurring in animals that have contact with swine.
- Characterized by sudden death, often without characteristic signs or with signs that include hypersalivation, intense pruritus, and neurologic changes.
- Also known as Aujeszky's disease, mad itch, or infectious bulbar paralysis.

SIGNALMENT

- Domestic and exotic dogs and cats.
- Other domestic animals—swine, cattle, sheep, and goats.
- Primarily farm dogs and cats, with no breed or age predilection.

SIGNS

- Sudden death.
- Hypersalivation.
- Rapid and labored breathing.
- Fever.
- Vomiting.
- Neurologic—depression and lethargy, ataxia, convulsions, reluctance to move, recumbency, intense pruritus and self-mutilation, coma, and death.

CAUSES & RISK FACTORS

- Pseudorabies virus (*Herpesvirus suid*)—an alphaherpesvirus.
- Contact with swine.
- Eating contaminated, uncooked meat or offal from swine.
- Ingestion of infected rats.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Rabies—in the furious form, affected dog or cat will attack anything that moves; no pruritus or sudden death; immunofluorescent antibody test of brain positive.
- Canine distemper—no hypersalivation, sudden death, or personality change; respiratory and gastrointestinal signs common.
- Poisoning (organophosphate, lead, strichnine, inorganic arsenic)—no pruritus or personality change; history of exposure to toxin; signs consistent with toxicity.

CBC/BIOCHEMISTRY/URINALYSIS

No characteristic changes

OTHER LABORATORY TESTS

Serologic assays—reveal pseudorabies virus antibodies if an animal recovers.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Immunofluorescent antibody test—brain tissue.
- Viral isolation—affected tissues.
- Animal (rabbit) inoculation.

PATHOLOGIC FINDINGS

- Severe skin lesions—caused by self-mutilation from intense pruritus.
- Histopathologic examination—glial and ganglion cells of neurologic tissues reveal Cowdry type A intranuclear inclusion bodies.
- Non-suppurative meningoencephalitis in the medulla oblongata.



TREATMENT

- Dogs and cats—no known effective treatment.
- General supportive therapy and prevention of self-injury indicated.



MEDICATIONS

DRUG(S)

- None specific.
- Antitherapeutic antivirals—not evaluated for dogs and cats.
- Rapid course makes successful use of antiviral drugs unlikely.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

None



FOLLOW-UP

PREVENTION/AVOIDANCE

- Avoid contact with infected swine, the reservoir host.
- Avoid ingestion of contaminated pork.
- Avoid ingestion of infected rats.
- Cat-to-cat and dog-to-dog transmission usually does not occur.

EXPECTED COURSE AND PROGNOSIS

- Classic (cats)—60% of cases; lasts 24–36 hours; almost invariably fatal.
- Atypical (cats)—40% of cases; lasts > 36 hours; almost invariably fatal.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Mild potential for human infection; take precautions when treating infected animals and handling infected tissues and fluids.

Suggested Reading

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Consulting Editor Stephen C. Barr

P

PTYALISM



BASICS

DEFINITION

- Excessive production and secretion of saliva.
- Pseudopytialism is the excessive release of saliva that has accumulated in the oral cavity due to the inability to swallow.

PATHOPHYSIOLOGY

- Saliva is constantly produced and secreted into the oral cavity from the salivary glands (parotid, sublingual, mandibular, zygomatic).
- Saliva production increases when salivary nuclei in the brainstem are stimulated.
- Higher centers in the CNS can also excite or inhibit the salivary nuclei. • Taste and tactile stimuli in the oral cavity increase saliva production. • Normal physiologic hypersalivation may occur with: anticipation of eating, hyperthermia and purring (cats).
- Saliva production may be increased with gastrointestinal or CNS disorders.

SYSTEMS AFFECTED

- Gastrointestinal • Hepatic
- Nervous/Neuromuscular • Renal/Urologic

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Breeds with a relatively higher incidence of congenital portosystemic shunts include: Yorkshire terrier, Maltese terrier, Australian cattle dog, miniature schnauzer, and Irish wolfhound. • Megesophagus is hereditary in wirehaired fox terrier and miniature schnauzer; familial predispositions have been reported in German shepherd, Newfoundland, Great Dane, Irish setter, Chinese Shar-Pei, greyhound, and retriever breeds, as well as in Siamese cats.
- Congenital hiatal hernia has been recognized in the Chinese Shar-Pei. • Giant breeds, such as Saint Bernard, Great Dane, and mastiff, typically exhibit excessive drooling due to lower lip conformation.

Mean Age and Range

- Congenital abnormalities (e.g., portosystemic shunt) are more likely to be diagnosed in younger animals. • Young animals may also be more likely to have ingested toxic or caustic agents or a foreign body.

SIGNS

Historical Findings

- Anorexia—seen most often in patients with oral lesions, gastrointestinal disease, and systemic disease. • Eating behavior changes—patients with oral disease or cranial nerve dysfunction may refuse to eat hard food, chew only on the unaffected side (if unilateral lesion), maintain an unusual head/neck position, or drop prehended food.

- Other behavioral changes—irritability, aggressiveness, and reclusiveness are common, especially in patients with a painful condition. • Dysphagia—may be seen with inability to swallow. • Nausea—may present as increased swallowing. • Regurgitation—in patients with esophageal disease.
- Vomiting—secondary to gastrointestinal or systemic disease. • Weight loss—as a consequence to many of the above findings.
- Pawing at the face or muzzle—patients with oral discomfort or pain. • Neurologic signs—patients that have been exposed to caustic drugs or toxins, those with hepatic encephalopathy, patients with seizure disorders or other intracranial disease.

Physical Examination Findings

- Periodontal disease. • Gingivitis/stomatitis caused by toxins, infection, immune-mediated disease or nutritional deficiency.
- Oral mass—neoplasia or granuloma.
- Glossitis caused by ulceration, mass or foreign body. • Lesions of the oropharynx may be due to inflammation, ulceration, mass, or foreign body. • Blood in the saliva suggests bleeding from the oral cavity, pharynx, or esophagus. • Halitosis is usually caused by oral disease, but may also be the result of esophageal and/or gastric disease.
- Facial pain may be seen with oral or pharyngeal disease. • Dysphagia may be caused by oral, pharyngeal, pharyngoesophageal, and esophageal causes, and can be precipitated by anatomic or structural causes or underlying neuropathic, myopathic, or junctionopathetic causes.
- Cranial nerve deficits—trigeminal nerve (CN V) lesions can cause drooling due to inability to close the mouth; facial nerve palsy (CN VII) can cause drooling from the affected side; glossopharyngeal (CN IX), vagus (CN X), and hypoglossal (CN XII) nerve lesions can cause a loss of the gag reflex or inability to swallow. • Cheilitis or acne—persistent drooling can lead to dermatologic lesions.

CAUSES

Conformational Disorder of the Lips

- Most common in giant-breed dogs

Oral and Pharyngeal Diseases

- Oral trauma. • Foreign body (e.g., stick, foxtail, or sewing needle). • Neoplasm.
- Abscess. • Gingivitis or stomatitis—secondary to periodontal disease, bacterial, viral (e.g., FeLV or FIV) or fungal infection, immune-mediated disease (e.g., lymphoplasmacytic stomatitis, pemphigus vulgaris), uremia, ingestion of a caustic agent, poisonous plants, effects of radiation therapy to the oral cavity or burns (e.g., biting on an electrical cord). • Neurologic or functional disorders affecting the swallowing center or oropharyngeal structural disease.

Salivary Gland Diseases

- Sialadenitis • Sialolithiasis • Sialadenosis (idiopathic enlargement) • Salivary mucocele

- Salivary gland fistula • Foreign body
- Neoplasm • Infarction • Immune-mediated disease (rare)

Esophageal or Gastrointestinal Disorders

- Esophageal foreign body • Esophageal neoplasm • Esophagitis • Gastroesophageal reflux • Infection (e.g., Spirocercosis, Pythiosis) • Hiatal hernia • Megesophagus
- Esophageal dysmotility • Gastric distension/volvulus • Gastric ulcer
- Gastroenteritis

Metabolic Disorders

- Hepatoencephalopathy (especially in cats)—caused by congenital or acquired portosystemic shunt or hepatic failure.
- Hyperthermia. • Uremia.

Neurologic Disorders

- Rabies—decreased swallowing causes increased drooling. • Pseudorabies in dogs.
- Botulism. • Tetanus. • Dysautonomia.
- Disorders that cause dysphagia. • Disorders that cause facial nerve palsy or a dropped jaw.
- Disorders that cause seizures—during a seizure, ptialism may occur because of autonomic discharge or reduced swallowing of saliva, and may be exacerbated by chomping of the jaws. • Nausea associated with vestibular disease. • Anxiety.

Drugs and Toxins

- Those that are caustic (e.g., household cleaning products and some common house plants). • Anesthesia may induce reflux esophagitis. Drugs used for premedication may induce nausea, vomiting or ptialism.
- Oral, otic or ophthalmic medications that are poorly palatable (especially in cats).
- Those that induce hypersalivation, including organophosphate compounds, cholinergic drugs, insecticides containing boric acid, pyrethrin and pyrethroid insecticides, ivermectin (dogs), fluids containing benzoic acid derivatives (cats), clozapine (a tricyclic dibenzodiazepine), caffeine, and illicit drugs such as amphetamines, cocaine, and opiates.
- Animal venom (e.g., black widow spider, Gila monster, and North American scorpion).
- Toad and newt secretions. • Plant consumption or prehension (e.g., poinsettia, Christmas trees, *Amanita* mushrooms) may cause increased salivation.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Differentiating causes of ptialism and pseudopytialism requires a thorough history, including vaccination status, current medications, possible toxin exposure, and duration of ptialism. • May be able to distinguish salivation associated with nausea (signs of depression, lip smacking, and retching) from dysphagia by observing the

(CONTINUED)

PTYALISM

patient. • Complete physical examination (with special attention to the oral cavity and neck) and neurologic examination are critical; wear examination gloves when rabies exposure is possible.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—often unremarkable; leukocytosis in patients with immune-mediated, inflammatory or infectious disease. • Stress leukogram—common in animals that have ingested a caustic agent or organophosphate.
- FeLV-infected cats may have leukopenia and nonregenerative anemia. • Serum creatine kinase (CK) activity should be evaluated in all dysphagic patients. • Possible microcytosis with portosystemic shunts. • Biochemical analysis—usually unremarkable except in patients with renal disease (azotemia, hyperphosphatemia), and hepatoencephalopathy (possibly elevated hepatic enzyme activities, decreased BUN, hypoalbuminemia, hypcholesterolemia, hyperbilirubinemia, and hypoglycemia).
- Marked ptalism can result in hypokalemia and acidosis from the loss of potassium and bicarbonate-rich saliva. • Urinalysis—often normal; decreased urine specific gravity with renal or hepatic disease. • Urate urolithiasis may be noted in patients with portosystemic shunts.

OTHER LABORATORY TESTS

- Fasting and postprandial bile acids and/or fasting ammonia when hepatoencephalopathy is suspected. • Serologic FeLV and FIV testing in cats with oral lesions. • Acetylcholine receptor antibody titer if focal myasthenia gravis is suspected to be cause of megaesophagus. • Serum cholinesterase level if organophosphate toxicosis is suspected.
- Post-mortem fluorescent antibody testing of brain tissue if rabies is suspected.

IMAGING

- Survey radiography of the oral cavity, neck, and thorax when foreign body, structural abnormality, or neoplasm is suspected.
- Abdominal radiographs ± abdominal ultrasound may help diagnose cause of vomiting; may also help diagnose hepatic or renal disease. • Ultrasonographic evaluation, portal venography, or portal scintigraphy may help diagnose a portosystemic shunt.
- Fluoroscopic evaluation of swallowing may be useful in dysphagic patients to evaluate esophageal function and motility; use caution during barium administration in animals that are dysphagic. • MRI or CT for suspected intracranial lesions. • CT of head may be more sensitive than radiographs, especially when foreign body or neoplasia is suspected.

DIAGNOSTIC PROCEDURES

- Biopsy and histopathology of mucocutaneous lesions—possibly including immunofluorescence testing when immune-mediated disease (e.g., pemphigus

vulgaris) is suspected. • Fine-needle aspiration of oral lesions and regional lymph nodes.

- Biopsy and histopathology of oral lesion, salivary gland, or mass. • Consider esophagoscopy or gastroscopy if lesions distal to the oral cavity are suspected; endoscopic removal of foreign bodies may be possible.

PATHOLOGIC FINDINGS

Varies as to the underlying condition.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Treat the underlying cause (refer to sections pertaining to specific conditions).
- Symptomatic treatment to reduce the flow of saliva—generally unnecessary, may be of little value to the patient, and may mask other signs of the underlying cause and thus delay diagnosis; only recommended when hypersalivation is prolonged and severe and, if possible, after the underlying condition has been diagnosed.

NURSING CARE

- Petroleum jelly can be applied to areas of the face constantly wet from saliva to help prevent moist dermatitis. • Astringent solutions applied for 10 minutes q8–12h can be used to treat areas of moist dermatitis.

DIET

- Enteral nutritional support (esophagostomy, gastrostomy tubes, etc.) may be needed in patients with ptalism and anorexia secondary to severe oral, gastrointestinal, or metabolic causes. • Reduced protein diets may be recommended for patients with hepatic encephalopathy or renal disease, but are not necessarily warranted in animals with portosystemic shunts that are not encephalopathic.

CLIENT EDUCATION

Client education will depend on the underlying disease process.

SURGICAL CONSIDERATIONS

Surgical procedures will vary depending on underlying cause; ligation of parotid salivary duct has been described.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Anticholinergic medications may be given symptomatically to reduce the flow of saliva; atropine (0.05 mg/kg SC PRN) or glycopyrrolate (0.01 mg/kg SC PRN).
- Antiemetics given in conjunction with opioid premedication have variable effects on nausea, vomiting, and ptalism (see chapter,

Vomiting, Acute, for list of antiemetics and dosages). • Crystallloid fluids may be given IV or SC to treat dehydration caused by prolonged or severe ptalism. • Phenobarbital (2 mg/kg PO q12h) has been effective in treating idiopathic hypersialosis.

- Anticonvulsant therapy is indicated for seizure activity.

**FOLLOW-UP****PATIENT MONITORING**

- Depends on the underlying cause (see “Causes”). • Continually monitor hydration, body weight, serum electrolytes, and nutritional status, especially in dysphagic or anorexic animals.

POSSIBLE COMPLICATIONS

- Metabolic acidosis • Dehydration
- Hypokalemia • Moist dermatitis
- Aspiration pneumonia

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

Rabies

SYNONYMS

- Drooling • Hypersalivation • Sialism
- Sialorrhea • Sialosis

SEE ALSO

- Dysphagia • Esophagitis • Hepatic Encephalopathy • Megaesophagus
- Periodontal Diseases • Stomatitis

ABBREVIATIONS

- CN = cranial nerve • CNS = central nervous system • CT = computed tomography • FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- MRI = magnetic resonance imaging

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PULMONARY CONTUSIONS



BASICS

OVERVIEW

- Hemorrhage in the lung parenchyma caused by tearing and crushing during direct thoracic trauma.
- Relatively small volumes of blood in the parenchyma markedly compromise lung function.
- Fluid resuscitation for treatment of shock can exacerbate lung dysfunction by producing edema.

SIGNALMENT

Dog and cat

SIGNS

- History of blunt trauma
- Tachypnea
- Abnormal respiratory effort
- Postural adaptations to respiratory distress
- Cyanotic or pale mucous membranes
- Auscultation of harsh bronchovesicular sounds or crackles
- Expectoration of blood or blood-tinged fluid
- Concurrent signs of shock can be present.
- Additional injuries secondary to blunt force trauma can also be noted.

CAUSES & RISK FACTORS

- Blunt trauma
- Motor vehicle accidents
- Falls from a height
- Abuse



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hemothorax—auscult dull lung sounds ventrally.
- Pneumothorax—auscult dull lung sounds dorsally.
- Diaphragmatic hernia—distinguished radiographically.
- Coagulopathy can result in pulmonary hemorrhage; identified by abnormal coagulation tests or platelet count.
- Acute onset of pulmonary hemorrhage—can be a feature of some neoplasms or pulmonary infarction associated with bacterial endocarditis or heartworm disease.
- Expectoration of bloody fluid (not frank hemorrhage) can occur in animals with ARDS or congestive heart failure.
- In animals without a known history of trauma, pneumonia, or edema (cardiogenic and noncardiogenic) are possible differentials.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—can reveal anemia or mature neutrophilia.
- Biochemistry profile—can demonstrate hypoproteinemia, indicating blood loss; can reveal damage to other organ systems.

IMAGING

Thoracic Radiography

- Usually a patchy alveolar pattern, often focal or asymmetrical but can be generalized.
- If there are concurrent rib fractures, contusions generally worse in the area of the fractures.
- Always perform thoracic radiographs in trauma patients after

stabilization to rule out hemothorax, pneumothorax, and diaphragmatic hernia.

DIAGNOSTIC PROCEDURES

- Coagulation tests for coagulopathy or disseminated intravascular coagulation.
- Pulse oximetry or arterial blood gas analysis—can confirm hypoxemia.
- Examination of tracheal wash cytology—can show excessive numbers of erythrocytes and macrophages; culture to detect bacterial infection.



TREATMENT

- Usually inpatient for stabilization.
- Support respiratory function, stabilize cardiovascular function.
- If concurrent pneumothorax suspected, thoracocentesis should be performed immediately.
- Assess and treat injuries to other organ systems.
- Restrict activity, minimize stress, and monitor carefully for deterioration of respiratory function.
- Respiratory support—oxygen supplementation for hypoxemia; intubation and positive-pressure ventilation if severe.
- Shock—fluids generally required; be conservative with fluid administration to avoid creation or exacerbation of pulmonary edema.
- Blood or plasma transfusion—consider if hemorrhage has resulted in anemia or if there is a coagulopathy.
- Nutritional support—as needed to maintain body condition and immune status.



MEDICATIONS

DRUG(S)

- Oxygen supplementation in animals with dyspnea or hypoxemia.
- Analgesics administered if warranted.
- Low-dose diuretics—furosemide (0.5–2 mg/kg IV, IM); use only when hemorrhage is accompanied by edema or suspected volume overload and respiratory distress is severe. Excessive diuresis can exacerbate shock.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Diuretics—no value in the early stages of pulmonary contusions and potentially harmful; decrease intravascular volume, which is contraindicated for shock.



FOLLOW-UP

PATIENT MONITORING

- Monitor respiratory rate and effort, mucous membrane color, heart rate and pulse quality, and lung sounds.
- Measure serial PCV and total solids and perform pulse oximetry and/or arterial blood gas analysis as needed

for the first 24 hours.

- Monitor ECG frequently to detect ventricular arrhythmias associated with hypoxemia or myocarditis
- Radiographs—repeated in 48–72 hours if clinically indicated, to ensure that the contusions are resolving.

PREVENTION/AVOIDANCE

Appropriate restriction of the animal to prevent trauma.

POSSIBLE COMPLICATIONS

- Bacterial pneumonia (uncommon)—owing to systemic immunosuppression from trauma, shock, and reduced pulmonary defenses.
- Development of a moist productive cough and failure to improve within 48 hours—suspect pneumonia.
- Patients with severe shock can develop ARDS (less common).

EXPECTED COURSE AND PROGNOSIS

- Respiratory function can deteriorate during the initial 12–24 hours after trauma and then should gradually improve.
- Clinical improvement within 48 hours with radiographic resolution likely in 7–10 days.
- If patient fails to improve clinically after 48 hours, evaluate for complications or concurrent disease.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Pneumothorax
- Fractured ribs
- Flail chest
- Ruptured trachea, bronchi, or esophagus
- Cardiac arrhythmias—ventricular
- Other possible complications of trauma

SEE ALSO

Pneumothorax

ABBREVIATIONS

- ARDS = acute respiratory distress syndrome
- ECG = electrocardiogram
- PCV = packed cell volume

Suggested Reading

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PULMONARY EDEMA, NONCARDIOGENIC



BASICS

DEFINITION

Accumulation of edema fluid in the pulmonary interstitium and alveoli, in the absence of heart disease.

PATHOPHYSIOLOGY

- Associated with increased pulmonary vascular permeability and leakage of fluid into the interstitium and alveoli; if severe, can be accompanied by an inflammatory response and accumulation of neutrophils and macrophages in the interstitium and alveoli.
- Several mechanisms contribute to changes in pulmonary vascular permeability.
- Stimulation of brainstem (medulla) vasomotor centers can lead to a reflex systemic release of catecholamines resulting in systemic vasoconstriction, temporary shunting of blood into the pulmonary circulation, transient pulmonary circulatory overload, and endothelial damage; probably occurs in patients with neurogenic edema, electric cord bites, and upper airway obstruction.
- In patients with upper airway obstruction, negative intrathoracic pressure from inspiratory attempts against an airway obstruction contributes to edema formation.
- Increased vascular permeability can be part of a generalized inflammatory response that develops in patients with SIRS, sepsis, or pancreatitis.
- The inciting insult can trigger a cascade inflammatory response that often worsens over 24 hours following the initial episode.
- Severity of clinical manifestation—varies, ranging from mild to severe; the most seriously affected patients can progress from normal to death in as little as a couple of hours after the incident.

SYSTEMS AFFECTED

- Respiratory.
- Cardiovascular—hypotension, tachycardia, and shock.
- Hemic/Lymphatic/Immune—if severe and causing respiratory failure, can be associated with DIC.
- Renal/Urologic—acute renal failure.

GENETICS

Unknown

INCIDENCE/PREVALENCE

Uncommon

SIGNALMENT

Species

Mainly dogs, occasionally cats. No breed or sex predilection except regarding airway obstruction.

Breed Predilections

None specific; brachycephalic dogs are more prone to airway obstruction, older large-breed dogs—laryngeal paralysis, small breed dogs—tracheal collapse.

Mean Age and Range

- Higher incidence in puppies < 1 year old—associated with strangulation, head trauma, and electric cord bites.
- Old—associated with laryngeal obstruction and neoplasia.

SIGNS

General Comments

Vary, depending on underlying cause and severity

Historical Findings

- Predisposing causes—airway obstruction; electric cord bite; seizures; head trauma; near drowning; smoke exposure; adverse drug effects.
- Acute onset of dyspnea.

Physical Examination Findings

- Mild to severe dyspnea.
- Increased respiratory rate and effort; open-mouthed breathing.
- Postural adaptations to respiratory distress (if severe).
- Unwillingness to lie down.
- Pale or cyanotic mucous membranes (severe).
- Harsh lung sounds (early, mild) or generalized crackles (late, severe) on auscultation.
- Expectoration of pink froth or bubbles; can have large volumes of bloody fluid flowing out through the endotracheal tube in severely affected intubated animals.
- Normal cardiac auscultation; can detect arrhythmias; tachycardia common.
- Oral ulceration or burns in cases of electrocution.
- Cranial nervous system abnormalities or other indications of previous seizure-like activity.
- Stridor over the upper airway in cases of brachycephalic syndrome, airway masses, foreign bodies, or abscesses.
- Smokey odor or burns indicative of smoke exposure.

CAUSES

- Upper airway obstruction—laryngeal paralysis; choke-chain injury; mass; abscess.
- Electric cord bite.
- Acute neurologic disease—head trauma; prolonged seizures.
- Smoke inhalation.
- Aspiration pneumonia.
- Systemic inflammatory response syndrome—sepsis; endotoxemia; pancreatitis.
- Anaphylaxis (cats).
- Near drowning.
- Adverse drug reactions including certain anesthetic drugs (ketamine), thiazides, or certain antineoplastics (vincristine, cisplatin in cats).
- Transfusion-related acute lung injury—not reported in veterinary medicine.

RISK FACTORS

- Hypoproteinemia
- Crystalloid fluid resuscitation



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cardiogenic pulmonary edema
- Pulmonary infection—bacterial, viral, or fungal pneumonia
- Pulmonary neoplasia
- Pulmonary hemorrhage (e.g., anticoagulant

rodenticide exposure)

- Pulmonary thromboembolism

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis common, leukopenia and thrombocytopenia possible—owing to neutrophil sequestration in the lung and platelet consumption.
- Biochemistries—usually normal; may note hypoalbuminemia owing to pulmonary protein loss; mild stress-related hyperglycemia.
- Urinalysis—usually normal.

OTHER LABORATORY TESTS

- Pulse oximetry and arterial blood gas analysis—usually demonstrates mild to severe hypoxemia and hypocapnia; results are not specific but indicate the severity of pulmonary dysfunction.
- Coagulation testing (severely affected patients)—mild to moderate prolongation of PT and PTT in animals with consumption and DIC. Severe coagulopathy could indicate hemorrhage as the cause for respiratory signs rather than noncardiogenic pulmonary edema.

IMAGING

- Thoracic radiographs—vital; can reveal prominent interstitial pattern with mild or early disease; alveolar infiltrates with moderate or severe disease; alveolar infiltrates commonly in dorsocaudal lung fields but can be seen in other lung fields, are sometimes asymmetrical and predominantly right-sided. Cardiac silhouette generally normal.
- Echocardiography—rule out cardiogenic pulmonary edema.

DIAGNOSTIC PROCEDURES

- Cytology of airway fluid—inflammatory with neutrophils and some alveolar macrophages. Fluid tends to have high protein values > 3 g/dL. Culture typically negative unless concurrent bacterial pneumonia.
- Edema fluid to plasma ratio (EF:PL) compares protein in the edema fluid to plasma protein. An increased ratio (> 0.65) is indicative of non-cardiogenic pulmonary edema.
- Pulse oximetry—non-invasive, continuous monitoring of arterial hemoglobin saturation with oxygen; provides information about the severity and progression of pulmonary dysfunction.
- Pulmonary artery wedge pressure—normal value confirms noncardiogenic origin; not commonly performed.
- NT Pro-BNP testing in cats and dogs can suggest underlying heart disease and thus support a diagnosis of cardiogenic edema.

PATHOLOGIC FINDINGS

- Gross—lungs usually heavy, red, or congested; fail to collapse; often exhibit a wet cut surface; can ooze foam from major airways.
- Histopathology—depends on severity of the insult; early, mild: may note eosinophilic amorphous material filling the alveoli or can be near normal because fluid removed in processing; severe: alveolar hyaline

PULMONARY EDEMA, NONCARDIOGENIC

(CONTINUED)

membranes, alveolitis, and interstitial inflammatory infiltrates with neutrophils and macrophages evident and accompanied by atelectasis, vascular congestion, and hemorrhage; lesions can be found within hours of a severe insult.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient versus outpatient—depends on the severity of respiratory dysfunction and the underlying cause of disease (e.g., dogs with upper airway obstruction or severe seizures generally require hospitalization).
- Make every effort to resolve and treat the underlying cause (e.g., relieve airway obstruction or treat seizures).
- Mild to moderate—patients generally improve on their own within 24–48 hours with complete resolution; offer support of pulmonary and cardiovascular function while the lung repairs.
- Severe—difficult to treat; usually requires PPV because of respiratory failure; many patients die despite intensive supportive care.

NURSING CARE

- Minimize stress.
- Oxygen therapy—vital in moderate to severe disease; administer via mask or hood, nasal catheter, or oxygen cage; inspired oxygen concentration depends on the severity of disease; most patients do well on 40–50% oxygen, but severe disease can require 80–100% to sustain life.
- Severe—can require PPV and PEEP.
- Fluid therapy with a balanced electrolyte—give as replacement solution with dehydration or shock; use cautious fluid administration.
- Plasma or synthetic colloids—consider with hypoproteinemia or low colloid osmotic pressure measurements; improve oncotic pressure, minimizing movement of fluid into the lungs.

P

ACTIVITY

Dogs with moderate to severe hypoxemia and respiratory distress—rest and minimal stress vital for minimizing oxygen requirements.

CLIENT EDUCATION

- Warn client that the condition can worsen before improving.
- Inform client that severe disease that progresses rapidly to fulminant pulmonary edema and respiratory failure is associated with a very poor prognosis.

SURGICAL CONSIDERATIONS

Relevant only for treating the underlying cause.



MEDICATIONS

DRUG(S) OF CHOICE

- Damaged endothelium in the pulmonary vasculature—no specific treatment available.

- Inflammatory response—generated by a variety of mediators and cascades; cannot be blocked by one specific anti-inflammatory drug to resolve edema.
- Diuretics—usually minimally effective; edema is caused by changes in permeability, not high hydrostatic pressure; can use furosemide cautiously in boluses of 0.5–2 mg/kg IV, IM or at 0.1–1 mg/kg/h IV in a continuous infusion. Additional beneficial effects may include decreases in bronchospasm and bronchodilation.
- Corticosteroids—used to reduce swelling in patients with upper airway obstruction; generally ineffective for pulmonary inflammatory response; may predispose patients to infectious complications (e.g., bacterial pneumonia); if used, recommend an anti-inflammatory dosage (e.g., dexamethasone sodium phosphate at 0.05–0.1 mg/kg IV).
- The use of beta-adrenergic agonists such as terbutaline may increase clearance of alveolar fluid.
- Sedatives can be used cautiously if patient's anxiety is contributing to respiratory distress or upper airway obstruction. The patient should be carefully monitored as sedation can decrease central respiratory drive leading to progression of respiratory failure.
- Additional therapy as indicated by underlying cause, such as anticonvulsants, analgesics for oral ulcerations.

PRECAUTIONS

- Diuretics (e.g., furosemide)—excessive use can cause dehydration and a marked decrease in intravascular volume with minimal resolution of edema; low intravascular volume can exacerbate cardiovascular collapse or shock.
- Corticosteroids—can predispose patients to infectious complications (e.g., bacterial pneumonia).



FOLLOW-UP

PATIENT MONITORING

- Observe respiratory rate and pattern and auscultate frequently (every 2–4 hours) for the first 24–48 hours, depending on severity of disease.
- Assess pulmonary function by pulse oximetry or arterial blood gas analysis (initially every 2–4 hours).
- Assess PCV and total solids and evaluate mucous membranes, pulse quality, heart rate, blood pressure, and urine output every 2–4 hours to monitor cardiovascular status and possible progression to shock.

PREVENTION/AVOIDANCE

- Avoid contact with electric wire.
- Correct and avoid airway obstruction.
- Treat seizures and high intracranial pressure.

POSSIBLE COMPLICATIONS

Usually none if patient recovers from the acute crisis.

EXPECTED COURSE AND PROGNOSIS

- Mild to moderate—resolution of signs in 24–72 hours; no specific treatment required except for oxygen and careful fluid supplementation.
- Severe—difficult to treat; can require PPV because of respiratory failure.
- Overall survival rates—80–90%.
- Long-term prognosis—excellent for recovered patients.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Acute respiratory distress syndrome

SYNOMYMS

- Acute alveolar failure
- Acute lung injury
- Capillary leak syndrome
- Congestive atelectasis
- Hemorrhagic lung syndrome
- Progressive respiratory distress
- Shock lung
- Traumatic wet lung

SEE ALSO

Acute Respiratory Distress Syndrome

ABBREVIATIONS

- DIC = disseminated intravascular coagulation
- PCV = packed cell volume
- PEEP = positive end-expiratory pressure
- PPV = positive-pressure ventilation
- PT = prothrombin time
- PTT = partial thromboplastin time
- SIRS = systemic inflammatory response syndrome

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PULMONARY THROMBOEMBOLISM



BASICS

DEFINITION

Develops when a thrombus lodges in the pulmonary arterial tree and occludes blood flow to the portion of lung supplied by that artery.

PATHOPHYSIOLOGY

- Pulmonary thromboemboli associated with heartworm disease occur *in situ* in the pulmonary vessels; in most other instances, the origin of the thrombus is unclear.
- Potential sites of origin include the right atrium, vena cavae, jugular veins, and femoral or mesenteric veins; these venous thrombi are carried in the venous circulation to the lungs, where they lodge in the pulmonary arteries.
- Abnormal blood flow (stasis), vascular endothelial damage, and altered coagulability (hypercoagulable state) are believed to predispose to thrombus formation. • In most patients, PTE is a complicating feature of another primary disease process.

SYSTEMS AFFECTED

- Cardiovascular—pulmonary hypertension may result, leading to right ventricular enlargement, right ventricular failure (*cor pulmonale*), and reduced cardiac output.
- Respiratory—diminished pulmonary blood flow leads to arterial hypoxemia and dyspnea.

INCIDENCE/PREVALENCE

- Not known—likelihood of pulmonary thromboembolism increases in animals with abnormal coagulation or severe systemic disease. • Uncommon diagnosis in the dog and cat; likely under-diagnosed due to nonspecific clinical signs, lack of clinical suspicion, and paucity of non-invasive, definitive diagnostic tests.

SIGNALMENT

Species

Dog and cat

Mean Age and Range

- More frequently seen in middle-aged to older dogs. • Bimodal age distribution reported in the cat with peak occurrence in cats less than 4 years and greater than 10 years of age.

SIGNS

Historical Findings

- Often reflect the primary disease process.
- Occasionally the reason for initial examination; in such a patient presenting signs may include paroxysmal dyspnea, anorexia, syncope or collapse, cough or hemoptysis, weakness, exercise intolerance, and inability to sleep or get comfortable.

Physical Examination Findings

- Tachypnea and dyspnea in most animals; adventitious lung sounds in some animals.
- Tachycardia, weak arterial pulses, jugular

vein distension, pale or cyanotic mucous membranes, delayed capillary refill time, right-sided cardiac murmur, and split or loud second heart sound in severely affected animals.

CAUSES

- Heartworm disease
- Neoplasia
- Hyperadrenocorticism (Cushing's disease) or corticosteroid administration
- Protein-losing nephropathy (renal loss of antithrombin) or enteropathy
- Immune-mediated hemolytic anemia
- Pancreatitis
- Pulmonary hypertension (primary or secondary)
- Orthopedic trauma or surgery
- Sepsis
- Disseminated intravascular coagulopathy
- Liver disease

RISK FACTORS

- Coagulopathy, especially any hypercoagulable state.
- Diseases listed under "Causes" are associated.
- Estrogen administration and air travel may be causative in humans.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other diseases that cause clinically important dyspnea and hypoxemia without profound radiographic findings include upper airway obstruction, laryngeal paralysis, and diffuse airway disease processes (e.g., toxin inhalation and interstitial lung disease).
- Upper airway obstruction often manifests as inspiratory dyspnea; breath sounds often loudest over the trachea or larynx. • Should be a leading diagnostic consideration in a patient with acute onset of dyspnea or collapse and a disease known to be associated with pulmonary thromboembolism.

CBC/BIOCHEMISTRY/URINALYSIS

CBC—may be normal; thrombocytopenia may be seen in up to 50% of dogs with PTE; leukocytosis may develop. Chemistry profile—results often reflect the underlying disease. Urinalysis—results often reflect the underlying disease; evaluate for proteinuria.

OTHER LABORATORY TESTS

- Arterial blood gases often show arterial hypoxemia (PaO_2 often $< 65 \text{ mmHg}$) and low PaCO_2 with respiratory alkalosis.
- Metabolic and respiratory acidosis may develop in severely affected patients.
- D-dimers result from the breakdown of cross-linked fibrin and are indicators of physiologic or pathologic thrombosis. D-dimer testing plays a pivotal role in diagnostic algorithms for PTE in humans; however, their utility for diagnosis of PTE in veterinary patients is uncertain. Plasma D-dimer levels may be inconsistently elevated in dogs with PTE and a low D-dimer level does not exclude the possibility of PTE.
- Thromboelastography is a technique that

provides a global assessment of coagulation and thrombolysis; may be useful in diagnosing systemic hypercoagulability but not widely available. • Coagulation profile may show high fibrin degradation products, abnormal fibrinogen, or alterations in one-stage PT and activated PTT. • Heartworm serology (antigen testing in dogs; both antigen and antibody testing in cats) should be performed in any animal with suspected PTE. • Cardiac biomarkers—cardiac troponin I and NT-proBNP levels may be elevated.

IMAGING

Thoracic Radiographic Findings

May be normal or show pulmonary artery enlargement or pruning, cardiomegaly, interstitial and alveolar lung patterns, small-volume pleural effusion, or areas of regional hyperlucency (Westerman sign).

Echocardiographic Findings

Right ventricular enlargement, an enlarged pulmonary artery segment, flattening of the interventricular septum, diminished size of the left ventricular cavity, or high velocity tricuspid or pulmonic regurgitation jets provide evidence of pulmonary arterial hypertension in some patients; infrequently a thrombus is imaged in the right heart or the main pulmonary artery segments.

Computed Tomography, Angiographic Findings, and Radionuclide Studies

- One or more of these tests are usually required for definitive diagnosis. • CT angiography is the gold standard for the diagnosis of PTE. • Spiral CT non-selective angiography may show intraluminal filling defects created by emboli, peripheral wedge-shaped pulmonary infiltrates, or pleural effusion. • Right-sided cardiac catheterization with pulmonary angiography may permit identification of intraluminal filling defects or regions of reduced pulmonary blood flow. • Non-selective angiography using conventional radiographic techniques has a low level of diagnostic success. • Combined ventilation and perfusion scans with radioisotopes permit identification of well-ventilated lung regions that are not receiving normal blood flow.

DIAGNOSTIC PROCEDURES

Electrocardiography

- Acute *cor pulmonale*—right axis deviation, *P pulmonale*, ST segment deviation, large T waves • Arrhythmias

PATHOLOGIC FINDINGS

- Thrombi in the major branches of the pulmonary arteries. • Some patients exhibit multiple smaller thrombi in small vessels of the pulmonary arteries, eventually leading to marked respiratory dysfunction and death.
- Concurrent pulmonary pathology such as pneumonia, pulmonary edema, pulmonary neoplasia or interstitial fibrosis is common.

PULMONARY THROMBOEMBOLISM

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

Treat patients documented to have pulmonary thromboembolism as inpatients until hypoxemia is resolved.

NURSING CARE

- Administer IV fluids cautiously unless pre-existing volume depletion exists; they may contribute to the development of right-sided congestive heart failure.
- Administer oxygen if dyspnea exists and/or $\text{PaO}_2 < 65 \text{ mmHg}$; response to oxygen therapy is variable.

CLIENT EDUCATION

- Alert client that disease is often fatal; further episodes are likely unless an underlying cause is identified and corrected; sudden death is not unusual.
- Treatment with traditional anticoagulant medications can lead to bleeding complications necessitating frequent re-evaluation of clotting times (e.g., PT and PTT) for successful management; LMWHs are safer and require less monitoring but are associated with greater expense; anticoagulant administration may be required for several months, even after resolution of the causative disease.



MEDICATIONS

DRUG(S) OF CHOICE

- Always identify and treat the underlying disease; if this is unlikely to be successful, aggressive efforts to treat pulmonary thromboembolism will probably be in vain.
- Unfractionated heparin may help to prevent further thrombi from developing; low dosages are probably inadequate for initial management; a dosage of 200–300 units/kg SC q8h or alternatively a bolus of 200 units/kg IV followed by a CRI at 15–30 units/kg/h adjusted to maintain the PTT at 1.5–2 times the baseline value.
- Thrombolytic drug administration (e.g., urokinase, streptokinase or tissue plasminogen activator) may also be useful in hemodynamically unstable cases; these drugs are expensive and carry a higher risk of bleeding complications.
- Warfarin—may be considered for long-term treatment (0.1 mg/kg q24h), with dosage adjustments to maintain a PT 1.5–2 times the baseline value; animals must be heparinized prior to warfarin therapy to avoid initial hypercoagulable phase.
- The low molecular weight heparins are likely associated with fewer bleeding complications than UFH or warfarin, require less intensive monitoring, and are more suitable for long-term management; however,

the expense of these drugs may be a limiting factor in their use.

- Thromboprophylactic effects have been demonstrated for dalteparin (150 units/kg SC q12h) in the absence of prolonged bleeding times or adverse effects; enoxaparin has been used at 1 mg/kg SC q12h.
- Sildenafil (1–2 mg/kg PO q 8–12 h) may be helpful in selected animals with PTE and concomitant pulmonary hypertension.

PRECAUTIONS

Warfarin—interacts with many other drugs; degree of anticoagulation may change after giving these drugs; or with diet alterations. Dose titration may be difficult in patients with diseases that result in coagulopathy. Review the mechanism of action and pharmacology of the antithrombotic drugs before use.



FOLLOW-UP

PATIENT MONITORING

- Serial arterial blood gases and/or pulse oximetry—may help determine improvement in respiratory function.
- Check PT every 3 days initially for adjusting warfarin dosage to achieve a PT 1.5–2 times the baseline value. International normalization ratios (INR) are recommended to minimize the effects of variability in thromboplastin preparations on PT results. Check weekly after an effective dosage is achieved (typically no sooner than 2 weeks).

PREVENTION/AVOIDANCE

- Activity or physical therapy may improve venous blood flow and prevent development of venous thrombi in immobile patients with severe systemic disease.
- Aspirin (0.5–5 mg/kg PO q12–24h) may have some preventive role but is inadequate as treatment.
- Clopidogrel (1–2 mg/kg PO q24h) is an alternative antiplatelet drug that may have some role in prevention. A single loading dose, up to 10 mg/kg, can be administered for rapid platelet inactivation in cases with active thrombosis.
- Heparin may be administered to animals predisposed to the development of pulmonary thromboembolism (200 units/kg IV initially and 75–200 units/kg SC q8h).
- Alternatively, dalteparin (150 units/kg SC q12h) may be used for thromboprophylaxis.
- Newer oral anticoagulants such as rivaroxaban, apixaban, or dabigatran may be as effective as warfarin for prevention of recurrent thrombosis in people and require less monitoring; these drugs may play a future role in longer-term anticoagulation of veterinary patients but further study on dosing and safety in animals is needed.

POSSIBLE COMPLICATIONS

Clinically important bleeding complications may arise in patients treated with

anticoagulant drugs. Bleeding may occur from any organ system. Anticipate active bleeding or anemia necessitating blood or plasma transfusion and have blood products readily available.

EXPECTED COURSE AND PROGNOSIS

Generally guarded to poor; depends on resolution of the precipitating cause. For irreversible diseases (e.g., some neoplasias and advanced protein-losing nephropathy), prognosis is poor long-term; it is somewhat better for patients with thromboembolism due to trauma or sepsis.



MISCELLANEOUS

SYNONYM

Pulmonary embolism

SEE ALSO

- Anemia, Immune-Mediated • Disseminated Intravascular Coagulation • Heartworm Disease—Cats • Heartworm Disease—Dogs
- Hyperadrenocorticism (Cushing's Syndrome)—Cats • Hyperadrenocorticism (Cushing's Syndrome)—Dogs • Nephrotic Syndrome • Sepsis and Bacteremia

ABBREVIATIONS

- CT = computed tomography • LMWH = low molecular weight heparin • PT = prothrombin time • PTE = pulmonary thromboembolism • PTT = partial thromboplastin time • UFH = unfractionated heparin

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Client Education Handout
available online

PULMONIC STENOSIS



BASICS

DEFINITION

Congenital narrowing of the right ventricular outflow tract, obstructing the passage of flow from the right ventricle to the pulmonary artery; usually valvular, but may be subvalvular or supravalvular. Double-chambered right ventricle is a variant of subvalvular pulmonic stenosis characterized by a focal muscular or fibromuscular stenosis in the mid right ventricle.

PATHOPHYSIOLOGY

The stenosis causes a pressure overload of the right ventricle, resulting in concentric hypertrophy. The right ventricle develops high systolic pressures to overcome the stenosis, whose magnitude correlates with the severity of the stenosis. The difference between the high right ventricular pressure and the normal pulmonary artery pressure (i.e., the pressure gradient) is often used to describe the severity of the stenosis. Hypertrophy of the right ventricle increases the risk of ischemia and arrhythmias. The geometric changes in right ventricular shape may result in secondary tricuspid insufficiency, although tricuspid insufficiency can also be associated with concurrent tricuspid dysplasia. With exercise, the right ventricle may be unable to increase stroke volume adequately. Tricuspid insufficiency with or without myocardial failure of the right ventricle may lead to high right atrial pressures and R-CHF. A concurrent atrial septal defect or patent foramen ovale may cause right-to-left shunting, especially with exercise, which may result in cyanosis on exertion. Mild pulmonic stenosis usually produces no significant hemodynamic effects apart from an ejection murmur.

SYSTEMS AFFECTED

- Cardiovascular—R-CHF, arrhythmias
- Hepatobiliary—hepatomegaly with R-CHF
- Nervous—cerebral hypoperfusion during exercise

GENETICS

Inherited defect in beagles; polygenic mode of transmission suggested.

INCIDENCE/PREVALENCE

- Most surveys show PS to be among the three most common congenital cardiac defects in dogs; comprising 21–32% of congenital heart defects.
- Uncommon in cats, especially as an isolated defect; comprised 3% of congenital heart defects in one study.

SIGNALMENT

Species

Dog and cat

Breed Predilections

English bulldog, Chihuahua, French bulldog, miniature schnauzer, West Highland white terrier, Samoyed, cocker spaniel, beagle, boxer, Pomeranian, German shepherd dog.

Mean Age and Range

Present from birth and may be detected as a murmur in puppies; if murmur is not detected, affected animals may not be identified until clinical signs develop later in life.

Predominant Sex

A predilection for males in English bulldogs and possibly other breeds.

SIGNS

General Comments

- Mild stenosis—usually no clinical signs.
- Severely affected patients—may develop CHF, exertional syncope, or sudden death.

Historical Findings

- Abdominal distension
- Dyspnea
- Exertional syncope, exercise intolerance, or sudden death
- Asymptomatic

Physical Examination Findings

- Systolic murmur loudest over the left heart base; may radiate widely but particularly dorsally on left.
- Murmur—midsystolic or holosystolic, and crescendo-decrescendo.
- Louder murmurs with a precordial thrill—generally associated with more severe stenosis.
- Arrhythmias may occur; the heart rate may be high in CHF.
- Other signs of CHF include ascites, jugular venous distension, and tachypnea.

CAUSES

Congenital



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Similar murmurs may be found with:
 - Aortic stenosis
 - Ventricular or atrial septal defects with marked left-to-right shunting
 - Tetralogy of Fallot.
- R-CHF associated with a left-sided murmur may be seen with:
 - Acquired valvular disease (endocardiosis)
 - Dilated cardiomyopathy.

CBC/BIOCHEMISTRY/URINALYSIS

- Generally unremarkable.
- Polycythemia may be present with right-to-left shunting.
- NT-proBNP is increased, particularly with severe stenosis or if clinical signs present.

IMAGING

Radiographic Findings

- Thoracic radiographs usually show right-sided cardiac enlargement, with a post-stenotic pulmonary artery bulge visible on the dorsoventral view at 1–2 o'clock.
- The caudal vena cava may be wide, and ascites may be present with or without pleural effusion in congestive failure.

Echocardiographic Findings

- Right ventricular hypertrophy, with flattening of the interventricular septum and a “figure-eight” appearance on short axis views in severe cases.
- Can usually image the site of the stenosis, but may be more difficult when the valve is hypoplastic; dysplastic pulmonic valves appear as thickened echodense leaflets; fused leaflets have abnormal motion with systolic doming; discrete subvalvular or supravalvular stenoses may appear as a localized hyperechoic narrowing.
- Post-stenotic dilation of the pulmonary artery often present.
- Double-chambered right ventricle can be difficult to image in conventional views.
- Localized hypertrophy may be seen in the right ventricular infundibular region.

Doppler Echocardiography

- Can use spectral Doppler to measure the elevated pulmonary artery flow velocity to calculate the pressure gradient across the stenosis. Pressure gradients under 50 mmHg generally represent mild stenosis; those over 100 mmHg indicate severe stenosis.
- Color-flow Doppler may reveal tricuspid regurgitation.

Angiography

- Selective cardiac angiography can help identify the precise morphologic abnormalities prior to surgery; may image dysplastic valves and hypertrophy of the infundibulum more clearly.
- Useful in identifying pulmonic stenosis caused by an anomalous coronary artery encircling the right ventricular outflow tract, which may affect the choice of therapy; recommended for English bulldogs (predisposed to this anomaly).

CT Angiography

Best technique to delineate coronary artery anomalies if resolution adequate and images are ECG-gated.

DIAGNOSTIC PROCEDURES

Electrocardiography

- QRS complex waveform changes include deep S waves in leads I, II, III, and aVF and right axis deviation.
- Atrial fibrillation may occur with severe right atrial enlargement.

PULMONIC STENOSIS

(CONTINUED)

PATHOLOGIC FINDINGS

- Various forms exist; most result in right ventricular hypertrophy and post-stenotic dilation of the pulmonary artery; infundibular hypertrophy may occur proximal to the obstruction.
- Hypoplastic pulmonic valve, with thickened leaflets ("dysplastic pulmonic valve").
- Normal pulmonic valve annulus with fused commissures, often attached to vessel at supravalvular level.
- Anomalous coronary arteries.
- Discrete supravalvular or subvalvular stenosis, with possible concurrent tricuspid dysplasia.
- Fibromuscular bands dividing the right ventricular inflow and outflow tracts in double-chambered right ventricle.



TREATMENT

APPROPRIATE HEALTH CARE

Most managed as outpatients.

NURSING CARE

Rarely, pleural effusions may need draining; ascites is usually treated medically.

ACTIVITY

Exercise should be restricted in cases with syncope or congestive failure, and severe exertion should be avoided in asymptomatic cases with severe stenosis.

DIET

Low-salt diets may benefit those with refractory ascites.

CLIENT EDUCATION

- Mildly affected animals may lead normal lives.
- Moderately severely affected patients may benefit from interventions such as balloon catheter dilation or surgery; improved clinical signs and survival has been associated with successful balloon procedures.
- Prognosis is guarded once congestive signs develop.
- Do not breed affected animals.

SURGICAL CONSIDERATIONS

Balloon catheter dilation—relatively safe procedure that involves passing a catheter across the stenosis and inflating a balloon to dilate the obstruction; in many cases, the pressure gradient is significantly reduced, especially when the lesion is caused by fused commissures; less successful with dysplastic or hypoplastic valves and should be used with caution with anomalous coronary arteries.

- Generally unsuccessful in double-chambered right ventricle.
- Alternative surgical techniques include valvulotomy or patch-graft procedures; mortality rates tend to be higher than with balloon valvuloplasty.



MEDICATIONS

DRUG(S) OF CHOICE

If signs of CHF, treat ascites with furosemide (2–4 mg/kg PO q8–12h); in refractory failure, it may be worth adding spironolactone (1–2 mg/kg PO q12h); aim should be to control CHF signs prior to catheter intervention.

CONTRAINDICATIONS

Vasodilators (e.g., hydralazine) may cause hypotension without relieving the stenosis, positive inotropes may further increase myocardial oxygen consumption.

PRECAUTIONS

Avoid overuse of diuretics. ACE inhibitors may be helpful with congestive signs, but may cause hypotension. Start with low doses and monitor blood pressure.



FOLLOW-UP

PATIENT MONITORING

Use serial echocardiograms to follow the pressure gradient and cardiac chamber size.

PREVENTION/AVOIDANCE

Do not breed affected animals.

POSSIBLE COMPLICATIONS

- R-CHF
- Arrhythmias
- Exercise intolerance
- Exertional syncope
- Sudden death

EXPECTED COURSE AND PROGNOSIS

- Mildly affected animals may remain asymptomatic with a normal lifespan.
- Severely affected animals have a guarded prognosis because they may develop CHF or sudden death; clinical signs are generally more common in animals > 1 year of age.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Ventricular septal defects, atrial septal defects, and patent foramen ovale.
- English bulldogs described with a single right coronary artery from which an anomalous left main coronary artery arises and then encircles and constricts the base of the pulmonic valve; other coronary variations have also been described.

AGE-RELATED FACTORS

Defect and murmur are present from birth

PREGNANCY/FERTILITY/BREEDING

Do not breed affected animals

SYNONYM

Pulmonary stenosis

SEE ALSO

- Congestive Heart Failure, Right-Sided
- Murmurs, Heart

ABBREVIATIONS

- ACE = angiotensin-converting enzyme
- PS = pulmonic stenosis
- R-CHF = right-sided congestive heart failure

Suggested Reading

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Fonfara S, Pereira YM, Swift S, et al. Balloon valvuloplasty for treatment of pulmonic stenosis in English bulldogs with an aberrant coronary artery. J Vet Intern Med 2010, 24:354–359.

Author Virginia Luis Fuentes

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Client Education Handout
available online

PUPPY STRANGLES (JUVENILE CELLULITIS)



BASICS

OVERVIEW

- Uncommon granulomatous and pustular disorder of puppies.
- Rarely seen in adult dogs.
- Affects primarily the face, pinnae, and submandibular lymph nodes.
- Immunopathogenesis unknown.

SIGNALMENT

- Dogs.
- Age range—usually between 3 weeks and 4 months.
- Predisposed breeds—golden retriever, dachshund, and Gordon setter.

SIGNS

- Acutely swollen face (eyelids, lips, and muzzle).
- Submandibular lymphadenopathy.
- Marked pustular and exudative dermatitis; frequently fistulates; develops within 24–48 hours.
- Purulent otitis externa.
- Lesions often become crusted.
- Affected skin is usually painful.
- Lethargy—50% of cases.
- Anorexia, pyrexia, and sterile suppurative arthritis—25% of cases.
- Sterile pyogranulomatous panniculitis (rare) over the trunk, preputial, or perianal area; lesions may appear as fluctuant subcutaneous nodules that fistulate.

CAUSES & RISK FACTORS

Unknown: an immune dysfunction with a heritable cause is suspected.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Bacterial folliculitis/furunculosis
- Demodicosis
- Drug reaction/eruption
- Deep fungal infection
- Cutaneous hypersensitivity
- Vaccination reaction
- Hymenoptera or insect envenomation

OTHER LABORATORY TESTS

- Cytology—pyogranulomatous inflammation with no microorganisms; non-degenerate neutrophils.
- Culture—often sterile in early cases; secondary infection with chronicity.

DIAGNOSTIC PROCEDURES

Skin biopsy

PATHOLOGIC FINDINGS

- Multiple discrete or confluent granulomas and pyogranulomas—clusters of large epithelioid macrophages and neutrophils.
- Sebaceous glands and apocrine glands may be obliterated.
- Suppurative changes in the dermis—predominate in later stages.
- Panniculitis.
- Exudate culture: important for selection of antibiotics if secondary infection suspected.



TREATMENT

- Early and aggressive therapy necessary because scarring may be severe.
- Topical therapy—may be soothing and palliative; adjunct to corticosteroids.



MEDICATIONS

DRUG(S)

- Corticosteroids—high doses required; prednisone (2.2 mg/kg divided q12h for at least 2 weeks then decreased over 2–4 weeks).
- Do not taper too rapidly.
- Chemotherapeutics—rare resistant cases.
- Adult dogs with panniculitis may require longer therapy.
- Antibiotics—only if there is evidence of secondary bacterial infection; as an adjunct therapy with immunosuppressive doses of corticosteroids.



FOLLOW-UP

- Most cases do not recur.
- Scarring may be a problem, especially around the eyes.



MISCELLANEOUS

SYNOMYMS

- Juvenile pyoderma
- Juvenile sterile granulomatous dermatitis and lymphadenitis

Suggested Reading

Miller WH, Griffin CE, Campbell KL. Muller & Kirk's Small Animal Dermatology, 7th ed. St. Louis, MO: Elsevier Mosby, 2013, pp. 708–709.

Author Karen Helton Rhodes

Consulting Editors Alexander H. Werner

PYELONEPHRITIS



BASICS

DEFINITION

Microbial colonization of the upper urinary tract including the renal pelvis, collecting diverticula, renal parenchyma, and ureters; because it is not usually limited to the renal pelvis and parenchyma, a more descriptive term is upper urinary tract infection; this chapter is limited to bacterial pyelonephritis.

PATOPHYSIOLOGY

- Infection of any portion of the urinary tract usually requires some impairment of normal host defenses against urinary tract infection (see Lower Urinary Tract Infection chapters); normal defenses against ascending urinary tract infection include mucosal defense barriers, ureteral peristalsis, ureterovesical flap valves, unidirectional flow of urine and an extensive renal blood supply. Pyelonephritis usually occurs by ascension of microbes causing lower urinary tract infection. In dogs and cats, hematogenous seeding of the kidneys does not usually cause pyelonephritis. Regardless of the route of infection, an upper urinary tract infection is frequently accompanied by lower urinary tract infection.
- Pyelonephritis can develop secondarily to infection of metabolic nephroliths. Upper urinary tract infection with urease-producing bacteria can predispose to formation of struvite nephroliths (see Urolithiasis, Struvite—Dogs).
- Obstruction of an infected kidney or ureter can rapidly cause septicemia (so-called urosepsis).

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SYSTEMS AFFECTED

- Renal/Urologic
- Can cause urosepsis, thus affecting any body system

INCIDENCE/PREVALENCE

- Unknown.
- Probably occurs much more commonly than is recognized clinically, because many animals with pyelonephritis are asymptomatic or have signs limited to lower urinary tract infection.

SIGNALMENT

Species

Detected more frequently in dog than cat

Mean Age and Range

- Dogs of any age can be affected.
- Cats urinary tract infection is uncommon (1–3%) in young to middle-age cats. It is more common in cats > 10 years of age (~10%).

Predominant Sex

- Unknown; dogs—urinary tract infection affects more females than males.
- Cats—similar frequency in males and females.

SIGNS

General Comments

Many patients are asymptomatic or have signs of lower urinary tract infection only.

Historical Findings

- Maybe asymptomatic.
- Polyuria/polydipsia.
- Abdominal or lumbar pain (uncommon).
- Signs associated with lower urinary tract infection—e.g., dysuria, pollakiuria, perirenia stranguria, hematuria, and malodorous or discolored urine.

Physical Examination Findings

- May be asymptomatic.
- Pain upon palpation of kidneys.
- Fever.
- One or both kidneys may be reduced in size, and/or increased in size.

CAUSES

Usually, ascending urinary tract infection caused by aerobic bacteria; most common isolates are *Escherichia coli* and *Staphylococcus* spp.; other bacteria, including *Proteus*, *Streptococcus*, *Klebsiella*, *Enterobacter*, and *Pseudomonas* spp., which frequently infect the lower urinary tract, may ascend into the upper urinary tract. Anaerobic bacteria, ureaplasma, and fungi uncommonly infect the upper urinary tract.

RISK FACTORS

- Ectopic ureters, vesicoureteral reflux, congenital renal dysplasia, and lower urinary tract infection.
- Conditions that predispose to urinary tract infection—e.g., diabetes mellitus, hyperadrenocorticism, exogenous steroid administration, renal failure, transurethral catheterization, urine retention, uroliths, urinary tract neoplasia, perineal urethrostomy.
- In cats with experimentally induced lower urinary tract disease, indwelling urinary catheters combined with administration of exogenous steroids frequently resulted in pyelonephritis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Clinical diagnosis of pyelonephritis is usually presumptive, based on results from CBC, biochemical analysis, urinalysis, urine culture, and diagnostic imaging; definitive diagnosis is not usually required for planning treatment.
- Since many dogs and cats lack specific symptoms attributable to pyelonephritis, any patient with urinary tract infection could potentially have pyelonephritis; the best methods for differentiating between upper and lower urinary tract infection are ultrasonography or excretory urography. Remember, most patients with pyelonephritis are asymptomatic.

- Consider pyelonephritis as a rule-out in dogs or cats with fever of unknown origin, PU/PD, chronic renal failure, and/or lumbar/abdominal pain.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—results often normal with chronic pyelonephritis; leukocytosis and immature neutrophilia may be detected in some patients.
- Biochemistry—values usually normal unless chronic pyelonephritis leads to chronic renal failure (azotemia with an inappropriate urinary specific gravity).
- Urinalysis reveals hematuria, pyuria, proteinuria, bacteriuria, and leukocyte casts in some animals. Leukocyte casts are diagnostic for renal inflammation, but unfortunately are very uncommon. Observe dilute urine specific gravity in patients with nephrogenic diabetes insipidus, which may occur secondary to pyelonephritis. Absence of these abnormalities does not rule out pyelonephritis.

OTHER LABORATORY TESTS

- Quantitative urine culture to confirm urinary tract infection; see Lower Urinary Tract Infection chapters for interpretation.
- Dogs with chronic pyelonephritis may have a negative urine culture and require multiple urine cultures to confirm urinary tract infection.

IMAGING

- Ultrasonography and excretory urography are the best methods for presumptively differentiating between upper and lower urinary tract infection. Ultrasonography is more sensitive than excretory urography for identification of mild-to-moderate acute pyelonephritis.
- Ultrasonographic findings supporting pyelonephritis include dilation of the renal pelvis and proximal ureter and a hyperechoic mucosal margin line within the renal pelvis and/or proximal ureter.
- Intravenous urography may reveal decreased opacity of the nephrogram phase of the IVU, dilation and blunting of the renal pelvis with lack of filling of the collecting diverticula, decreased opacity of contrast media in the collecting system, and dilation of the proximal ureter.
- In patients with acute pyelonephritis, the kidneys may be large; in patients with chronic pyelonephritis, the kidneys may be small, with an irregular surface contour.
- Concomitant nephroliths detected in some patients by survey radiography, ultrasonography, or excretory urography.

DIAGNOSTIC PROCEDURES

- Definitive diagnosis requires urine cultures obtained from the renal pelvis or parenchyma, or histopathology from a renal biopsy. Pyelocentesis can be performed percutaneously using ultrasound guidance or during exploratory surgery; can obtain

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- specimen for culture from the renal pelvis (or from nephroliths) during nephrotomy.
- To confirm the diagnosis, the biopsy specimen must include the renal cortex and medulla; thus renal biopsy should be performed by an individual very familiar with the technique of ultrasound guided renal biopsy, or by open surgery and only if necessary.
 - The renal lesions may be patchy in distribution and therefore the renal biopsy sample may not be representative of the light microscopic lesions.

PATHOLOGIC FINDINGS

- Kidneys affected by chronic pyelonephritis may have areas of infarction and scarring on the capsular surface. The renal pelvis and collecting diverticula may be dilated and distorted from chronic infection and inflammation. Purulent exudate is occasionally observed in the renal pelvis.
- Light microscopic findings include papillitis, pyelitis, interstitial nephritis, and leukocyte casts in tubular lumens.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient unless animal has septicemia or symptomatic renal failure.

ACTIVITY

Unlimited

DIET

Modified renal diet (e.g., Prescription Diet k/d for dogs or cats) recommended in cats or dogs with concomitant chronic renal failure or nephrolithiasis.

CLIENT EDUCATION

- Recurrent pyelonephritis may be asymptomatic. Unresolved chronic pyelonephritis may lead to chronic renal failure; diagnostic follow-up is important to document resolution or progression of pyelonephritis.
- In patients with nephroliths, resolution is unlikely unless the nephroliths are removed.

SURGICAL CONSIDERATIONS

- Complete obstruction of the upper urinary tract of a patient with pyelonephritis may rapidly progress to septicemia and therefore should be regarded as a medical emergency. The cause of the obstruction should be corrected by surgery (or lithotripsy for nephroliths).
- Infected nephroliths—surgically remove, medically dissolve (struvite), or fragment by extracorporeal shock wave lithotripsy; use periprocedural antibiotics to reduce the risk of urosepsis when manipulating infected nephroliths.

- Unilateral nephrectomy is usually not effective for elimination of suspected unilateral pyelonephritis.



MEDICATIONS

DRUG(S) OF CHOICE

- Base antibiotic selection on urine culture and susceptibility testing.
- Antibiotics should be bactericidal, achieve good serum and urine concentrations, and not be nephrotoxic.
- High serum and urinary antibiotic concentrations do not necessarily ensure high tissue concentrations in the renal medulla; thus chronic pyelonephritis may be difficult to eradicate.
- Give orally administered antibiotics at full therapeutic dosages for 4–6 weeks.
- Do not use drugs that achieve good concentrations in urine but poor concentrations in serum (e.g., nitrofurantoin).

CONTRAINdications

Do not use aminoglycosides unless no other alternatives exist on the basis of urine culture and susceptibility testing.

PRECAUTIONS

Trimethoprim/sulfa combinations can cause side effects (keratoconjunctivitis sicca, blood dyscrasias, and polyarthritis) when administered for more than 4 weeks.



FOLLOW-UP

PATIENT MONITORING

Perform urine cultures and urinalysis during antibiotic administration (~5–7 days into treatment) and 1 and 4 weeks after antibiotics are finished.

PREVENTION/AVOIDANCE

Eliminate factors predisposing to urinary tract infection; correct ectopic ureters.

POSSIBLE COMPLICATIONS

Renal failure, recurrent pyelonephritis, struvite nephrolithiasis, septicemia, septic shock, metastatic infection (e.g., endocarditis, polyarthritis).

EXPECTED COURSE AND PROGNOSIS

- Patients with acute or subacute pyelonephritis—fair to good, with a return to normal health unless the patient also has nephrolithiasis, chronic renal failure, or some other underlying cause for urinary tract infection (e.g., obstruction or neoplasia).
- Established chronic infection of the renal medulla may be difficult to resolve because of poor tissue penetration of antibiotics.

PYELONEPHRITIS

- Patients with chronic renal failure caused by pyelonephritis—prognosis determined by the severity and rate of progression of the chronic renal failure.
- Recurrent pyelonephritis is likely if infected nephroliths are not removed.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Hyperadrenocorticism, exogenous glucocorticoid administration, chronic renal failure, hyperthyroidism (cats), and diabetes mellitus are associated with lower urinary tract infection, which can ascend into the ureters and kidneys.

PREGNANCY/FERTILITY/BREEDING

Use antibiotics that are safe for the pregnant bitch or queen.

SYNONYMS

Upper urinary tract infection, pyelitis

SEE ALSO

- Lower Urinary Tract Infection chapters
- Nephrolithiasis
- Renal Failure, Chronic
- Urinary Tract Obstruction
- Urolithiasis, Struvite—Cats
- Urolithiasis, Struvite—Dogs

ABBREVIATIONS

- IVU = intravenous urogram
- PU/PD = polyuria and polydipsia

Suggested Reading

Bartges JW. Urinary tract infection. In: Ettinger SJ, Feldman EC, eds., Textbook of Veterinary Internal Medicine, 6th ed. St. Louis: Elsevier, 2005, pp. 1800–1808.
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Authors Carl A Osborne and Larry G. Adams
Consulting Editor Carl A. Osborne



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PYODERMA



BASICS

DEFINITION

- Bacterial infection of the skin.
- Surface bacterial infections—often referred to as a “hot spot;” represents an acute moist dermatitis involving the surface of the skin.
- Superficial pyoderma—involves the epidermis and the intact hair follicle; includes mucocutaneous pyoderma.
- Deep pyoderma—involves the dermis and possibly subcutis; furunculosis is often present; patients can be systemically ill.

PATOPHYSIOLOGY

- Skin infections occur when the surface barrier of the skin has been broken, the skin has become macerated by chronic exposure to moisture, the population of resident bacterial flora has been altered, circulation has been impaired, and/or immunocompetency of the patient has been negatively impacted by systemic illness or immunosuppressive therapy.
- Pyoderma is usually secondary to an underlying cause; the primary, underlying cause should be identified and managed to reduce the frequency and recurrence of skin infections.

SYSTEMS AFFECTED

Skin/Exocrine

GENETICS

N/A

INCIDENCE/PREVALENCE

- Dogs—very common
- Cats—uncommon

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GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Dog—short-coated breeds, especially those with excessive skin folds.
- German shepherd dog—severe, deep pyoderma that responds to antibiotics and may frequently relapse.

Mean Age and Range

Age of onset is usually directly related to the underlying cause.

Predominant Sex

None

SIGNS

General Comments

- Superficial—usually involves the trunk; extent of lesions may be obscured by hair coat.
- Deep—often affects the chin, bridge of the nose, pressure points, and feet; may be generalized and associated with symptoms of systemic illness, such as pyrexia and/or pain.

Historical Findings

- Acute or gradual onset.
- Variable pruritus—typically pruritic; the underlying cause may be pruritic or the staphylococcal infection itself may be pruritic; may not be pruritic if associated with hypercortisolism.

Physical Examination Findings

- Papules
- Pustules
- Crusted papules
- Crusts
- Epidermal collarettes
- Circular erythematous or hyperpigmented patches (macules)
- Alopecia; moth-eaten hair coat
- Hemorrhagic bullae
- Scaling
- Lichenification
- Target lesions
- Abscess
- Furunculosis, cellulitis

CAUSES

- *Staphylococcus pseudintermedius*—most frequent.
- *Pasteurella multocida*—cats.
- Deep bacterial skin infections may be complicated by gram-negative organisms (e.g., *Escherichia coli*, *Proteus* spp., *Pseudomonas* spp.).
- Rarely caused by higher bacteria (e.g., *Actinomycetes*, *Nocardia*, *Mycobacteria*, *Actinobacillus*).

RISK FACTORS

- Hypersensitivity—flea allergic dermatitis; atopic dermatitis; cutaneous adverse reaction to food; contact allergic dermatitis.
- Parasites—especially *Demodex* spp.
- Fungal infection—dermatophytosis (*Microsporum canis*, *Microsporum gypseum*, or *Trichophyton mentagrophytes*) most common.
- Endocrine diseases—hypothyroidism; hyperadrenocorticism; sex hormone imbalance.
- Immunosuppression—excessive corticosteroid administration; young animals.
- Seborrhea—chin acne; schnauzer comedo syndrome.
- Conformation—short coat; skin folds; redundant interdigital skin.
- Trauma—pressure points; grooming; scratching; rooting behavior; irritants.
- Foreign body—foxtail; grass awn.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hypersensitivity—pruritus precedes lesions; persists with resolution of pyoderma.
- Endocrinopathy—relapsing pyoderma; consider if pruritus resolves with resolution of the pyoderma; may be associated with systemic symptoms.

- Flea allergic dermatitis or atopic dermatitis—may be seasonal.

- Pustular diseases—dermatophytosis; demodicosis; pemphigus foliaceus; and subcorneal pustular dermatosis.

- Furunculosis—higher bacterial infection; demodicosis; dermatophytosis; opportunistic fungal infections; deep fungal infections; panniculitis; and zinc-responsive dermatosis.
- Superficial pyoderma in short-coated breeds often misdiagnosed as urticaria due to acute onset of pruritic papules and follicular tufting.

CBC/BIOCHEMISTRY/URINALYSIS

- Superficial pyoderma—normal or may reflect underlying cause (e.g., anemia due to hypothyroidism; stress leukogram and high serum alkaline phosphatase due to hyperadrenocorticism; eosinophilia due to parasitism).
- Generalized, deep pyoderma—may show leukocytosis with a regenerative left shift and hyperglobulinemia; abnormalities related to an underlying cause may be present.

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Multiple skin scrapings—demodicosis.
- Direct smear from intact pustule—neutrophils with intracellular bacteria, typically cocci.
- Cytology from underneath a crust or edge of an epidermal collarette; help differentiate pemphigus foliaceus (acantholytic keratinocytes) and deep fungal infections (blastomycosis, cryptococcosis) from pyoderma; tissue grains may identify filamentous organisms characteristic of higher bacteria.
- Skin scrapings—demodicosis.
- Trichograms—dermatophytosis, follicular abnormalities.
- Dermatophyte culture—fungal infection.
- Surface or papule/pustule cytology—pemphigus foliaceus.
- Intradermal allergy testing—atopy.
- Elimination diet trial—food hypersensitivity.
- Endocrine tests—hypothyroidism, hyperadrenocorticism.
- Skin biopsy is rarely useful unless the infection is deep in nature; utilized to obtain tissue sample for macerated tissue culture.

Culture

- Usually positive for *S. pseudintermedius*.
- Other organisms besides staphylococci and higher bacteria may be cultured from the lesions of deep pyoderma.
- Contents of an intact pustule—most reliable results for superficial infections.
- Punch biopsy obtained by sterile technique for macerated tissue culture; especially for

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PYODERMA

deep pyoderma; more likely false-negative results with superficial pyoderma.

- Freshly expressed exudate from a draining tract or beneath a crust—may yield the pathogen or a contaminant if the lesion is not intact; least reliable method.

PATHOLOGIC FINDINGS

- Subcorneal pustules.
- Intraepidermal neutrophilic microabscesses.
- Perifolliculitis.
- Folliculitis.
- Furunculosis.
- Nodular to diffuse dermatitis.
- Panniculitis.
- Inflammatory reaction—suppurative or pyogranulomatous.
- Tissue grains within pyogranulomas—observed most often with *Actinomyces*, *Actinobacillus*, and *Nocardia*.
- Special stains—used to identify gram-negative bacteria or acid-fast organisms.

**TREATMENT****APPROPRIATE HEALTH CARE**

Usually outpatient, except for severe, generalized deep pyoderma.

NURSING CARE

- Severe, generalized, deep pyoderma—may require IV fluids, parenteral antibiotics, and/or daily whirlpool baths.
- Benzoyl peroxide or chlorhexidine shampoos—remove surface debris.
- Whirlpool baths—deep pyoderma; remove crusted exudate; encourage drainage; decrease inflammation and improve tissue oxygenation.

ACTIVITY

No restriction

DIET

- Novel protein or hydrolysate diet if secondary to cutaneous adverse reaction to food.

CLIENT EDUCATION

N/A

SURGICAL CONSIDERATIONS

Fold pyoderma may require surgical correction to prevent recurrence; frequent topical therapy can help reduce the severity and frequency of recurrence.

**MEDICATIONS****DRUG(S) OF CHOICE**

- *S. pseudintermedius* isolates—usually susceptible to cephalosporins, cloxacillin, oxacillin, methicillin, amoxicillin-clavulanate, erythromycin, clindamycin, and trimethoprim-sulfamethoxazole; somewhat

less responsive to lincomycin; frequently resistant to amoxicillin, ampicillin, penicillin.

- Amoxicillin-clavulanate—most isolates of *Staphylococcus* and *P. multocida* susceptible; generally effective for skin infections in cats.
- Superficial pyoderma—initially treated empirically with one of the antibiotics listed above.
- Recurrent, resistant, or deep infections—choose antibiotic therapy based upon culture and sensitivity testing (e.g., chloramphenicol).
- Multiple organisms with different antibiotic sensitivities—choose antibiotic on basis of the staphylococcal susceptibility.

CONTRAINdications

Corticosteroids—mask inflammation causing therapy to be discontinued prematurely and resulting in selection for resistant organisms; if used concurrently, therapy should be extended and the infection should be re-evaluated before discontinuing antibiotics.

PRECAUTIONS

- Cephalosporins, erythromycin, lincomycin, clindamycin and oxacillin—vomiting; administer with food.
- Aminoglycosides—renal toxicity usually precludes prolonged systemic use.
- Trimethoprim-sulfamethoxazole—keratoconjunctivitis sicca, fever, hepatotoxicity, polyarthritis, and hematologic abnormalities, especially neutropenia.
- Chloramphenicol—use with caution in cats; may cause mild, reversible anemia in dogs; associated with aplastic anemia in humans; rear limb muscle weakness should be mentioned to owners as a possible side effect.

POSSIBLE INTERACTIONS

Trimethoprim-sulfamethoxazole—falsey decrease thyroid hormone test results.

ALTERNATIVE DRUG(S)

Bacterin (Staphage Lysate—Delmont Laboratories), staphoid AB, or autogenous injections—may improve antibiotic efficacy and decrease infection recurrence.

**FOLLOW-UP****PATIENT MONITORING**

Administer antibiotics for a minimum of 7–10 days beyond clinical cure; approximately 3–4 weeks for superficial pyoderma; 6–10 weeks for deep pyoderma.

PREVENTION/AVOIDANCE

- Routine bathing with benzoyl peroxide or chlorhexidine shampoos—may help prevent recurrences.
- Padded bedding—may ease pressure point pyoderma; also consider causes for poor wound healing including hypothyroidism.
- Topical benzoyl peroxide gel or mupirocin 2% ointment may be helpful adjunct

therapies—chin acne, fold pyoderma, respectively.

- Identification and management of the underlying cause is crucial to prevent recurrence.

POSSIBLE COMPLICATIONS

Bacteremia and septicemia

EXPECTED COURSE AND PROGNOSIS

Likely to be recurrent or non-responsive if underlying cause is not identified and effectively managed.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

- Impetigo—affects young dogs before puberty; can be associated with poor husbandry; often requires only topical therapy.
- Superficial pustular dermatitis—occurs in kittens; associated with overzealous “mouthing” by the queen.
- Pyoderma secondary to atopic dermatitis—usually begins between 1 and 3 years of age.
- Pyoderma secondary to endocrine disorders—usually begins in middle adulthood.

ZOONOTIC POTENTIAL

- Cutaneous tuberculosis—rare
- Feline leprosy—unknown

PREGNANCY/FERTILITY/BREEDING

N/A

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SEE ALSO

- Acne—Cats
- Acne—Dogs
- Perianal Fistula
- Pododermatitis

Suggested Reading

Miller WH, Griffin CE, Campbell KL, Muller & Kirk's Small Animal Dermatology, 7th ed. St. Louis, MO: Saunders, 2013, pp. 184–217.

Author Elizabeth R. May

Consulting Editor Alexander H. Werner



Client Education Handout
available online

PYODERMA—METHICILLIN-RESISTANT



BASICS

OVERVIEW

- Staphylococcal bacterial skin infection resistant to all β -lactam antibiotics; associated with exposure to one or more courses of antibiotic therapy.
- Most often caused by *Staphylococcus pseudintermedius*; rarely *Staphylococcus aureus*.

SIGNALMENT

Dogs

- Any age, breed, sex, size.
- More common with chronic, primary skin conditions, especially patients with recurrent skin infection.

Cats

- Any age, breed or sex may be affected.
- Pyoderma less common in cats.

SIGNS

Dogs & Cats

- Papules • Pustules • Crusts • Crusted papules • Epidermal collarettes
- Furunculosis, cellulitis if deep • Circular erythematous or hyperpigmented spots (macules) • Alopecia, moth-eaten hair coat, especially in short-coated breeds
- Hemorrhagic bullae • Scale
- Lichenification • Abscess • Pyoderma that persists when active disease remains or develops during appropriate therapy.

CAUSES & RISK FACTORS

- Hypersensitivity—flea allergic dermatitis; atopic dermatitis; cutaneous adverse reaction to food; contact allergic dermatitis.
- Parasites—especially *Demodex* spp.
- Endocrine—hypothyroidism; hyperadrenocorticism (especially if non-pruritic); sex hormone imbalance.
- Immunosuppression—iatrogenic due to chronic glucocorticoid therapy; young animals.
- Seborrhea—chin acne; schnauzer comedo syndrome.
- Additional—short coat; skin folds; redundant interdigital skin; trauma of pressure points, especially in hypothyroid dogs; excessive grooming; scratching; rooting behavior; irritants; foreign bodies (foxtail; grass awn).

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DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Dogs

- Demodicosis • Dermatophytosis
- Methicillin-sensitive pyoderma
- Pemphigus foliaceus • Systemic lupus erythematosus • Other primary causes for pyoderma • Epitheliotropic lymphoma (older animals)

Cats

- Dermatophytosis • Flea-allergic dermatitis
- Demodicosis • Pemphigus foliaceus
- Methicillin-sensitive pyoderma
- Epitheliotropic lymphoma in older animals

CBC/BIOCHEMISTRY/URINALYSIS

- Superficial pyoderma—normal or may reflect underlying cause.
- Generalized, deep pyoderma—may demonstrate leukocytosis with regenerative left shift and hyperglobulinemia; in addition, may reflect underlying cause; sepsis a concern, especially if patient is immunosuppressed.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Multiple skin scrapings—demodicosis.
- Direct smear from intact pustule—neutrophils with intracellular bacteria.
- Cytology from underneath crust or edge of epidermal collarette useful if intact pustules absent; cytology utilized to help differentiate pemphigus foliaceus (acantholytic keratinocytes) and deep fungal infections (blastomycosis) from pyoderma.
- Culture and sensitivity essential when MR infection suspected.
- Skin biopsy rarely useful unless infection deep; used to obtain tissue sample for macerated tissue culture.
- Dermatophyte culture—fungal infection.
- Intradermal allergy testing—atopy.
- Elimination diet trial—food hypersensitivity.
- Endocrine tests—hypothyroidism, hyperadrenocorticism.

PATHOLOGIC FINDINGS

- Subcorneal pustules • Intraepidermal neutrophilic microabscesses • Perifolliculitis
- Folliculitis • Furunculosis—deep infection
- Nodular to diffuse dermatitis
- Panniculitis—deep infection
- Inflammatory reaction—suppurative; pyogranulomatous with deep infections



TREATMENT

- Antibiotic choice based on culture and sensitivity.
- Topical therapy.
- Generalized, deep pyoderma—hospitalization, IV fluids, IV antibiotics, whirlpool baths, depending on severity and risk for sepsis.



MEDICATIONS

DRUG(S)

- Antibiotic therapy must be based on culture and sensitivity.
- Topical therapy essential—chlorhexidine shampoo or spray, dilute bleach bathing, mupirocin ointment, for localized disease.
- Some cases resolve with topical therapy only—must be consistent/frequent.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Corticosteroid therapy—masks inflammation and suppresses immune system function; therapy should be discontinued.



FOLLOW-UP

PATIENT MONITORING

- Recheck examinations crucial, since fewer antibiotics to choose from.
- Re-evaluation of patient while still receiving treatment aids in decision making regarding continuation of therapy, or need for additional diagnostic tests.

PREVENTION/AVOIDANCE

- Choose antibiotic therapy from culture and sensitivity data—treatment failure occurs when antibiotic changes made without evidence.
- Successful management of underlying disease.
- Hand washing before and after handling patient.

EXPECTED COURSE AND PROGNOSIS

- Good if antibiotic choice is based on culture and sensitivity data and underlying cause is managed.
- MR infections not more virulent, but fewer antibiotic medications for treatment.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Exposure of humans and animals to MRSA and MRSP is common.
- MRSP infections in humans are rare.
- MRSP is not MRSA.
- MRSA infections in animals are rare and most associated with exposure to humans with MRSA infection.

SEE ALSO

- Pyoderma • Pododermatitis

ABBREVIATIONS

- MR = Methicillin resistant
- MRSP = Methicillin resistant *S. pseudintermedius*
- MRSa = Methicillin resistant *S. aureus*

INTERNET RESOURCES

Weese SJ. www.wormsandgermsblog.com

Suggested Reading

Miller WH, Griffin CE, Campbell KL. Muller & Kirk's Small Animal Dermatology, 7th ed. St. Louis, MO: Saunders, 2013, pp. 184–207.

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BASICS

DEFINITION

Pyometra is an acute or chronic suppurative inflammation of the endometrium in ovary-intact bitches which leads to intraluminal accumulation of purulent exudates.

PATOPHYSIOLOGY

- Incompletely understood and multifactorial in origin.
- Classic description: Normal cycling bitches—repeated exposure of the endometrium to high concentrations of estrogen during proestrus and estrus followed by high concentrations of progesterone for 2 months during diestrus without pregnancy—leads to development of cystic endometrial hyperplasia (CEH), which predisposes the uterus to a secondary bacterial infection.
- Strains of *Escherichia coli* with uropathogenic virulence factors that allow adhesion to the endometrium and establishment of an infection without the presence of CEH enter the uterus during proestrus and estrus and act as a mucosal irritant—stimulating the development of CEH under the influence of progesterone during diestrus.
- Combination of both disease entities—occurring concurrently.
- Bacteria—ascend from the vagina through the partially open cervix during proestrus and estrus; uterine secretions provide excellent media for growth; uropathogenic *E. coli* most common isolate.
- Regardless of underlying cause—pyometra does not occur without the presence of progesterone (endogenous or exogenous source).

SYSTEMS AFFECTED

- Reproductive
- Hemic/Lymphatic/Immune
- Hepatobiliary
- Renal/Urologic

GENETICS

- Genetic predisposition suspected in some ‘lines’ of related bitches.
- Breed predisposition has been suggested: Bernese mountain dogs, rottweiler, rough-coated collie.

INCIDENCE/PREVALENCE

Incidence—accurate assessment cannot be made because most dogs and cats in the United States undergo elective ovariohysterectomy.

SIGNALMENT

Species

Dog and cat

Mean Age and Range

- Usually > 6 years old; range 4 months to 16 years in dogs.
- Animals treated with exogenous estrogen or progestagen.
- Pyometra of the uterine stump in spayed animals—may develop any time after ovariohysterectomy.

Predominant Sex

Female—ovary intact

SIGNS

Historical Findings

- Dogs—present within 12 weeks after their last estrus.
- Cats—present within 4 weeks of last call (estrus).
- History of treatment with exogenous hormones.

Physical Examination Findings

- Uterus—with closed cervix palpably enlarged; palpate carefully to avoid rupture; with open cervix, may not be palpably enlarged.
- Vaginal discharge and systemic illness—depends on patency of cervix.
- Open cervix—blood-stained, purulent vaginal discharge often only presentation.
- Closed cervix—systemically ill from endotoxemia and bacteremia: polyuria, polydipsia, lethargy, anorexia, vomiting, abdominal distension, dehydration.
- May or may not have pyrexia.

CAUSES

- Dogs—the unique, repeated exposure of the endometrium to estrogen followed by exposure to progesterone without pregnancy.
- Cats—may be the result of estrogen at estrus followed by a progestational (pseudopregnancy) phase, caused by induction of ovulation by coitus, mechanical stimulation, hormones (hCG, GnRH), or spontaneous ovulation (incidence of 30% reported).

RISK FACTORS

- Middle-aged to older, nulliparous ovary-intact females may be predisposed.
- Pharmacologic use of estrogen (mismate) shots during midestrus to early diestrus.
- No correlation with pseudopregnancy in dogs.
- Use of progestagens in both queens and bitches for estrus prevention.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pregnancy
- Other causes of polyuria and polydipsia—diabetes mellitus; hyperadrenocorticism; primary renal disease
- Severe vaginal disease
- Metritis and retained fetal membranes (associated within first days postpartum)
- Hydrometra (serous intrauterine discharge); mucometra (mucoïd intrauterine discharge); hematometra (hemorrhagic intrauterine discharge)

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilia—left shift +/− toxic changes; more severe with closed cervix
- Mild, normocytic, normochromic, nonregenerative anemia
- Hyperglobulinemia, hyperproteinemia, hypoalbuminemia, hypercholesterolemia, elevated C-reactive protein
- Azotemia (elevated BUN and creatinine)
- ALT and ALP—high with

septicemia or severe dehydration • Electrolyte disturbances—depend on clinical course

- Urinalysis—isosthenuria, bacteriuria, glucosuria, and proteinuria can be found. Collect sample by catheterization of urinary bladder or ultrasound-guided cystocentesis to avoid risk of uterine puncture. Midstream urine sample not recommended as contamination with vaginal discharge likely.

OTHER LABORATORY TESTS

- Cytologic examination of vulvar discharge—degenerative polymorphonuclear cells and phagocytized bacteria; may be indistinguishable from the purulent discharge associated with vaginal disease (e.g., vaginitis, vaginal mass, foreign object, and vaginal anatomic anomaly).
- Bacterial culture and sensitivity test of vulvar discharge—not helpful in confirming diagnosis (bacteria cultured are usually normal vaginal flora); useful in determining appropriate antibiotic use—if sample directly taken from the uterus transcervically or the cranial vagina with the aid of a vaginal speculum (guarded swab from caudal vagina/vestibule bacteria).
- Serologic testing for *Brucella canis*—rapid slide agglutination test used as a screen (D-Tec CB®, Zoetis, Corp., (888)-963-8471); sensitive but not specific. If positive, recheck by an agar gel immunodiffusion test (Cornell University Diagnostic Laboratory, (607)253-3900) or bacterial culture of whole blood, lymph node aspirate, or vulvar discharge.
- Prostaglandin $F_{2\alpha}$ metabolites (PGFM) are elevated in dogs with pyometra compared to those with hydrometra or mucometra.
- Hormone assay: progesterone concentration > 2 ng/mL.

P

IMAGING

Radiography

- Detect an enlarged and distended uterus (see Web Figure 1).
- Rule out pregnancy—45 days after ovulation when fetal skeletal ossification is present.

Ultrasonography

- Uterine horns distended with hypo- to hyperechoic intraluminal fluid, with or without flocculation. Uterine wall often thickened with irregular edges and small hypoechoic areas consistent with cystic change (CEH) (see Web Figure 2) or can be thin if uterus is severely distended as with a closed cervix pyometra.
- Rule out pregnancy—20–24 days after ovulation.
- Pyometra—may occur with pregnancy in dogs (rare).

DIAGNOSTIC PROCEDURES

- Vaginoscopy—indicated in dogs with purulent vulvar discharge and no apparent uterine enlargement; allows determination of site of origin of the vulvar discharge; not possible in cats.

PYOMETRA

(CONTINUED)

PATHOLOGIC FINDINGS

- Endometrium (dogs and cats)—described as cobblestone appearance (see Web Figure 3).
- Cystic endometrial surface—covered by malodorous, mucopurulent exudate; thickened because of increased endometrial gland size and cystic gland distension.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient • Pyometra—life-threatening condition if the cervix is closed and bitch is systemically ill.

NURSING CARE

Supportive care—immediate intravenous fluid administration and broad-spectrum antibiotics.

CLIENT EDUCATION

- Recommend medical treatment only for valuable, young breeding animals that are not azotemic and present systemically well. For all other animals not intended for breeding, ovariohysterectomy is the treatment of choice.
- Historically, medical treatment of closed-cervix pyometra can be associated with uterine rupture and peritonitis, but with the development of new pharmacologic agents and treatment protocols this is now a rare event.
- Bitches that are refractory or chronic cases that do not readily respond to medical treatment are candidates for ovariohysterectomy.
- Warn of possible recurrence of pyometra after medical therapy—important to breed at very next heat and spay when desired number of litters is achieved.

SURGICAL CONSIDERATIONS

- Ovariohysterectomy is the preferred treatment in all animals not intended for breeding, older (> 4 years) bitches, bitches with evidence of chronic CEH changes, bitches that present systemically unwell and require immediate emergency care and stabilization. The pus-filled uterus, both ovaries and the entire cervix should all be removed.
- Closed-cervix pyometra—exercise great care in handling the enlarged and friable uterus (see Web Figure 4).
- Place saline-soaked laparotomy sponges in the abdomen to prevent leakage of purulent material into the peritoneal cavity.
- Patients should be systemically stabilized prior to anesthesia for surgery (correction of any acid-base derangements, dehydration, hypotension, shock, electrolyte abnormalities,

arrythmias and endotoxemia) and started on IV fluids and IV broad-spectrum antibiotics.



MEDICATIONS

DRUG(S) OF CHOICE

Antibiotics

- All patients with pyometra • Empirical (*E. coli* most common isolate)—pending results of bacterial culture and sensitivity test
- Start on broad-spectrum antibiotics prior to receiving culture and sensitivity results—ampicillin (22 mg/kg PO q8h); amoxicillin and clavulanic acid (12.5–25 mg/kg PO q12h) or cefazolin (22 mg/kg IV or IM q8h). Exercise care when using cephalosporins, potentiated sulfonamides and enrofloxacin in dehydrated, potentially septicemic patients with impaired renal or liver function.

Prostaglandins (PGF_{2α})

- Doses listed below for native compound only (dinoprost tromethamine; Lutalyse®); has both luteolytic and ecobolic actions.
- New low-dose protocol: start with low doses to minimize side effects and ecobolic effect especially in closed pyometra cases. Once luteolysis has occurred and the cervix is fully open the dose can be gradually increased depending of the individual patient's tolerance to the drug.
- Side effects: dose dependent and usually not seen with new low dose protocol; tachypnea, vomiting, diarrhea, urination, anxiety; side effects are seen 20 minutes after administration of the drug and last for 15–30 minutes.
- Animals should be hospitalized for 1 hour after each treatment.
- Dogs and cats—10 µg/kg SC q6h for 1 day then 25 µg/kg q6h for 1–2 days; then 50 µg/kg q6h for 3–4 days. The queen is more resistant to the luteolytic effects of PGF_{2α} than bitches—often higher doses for longer periods are required.
- Ovariohysterectomy—performed in patients not responding well to treatment within 5 days and are refractory to prostaglandin treatment (persistent or recurring uterine fluid and vulvar discharge).

Cloprostenol

- Synthetic form of PGF_{2α} • Dogs—1 µg/kg SC daily for 7–14 days; greater side effects and prolonged time to resolution compared to the natural form of PGF_{2α}

Miscellaneous

Transcervical endoscopic catheterization of open- and/or closed-cervix pyometra—a recently described technique; involves

flushing the uterus with warm saline and PGF_{2α}; reported resolution within 3–5 days; no uterine rupture or leakage reported but still should be considered a risk—patient selection important.

CONTRAINDICATIONS

- High-dose PGF_{2α} and cloprostenol with closed-cervix pyometra—strong myometrial contractions may cause uterine rupture or force purulent exudate through the oviducts, causing secondary peritonitis.

PRECAUTIONS

- PGF_{2α} (dinoprost tromethamine) and cloprostenol—not approved for use in dogs and cats.

ALTERNATIVE DRUG(S)

- Progesterone receptor antagonist—aglepristone (10 mg/kg SC days 1, 2, and 8) competitively binds to the progesterone receptor with greater affinity than natural progesterone. Minimal side effects. Excellent choice for closed pyometra cases as it dilates the cervix with minimal uterine contractions. Best results achieved when used in combination with prostaglandin—PGF_{2α} is started 24–48h after aglepristone, allowing the cervix to open prior to stimulation of uterine contractions by PGF_{2α}; not registered in United States; not suitable for use in bitches with poor liver and/or kidney function.
- Dopamine agonists—cabergoline (5 µg/kg PO q24h for 7–14 days) or bromocryptine (10–20 µg/kg q8h); both given with food to reduce risk of vomiting; act as prolactin antagonists; best used in combination with PGF_{2α} to potentiate the ecobolic effect—should see cervical opening within 24–48 h.



FOLLOW-UP

PATIENT MONITORING

- Antibiotics—continued for at least 14 days after resolution of vulvar discharge and removal of all fluid from the uterine lumen (confirmed by ultrasound).
- Clinical improvement and a significant increase in vaginal discharge should be noted within 24 hours of commencing PGF_{2α} treatment; vaginal discharge will change from purulent to serosanguineous to serous; a reduction in the uterine lumen should be seen on ultrasound within 3 days after the start of treatment; resolution of clinical signs (no vulvar discharge and no intrauterine fluid visible by ultrasound) should occur within

(CONTINUED)

PYOMETRA

7 days. • Serum progesterone concentrations decline within 48 hours of treatment and should be < 2 ng/mL at 5–7 days; CBC and neutrophil count normal after 10–15 days. • Follow-up ultrasound of the uterus 4 weeks after discontinuation of treatment to assess uterine health—confirm no intraluminal fluid and determine CEH changes (predictor of future fertility).

PREVENTION/AVOIDANCE

- Animals not intended for breeding should be spayed.
- Breeding females should be spayed as soon as the desired number of litters has been obtained.
- Females should be bred when they are young (< 4 years) and subsequently have the desired number of litters as soon as possible—a pregnant uterus reduces the risk of developing pyometra and maximizes uterine health of the bitch.
- Breed during the estrus immediately following treatment—the gravid uterus is less susceptible to reinfection; a bitch with underlying cystic endometrial hyperplasia has limited breeding life (best to get the desired number of pups as soon as possible); ultrasound examination 28 days after the LH surge for early detection of recurring pyometra allows surgical management before the bitch becomes systemically ill.
- Breeding management at the subsequent heat is important to maximize the chance of pregnancy—use of high-quality semen, timed insemination with extenders containing antibiotics, or timed natural mating with young proven stud dog.
- Antibiotic therapy at subsequent heat—vaginal cytology monitoring; presence of neutrophils during estrus indication to start broad-spectrum antibiotic (amoxicillin or amoxicillin and clavulonic acid) until early ultrasound (for 4 weeks after the LH surge).
- Medical treatment can result in a shortened interestrus interval which can be associated with decreased fertility—lengthen interestrus interval with an androgen-receptor agonist

such as mibolerone to allow sufficient time for the uterus to remodel/recover; start mibolerone 1 month after the end of treatment and continue for 2–3 months to ensure a minimum interval of 6 months from the last heat.

POSSIBLE COMPLICATIONS

- Bitch may enter estrus sooner after treatment than anticipated if medical treatment induces premature luteolysis (see “Prevention/Avoidance”).
- Recurrence of pyometra at subsequent heats.

EXPECTED COURSE AND PROGNOSIS

- Prognosis for survival is good with both medical and surgical treatment if uterine rupture does not occur; 4% mortality rate reported in bitches and 8% in queens.
- Recurrence rate of pyometra is dependent on age, parity, and pre-existing uterine pathology.
- Variable pregnancy rates reported after treatment for pyometra (50–90%).

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Pyometra of the uterine stump in spayed animals—may develop any time after ovariohysterectomy; may be associated with the presence of an ovarian remnant.

PREGNANCY/FERTILITY/BREEDING

- Any of the drugs used for the treatment of pyometra are also abortifacients—always rule out pregnancy before administration to valuable breeding animals.
- See “Prevention/Avoidance” and “Expected Course and Prognosis” for future breeding/fertility after treatment of a pyometra and ways to reduce incidence of pyometra.

SEE ALSO

- Breeding, Timing
- Infertility, Female—Dogs
- Ovarian Remnant Syndrome

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- CEH = cystic endometrial hyperplasia
- PGF_{2α} = prostaglandin F_{2α}
- WBC = white blood cell

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Client Education Handout available online

PYOTHORAX



BASICS

DEFINITION

Accumulation of septic suppurative inflammation in the pleural cavity.

PATHOPHYSIOLOGY

- Infectious—from transpulmonary, transesophageal, or transthoracic inoculation of bacteria into the pleural space, with subsequent suppurative pleuritis.
- Dogs—often associated with an inhaled grass awn or other foreign object or a penetrating wound to the thorax.
- Cats—most commonly associated with penetrating bite wounds, foreign bodies, or possibly by extension of pneumonia into the pleural space following aspiration of oropharyngeal flora. • Other causes include extension of discospondylitis, esophageal perforation, parasitic migration, hematogenous spread, previous thoracic surgery, and neoplasia with abscess formation.

SYSTEMS AFFECTED

- Respiratory • Hemic/Lymphatic/Immune
- Renal/Urologic—protein-losing nephropathy

GEOGRAPHIC DISTRIBUTION

Etiology is regionally dependent. For example, inhaled grass awn or foxtails are common in California. *Spirocera lupi* should be considered as a predisposing cause in endemic areas (Africa, Asia, southeastern United States).

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Dogs—hunting and sporting breeds; specifically, Labrador retrievers, springer spaniels, and border collies • Cats—domestic shorthair.

Mean Age and Range

Median ~ 4 years, although there is wide variation.

Predominant Sex

Male animals overrepresented.

SIGNS

General Comments

- Often insidious in onset, with few clinical signs until late in the course of disease.
- Respiratory compromise—often not severe unless disease is advanced. • Vomiting/diarrhea may be initial presenting complaint in 25% of canine cases.

Historical Findings

- Diminished activity. • Collapse after exercising and slow recovery. • Weight loss and partial anorexia can be the only clinical signs. • Temporary improvement with antibiotic therapy. • Confirm history of fights or puncture wounds.

Physical Examination Findings

- Tachypnea—usually apparent; may be mild and not associated with respiratory difficulty.
- Cachexia—often observed. • Cough—may be observed. • Pyrexia—usually low-grade, may be observed. • Thoracic auscultation—may reveal muffled heart sounds, diminished lung sounds ventrally, and amplified lung sounds dorsally. • Cats—may show few clinical signs before onset of apparently acute respiratory distress, collapse, and septic shock; bradycardia and hypersalivation associated with poor outcome.
- Injury to the thoracic wall—may not be apparent or may be healed at the time of examination.
- Perform thorough palpation and inspection of the thorax for evidence of scarring or cellulitis.

CAUSES

- Infectious—dogs: *Actinomyces* spp., *Nocardia* spp., Anaerobes (*Bacteroides*, *Peptostreptococcus*, *Fusobacterium*), *Corynebacterium*, *Escherichia coli*, *Pasteurella*, and *Streptococcus* spp.; fungal agents.
- Infectious—cats: oral commensals (e.g., *Pasteurella multocida* and *Bacteroides* spp.) most common; obligate anaerobes (*Peptostreptococcus*, *Fusobacterium*) common.
- Parasitic—dogs: esophageal rupture of *Spirocera lupi* granuloma.
- Neoplastic—rarely with intrathoracic tumors secondary to tumor necrosis.
- Lung lobe torsion—occasionally associated with pyothorax.

RISK FACTORS

- Dogs—hunting, field trials, and other strenuous outdoor sporting activities; *S. lupi* endemic areas.
- Cats—multiple cat households, outdoor cats, pneumonia, upper-respiratory infection.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other pleural effusions—chylothorax and hemothorax; non-septic exudates (FIP or neoplasia); transudative effusions; differentiated via cytologic examination.
- Other systemic diseases should be considered for nonspecific findings.
- Diseases associated with fever of unknown origin should be considered for animals with non-localizing signs.

CBC/BIOCHEMISTRY/URINALYSIS

- Marked neutrophilic leukocytosis with left shift, monocytosis, and anemia of chronic disease.
- Regenerative anemia—can be seen with substantial hemorrhage into the pleural cavity.
- Hyperglobulinemia—possible due to chronic inflammation.
- Hypoalbuminemia as a negative acute phase reactant or due to renal loss, if glomerulonephritis results from chronic antigenic stimulation.
- Alkaline phosphatase—mildly elevated from

hypoxemia. • Prerenal azotemia—if the patient is dehydrated. • Organ-specific changes—if other organs are secondarily infected (e.g., pyelonephritis and hepatitis).

IMAGING

- Radiography—unilateral or bilateral pleural effusion with pleural fissure lines; pulmonary parenchymal lesions (consolidation, atelectasis, masses) common; mediastinal lesions possible.
- Ultrasonography—pleural effusion; may show marked amount of fibrinous deposition in the pleural space; may identify consolidated lung masses, mediastinal masses, and abscessed or neoplastic lung nodules.
- CT—focal interstitial to alveolar pulmonary opacities; pleural thickening; enlarged intrathoracic lymph nodes; pleural effusion; pneumothorax; and foreign body identification.

DIAGNOSTIC PROCEDURES

Thoracocentesis

- Cytologic evaluation—necessary to confirm the diagnosis; many effusions appear grossly hemorrhagic.
- Gram stains—can facilitate early identification of pathogenic organisms.
- Sulfa granules (small accumulations of purulent debris) in the exudate—characteristic of infection by filamentous organisms (e.g., *Actinomyces* and *Nocardia*).
- Organisms are often seen on cytologic examination, often within degenerative neutrophils.
- The effusion is often malodorous, especially in cats.

Microbiology

- Culture fluid samples aerobically and anaerobically. Consider *Mycoplasma* culture if standard cultures are negative.
- Many of the filamentous, microaerophilic, and anaerobic organisms are slow-growing, so cultures should be maintained longer than standard samples.
- Sulfa granules—maceration may enhance culturing; contain higher concentrations of bacteria.
- Often mixed bacterial populations.
- Fungal organisms—culture depends on history and geographic location.
- Urine samples—culture with suspected pyelonephritis.

Esophagoscopy

- If *S. lupi* is suspected.

PATHOLOGIC FINDINGS

- Fibrinous and suppurative pleuritis, with or without pulmonary abscessation.
- Glomerulonephritis.
- Caudal vena-caval thrombosis (rare).



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—often for several days to weeks.
- Treat like any abscess; drainage is critical, without which resolution is highly unlikely.
- Surgical exploration, debridement, and potential lobectomy required in some cases.

(CONTINUED)

PYOTHORAX**NURSING CARE**

- Continuous evacuation via tube thoracostomy with low-pressure suction through a perforated tube; use a large-bore tube to minimize occlusion; continue until net drainage is < 2–3 mL/kg/day and intracellular bacteria are no longer visible on gram stain; drainage may be slightly higher with red rubber tubes because they are more irritating.
- Cats—usually require general anesthesia for tube placement.
- Dogs with severe respiratory compromise—may substitute local anesthesia and regional analgesia for general anesthesia.
- Periodic thoracic radiography—to ensure proper tube placement, and lack of pocketing or loculation of exudate, determine whether bilateral tube placement is necessary; document primary pulmonary pathology that may not have been apparent on initial examination.
- Thoracic lavage—every 6–8 hours with warm, sterile saline; may help break down consolidated debris. Consider addition of heparin (1,500 units/liter) to lavage fluid.
- Coupage (rapid thoracic percussion)—may help remove consolidated debris.
- Repeat bacterial culture if the patient fails to improve.

ACTIVITY

- Inpatient—encourage light exercise (10 minutes every 6–8 hours); promotes ventilatory efforts and helps break down pleural adhesions.
- After discharge, gradually increase exercise over 2–4 months.

DIET

- High-calorie food
- Consider feeding tube placement if prolonged anorexia.

CLIENT EDUCATION

Warn client that the duration of treatment (inpatient and outpatient) is long and expensive; recurrence is possible with either medical or surgical management.

SURGICAL CONSIDERATIONS

- Surgery—higher cure rate expected with surgery if pulmonary abscessation, pleural fibrosis, lung-lobe torsion, extensive loculation of pus is present, or if mediastinum is involved.
- Thoracoscopy can be utilized as an intermediate step to assess degree of severity and need for more aggressive intervention.
- Identified foreign body via thoracic imaging (radiography, ultrasound, or CT)—thoracotomy and retrieval indicated; grass awns are uncommonly found, even during surgery.

**MEDICATIONS****DRUG(S) OF CHOICE****Antimicrobials**

- Ultimately, choice determined by results of in vitro sensitivity testing.
- Suspected specific pathogen—initiate treatment before culture

results are available; choose on the basis of common antibiotic sensitivities of particular organisms; *Actinomycetes* spp. and *Bacteroides* (non-*fragilis*) spp. often susceptible to amoxicillin; *Nocardia* spp. often susceptible to potentiated sulfonamides; obligate anaerobic bacteria (including *B. fragilis*) susceptible to amoxicillin-clavulanic acid, chloramphenicol, and usually metronidazole; *Pasteurella* spp. often susceptible to potentiated penicillins.

- Ampicillin or amoxicillin with a β -lactamase inhibitor—good initial choice for most patients; ampicillin and sulbactam (20 mg/kg IV q8h) followed by amoxicillin clavulanic acid (25 mg/kg PO q8h) when medications can be given orally.
- Trimethoprim-sulfa, aminoglycosides, and quinolones—generally ineffective.
- Multiple antibiotics occasionally necessary.
- Dosages are generally high (e.g., amoxicillin, 40 mg/kg PO q8h) to allow adequate distribution into the pleural cavity; may need to continue drug for several months and occasionally indefinitely.

Analgesics

- Required following thoracotomy or during thoracocentesis.
- Consider multimodal analgesia: systemic opioids, nonsteroidal anti-inflammatory drugs; intrapleural analgesia.

CONTRAINdications

Glucocorticoids and immunosuppressive agents—avoid with infectious pyothorax.

PRECAUTIONS

Potentiated sulfas—can be associated with keratoconjunctivitis sicca, polyarthropathy, hypothyroidism, thrombocytopenia, and anemia, especially with prolonged use.

**FOLLOW-UP****PATIENT MONITORING**

- Decreasing thoracic fluid production, decrease in cell count in pleural fluid, and absence of bacteria usually noted within 4–7 days indicate that drains can be removed. Fluid should be submitted for aerobic and anaerobic culture at the time of drain removal.
- Evaluate thoracic radiographs—ensure adequate evacuation of fluid.
- Antibiotics—continue for 1 month after the patient is clinically normal, the hemogram is normal, and there is no radiographic evidence of fluid reaccumulation; average duration of therapy is 3–4 months but may continue for 6–12 months or longer.
- Assess CBC and radiographs monthly—residual radiographic changes may be permanent, but fluid should be absent.

POSSIBLE COMPLICATIONS

- Incorrect insertion of the drainage tube—may prevent adequate drainage or produce pneumothorax; placement too far cranially may put pressure on brachial arteries

and veins, resulting in unilateral limb edema or lameness; lung laceration during placement.

- Persistent, recurrent pyothorax—compartmentalization of pus; premature discontinuation of treatment; pulmonary lesions.
- Chronic fibrosing pleuritis and poor performance after apparent recovery—may occasionally respond to further surgery.
- Persistent granulomatous mediastinitis.

EXPECTED COURSE AND PROGNOSIS

- With aggressive management—prognosis fair to excellent (60–90% survival).
- Dependent on severity of clinical signs.
- Overall better prognosis in dogs (83%) than in cats (62%).
- Return to performance—depends on chronicity of disease and level of management.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Retroperitoneal abscessation and discospondylitis caused by migration of a foreign body through the diaphragm into the retroperitoneal space—occasionally seen.
- Glomerulonephropathy—can be reversible with successful resolution of pyothorax.

ZOONOTIC POTENTIAL

Fungal infection during *in vitro* isolation.

SYNOMYS

- Empyema • Pleurisy • Suppurative pleuritis

SEE ALSO

- Chylothorax • Dyspnea and Respiratory Distress • Panting and Tachypnea • Pleural Effusion

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ABBREVIATIONS

- CT = computed tomography
- DIC = disseminated intravascular coagulation
- FIP = feline infectious peritonitis
- MRI = magnetic resonance imaging

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Client Education Handout
available online

PYRETHRIN AND PYRETHROID TOXICOSIS



BASICS

OVERVIEW

- Insecticides.
- Pyrethrins—natural.
- Pyrethroids—synthetic; include acrinathrin, allethrin, barthrin, bifenthrin, bioresmethrin, cismethrin, cypermethrin, dimethrin, deltamethrin, cyfluthrin, cyhalothrin, cyphenothrin, esfenvalerate, fenpropothrin, fenvalerate, flumethrin, fluvalinate, imiprothrin, permethrin, phenothrin, tefluthrin, tetramethrin, tralomethrin, and the ether etofenprox.
- Affect the nervous system—reversibly prolong sodium conductance in nerve axons, resulting in repetitive nerve discharges.
- Pyrethrin/pyrethroid exposures represent 45% of all insecticide-related calls to the ASPCA Animal Poison Control Center.

SIGNALMENT

Adverse reactions occur more frequently in cats; small dogs; and young, old, sick, anemic, or debilitated animals. Reactions may occur in cats through direct contact with permethrin spot-on treated dogs.

SIGNS

- Result from immune-mediated allergic hypersensitivity and anaphylactic reactions, genetic-based idiosyncratic reactions, and neurotoxic reactions.
- Mild—hypersalivation; paw flicking; ear twitching; mild depression; vomiting; diarrhea.
- Moderate—protracted vomiting and diarrhea; marked depression; ataxia; muscle tremors.
- Extreme dermal or oral overdose—may produce seizures or death.
- Cats—sensitive to pyrethroids. Cats inappropriately treated with permethrin-containing products for use on dogs, often develop muscle tremors, ataxia, seizures, hyperthermia, and death within hours if not treated.
- Dogs may develop tremors following exposure to liquid or granular lawn products containing bifenthrin.
- Allergic reactions—urticaria; hyperemia; pruritus; anaphylaxis; shock; respiratory distress; (rarely) death.

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CAUSES & RISK FACTORS

- Cats—more sensitive; less-efficient metabolic pathways, combined with grooming habits.
- Patients with subnormal body temperatures after bathing, anesthesia, or sedation—predisposed to clinical signs.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Exposure history (amount and frequency of product usage), type and severity of clinical signs, and onset and duration of clinical

signs—must be consistent before a tentative diagnosis can be made.

- Misapplication of permethrin-containing dog-only flea product on cats.
- Organophosphorous compounds, carbamate, or d-limonene toxicosis.
- Strychnine, metaldehyde, tremorgenic mycotoxins, methylxanthines, amphetamines, serotonergic drug overdose, alcohol intoxication from isopropyl alcohol-based sprays.

OTHER LABORATORY TESTS

- Pyrethrins—analytical tests not generally available.
- Pyrethroids—some compounds can be detected in tissues, especially on hair, to confirm exposure. Hair analysis for permethrin can be valuable when severity of the adverse event in cats is much greater than anticipated based on the reported product application. Cats with generalized full-body tremors or seizures after reported application of a cat-approved flea product are suspect for exposure to a permethrin-containing product.



TREATMENT

- Mild adverse reactions (salivation, paw flicking, and ear twitching)—often mild and self-limiting and resolve with no care.
- Patient saturated with spray products—dry with a warmed towel; brush.
- Continued mild signs—bathe at home with a mild hand dish-washing detergent (strictly avoid hypothermia).
- Progression to tremors and ataxia—hospitalize.
- Seriously affected patient—intravenous fluid support recommended.
- Maintenance of a normal body temperature—critical.
- Bathing upon stabilization (tremors controlled) with liquid hand dish-washing detergent and warm water is critical.



MEDICATIONS

DRUG(S)

- Tremors or seizures—especially for cats exposed to permethrin; methocarbamol (Robaxin-V injectable at 55–220 mg/kg IV not to exceed 330 mg/kg/day; administer one-half dose slowly IV, wait until the patient begins to relax, continue administration to effect; do not exceed 2 mL/minute injection rate, and start with lower dose initially).
- Diazepam at low dosages has been used to control minor hyperesthesia. Seizure control has been achieved with pentobarbital, propofol (3–6 mg/kg IV or 0.1 mg/kg/min CRI) and inhalant anesthetics.

Methocarbamol remains the agent of choice and can also be used orally for treating mild tremors (50–100 mg/kg q8h; 30 minutes onset time).

- Activated charcoal (2 g/kg PO) is rarely beneficial or recommended.
- Emetics—rarely warranted.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Atropine sulfate—not antidotal; avoid; may cause tachycardia, CNS stimulation, disorientation, drowsiness, respiratory depression, and even seizures.



FOLLOW-UP

PREVENTION/AVOIDANCE

- Proper application of flea-control products—greatly reduces reactions.
- Reduction of salivation—spray onto a grooming brush; evenly brush through hair coat.
- Liquids—term *dip* common; never submerge animal; pour on body; sponge to cover dry areas.
- Premise products—do not apply topically unless labeled for such use; after treating house or yard, do not allow animal in the area until product has dried and environment has been ventilated.
- Do not apply dog-only products on cats.
- Do not use permethrin spot-on products on dogs in households where cats groom or sleep in physical contact with dogs.

EXPECTED COURSE AND PROGNOSIS

- Hypersalivation—may recur for several days after use of flea-control product when patient (especially cat) grooms itself.
- Most clinical signs (mild to severe) resolve within 24–72 hours.



MISCELLANEOUS

Suggested Reading

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PYRUVATE KINASE DEFICIENCY



BASICS

OVERVIEW

- RBCs require energy in the form of ATP for maintenance of shape, deformability, active membrane transport, and limited synthetic activities; mature RBCs lack mitochondria and depend on anaerobic glycolysis for ATP generation.
- PK catalyzes an important rate-controlling, ATP-generating step in glycolysis; consequently, energy metabolism is markedly impaired in PK-deficient RBCs, resulting in shortened RBC lifespan and anemia; bone marrow attempts to compensate by erythroid hyperplasia, with marked reticulocytosis in peripheral blood.

SIGNALMENT

- Autosomal recessive trait recognized in basenji, beagle, West Highland white terrier, cairn terrier, miniature poodle, dachshund, Chihuahua, pug, American Eskimo, and Labrador retriever dogs, and in Abyssinian, Somali, and domestic shorthair cats.
- Affected homozygous animals generally not recognized as abnormal until several months of age or adulthood.

SIGNS

- Affected cats are often asymptomatic.
- Lethargy or exercise intolerance.
- Pale mucous membranes.
- Often splenomegaly.
- Tachycardia.
- Systolic heart murmurs reported in dogs.
- Icterus is occasionally seen in cats but rarely seen in dogs.
- Affected dogs may be slightly smaller than normal for their breed and age and may exhibit weakness and muscle wasting.
- Affected cats may exhibit diarrhea, inappetence, poor coat quality, and weight loss.

CAUSES & RISK FACTORS

- RBCs from normal adult dogs exhibit only one PK isozyme (the R-type).
- Breed-specific defects in the *PKLR* gene result in erythrocyte PK deficiency in dogs.
- A common molecular defect has been described in cats.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of hemolytic anemia—immune-mediated hemolytic anemia, hemotropic mycoplasmosis, babesiosis, Heinz body hemolytic anemia, microangiopathic hemolytic anemia, and phosphofructokinase deficiency (dogs).
- Affected animals—negative Coombs' test, no parasites or Heinz bodies in stained blood films, seronegative for *Babesia* spp., and no evidence of DIC or heartworm disease.
- In contrast to phosphofructokinase deficiency, PK-deficient

dogs do not exhibit episodes of intravascular hemolysis and hemoglobinuria; these deficiencies are differentiated by specific enzyme assays or DNA tests.

CBC/BIOCHEMISTRY/URINALYSIS

- Persistent macrocytic hypochromic anemia, with HCT values of 16–28% and uncorrected reticulocyte counts of 15–50% in dogs.
- Anemia is intermittent (HCT 13–40%), with slightly to markedly increased aggregate reticulocyte counts in cats.
- Normal or slightly high total leukocyte counts.
- Normal to slightly high platelet count.
- Moderate to marked polychromasia, anisocytosis, and increased nucleated RBCs on stained blood films.
- Poikilocytosis reported in splenectomized dogs.
- Possible abnormal clinical chemistry findings, such as hyperferremia, hyperbilirubinemia, and slightly high ALT and ALP activities; hyperglobulinemia common in cats; dogs with liver failure may have hypoalbuminemia.
- Normal urinalysis, except for bilirubinuria in dogs.

OTHER LABORATORY TESTS

- Total RBC PK activity—low value diagnostic in cats and some dogs; many affected dogs have normal or high activities because of the expression of an M2 isozyme that does not normally occur in mature RBCs; approximately 50% of normal activity in heterozygous animals.
- Additional assays (e.g., enzyme heat stability test, measurement of RBC glycolytic intermediates, electrophoresis of isozymes, and enzyme immunoprecipitation)—to reach a diagnosis in dogs whose total enzyme activity is not low.
- DNA diagnostic tests—for screening several breeds.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Affected animals can only be cured by bone marrow transplantation.
- Splenectomy may reduce the severity of the anemia in cats.



MEDICATIONS

DRUG(S)

Although not adequately evaluated, long-term treatment with iron-chelating drugs might prolong the life expectancy of an affected dog.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

None



FOLLOW-UP

- Hepatic iron overload—develops in affected dogs; can result in cirrhosis and liver failure.
- Myelofibrosis and osteosclerosis—develop in affected dogs with age; thus most die by 5 years of age as a result of bone marrow or liver failure.
- Severe anemia with minimal reticulocytosis or abnormal liver function tests and ascites secondary to hypoalbuminemia indicate the terminal stage of the disease in dogs.
- Extrahepatic biliary obstruction with bilirubin cholelithiasis has been reported in two cats.



MISCELLANEOUS

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- ATP = adenosine triphosphate
- DIC = disseminated intravascular coagulation
- HCT = hematocrit
- PK = pyruvate kinase
- RBC = red blood cell

INTERNET RESOURCES

<http://research.vet.upenn.edu/penngen>

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PYTHIOSIS



BASICS

DEFINITION

An infectious disease primarily affecting the skin or GI tract of dogs and cats. It is caused by the aquatic pathogen *Pythium insidiosum*, an organism in the class Oomycetes.

PATHOPHYSIOLOGY

- The infective form of *P. insidiosum* is thought to be the motile biflagellate zoospore, which is released into warm water environments and is chemotactically attracted to damaged tissue and animal hair. Animals are likely infected when they enter or ingest water that contains infective zoospores.
- P. insidiosum* is considered a pathogenic rather than opportunistic organism because immune suppression is not a prerequisite for infection.
- In the GI tract, *P. insidiosum* infection causes chronic pyogranulomatous disease manifested by severe segmental transmural thickening of one or more areas of the stomach or intestine.
- In the skin, pythiosis typically results in the development of non-healing wounds and invasive masses that contain ulcerated nodules and draining tracts.

SYSTEMS AFFECTED

GI and cutaneous forms of the disease are encountered with equal frequency in the dog. In cats, which are infrequently infected, the cutaneous form is more common. With the exception of occasional dissemination to regional lymph nodes, pythiosis usually affects only one body system in each patient.

- GI pythiosis most often affects the gastric outflow region, proximal small intestine, ileocolic junction, or colon. The surrounding mesentery is often involved. Rarely, the esophagus may be affected.
- In dogs with GI disease, *P. insidiosum*-induced local thromboembolic events or vascular invasion may lead to bowel wall ischemia and GI perforation or hemoabdomen.
- Dogs with cutaneous pythiosis most often are presented for solitary or multiple cutaneous or subcutaneous lesions involving the extremities, tailhead, ventral neck, or perineum.
- In cats, cutaneous lesions or subcutaneous masses involving retrobulbar, periorbital, or nasopharyngeal regions, the tailhead, or the footpads have been observed.

GI lesions are rare in cats.

- Multisystemic involvement is rare.

GENETICS

Although large-breed dogs are most often affected, no genetic predisposition has been documented.

INCIDENCE/PREVALENCE

- Dependent on geographic distribution.
- Affected animals more often are presented for signs of disease in the fall or early winter months.

GEOGRAPHIC DISTRIBUTION

Disease caused by *P. insidiosum* occurs primarily in tropical and subtropical areas of the world.

- In the United States, pythiosis occurs most often in states bordering the Gulf of Mexico; however, it has also been documented in Oklahoma, Arkansas, Missouri, Kentucky, Tennessee, North and South Carolina, Virginia, southern Indiana, New Jersey, Arizona, Wisconsin, and California.
- Outside the United States, pythiosis has been reported in Australia, Brazil, Burma, Colombia, Costa Rica, Indonesia, Japan, New Guinea, and Thailand.

SIGNALMENT

Species

Dog and less commonly cat

Breed Predilections

- Large-breed dogs, especially those used in hunting or field trial work near water.
- Labrador retrievers are overrepresented.
- German shepherds may be predisposed to cutaneous pythiosis.

Mean Age and Range

Animals < 6 years old are most likely to be infected.

Predominant Sex

Males are affected more often than females, possibly because of increased exposure.

SIGNS

General Comments

Affected dogs are not usually severely ill until late in the course of disease.

Historical Findings

- Chronic weight loss and intermittent vomiting are the most common signs.
- Diarrhea may be evident if the colon or a large segment of the small intestine is affected.
- Regurgitation is noted with esophageal disease.
- Cutaneous disease is characterized by non-healing wounds with nodules that ulcerate and drain.

Physical Examination Findings

GI Pythiosis

- Emaciation is common.
- An abdominal mass is often palpable.
- Despite severe weight loss, affected dogs are usually bright and alert.
- Fever is usually absent.
- Systemic signs and abdominal pain may occur with intestinal obstruction, infarction, or perforation.

Cutaneous Pythiosis

- Cutaneous or subcutaneous lesions appear as non-healing wounds; boggy, edematous regions; or poorly defined nodules that become ulcerated.
- Multiple tracts draining a serosanguineous or purulent exudate often are present.

CAUSES

P. insidiosum

RISK FACTORS

- Environmental exposure to swampy areas, bayous, ponds, or lakes containing infective

zoospores.

- Outdoor activities such as hunting.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

GI Pythiosis

- Intestinal obstruction caused by a foreign body or chronic intussusception.
- Histoplasmosis.
- Gastric or intestinal lymphosarcoma.
- Gastric carcinoma.
- Other GI neoplasia.
- Inflammatory bowel disease.
- Basidiobolomycosis, protothecosis.
- Histiocytic or idiopathic colitis.

Cutaneous Pythiosis

- Lagenidiosis (caused by oomycotic pathogens in the genus *Lagenidium*).
- Zygomycosis (infections caused by *Basidiobolus* or *Conidiobolus* spp.).
- Other mycotic skin diseases, such as cryptococcosis, coccidioidomycosis, sporotrichosis, eumycotic mycetoma, and phaeohyphomycosis.
- Nodular bacterial skin diseases, such as actinomycosis, mycobacteriosis, botryomycosis, and brucellosis.
- Protothecosis or nodular leishmaniasis.
- Non-infectious pyogranulomatous diseases, such as foreign-body reaction, idiopathic nodular panniculitis, sebaceous nodular adenitis, and canine cutaneous sterile pyogranuloma/granuloma syndrome.
- Cutaneous neoplasia.
- Systemic vasculitis and cutaneous embolic disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Laboratory findings are nonspecific.
- Eosinophilia, leukocytosis, and anemia of chronic disease may occur.
- Hyperglobulinemia and/or hypoalbuminemia may be noted in chronically affected dogs.
- Hypokalemia, hyponatremia, hypochloridemia, and metabolic alkalosis may be noted in dogs with gastric outflow obstruction.
- Hypercalcemia was reported in a single affected dog.
- Urinalysis usually normal.

OTHER LABORATORY TESTS

Serology—a sensitive and specific ELISA test for anti-*Pythium* antibody is available at Auburn University College of Veterinary Medicine.

IMAGING

- Abdominal radiography may reveal an obstructive pattern, bowel wall thickening, or abdominal mass.
- Abdominal ultrasonography may reveal segmental transmural thickening of the stomach, proximal small intestine, or ileocolic junction. Granulomas or enlarged lymph nodes may be evident in the mesentery.

DIAGNOSTIC PROCEDURES

- Biopsy of gastrointestinal or skin lesions demonstrates histologic changes that are

(CONTINUED)

PYTHIOSIS

suggestive of, but not definitive for, pythiosis. • Definitive diagnosis is based on serology or culture; tissue samples should be submitted to an experienced laboratory via overnight shipping at room temperature. • A nested PCR assay can be used for the definitive identification of cultured isolates or organisms in tissue samples.

PATHOLOGIC FINDINGS

- Histologically, GI and skin lesions are characterized by pyogranulomatous and eosinophilic inflammation associated with broad (4–6 micron), irregularly branching, infrequently septic hyphae with thick, non-parallel walls. • Predominance of eosinophils within the inflammatory reaction helps to differentiate pythiosis, lagenidiosis, and zygomycosis from other mycotic infections. • Hyphal organisms are usually not visible on hematoxylin and eosin-stained sections, but are readily visualized with a silver stain. • Dogs with GI lesions typically have severe segmental thickening of portions of stomach and/or bowel, often with obstruction of the intestinal lumen. • Mesenteric lymphadenopathy is often noted, but the presence of *P. insidiosum* hyphae within lymph nodes is uncommon. • Histologically, GI pythiosis is characterized by eosinophilic and pyogranulomatous inflammation with necrotic foci and discrete granulomas that contain hyphae.

**TREATMENT****APPROPRIATE HEALTH CARE**

The treatment of choice is aggressive surgical excision of all infected tissue. Unfortunately, many animals are not presented to the veterinarian until late in the disease, when complete resection is not possible.

NURSING CARE

Supportive care should include fluids, potassium, and nutritional support. Antibiotics may be indicated to treat secondary pyoderma in dogs with cutaneous lesions.

ACTIVITY

Limit activity

DIET

Feed a highly digestible, calorie-dense diet

CLIENT EDUCATION

- Treatment is expensive. • Prognosis is guarded to poor unless a complete resection is feasible.

SURGICAL CONSIDERATIONS

- Attempt wide surgical excision to obtain 5- to 6-cm margins even if medical therapy is contemplated. • Amputation is recommended for treatment of extremity lesions. • Enlarged

mesenteric lymph nodes should be biopsied but often do not contain infective hyphae, thus do not have to be removed. • Dogs often improve after obstructive lesions are resected, even if significant disease is still grossly evident. • Postoperative medical therapy with itraconazole and terbinafine (see below) for 2–3 months may decrease the chance of recurrence. • Reevaluation of ELISA serology 2–3 months after surgery is an excellent prognostic indicator.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Itraconazole (10 mg/kg PO daily) combined with terbinafine (10 mg/kg PO daily) appears to be most effective. Although controlled studies have not been performed, the efficacy of this combination is probably < 10% in dogs with non-resectable or partially resectable lesions. • Prednisone (1–2 mg/kg PO daily and then tapered over 2–3 months) added to antifungal drugs may improve clinical outcome. • Medical therapy should be continued for a minimum of 6 months.
- Give itraconazole with food.

PRECAUTIONS

- Azole drugs should not be used in animals with severe liver disease. • Anorexia, high liver enzymes, and cutaneous vasculitis are the most common adverse effects of itraconazole.

POSSIBLE INTERACTIONS

Antacids and anticonvulsants may decrease blood levels of itraconazole.

ALTERNATIVE DRUG(S)

Prednisone (1–2 mg/kg PO daily and then tapered over several months) routinely improves clinical signs in the short term. In addition, the author has observed complete long-term resolution of clinical signs in a small number of dogs with GI pythiosis treated with prednisone alone. This is not recommended as a primary treatment for dogs with resectable lesions, but should be considered as palliative therapy in dogs with nonresectable disease.

**FOLLOW-UP****PATIENT MONITORING**

- ELISA serology can be used to monitor response to therapy; serology should be checked 2–3 months after surgery or every 3 months during medical therapy.
- Abdominal ultrasonography is useful in reevaluating intestinal lesions. • Liver enzymes should be evaluated monthly while patient is on itraconazole.

PREVENTION/AVOIDANCE

Monitor for signs of recurrence.

POSSIBLE COMPLICATIONS

Acute abdomen and death from GI thrombosis and perforation

EXPECTED COURSE AND PROGNOSIS

Prognosis is guarded to poor unless a complete resection is possible.

**MISCELLANEOUS****AGE-RELATED FACTORS**

Young animals are predisposed.

ZOONOTIC POTENTIAL

Infections in humans are very rare and are from a common environmental source. There is no evidence of direct transmission from animals to humans.

PREGNANCY/FERTILITY/BREEDING

Azole antifungals are teratogenic and should not be used in pregnant animals.

SYNONYMS

- Phycomycosis • Swamp Cancer

ABBREVIATIONS

- ELISA = enzyme-linked immunosorbent assay • GI = gastrointestinal • PCR = polymerase chain reaction

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Consulting Editor Stanley L. Marks



Client Education Handout
available online

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PYURIA



BASICS

DEFINITION

- WBCs (i.e., neutrophils, eosinophils, monocytes, lymphocytes, or plasma cells) in urine.
- More than 5 WBCs per high-power field is generally considered abnormal, but the number of WBCs found in urinary sediment varies with method of collection, sample volume and concentration, degree of cellular destruction after collection, and laboratory technique.

PATHOPHYSIOLOGY

- Large numbers of WBCs in voided urine samples indicate active inflammation somewhere along the urogenital tract.
- Can be associated with any pathologic process (infectious or non-infectious) that causes cellular injury or death; tissue damage evokes exudative inflammation characterized by evidence of leukocytic extravasation (pyuria) and increased vascular permeability (hematuria and proteinuria).

SYSTEMS AFFECTED

- Renal/Urologic—urethra, urinary bladder, ureters, and kidneys
- Genital—prepuce, prostate, vagina, and uterus

SIGNALMENT

Dog and cat

SIGNS

General Comments

- Inflammation can cause clinical signs localized to the site(s) of injury or may be accompanied by systemic manifestations. Historical and physical examination findings depend on the underlying cause, organ(s) affected, degree of organ dysfunction, and magnitude of systemic inflammatory responses.
- Non-obstructive lesions confined to the urinary bladder, urethra, vagina, or prepuce rarely cause systemic signs of inflammation. Systemic signs may accompany generalized inflammatory lesions of the kidneys, prostate, or uterus.

Physical Examination Findings

Local Effects of Inflammation

- Erythema of mucosal surfaces—e.g., redness of vaginal or preputial mucosa
- Tissue swelling—e.g., renomegaly, prostatomegaly, mural thickening of urinary bladder or urethra
- Exudation of leukocytes and protein-rich fluid—e.g., pyuria, purulent urethral or vaginal discharge, pyometra, or prostatic abscess
- Pain—e.g., adverse response to palpation, dysuria, pollakiuria, stranguria
- Loss of function—e.g., polyuria, dysuria, pollakiuria, urinary incontinence

Systemic Effects of Inflammation

- Fever
- Depression
- Anorexia
- Dehydration

CAUSES

Kidney

- Pyelonephritis—e.g., bacterial, fungal, parasitic, or mycoplasmal
- Nephrolith(s)
- Neoplasia
- Trauma
- Immune-mediated

Ureter

- Ureteritis—e.g., bacterial
- Ureterolith(s)
- Neoplasia

Urinary Bladder

- Cystitis—e.g., bacterial, mycoplasmal, fungal, or parasitic
- Urocystolith(s)
- Neoplasia
- Trauma
- Overdistension—urethral obstruction
- Pharmacologic—cyclophosphamide

Urethra

- Urethritis—e.g., bacterial, fungal, or mycoplasmal
- Urethrolith(s)
- Neoplasia
- Trauma
- Foreign body

Prostate

- Prostatitis/abscess—e.g., bacterial or fungal
- Neoplasia

Penis/Prepuce

- Balanoposthitis
- Neoplasia
- Foreign body

Uterus

Pyometra/metritis—e.g., bacterial

Vagina

- Vaginitis—bacterial, mycoplasmal, viral, or fungal
- Neoplasia
- Foreign body
- Trauma

RISK FACTORS

- Any disease process, diagnostic procedure, or therapy that alters normal host urinary tract defenses and predisposes to infection.
- Any disease process, dietary factor, or therapy that predisposes to formation of metabolic uroliths.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Voided Specimens

- Rule out vaginitis—signs include vaginal discharge, erythema of vaginal mucosa, licking of vulva, and attracting male dogs.
- Rule out pyometra, metritis—signs include vaginal discharge, large uterus, pyrexia, depression, anorexia, polyuria, polydipsia, and a recent history of estrus, parturition, or progestin administration.
- Rule out balanoposthitis—signs include preputial discharge, erythema of preputial or penile mucosa, and licking of prepuce.
- Rule out prostatitis, prostatic abscess, or prostatic neoplasia—signs include urethral discharge, prostatomegaly, pyrexia, depression, dysuria, tenesmus, caudal abdominal pain, and stiff gait.
- Rule out urethritis, urethroliths, urethral neoplasms—signs include dysuria, pollakiuria, stranguria, and/or palpable uroliths or mass lesions in the urethra.
- Rule out inflammatory disorders of urinary bladder and kidneys.

Specimens Collected by Cystocentesis

- Rule out urethral obstruction—signs include stranguria, anuria, and a large overdistended urinary bladder.
- Rule out prostatic and urethral disorders (see above); purulent prostatic or urethral exudates can reflux into the urinary bladder.
- Rule out cystitis, urocystoliths, and urinary bladder neoplasia—signs may include dysuria, pollakiuria, stranguria, and/or palpable uroliths or mass lesions in the urinary bladder.
- Rule out pyelonephritis—signs may include pyrexia, depression, anorexia, polyuria, polydipsia, renal pain, and renomegaly.
- Rule out post-traumatic pyuria—signs may include history of trauma, including iatrogenic causes.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

- WBCs lyse rapidly in hypotonic or alkaline urine. Administration of alkalinizing agents (e.g., sodium bicarbonate, potassium citrate, chlorothiazide, or acetazolamide) or agents that produce hypotonic urine (e.g., diuretics and glucocorticoids) may falsely decrease urine WBC numbers.
- Leukocyte esterase reagent strip (dipstick) methods are not recommended for use in canine (not sensitive) or feline (not specific) urine samples. In addition, nitrofurantoin, cephalosporins, and gentamicin can cause false-positive leukocyte esterase reactions.
- Urinary WBC concentrations can be low in patients with inflammatory disorders who have been given steroidal or nonsteroidal anti-inflammatory drugs.

Disorders That May Alter Laboratory Results

- Disorders associated with diminished WBC function or absolute neutropenia can artificially lower WBC values.
- Disorders associated with production of hypotonic urine or alkaline urine artificially lower WBC values.

Miscellaneous Factors That May Alter Laboratory Results

- False-negative leukocyte esterase reaction in dogs when urine is tested by the reagent strip (dipstick) method.
- False-positive and false-negative leukocyte esterase reaction in cats when urine is tested by the reagent strip (dipstick) method.

Valid if Run in Human Laboratory?

Valid if urinary sediment is examined microscopically; invalid if only leukocyte esterase reagent strip (dipstick) method is used.

CBC/BIOCHEMISTRY/URINALYSIS

- Pyuria in specimens collected by voiding, manual compression, or transurethral catheterization indicates an inflammatory lesion involving at least the urinary or genital tracts.
- Pyuria in specimens collected by cystocentesis localizes the site of inflammation

(CONTINUED)

PYURIA

to at least the urinary tract, but does not exclude the urethra and genital tract. Reflux of prostatic exudates into the urinary bladder may result in pyuria in patients with prostatic disease. • Pyuria associated with WBC casts is unequivocal evidence of renal parenchymal inflammation. • Generalized renal injury may be associated with concomitant leukocytosis, isosthenuria, and azotemia. • Pyuria associated with bacteria, fungi, or parasite ova in sufficient numbers to be seen by microscopic sediment examination indicates that the inflammatory lesion was caused or complicated by urinary tract infection. Detection of bacteria in urine sediment by light microscopy may be enhanced by placing a drop (20 µL) of urine sediment on a glass slide, allowing it to dry without spreading, staining with Diff-Quik and examining for bacteria under oil immersion (1,000 ×).

- Pyuria associated with neoplastic cells indicates neoplasia. Diagnosis of urinary tract neoplasia by cytologic examination of urine may be complicated by epithelial cell hyperplasia and atypia caused by urinary tract inflammation or the physicochemical properties of urine (pH and tonicity causing cell scalding).

OTHER LABORATORY TESTS

- Perform quantitative urine culture on all patients with pyuria; it provides the most definitive means of identifying and characterizing bacterial urinary tract infection. It is important to note that the absence of pyuria does not rule out the bacteriuria as patients with bacteriuria frequently do not have pyuria. • Negative urine culture results suggest a non-infectious cause of inflammation (e.g., uroliths, neoplasia) or inflammation associated with urinary tract infection caused by fastidious organisms (e.g., mycoplasmas and viruses) or by organisms capable of forming intracellular bacterial colonies or biofilms. False-negative culture results may also be due to recent antimicrobial therapy, sample mishandling, or delays between specimen collection and culture. • Cytologic evaluation of urinary sediment, prostatic fluid, urethral or vaginal discharges, or biopsy specimens obtained by catheter or needle biopsy may help evaluate patients with localized urinary or genital tract disease. Cytologic examination may establish a definitive diagnosis of urinary tract neoplasia, but negative cytologic findings do not rule out neoplasia.

IMAGING

Survey abdominal radiography, contrast urethrocystography and cystography, urinary tract ultrasonography, and excretory urography are important means of identifying and localizing underlying causes.

DIAGNOSTIC PROCEDURES

- Urethrocystoscopy—indicated in patients with persistent lesions of the lower urinary tract for which a definitive diagnosis has not been established by other, less invasive, means. • Light microscopic evaluation of tissue specimens—indicated in patients with lesions of the urinary or genital tracts for which a definitive diagnosis has not been established by other, less invasive, means; tissue specimens may be obtained by membrane disruption (traumatic) catheterization biopsy, cystoscopy and forceps biopsy, or exploratory laparotomy; aspiration and punch biopsy techniques may be used to evaluate the prostate gland.

**TREATMENT**

- Treatment varies, depending on the underlying cause and specific organs involved.
- Pyuria associated with systemic signs of illness (i.e., pyrexia, depression, anorexia, vomiting, dehydration, leukocytosis, polyuria, and polydipsia) or urinary obstruction warrants aggressive diagnostic evaluation and initiation of specific, supportive, and/or symptomatic treatment.

**MEDICATIONS****DRUG(S)**

Depend on underlying cause

CONTRAINDICATIONS

- Avoid glucocorticoids or other immunosuppressive agents in patients suspected of having urinary or genital tract infection. • Avoid potentially nephrotoxic drugs (e.g., gentamicin) in febrile, dehydrated, or azotemic patients and those suspected of having pyelonephritis, septicemia, or pre-existing renal disease.

**FOLLOW-UP****PATIENT MONITORING**

Response to treatment by serial urinalyses, including examination of urine sediment; collect specimens from most patients by cystocentesis to avoid contamination by preputial or vaginal exudates; perform transurethral catheterization if the expected benefits outweigh the risk of iatrogenic bacterial urinary tract infection.

POSSIBLE COMPLICATIONS

- Infectious and non-infectious inflammatory disorders of the urinary tract can cause primary renal failure, urinary obstruction, uremia, septicemia, and death. • Pyuria is a potential risk factor for formation of matrix or matrix-crystalline urethral plugs and subsequent urethral obstruction in male cats.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Hematuria • Proteinuria • Bacteriuria

SYNOMYMS

Leukocyturia

SEE ALSO

- Dysuria and Pollakiuria • Hematuria
- Lower Urinary Tract Infection chapters
- Proteinuria • Pyelonephritis

ABBREVIATION

WBC = white blood cell

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Q FEVER



BASICS

OVERVIEW

- Caused by the zoonotic rickettsia *Coxiella burnetii*.
- Infection—most commonly by inhalation or ingestion of organisms while feeding on infected body fluids (urine, feces, milk, or parturient discharges), tissues (especially placenta), or carcasses of infected animal reservoir hosts (cattle, sheep, goats); can occur after tick exposure (many species of ticks implicated).
- Lungs—thought to be main portal of entry to systemic circulation.
- Organism replicates in vascular endothelium; causes widespread vasculitis; severity depends on the pathogenicity of the strain of organism; vasculitis results in necrosis and hemorrhage in lungs, liver, and CNS.
- An extended latent period exists after recovery until chronic immune-complex phenomena develop; organism reactivated out of the latent state during parturition, resulting in large numbers entering the placenta, parturient fluids, urine, feces, and milk.
- Endemic worldwide. Most cases in the United States occur in western states.

SIGNALMENT

Cats and dogs of any age, sex, or breed.

SIGNS

Historical Findings

- Often a history of contact with farm animals or ticks.
- Fever.
- Lethargy.
- Depression.
- Anorexia.
- Abortion—especially cats.
- Ataxia and seizures—especially dogs.

Physical Examination Findings

- Usually asymptomatic.
- Splenomegaly is often the only clinical finding.
- Multifocal neurologic signs—dogs.

CAUSES & RISK FACTORS

- *C. burnetii*.
- Exposure to infected animals (especially following parturition) and ticks.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cats—other causes of abortion: infections (viral rhinotracheitis, panleukopenia, FeLV,

toxoplasmosis, bacteria including coliforms, streptococci, staphylococci, salmonellae); fetal defects; maternal problems (nutrition, genital tract abnormalities); environmental stress; endocrine disorders (hypoluteidism).

- Dogs—other causes of encephalitis.

CBC/BIOCHEMISTRY/URINALYSIS

Nonspecific

OTHER LABORATORY TESTS

Serology

- Serology—IF and ELISA methods are available; a four-fold increase in IgG titer over a 4-week period is diagnostic; the use of newer serologic techniques that measure IgM on one sample have not been well documented in small animals.
- Collect 2–3 mL of serum and refrigerate, for organism identification.
- Collect tissue sample (e.g., placenta) and refrigerate, for animal inoculation.
- Tests available from the New Mexico Department of Agriculture, Veterinary Diagnostic Services, 700 Camino de Salud NE, Albuquerque, NM 87106.
- PCR—also performed by above laboratory; used to detect organisms in tissue culture or tissue specimens derived from the patient.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Alert client of possible zoonotic risk.
- Inpatient—avoids zoonotic risk to client.
- Wear gloves and masks when treating an infected animal or when attending an aborting cat.



MEDICATIONS

DRUG(S)

- Tetracycline 22 mg/kg PO q8h for 2 weeks.
- Doxycycline 20 mg/kg PO q12h for 1 week.
- Enrofloxacin 10 mg/kg PO q12h for 1 week; should be effective but no clinical reports; effective in vitro.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Tetracycline drugs are associated with yellowing of teeth in young animals; do not use in animals with renal failure.

- Doxycycline may cause esophagitis and stricture.

- Enrofloxacin may cause cartilage defects in young animals.

- Enrofloxacin may cause retinal degeneration when used in cats with concurrent liver or kidney disease or at high doses.



FOLLOW-UP

- Difficult to determine success of therapy because many animals spontaneously improve.
- Even asymptomatic cases should be aggressively treated because of the zoonotic potential.
- Utility of predicting success of therapy based on serologic improvement unknown.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Major zoonotic potential.
- By the time a diagnosis is made in a cat or dog, human exposure and infection have occurred.
- Instruct owners and people in contact with the pet to seek medical advice immediately.
- Humans contract the disease by inhaling infected aerosols (e.g., after parturition); children commonly infected from ingesting raw milk but are usually asymptomatic.
- Previous urban outbreaks have been related to exposure to infected cats.
- Incubation period from time of contact until the first signs of illness—5–32 days.
- Person-to-person transmission possible.

ABBREVIATIONS

- CNS = central nervous system
- ELISA = enzyme-linked immunosorbent assay
- FeLV = feline leukemia virus
- IF = immunofluorescence
- PCR = polymerase chain reaction

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Author Stephen C. Barr

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QUADRIGEMINAL CYST



BASICS

OVERVIEW

- CSF-filled diverticula within the subarachnoid space at the quadrigeminal cisterna (dorsal to the midbrain and adjacent to the third ventricle). CSF may be secreted by the arachnoid cells lining the cyst cavity. It is suspected that an anomaly of CSF flow from the choroid plexus during the stage of development forces a separation within the arachnoid layer.
- Clinical signs may develop as a result of gradual expansion of the subarachnoid space by a valve mechanism associated with pulsating CSF flow.
- May be an incidental finding.

SIGNALMENT

Dog and cat

Breed Predilections

Mainly in small breeds and brachycephalic patients—Shih Tzu, Maltese, Pug, Cavalier King Charles, Yorkshire terrier, Lhasa Apso, Chihuahua, Pekingese, Pomeranian and Bulldog.

Mean Age and Range

- Mean—5 years
- Range—2 months–10 years

SIGNS

- Seizures.
- Abnormal behavior.
- If associated with hydrocephalus, could manifest with disorientation, behavioral changes, cortical blindness, compulsive circling, head pressing.

CAUSES & RISK FACTORS

- Disturbance of embryogenesis where splitting of the primitive arachnoid membrane leads to fluid accumulation.
- Inflammatory conditions affecting the meninges.
- Post-surgical trauma (intervertebral disc disease, spinal tumor).
- Neoplasia and hemorrhage.
- Intracystic hemorrhage secondary to trauma may result in expansion of the cyst and subsequent compression of the adjacent brain parenchyma.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Congenital brain anomalies (anencephaly, hydrocephalus, other).
- Storage disease.
- Infectious inflammatory diseases—viral (distemper virus, other viruses); fungal (*Blastomyces dermatitidis*, *Coccidioides* spp., *Cryptococcus neoformans*); rickettsial (*Rickettsia rickettsii*); bacterial (*Ehrlichia* spp., *E. coli*, *Streptococcus*); protozoal (*Neospora caninum*, *Toxoplasma gondii*).
- Other inflammatory disease—breed-related encephalitis (necrotizing encephalitis of the Yorkshire terrier, Maltese, and Pug).
- Brain tumor—

meningioma, glioma, choroid plexus papilloma, lymphoma.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

IMAGING

- MRI—extra-axial CSF-filled cyst at the quadrigeminal cisterna. On T1-weighted images, the lesion is hypointense to brain tissue and isointense to CSF. On T2-weighted images, the lesion is hyperintense to brain tissue and isointense to CSF. On fluid attenuated inversion recovery (FLAIR) sequences, the cyst is hypointense, confirming the presence of CSF. Dilation of the ventricular system may be present if the cyst is obstructing CSF flow.
- MRI may reveal other compressive, parenchymal (syringohydromyelia) or space occupying lesions.

DIAGNOSTIC PROCEDURES

CSF—rule out concomitant inflammation. If CSF inflammatory, the cyst may be an incidental finding.



TREATMENT

- Medical therapy to control seizures and reduce CSF production.
- If signs are progressive, surgical cyst fenestration through craniotomy or craniectomy can result in clinical improvement. When hydrocephalus is present surgical shunting can be considered.
- Other disease process must be ruled out before considering surgery. The cystic structure may be an incidental finding.
- Stable patients can be discharged with recommended medical therapy.
- Inpatient—for severely affected dogs; monitor patient closely to assess progression of neurologic deficits.
- Sequential assessment of pupillary size and reaction to light, and mentation are helpful to determine risk of brain herniation.



MEDICATIONS

DRUG(S)

- Glucocorticosteroids—dexamethasone 0.1 mg/kg IV or PO q24h for 3 days followed by prednisone 0.25–0.5 mg/kg PO q24h for 10 days, then reassess response and adjust dose. To prevent gastrointestinal ulceration, add omeprazole 0.5 mg/kg PO q 24h or famotidine 0.5–1 mg/kg IV or PO q12h to steroid therapy.
- Antiepileptic drugs—phenobarbital 2 mg/kg IV or PO q12h, levetiracetam 20 mg/kg PO q8–12h or zonisamide 5–10 mg/kg PO q12h.
- Diuretic—acetazolamide 10 mg/kg q6–8h as a carbonic anhydrase inhibitor that may help reduce CSF production and intracranial pressure. Omeprazole may act as an agent to

reduce CSF production and provide gastric protection during steroid therapy.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Do not use acetazolamide in dehydrated patients.
- The combination of glucocorticosteroid and diuretic may cause marked dehydration and increased blood viscosity that can result in poor cerebral perfusion and neurologic deterioration.



FOLLOW-UP

PATIENT MONITORING

- Repeat neurologic examination periodically (every 2–4 weeks).
- Corticosteroid may be necessary for a long period or for life. The goal is to find the dose that keeps the clinical signs controlled with minimal side effects.
- Evaluate phenobarbital levels after 4–5 weeks of starting therapy.
- If phenobarbital is continued, recheck biochemical profile and bile acids to assess hepatic function every 6 months.

POSSIBLE COMPLICATIONS

- Deterioration of clinical signs despite aggressive treatment.
- Status epilepticus, dementia, brain herniation, and death.

EXPECTED COURSE AND PROGNOSIS

- Prognosis is variable depending on severity of clinical signs and response to therapy.
- Quadrigeminal cyst may be incidental or may result in progressive neurologic deterioration.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Hydrocephalus

PREGNANCY/FERTILITY/BREEDING

Corticosteroids—may affect pregnancy

ABBREVIATIONS

- CSF = cerebrospinal fluid
- MRI = magnetic resonance imaging

INTERNET RESOURCES

- IVIS: <http://www.ivis.org>
- VIN: <http://www.vin.com>

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RABIES



BASICS

DEFINITION

A severe, invariably fatal, viral polioencephalitis of warm-blooded animals, including humans.

PATHOPHYSIOLOGY

Virus—enters body through a wound (usually from a bite of rabid animal) or via mucous membranes; replicates in myocytes; spreads to the neuromuscular junction and neurotendinal spindles; travels to the CNS via intra-axonal fluid within peripheral nerves; spreads throughout the CNS; finally spreads centrifugally within peripheral, sensory, and motor neurons.

SYSTEMS AFFECTED

- Nervous—clinical encephalitis, either paralytic or furious.
- Salivary glands—contain large quantities of infectious virus particles that are shed in saliva.

GENETICS

None

INCIDENCE/PREVALENCE

- Incidence of disease within infected animals—high (approaches 100%).
- Prevalence—overall low; can be significant in enzootic areas; especially high in underdeveloped countries where vaccination of dogs and cats is not routine.

GEOGRAPHIC DISTRIBUTION

- Worldwide.
- Exceptions—New Zealand, Hawaii, Japan, Iceland, and parts of Scandinavia.
- Species-adapted strains—specific geographic distributions within endemic countries.

SIGNALMENT

Species

- All warm-blooded mammals, including dogs, cats, and humans.
- United States—five strains endemic within fox, raccoon, skunk, coyote, and insectivorous bat populations; all five strains can be transmitted to dogs and cats.

Breed Predilections

None

Mean Age and Range

None, but adult animals that come in contact with wildlife at most risk.

Predominant Sex

None

SIGNS

General Comments

- Quite variable; atypical presentation is the rule rather than the exception.
- Three progressive stages of disease—prodromal; furious; and paralytic; 90% of rabid cats have the furious form.

Historical Findings

- Change in attitude—solitude; apprehension, nervousness, anxiety; unusual shyness or aggression.
- Erratic behavior—biting or snapping; licking or chewing at site of wound; biting at cage; wandering and roaming; excitability; irritability; viciousness.
- Disorientation.
- Muscular—incoordination; seizures; paralysis.
- Change in tone of bark.
- Excess salivation or frothing.

Physical Examination Findings

- All or some of the historical findings.
- Mandibular and laryngeal paralysis, with dropped jaw.
- Inability to swallow.
- Hypersalivation.
- Fever.
- Dilated pupils—unresponsive to light; anisocoria.

CAUSES

Rabies virus—a single-stranded, enveloped, bullet-shaped RNA virus; genus *Lyssavirus*; family *Rhabdoviridae*.

RISK FACTORS

- Exposure to wildlife, especially skunks, raccoons, bats, and foxes.
- Inadequate vaccination against rabies.
- Bite or scratch wounds from unvaccinated dogs, cats, or wildlife.
- Exposure to aerosols in bat caves.
- Immunocompromised animal—use of modified live virus rabies vaccine.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Must seriously consider rabies for any dog or cat showing unusual mood or behavior changes or exhibiting any unaccountable neurologic signs; caution: handle with considerable care to prevent possible transmission of the virus to individuals caring for or treating the animal.
- Any neurologic disease—brain tumor; viral encephalitis.
- Head wound—identify lesions from wound.
- Laryngeal paralysis.
- Choking.
- Pseudorabies virus infection.

CBC/BIOCHEMISTRY/URINALYSIS

No characteristic hematologic or biochemical changes

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- CSF—minimal increased protein and leukocyte counts may be seen.
- DFA test of nervous tissue—rapid and sensitive test; collect brain, head, or entire body of a small animal that has died or has been euthanized; chill sample immediately; submit to a state-approved laboratory for rabies diagnosis; CAUTION: use extreme care when collecting, handling, and shipping these specimens.
- DFA test of dermal tissue—skin biopsy of the sensory vibrissae of the maxillary area, including deeper subcutaneous hair follicles; approved for human diagnostics, but not for animal diagnostics; accurate if positive, but negative test does not rule out rabies.
- Rabies antibody titer—a serologic antibody titer of 0.5 IU/ml is considered adequate for protection in vaccinated people and animals.

PATHOLOGIC FINDINGS

- Gross changes—generally absent, despite dramatic neurologic disease.
- Histopathologic changes—acute to chronic polioencephalitis; gradual increase in the severity of the non-suppurative inflammatory process in the CNS as disease progresses; large neurons within the brain may contain the classic intracytoplasmic inclusions (Negri bodies).



TREATMENT

APPROPRIATE HEALTH CARE

Strictly inpatient

NURSING CARE

Administer with extreme caution

ACTIVITY

- Confine to secured quarantine area with clearly posted signs indicating suspected rabies.
- Runs or cages should be locked; only designated people should have access.
- Feed and water without opening the cage or run door.

DIET

Soft, moist food; most patients will not eat.

CLIENT EDUCATION

- Thoroughly inform client of the seriousness of rabies to the animal and the zoonotic potential.
- Ask client about any human exposure (e.g., contact, bite) and strongly urge client to see a physician immediately.
- Local public health official must be notified.

SURGICAL CONSIDERATIONS

- Generally none.
- Skin biopsy—may help establish antemortem diagnosis; must be confirmed by identification from CNS tissue.

(CONTINUED)

RABIES**MEDICATIONS****DRUG(S) OF CHOICE**

- No treatment.
- Once the diagnosis is certain, euthanasia is indicated.

CONTRAINDICATIONS

None

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

- All suspected rabies patients should be securely isolated and monitored for any development of mood change, attitude change, or clinical signs that might suggest the diagnosis.
- An apparently healthy dog or cat that bites or scratches a person should be monitored for a period of 10 days; if no signs of illness occur in the animal within 10 days, the person has had no exposure to the virus; dogs and cats do not shed the virus for more than 3 days before development of clinical disease.
- An unvaccinated dog or cat that is bitten or exposed to a known rabid animal must be quarantined for up to 6 months or according to local or state regulations.

PREVENTION/AVOIDANCE

- Vaccines (dogs and cats)—vaccinate according to standard recommendations and state and local requirements; all dogs and cats with any potential exposure to wildlife or

other dogs; vaccinate after 12 weeks of age; then 12 months later; then every 3 years using a vaccine approved for 3 years; use only inactivated or recombinant vector vaccines for cats.

- Rabies-free countries—entering dogs and cats are quarantined for long periods, usually 6 months.
- Disinfection—any contaminated area, cage, food dish, or instrument must be thoroughly disinfected; use a 1:32 dilution (4 ounces/gallon) of household bleach to quickly inactivate the virus.

POSSIBLE COMPLICATIONS

From paralysis or attitude changes

EXPECTED COURSE AND PROGNOSIS

- Prognosis—grave; almost invariably fatal.
- Dogs and cats with clinical infection usually succumb within 1–10 days of onset of clinical signs; often within 3–4 days.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

None

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

- Extreme.
- Humans must avoid being bitten by a rabid animal or an asymptomatic animal that is incubating the disease.
- Rabies cases must be strictly quarantined and confined to prevent exposure to humans and other animals.
- Local and state regulations must be adhered to carefully and completely.

PREGNANCY/FERTILITY/BREEDING

Infection during pregnancy is fatal to dam

SYNONYMS

Rage

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- DFA = direct immunofluorescent antibody

INTERNET RESOURCESwww.cdc.gov/rabies/.*Suggested Reading*

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Author Fred W. Scott**Consulting Editor** Stephen C. Barr

**Client Education Handout
available online**

R

RECTAL AND ANAL PROLAPSE



BASICS

OVERVIEW

- Eversion of one or more layers of the rectum through the anus.
- An anal prolapse (incomplete prolapse) is a protrusion of anorectal mucosa through the external anal orifice.
- A rectal prolapse (complete prolapse) is a double-layer invagination of the full thickness of the rectal tube through the anal orifice.

SIGNALMENT

- Dog and cat (especially Manx).
- Any age, sex, or breed.
- High prevalence for young, parasitized dogs or cats with diarrhea.

SIGNS

- Persistent tenesmus.
- Incomplete prolapse—protrusion of a portion of the circumference of the rectal mucosa that typically appears worse immediately after defecation and then subsides.
- Complete prolapse appears as a tubular hyperemic mass protruding from the anus.
- Chronic prolapses may be dark blue or black in color or the mucosa may be ulcerated.

CAUSES & RISK FACTORS

- Gastrointestinal disorders that cause diarrhea and tenesmus, such as parasitism, colitis/enteritis, constipation/obstipation, rectal foreign body, rectal deviation and diverticulum, proctitis, and rectal or anal tumors.
- Urogenital disorders, such as cystitis, urolithiasis, prostatitis, prostatic hypertrophy, and dystocia.
- Tenesmus following perineal, rectal, or urogenital surgery (e.g., perineal herniorrhaphy).

R



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Prolapsed intussusception—rule-out by passing a finger or blunt probe between the mass and the anus (the probe should not penetrate more than 1–2 cm before contacting the fornix; if the probe easily passes 5–6 cm, then suspect prolapsed intussusception) or by abdominal ultrasonography (look for increased intestinal layering).
- Neoplasia—rule-out by palpation, fine-needle aspiration and cytology, and/or biopsy and histopathology.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually unremarkable.
- Inflammatory or stress leukogram may be present.

OTHER LABORATORY TESTS

Fecal examination may confirm parasitism.

IMAGING

- Abdominal radiography and ultrasonography—usually unremarkable.
- Abdominal radiography—may demonstrate foreign body, prostatomegaly, cystic calculi, or colonic fecal distention.
- Abdominal ultrasonography—may demonstrate prostatomegaly, cystic calculi, bladder wall thickening, or intussusception.

DIAGNOSTIC PROCEDURES

- Rectal examination to palpate for perineal hernia.
- Colonoscopy may help evaluate recurrent prolapse for an underlying cause.

PATHOLOGIC FINDINGS

Assess viability of the prolapsed tissue by surface appearance and tissue temperature—vital tissue appears swollen and hyperemic, and red blood exudes from the cut surface; devitalized tissue appears dark purple or black, and dark cyanotic blood exudes from the cut surface; ulcerations may be present.



TREATMENT

- Must identify and treat underlying cause.
- Conservative medical management—gently replace prolapsed tissue through the anus with the use of lubricants and gentle massage; osmotic agents may help if severe swelling exists.
- Use of an epidural may facilitate treatment and relieve discomfort.
- Place a purse string suture to aid retention and prevent acute recurrence; place the suture loose enough to allow room for defecation.
- Decrease straining with stool softeners.
- Colopexy recommended for recurrent viable prolapses or if straining persists after rectal resection and anastomosis.
- When prolapse is non-reducible and/or devitalized, rectal resection and anastomosis are necessary.



MEDICATIONS

DRUG(S) OF CHOICE

- Appropriate anesthetic/analgesics as needed.
- Consider epidural to facilitate surgery and

reduce postoperative straining.

- Appropriate perioperative antibiotics are recommended (e.g., cefoxitin sodium 30 mg/kg IV) for resection anastomosis.
- Topical agents to aid in reduction—50% dextrose solution and KY Jelly.
- Stool softeners—docusate sodium (dogs, 50–200 mg PO q8–12h; cats, 50 mg PO q12–24h) or lactulose (10 g/15 mL solution or syrup, 1 mL/4.5 kg q8–12h to effect); continue for 2–3 weeks after removal of the purse-string suture.
- Feed a low-residue diet until purse-string suture is removed.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Purse-string suture removal in 3–7 days.
- Examine for rectal stricture if straining persists following anastomosis.

POSSIBLE COMPLICATIONS

- Recurrence—especially if underlying cause is not eliminated.
- Postoperative—may include infection, anastomosis dehiscence within 5–7 days postoperatively, or rectal stricture.
- Fecal incontinence after resection (sensory incontinence resulting from removal of receptors in rectal wall).



MISCELLANEOUS

ASSOCIATED CONDITIONS

Intestinal parasitism

SEE ALSO

- Colitis and Proctitis
- Dyschezia and Hematochezia
- Intussusception

Suggested Reading

- Aronson LR. Rectum, anus, perineum. In Tobias KM, Johnston SA, eds, Veterinary Small Animal Surgery, St. Louis, MO: Elsevier Saunders, 2012, pp 1564–1600.
Radlinsky MG. Rectal prolapse. In: Fossum TW, ed., Small Animal Surgery, 4th ed. St. Louis, MO: Elsevier Mosby, 2013, pp. 577–580.

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RECTAL STRICTURE



BASICS

OVERVIEW

- Diminution in the size of the rectal or anal lumen either from cicatricial contracture or scarring as a result of wound healing or chronic inflammation or from proliferative neoplastic disease.
- Gastrointestinal function is compromised because of outflow obstruction.
- No genetic basis reported.

SIGNALMENT

- Dog and cat
- No age, breed, or gender predilection reported

SIGNS

- Vary with severity of the lesion
- Tenesmus
- Dyschezia
- Constipation
- Hematochezia
- Mucoid feces
- Large-bowel diarrhea
- Secondary megacolon can develop

CAUSES & RISK FACTORS

- Inflammatory—rectoanal abscess, anal sacculitis, perianal fistulas, proctitis, foreign body, fungal infection (e.g., histoplasmosis, pythiosis).
- Traumatic—lacerations.
- Neoplastic—rectal adenocarcinoma, leiomyoma, rectal polyps.
- Iatrogenic—rectal anastomosis, rectal mass excision, rectal biopsy.
- Congenital—atresia ani.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Space-occupying processes that lead to diminished rectal capacity (extraluminal rectal compression [e.g., prostatic disease, pelvic fractures], intraluminal rectal obstruction [e.g., pseudocoprostasis, foreign body]) and functional constriction (rectal muscle spasms).
- Differentiate by rectal palpation and imaging.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually unremarkable.
- Patients with inflammation or infection may have an inflammatory leukogram.

OTHER LABORATORY TESTS

N/A

IMAGING

- Survey abdominal radiography and contrast studies (e.g., barium, air, or double-contrast enema and barium gastrointestinal series) may reveal consistent narrowing of the rectal luminal diameter.
- A combination of air and barium allows the best visualization of the colonic mucosa and aids in determining the extent of the lesion.
- Abdominal ultrasonography may reveal thickening and altered architecture if infiltrative rectocolonic disease is present (e.g., pythiosis, neoplasia).

DIAGNOSTIC PROCEDURES

- Digital rectal palpation.
- Proctoscopy/colonoscopy may be useful to

visualize a stricture, determine the extent of the lesion, and procure a biopsy specimen.

- Colonic scrapings may aid in cytologic diagnosis of fungal (histoplasmosis) and neoplastic diseases.
- Biopsy and evaluate the lesion histopathologically to classify the disease process and establish a prognosis.



TREATMENT

- Resolve the underlying cause before specifically treating the stricture when possible.
- Medical treatment directed at either palliation by use of stool softeners and enemas or the elimination of infective agents or inflammatory conditions.
- Give fluid therapy to optimize hydration prior to administering an enema to constipated or obstipated patients.
- Anesthesia may be necessary for enema administration.
- Balloon dilatation of non-neoplastic and postoperative strictures—more than one procedure may be needed based on patient response.
- Surgical reconstruction of focal strictures (plasty procedures) (see “Suggested Reading” for greater detail).
- Complete resection and anastomosis may be necessary for extensive lesions and recurrent strictures.
- Placement of a colorectal stent may be successful in relieving obstructions due to nonresectable neoplasms and potentially for non-neoplastic lesions.
- Radiotherapy and/or chemotherapy may benefit the treatment of some neoplasms.



MEDICATIONS

DRUG(S)

- Stool softeners—docusate sodium; lactulose (see Appendix IX for dosages). Intraluminal injection of corticosteroids such as triamcinolone prior to dilatation may improve outcome and reduce the likelihood of recurrence. Injection can be repeated one time if additional dilatations are necessary.
- Corticosteroids—can use prednisone to treat non-infectious inflammatory conditions (0.5–1 mg/kg PO q24h or divided q12h) and after balloon dilation or bougienage to prevent stricture recurrence.
- Chemotherapy may be indicated for various neoplasms.
- Antifungal therapy if fungal infection present.
- Appropriate perioperative antimicrobial therapy with a broad spectrum of activity against anaerobes and coliforms (e.g., cefoxitin sodium 30 mg/kg IV) in conjunction with balloon dilation or surgical therapy.
- Antibiotics can be administered after dilatation if mucosal tearing occurs (e.g., amoxicillin or metronidazole).

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Corticosteroids when infection is possible.
- Corticosteroids may adversely affect healing after surgical correction of the stricture.



FOLLOW-UP

PATIENT MONITORING

- Resolution or recurrence of clinical signs.
- Patients with neoplastic lesions—recurrence and metastatic disease.
- Patients with strictures that have undergone balloon dilation should be re-evaluated for restenosis formation within 7–14 days of the dilation procedure to determine the need for additional dilation procedures.

POSSIBLE COMPLICATIONS

- Medical treatment—can include inefficacy, diarrhea, and adverse effects of medications.
- Balloon dilation can result in deep rectal tears, hemorrhage, or possibly full-thickness perforation.
- Surgical treatment—fecal incontinence, secondary stricture formation, and wound dehiscence.

EXPECTED COURSE AND PROGNOSIS

- Varies with the severity of the stricture.
- Patients with benign strictures that are readily managed medically or with balloon dilation or bougienage may have a good long-term outcome.
- Surgical resection has more guarded prognosis because of the frequency of complications.
- Most patients with recognizable clinical signs due to neoplasia have a guarded-to-poor prognosis for complete resolution.



MISCELLANEOUS

AGE-RELATED FACTORS

Atresia ani is seen within weeks of birth.

SEE ALSO

- Colitis and Proctitis
- Constipation and Obstipation
- Dyschezia and Hematochezia
- Histoplasmosis
- Perianal Fistula
- Pythiosis
- Rectoanal Polyps

Suggested Reading

- Aronson LR. Rectum, anus, perineum. In Tobias KM, Johnston SA, eds, Veterinary Small Animal Surgery, St. Louis, MO: Elsevier Saunders, 2012, pp. 1564–1600.
- Culp WT, Macphail CM, Perry JA, Jensen TD. Use of a nitinol stent to palliate a colorectal neoplastic obstruction in a dog. J Am Vet Med Assoc 2011, 239:222–227.

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RECTOANAL POLYPS



BASICS

OVERVIEW

Most rectoanal polyps are benign growths located in the distal rectum. Histopathologic evaluation typically reveals adenomas, but lesions may undergo malignant transformation.

SIGNALMENT

- Dog and rarely cat
- Middle-aged to old
- No breed or sex predilection

SIGNS

- Hematochezia with relatively well-formed feces.
- Mucus-covered feces.
- Pencil-thin or ribbon-like feces.
- Tenesmus.
- Dyschezia.
- Soft, well-vascularized, friable, and often ulcerated mass(es) may be seen or palpated rectally.
- Usually single but multiple polyps can occur.
- May be pedunculated or broad-based sessile masses.

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Carcinoma *in situ* and adenocarcinoma.
- Other neoplasias—leiomyoma, lymphoma, papilloma.
- Proctitis.
- Pythiosis.
- Colitis (clinical signs are characterized by diarrhea with a marked increase in frequency, scant volume of feces, increase fecal mucus, and tenesmus. These clinical signs are vastly different to those of dogs with rectoanal polyps which do not cause diarrhea).
- Incomplete rectal prolapse.

CBC/BIOCHEMISTRY/URINALYSIS

Usually unremarkable

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Rectal palpation.
- Direct visualization through anus.

• Proctoscopy—viable low-cost procedure that allows one to visualize the descending colon after cleansing the animal's colon. This method is suitable in most dogs and cats because the polyps are usually localized to the rectoanal or colorectal region and tend not to metastasize.

- Colonoscopy—recommended to evaluate the entire rectum and colon for additional polyps.
- Cytologic examination of polyp aspirate or scraping may help the initial diagnosis, although cytology should be interpreted with caution given the inherent challenges of differentiating benign adenomas from adenocarcinomas cytologically.
- Histopathologic examination of excised tissue is required for definitive diagnosis and to assess completeness of the excision.

PATHOLOGIC FINDINGS

- Adenomatous polyp
- Adenomatous hyperplasia
- Carcinoma *in situ*



TREATMENT

- Surgical excision is the treatment of choice.
- Most polyps can be exteriorized directly through the anus and removed with submucosal resection.
- Close the mucosal defect with absorbable sutures, avoiding compromise of the lumen diameter.
- Lesions that cannot be exteriorized may be removable transanally by electrosurgery with endoscopic guidance or can be directly exposed through a dorsal rectal approach.
- One study in dogs showed significant improvement in clinical signs following administration of piroxicam, but long-term follow-up is not available. Numerous NSAIDs have been evaluated in humans with mixed results (see "Internet Resources").



MEDICATIONS

DRUG(S)

- Appropriate perioperative antibiotics are recommended (e.g., cefoxitin sodium 30 mg/kg IV).
- Stool softeners may help decrease tenesmus—docusate sodium (dogs, 50–200 mg PO q8–12h; cats, 50 mg PO q12–24h) or docusate calcium (dogs, 50–100 mg PO q12–24h; cats, 50 mg PO q12–24h).

- Alternative stool softener—lactulose (1 mL/4.5 kg PO q8h to effect).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Examine the excision site 14 days after surgery and again at 3 and 6 months to ensure absence of recurrence or stricture.
- Twice yearly examination thereafter to assess for recurrence.

POSSIBLE COMPLICATIONS

- Recurrence
- Rectal stricture (rare)

EXPECTED COURSE AND PROGNOSIS

- Dogs with focal single adenomas have a good prognosis with a low rate of recurrence.
- Dogs with multiple and/or diffuse lesions (involvement of > 50% of circumference of rectal wall) have much higher rates of recurrence.
- Malignant transformation of benign lesions can occur in up to 50% of dogs.
- Excised tissues should be submitted for histopathology even when preoperative biopsies have been performed. The diagnosis may change in up to one-third of the cases in which preoperative endoscopic biopsies are performed.



MISCELLANEOUS

SEE ALSO

- Adenocarcinoma, Anal Sac
- Dyschezia and Hematochezia
- Rectal and Anal Prolapse

ABBREVIATION

- NSAID = nonsteroidal anti-inflammatory drug

INTERNET RESOURCES

<http://www.jr2.ox.ac.uk/Bandolier/band129/b129-6.html>. This site reviews the mixed results of clinical trials using various NSAIDs in humans.

Suggested Reading

Aronson LR. Rectum, anus, perineum. In Tobias KM, Johnston SA, eds. Veterinary Small Animal Surgery, St. Louis, MO: Elsevier Saunders, 2012, pp. 1564–1600.

Author Eric R. Pope

Consulting Editor Stanley L. Marks

RED EYE



BASICS

DEFINITION

Hyperemia of the eyelids or ocular vasculature, or hemorrhage within the eye.

PATHOPHYSIOLOGY

- Active dilation of ocular vessels—in response to extraocular or intraocular inflammation or passive congestion.
- Hemorrhage from existing or newly formed blood vessels.

SYSTEMS AFFECTED

Ophthalmic—eye and/or ocular adnexa

SIGNALMENT

Dog and cat

SIGNS

Historical Findings

Depends on cause

Physical Examination Findings

- Depends on cause.
- May affect one or both eyes.
- Result of systemic disease—abnormalities in other organ systems common.

CAUSES

- Virtually every case fits into one or more of the following categories.
- Blepharitis.
- Conjunctivitis.
- Keratitis.
- Episcleritis or scleritis.
- Anterior uveitis.
- Glaucoma.
- Hyphema.
- Orbital disease—usually the orbital abnormality is more prominent.

RISK FACTORS

- Systemic infectious or inflammatory diseases.
- Immunocompromise.
- Coagulopathies.
- Systemic hypertension.
- Irritation by potentially any topical ophthalmic medication.
- Neoplasia.
- Trauma.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

More than one cause may occur simultaneously.

Similar Signs

- Rule out normal variations.
- Palpebral conjunctiva—normally redder than bulbar conjunctiva.
- One or two large episcleral vessels—may be normal if the eye is otherwise quiet.

- Transient mild hyperemia—with excitement, exercise, and straining.
- Horner's syndrome—may cause mild conjunctival vascular dilation; differentiated by other signs and pharmacologic testing.

Causes

- Superficial (conjunctival) vessels—originate near the fornix; move with the conjunctiva; branch repeatedly; blanch quickly with topical 2.5% phenylephrine or 1:100,000 epinephrine; suggest ocular surface disorders (e.g., conjunctivitis, superficial keratitis, blepharitis).
- Deep (episcleral) vessels—originate near the limbus; branch infrequently; do not move with the conjunctiva; blanch slowly or incompletely with topical sympathomimetics; suggest episcleritis or intraocular disease (e.g., anterior uveitis or glaucoma).
- Discharge—mucopurulent to purulent: typical of ocular surface disorders and blepharitis; serous or none: typical of intraocular disorders.
- Swollen or inflamed eyelids—suggest blepharitis.
- Corneal opacification, neovascularization, or fluorescein stain retention—suggest keratitis.
- Aqueous flare or cell (increased protein or cells in the anterior chamber)—confirms diagnosis of anterior uveitis.
- Pupil—miotic: common with anterior uveitis; dilated: common with glaucoma; normal: with blepharitis and conjunctivitis.
- Abnormally shaped or colored irides—suggest anterior uveitis.
- Luxated or cataractous lenses—suggest glaucoma or anterior uveitis.
- IOP—high: diagnostic for glaucoma; low: suggests anterior uveitis.
- Loss of vision—suggests glaucoma, anterior uveitis, or severe keratitis.
- Glaucoma and anterior uveitis—may complicate hyphema.

CBC/BIOCHEMISTRY/URINALYSIS

- Typically normal, except with anterior uveitis, glaucoma, or hyphema secondary to systemic disease.
- See Anterior Uveitis—Dogs; Anterior Uveitis—Cats; Hyphema.

OTHER LABORATORY TESTS

Depends on cause

IMAGING

- Chest radiographs—consider with anterior uveitis or if intraocular neoplasia is a possibility.
- Abdominal radiography or ultrasonography—may help rule out infectious or neoplastic causes.
- Ocular ultrasonography—if the ocular media are opaque; may define the extent and nature of intraocular disease or identify an intraocular tumor.

DIAGNOSTIC PROCEDURES

Tonometry—must perform in every patient with an unexplained red eye.

Ocular Surface Disorders

- Aerobic bacterial culture and sensitivity profile—with a purulent discharge, chronic disease, or if the response to treatment is poor.
- Schirmer tear test.
- Cytologic examination of affected tissue—lid; conjunctiva; cornea.
- Cats—consider PCR or IFA test on corneal or conjunctival scrapings for feline herpesvirus and *Chlamydia*; collect sample before fluorescein staining to avoid false-positive results on IFA.
- Fluorescein stain.
- Conjunctival biopsies—with chronic conjunctivitis or with a mass lesion.
- See specific disease—Conjunctivitis—Cats; Conjunctivitis—Dogs; Blepharitis; Keratitis chapters.

Intraocular Disorders

- Fluorescein stain.
- See specific disease—Anterior Uveitis—Cats; Anterior Uveitis—Dogs; Hyphema; Glaucoma.



TREATMENT

- Usually outpatient.
- Elizabethan collar—considered to prevent self-trauma.
- Avoid dirty environments or those that may lead to ocular trauma, especially if topical corticosteroids are used.
- Because there is a narrow margin for error, consider referral if you cannot attribute the condition to one of the listed causes, if you cannot rule out glaucoma on the initial visit, or if the diagnosis is so uncertain that administration of a topical antibiotic alone or a topical corticosteroid alone would be questionable.
- Few causes are fatal; however, a workup may be indicated (especially with anterior uveitis and hyphema) to rule out potentially fatal systemic diseases.
- Deep corneal ulcers and glaucoma—may be best treated surgically.

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MEDICATIONS

DRUG(S)

- Depends on specific cause.
- Generally, control ocular pain, inflammation, infection, and IOP.
- Aspirin 10–15 mg/kg PO q8–12h (dogs); may control mild ocular inflammation and pain pending test results.
- Carprofen 2.2 mg/kg q12h or 4.4 mg/kg q24h.

RED EYE

(CONTINUED)

- Flunixin meglumine 0.5 mg/kg IV once; may be used in dogs with severe ocular inflammation pending test results.

CONTRAINDICATIONS

- Topical corticosteroids—contraindicated if the cornea retains fluorescein stain.
- Systemic corticosteroids—avoid until infectious systemic causes have been ruled out.

PRECAUTIONS

- Topical aminoglycosides—may be irritating; may impede reepithelialization if used frequently or at high concentrations.
- Topical solutions—may be preferable to ointments if corneal perforation is possible.
- Atropine—may exacerbate KCS and glaucoma.
- NSAIDs—use with caution in hyphema.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

- Depends on cause.
- Repeat ophthalmic examinations—as required to ensure that IOP, ocular pain, and inflammation are well controlled.
- The greater the risk of loss of vision, the more closely the patient needs to be followed; may require daily or more frequent examination.

POSSIBLE COMPLICATIONS

- Death
- Loss of the eye or permanent vision loss
- Chronic ocular inflammation and pain

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Numerous systemic diseases

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

See Anterior Uveitis—Dogs; Anterior Uveitis—Cats; Conjunctivitis—Dogs; Conjunctivitis—Cats; Episcleritis; Glaucoma; Keratitis, Ulcerative

PREGNANCY/FERTILITY/BREEDING

Systemic corticosteroids may complicate pregnancy.

ABBREVIATIONS

- IFA = immunofluorescent antibody
- IOP = intraocular pressure
- KCS = keratoconjunctivitis sicca
- NSAID = nonsteroidal anti-inflammatory drug
- PCR = polymerase chain reaction

Suggested Reading

Maggs DJ, Miller PE, Ofri R. Slatter's Fundamentals of Veterinary Ophthalmology, 5th ed. St. Louis, MO: Saunders, 2013.

Author Paul E. Miller**Consulting Editor** Paul E. Miller

**Client Education Handout
available online**



BASICS

DEFINITION

Passive, retrograde movement of undigested gastric or esophageal contents into the oral cavity. Reflux refers to the retrograde movement of gastric juice across the gastroesophageal sphincter into the esophagus.

PATOPHYSIOLOGY

Regurgitation results from a loss of normal esophageal motility. In the normal esophagus, the presence of a food bolus in the proximal esophagus stimulates afferent sensory neurons. Signals are transferred centrally, via the vagus and glossopharyngeal nerves, to the tractus solitarius and nucleus ambiguus. Motor impulses travel back via the vagus nerve to stimulate striated muscle (canine) and striated and smooth muscle (feline) to cause esophageal peristalsis. Lesions anywhere along this pathway may lead to regurgitation.

SYSTEMS AFFECTED

- Gastrointestinal—dysphagia, weight loss
- Musculoskeletal—weakness, weight loss
- Nervous—polyneuropathies, CNS disease
- Respiratory—aspiration pneumonia

GENETICS

• Regurgitation due to megaesophagus can be inherited in wirehaired fox terriers (autosomal recessive) and miniature schnauzers (autosomal dominant or 60% penetrance autosomal recessive). A breed predisposition also exists for the German shepherd, great Dane and Irish setter. The site and pathogenesis of the lesion in idiopathic megaesophagus is unknown. Suggested hypotheses include abnormalities of the afferent limb of the reflex arc (receptors, neurons) or of the swallowing center in the CNS.

• Boxers and Newfoundlands have a genetic predisposition for inflammatory myopathy that is associated with esophageal dysmotility.

• Brachycephalic breeds are predisposed to sliding hiatal hernias (type I) that is typically associated with gastroesophageal reflux.

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog (more commonly) and cat

Breed Predilections

- Wirehaired fox terriers, miniature schnauzers. Other predisposed breeds include Great Dane, German shepherd, Irish setter, Labrador retriever, Newfoundland, and boxer, brachycephalic breeds (Shar-Pei, pug, Boston terrier, English bulldog, French bulldog).
- Siamese and Siamese-related cats.

Mean Age and Range

- Congenital cases present soon after birth (congenital megaesophagus) or at weaning (vascular ring anomalies) from liquid diet to solid foods.
- Acquired cases may be seen at any age, depending on the etiology.

Predominant Sex

No gender predilection has been identified.

SIGNS

General Comments

- Clients often report vomiting; the veterinarian must differentiate vomiting from regurgitation using a comprehensive history. Having owner videotape events may be helpful.
- Regurgitation: passive process; little to no abdominal effort; no prodromal phase; regurgitated material has increased amounts of thick mucus.
- Vomiting: active process; prodromal phase is identified; vomited material may have increased amounts of bile staining.
- The shape of the expelled material (i.e., tube-like), presence of undigested food, and length of time from ingestion to regurgitation or vomiting are less helpful to differentiate.

Historical Findings

- Vomiting (as perceived by owner)
- Dysphagia
- Coughing
- Ravenous appetite
- Weight loss
- Ptyalism
- Other signs, depending upon underlying etiology

Physical Examination Findings

- Cervical swelling may be noted
- Ptyalism
- Halitosis
- Increased respiratory noises
- Nasal discharge and fever (if concurrent pneumonia)
- Cachexia
- Weakness

CAUSES

Congenital Pharyngeal or Pharyngoesophageal

- Cleft or short palate (typically associated with nasal reflux)
- Cricopharyngeal achalasia (typically associated with nasal reflux and dysphagia)
- Myasthenia gravis

Congenital Esophageal

- Vascular ring anomaly (e.g., persistent right aortic arch)
- Megaesophagus
- Glycogen storage disease
- Esophageal diverticulum
- Bronchoesophageal fistula

Acquired Pharyngeal or Pharyngoesophageal

- Cricopharyngeal dysphagia
- Foreign bodies
- Neoplasia

Rabies

- Toxicity (botulism)
- Myopathy/neuropathy/junctionopathy

Acquired Esophageal

- Megaesophagus
- Myasthenia gravis
- Stricture
- Neoplasia
- Hypoadrenocorticism
- Hypothyroidism
- Hiatal hernia
- Dysmotility
- Gastroesophageal intussusception
- Gastroesophageal reflux
- Periesophageal masses
- Dysautonomia
- Myopathy/neuropathy
- Foreign bodies
- Granulomatous disease
- Toxicity (lead)
- Idiopathic
- Gastric dilatation/volvulus
- Parasitic infection (*Spirocerca lupi*)
- Bronchoesophageal fistula

RISK FACTORS

Increased risk of gastroesophageal reflux with general anesthesia; the resultant esophagitis may lead to stricture formation and regurgitation.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Regurgitation is a clinical sign, not a diagnosis, and is the hallmark of esophageal disease.
- It is important to differentiate vomiting from regurgitation.

CBC/BIOCHEMISTRY/URINALYSIS

- There are no pathognomonic changes for regurgitation.
- Inflammatory leukogram may be seen if aspiration pneumonia is present.
- Most helpful for evaluation of possible underlying etiologies: e.g., erythrocyte changes with lead toxicosis, elevated CK with myopathy, hyperkalemia and hyponatremia with hypoadrenocorticism, hypercholesterolemia with hypothyroidism.

OTHER LABORATORY TESTS

These elucidate etiologies of acquired conditions causing regurgitation and include ACTH stimulation test or baseline cortisol level (hypoadrenocorticism); thyroid serology (hypothyroidism); acetylcholine receptor antibody level (myasthenia gravis); blood lead levels (toxicosis).

IMAGING

- Thoracic and cervical radiography—evidence of a gas-, fluid-, or ingesta-filled esophagus with megaesophagus; may also show aspiration pneumonia, neoplasia, foreign bodies, hiatal hernia, etc.

REGURGITATION

(CONTINUED)

- Contrast studies—both liquid barium and barium-coated food for radiolucent foreign bodies or esophageal strictures. Iohexol may also be used. Esophagram does not allow one to evaluate functional disorders such as intestinal dysmotility or cricopharyngeal achalasia. **Caution:** contrast studies may increase the risk for aspiration pneumonia with regurgitation.
- Videofluoroscopy—for pharyngeal weakness, cricopharyngeal dysphagia, esophageal motility disorders, hiatal hernia or gastroesophageal reflux.
- Other imaging studies include scintigraphy and high-resolution manometry for motility evaluation and ultrasound for pharyngeal or cervical masses.
- Cervical and thoracic CT scans may also be utilized.

DIAGNOSTIC PROCEDURES

- Esophagoscopy can be useful for esophagitis, strictures, vascular ring anomalies, neoplasia, and foreign bodies.
- Electromyography and nerve/muscle biopsies may be used for neuropathic or myopathic conditions.
- Transtracheal wash or bronchoalveolar lavage if aspiration pneumonia is present or suspected.

PATHOLOGIC FINDINGS

Gross and histologic findings depend upon the underlying etiology and the presence of complicating factors.



TREATMENT

APPROPRIATE HEALTH CARE

- Therapy for underlying etiology should be instituted.
- Important to meet nutritional requirements and treat or prevent aspiration pneumonia.

NURSING CARE

- Aspiration pneumonia may require supplemental oxygen therapy, nebulization/coupage, and fluid therapy with balanced electrolyte solution.
- These animals may be recumbent and require soft bedding. They should be maintained in sternal recumbency or turned to alternate down sides every 4 hours.

ACTIVITY

Depending on etiology, restricted activity is not necessary.

DIET

- Experimentation with different food consistencies is essential. Liquid gruel, small meatballs, or blenderized slurries may be used.
- Some cases benefit from gastrostomy feedings, though regurgitation may still occur.
- Both food and water should be elevated, and animal should be maintained in an upright position for 10–15 minutes after

eating or drinking. Use of a Bailey chair facilitates keeping the dog upright for 10–15 minutes after a meal.

- The recommended caloric requirement amount should be calculated and the diet should be monitored so that basic energy requirements are met.

CLIENT EDUCATION

- If regurgitation is due to megaesophagus, most cases require life-long therapy, even if an underlying etiology is found. Client dedication is important for long-term management.
- Most animals succumb to aspiration pneumonia or intractable regurgitation.
- Placement of a PEG tube in dogs with megaesophagus can reduce the frequency of aspiration pneumonia.

SURGICAL CONSIDERATIONS

- Surgical intervention is indicated for vascular ring anomalies, cricopharyngeal achalasia, bronchoesophageal fistula, and others.
- Esophageal dysfunction is permanent in most cases.
- Balloon dilation is indicated for cases of esophageal stricture.



MEDICATIONS

DRUG(S) OF CHOICE

- Antibiotics for aspiration pneumonia (broad-spectrum or based on culture and sensitivity from TTW or BAL).
- Specific therapy for underlying etiology if indicated.
- Prokinetics—metoclopramide (0.2–0.4 mg/kg SC or PO q6–12h, or 1–2 mg/kg q24h as a CRI) increases lower esophageal sphincter tone and increases gastric motility. Cisapride (0.5 mg/kg PO q8–12h) is more effective for esophageal reflux than metoclopramide and has been documented to enhance gastric emptying and increase lower esophageal sphincter tone in dogs.
- Other motility agents (e.g., nizatidine) have not been evaluated for esophageal motility.
- H₂ blockers for esophagitis—ranitidine (1–2 mg/kg PO, IV q12h), famotidine (0.5–1 mg/kg PO, SC, IM, IV q12h). Proton pump inhibitors may be used in severe cases—omeprazole (0.7–1.5 mg/kg PO q24h).

CONTRAINDICATIONS

N/A

PRECAUTIONS

- Absorption of orally administered drugs may be compromised.
- Injectable forms should be used when applicable.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Animals with aspiration pneumonia should have thoracic radiographs and complete blood counts checked until resolution, or if recurrence is suspected.
- Animals should be monitored, weighed, and body condition scores applied to ensure adequate caloric intake.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Aspiration pneumonia.
- Others depending on presence of underlying diseases (e.g., hypothyroidism).

EXPECTED COURSE AND PROGNOSIS

- Older animals with idiopathic megaesophagus have a poor prognosis.
- Aspiration pneumonia is the typical cause of death or euthanasia.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Aspiration pneumonia
- Megaesophagus

AGE-RELATED FACTORS

Young animals may regain some esophageal function with appropriate therapy, depending on etiology.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Dysautonomia (Key-Gaskell Syndrome)
- Dysphagia
- Esophagitis
- Megaesophagus
- Myasthenia Gravis
- Pneumonia, Bacterial

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- BAL = bronchoalveolar lavage
- CK = creatine kinase
- CT = computed tomography
- PEG = percutaneous gastrostomy tube
- TTW = transtracheal wash

Suggested Reading

Guilford G, Strombeck D. Diseases of swallowing. In: Strombeck's Small Animal Gastroenterology, 3rd ed. Philadelphia: Saunders, 1996, pp. 211–235.

Author Stanley L. Marks

Consulting Editor Stanley L. Marks



Client Education Handout
available online

RENAL FAILURE, ACUTE



BASICS

DEFINITION

Acute uremia is a clinical syndrome characterized by sudden onset of renal outflow or excretory failure; accumulation of uremic toxins; dysregulation of fluid, electrolyte, and acid-base balance; and clinical signs of uremia. Depending on the underlying cause, acute uremia is potentially reversible if diagnosed quickly and treated aggressively. This chapter refers to intrinsic acute kidney injury and ureteral obstruction.

PATHOPHYSIOLOGY

- AKI may be initiated by ischemia, nephrotoxins, infection, prolonged urine outflow obstruction and severe non-renal systemic diseases (e.g., pancreatitis, neoplasia).
- AKI may be divided into four sequential stages: (1) initiation, (2) extension, (3) maintenance, and (4) recovery. Clinically, transition from one stage to the next may not be clearly evident, and not all stages need be present in an individual patient.
- Renal excretory failure is perpetuated by multiple factors including (1) reduced glomerular surface area and permeability, (2) low renal blood flow, (3) intratubular obstruction by tubular debris, (4) cellular and interstitial edema, and (5) “backleak” of filtrate across damaged tubular epithelia. Resolution occurs by renal regeneration and repair.
- Ureteral obstruction results from ureteroliths, inspissated blood, strictures or inflammatory debris.

SYSTEMS AFFECTED

- Renal/Urologic
- Endocrine/Metabolic
- Gastrointestinal
- Hemic/Lymph/Immune
- Musculoskeletal
- Nervous
- Respiratory

INCIDENCE/PREVALENCE

- Prevalence is lower than chronic kidney disease.
- Prevalence may increase in the fall and winter with greater exposure to antifreeze containing ethylene glycol, and wet environments that support *Leptospira*.
- Ureteral obstruction is the most common cause of severe acute uremia in cats.

SIGNALMENT

Species

Dog and cat

Breed Predilections

None

Mean Age and Range

• 6–8 years peak prevalence in dogs and cats.

- Older animals at greater risk due to decreased renal reserve.

SIGNS

Historical Findings

Sudden onset of anorexia, listlessness, depression, vomiting (\pm blood), diarrhea (\pm blood), halitosis, ataxia, seizures, known toxin or drug exposure, recent medical or surgical procedure, and oliguria/anuria.

Physical Examination Findings

Normal body condition and hair coat, depression, dehydration (or iatrogenic overhydration), scleral injection, oral ulceration, glossitis, necrosis of the tongue, uremic breath, hypothermia, fever, tachypnea, bradycardia, non-palpable urinary bladder, and asymmetrically enlarged, painful, firm, kidneys.

CAUSES

Hemodynamic/Hypoperfusion

Shock, trauma, thromboembolism (e.g., DIC, vasculitis, transfusion reaction), heatstroke, excessive vasoconstriction (e.g., administration of NSAIDs), adrenal insufficiency, excessive vasodilation (e.g., ACEI or antihypertensive drugs), prolonged anesthesia, significant hypertension, heart failure.

Nephrotoxic

Ethylene glycol, aminoglycoside, amphotericin B, chemotherapeutic agent (e.g., cisplatin, doxorubicin), thiocetarsamide, NSAIDs, radiographic contrast agents, heavy metals (e.g., lead, mercury, arsenic, thallium), insect or snake venom, heme pigment, calcium, grape or raisin ingestion (dogs), and lily ingestion (cats).

Intrinsic and Systemic Disease

Leptospirosis, Lyme disease, immune-mediated glomerulonephritis, pancreatitis, septicemia, DIC, hepatic failure, heat stroke, transfusion reaction, bacterial endocarditis, pyelonephritis, cortical necrosis, and lymphoma. Unilateral or bilateral ureteral obstruction.

RISK FACTORS

- Endogenous—preexisting CKD, dehydration, sepsis, hypovolemia, hypotension, advanced age, concurrent disease, hyponatremia, hypokalemia, hypocalcemia, and acidosis.
- Exogenous—drugs (e.g., furosemide, NSAIDs, ACEI, aminoglycoside), prolonged anesthesia, acidifying diets, trauma, multiple organ disease, and high environmental temperature.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Prerenal azotemia—oliguria, concentrated USG (dogs, ≥ 1.030 ; cats, ≥ 1.035), correctable with fluid repletion.

- Post-renal azotemia—anuria, dysuria, stranguria, large bladder, urethral obstruction, enlarged prostate, urethral tear, uroperitoneum.

- CKD—polyuria, polydipsia, history of chronic illness, loss of body condition, anemia.

- Prerenal on CKD—clinical and laboratory features of CKD but partially correctable with fluid repletion.

- Prerenal on AKI—acute onset uremia, partially correctable with fluid repletion.

- Hypoadrenocorticism—hyponatremia, hyperkalemia, low serum cortisol.

- Pancreatitis—cranial abdominal pain, high trypsin-like immunoreactivity, hyperbilirubinemia, and increase in liver enzyme activity.

CBC/BIOCHEMISTRY/URINALYSIS

- Normal or high PCV, variable leukocytosis, and lymphopenia.

- Progressive (moderate to severe) increases in SUN, creatinine, and phosphorus; variably high potassium and glucose; and variably low bicarbonate and calcium concentration.

- USG ≤ 1.020 , mild-to-moderate proteinuria, glucosuria; variable number of cellular, and/or granular casts, WBCs, RBCs, and tubular epithelial cells; variable bacteriuria and calcium oxalate monohydrate crystalluria (sometimes seen in association with ethylene glycol toxicosis).

OTHER LABORATORY TESTS

- Metabolic acidosis common; mixed disorders may occur.

- *Leptospira* titer $\geq 1:800$ to non-vaccinal serovar, or rising titers.

- Ethylene glycol concentration—“spot test” positive if ingested, increased serum osmolality and/or osmolar or anion gap.

IMAGING

- Survey and contrast radiography—kidneys are normal to large, with bilateral smooth contours; asymmetric kidneys in cats (“big kidney-little kidney” syndrome) with ureteral obstruction—small radiodense uroliths may be visible in the retroperitoneum.

- Percutaneous nephropyleography or contrast CT for ureteral obstruction.

- Ultrasonography—severe cortical hyperechogenicity suggests ethylene glycol toxicosis. Moderate cortical hyperechogenicity suggests glomerulonephritis or nephrosis. Pelvic and/or ureteral dilation or calcific densities suggest outflow obstruction.

DIAGNOSTIC PROCEDURES

- Monitor urine output—helps establish diagnosis and helps in formulation of therapy and prognosis: anuria; oliguria, ≤ 0.25 mL/kg/h (≤ 1 mL/kg/h during fluid administration); non-oliguria, ≥ 2 mL/kg/h.

- Fine-needle aspiration—may establish lymphoma as cause of renomegaly.

RENAL FAILURE, ACUTE

(CONTINUED)

- Percutaneous renal biopsy—helps establish the cause, severity, and potential reversibility of injury; later in the course of disease (4–6 weeks) it may help predict ongoing renal repair and permanence of renal damage.

PATHOLOGIC FINDINGS

Nephrosis or nephritis, glomerulonephritis, calcium oxalate crystals, interstitial edema, and lack of interstitial fibrosis; the subacute stage is characterized by attenuated tubular epithelium, interstitial fibrosis and mineralization, cellular infiltration, and variable tubular regeneration.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient management; eliminate inciting causes; discontinue nephrotoxic drugs; establish and maintain hemodynamic stability; ameliorate life-threatening fluid imbalances, biochemical abnormalities, and uremic toxicities; initiate gastric lavage, induce emesis and administer activated charcoal, cathartics, and specific antidotes to patients with acute poisoning; early hemodialysis/hemoperfusion can eliminate many toxins.

NURSING CARE

- Hypovolemia—correct estimated fluid deficits with 0.9% saline or balanced polyionic solution within 2–4 hours if patient condition permits; once hydrated, ongoing fluid requirements are provided by 5% dextrose for insensible requirements (approximately 20–25 mL/kg/day) and balanced electrolyte solution equal to urinary and other losses (i.e., vomiting and diarrhea); avoid overhydration; replace blood losses by blood transfusion.
- Hypervolemia—stop fluid administration and eliminate excess fluid by diuretics or dialysis.
- Monitor body weight at least four times daily and adjust fluids to maintain stable weight once rehydrated. Avoid overhydration.

DIET

- Rapid control of vomiting and early nutritional support. Endogenous fat and protein stores are consumed while patient is anorexic; resting energy requirements must be provided within 3 days using moderately protein-restricted diets, or enteral feeding solutions formulated to control azotemia and supply caloric requirements.
- Parenteral nutrition (intractable vomiting)—provide caloric requirements by dextrose and emulsified lipid solution; protein requirements (dogs, 2–3 g/100 kcal; cats, 3–4 g/100 kcal) provided by amino acid mixtures.

- Enteral feeding (anorectic, non-vomiting animals)—caloric and protein requirements supplied by blended renal diets, liquid enteral solutions, or formulated diets delivered by nasoesophageal, esophagostomy, gastrostomy, or enterostomy tube.

CLIENT EDUCATION

Guarded prognosis for complete recovery; potential for morbid complications of treatment (e.g., fluid overload, sepsis, and multiple organ failure); expense of prolonged hospitalization; alternatives to conventional medical management (i.e., peritoneal dialysis, hemodialysis, and renal transplantation); zoonotic potential of leptospirosis.

SURGICAL CONSIDERATIONS

- For acute ureteral obstruction unresponsive to medical management, consider surgical intervention via ureteral stenting, subcutaneous ureteral bypass or ureteral resection and re-implantation.
- Renal transplantation may provide long-term survival for cats with fulminating, nonresponsive AKI.

Peritoneal or Hemodialysis

- Dialysis can stabilize the patient until renal function is restored or corrective surgery (removal of ureteral obstruction, renal transplantation); without dialysis, most oliguric patients die before renal repair occurs.
- Specific indications include severe oliguria or anuria, life-threatening fluid overload or acid-base/electrolyte disturbances, $\text{SUN} \geq 100 \text{ mg/dL}$, serum creatinine $\geq 10 \text{ mg/dL}$, clinical course refractory to conservative treatment, perioperative stabilization, and poisoning/overdosage with a dialyzable toxin.



MEDICATIONS

DRUG(S) OF CHOICE

Inadequate Urine Production

- Ensure patient is fluid-volume-replete; provide additional isonatric fluid to achieve 3% volume expansion; failure to induce diuresis indicates severe parenchymal damage or underestimation of fluid deficit; if fluid-replete, administer diuretics.
- Hypertonic mannitol (20%) 0.5 g/kg IV over 15–30 minutes; if effective, continue as intermittent IV bolus q6h; do not repeat dosage if ineffective.
- Furosemide (alternative or subsequent to mannitol)—4 mg/kg IV; if effective, continue CRI at 0.5 mg/kg/h or 2 mg/kg q6h; discontinue if ineffective.
- Dopamine—lack of documented efficacy and potential side effects contraindicate its use except for pressor control.
- If these treatments fail to induce diuresis within 4–6 hours, consider dialysis.

Metabolic Disorders, Acid-Base Disorders

Administer bicarbonate if serum bicarbonate $\leq 16 \text{ mEq/L}$; bicarbonate replacement: $\text{mEq} = \text{bicarbonate deficit} \times \text{body weight (kg)} \times 0.3$; give half IV over 30 minutes and the remainder over 2–4 hours; then reassess.

Hyperkalemia

- Correct dehydration with potassium free (0.9% NaCl) fluids.
- Minimize potassium intake.
- Discontinue medications that promote hyperkalemia (e.g., ACEI, potassium sparing diuretics).
- Loop diuretics: furosemide 2–4 mg/kg IV.
- Sodium bicarbonate, sufficient to correct existing bicarbonate deficit, if bicarbonate status unknown, 1–2 mEq/kg IV.
- Dextrose \pm insulin: 1–2 mL/kg of 50% dextrose (diluted to 25%) IV or regular insulin 0.1–0.2 U/kg IV bolus followed by 1–2 g dextrose/unit insulin.
- Calcium gluconate: 0.5–1.0 mL/kg of 10% calcium gluconate IV over 10–15 minutes.
- Refractory hyperkalemia—dialysis.

Vomiting

- Reduce gastric acid production—famotidine (0.5 mg/kg IM, IV q24h) or omeprazole (0.5–1 mg/kg PO q24h [dogs]).
- Mucosal protectant—sucralfate (0.25–1 g PO q6–8h).
- Antiemetics—maropitant (1 mg/kg SC/IV q24h); or ondansetron (0.1–0.3 mg/kg IV q8–12h); or dolasetron (0.5 mg/kg SC, IV q24h).

PRECAUTIONS

Modify dosages of all drugs that require renal metabolism or elimination.



FOLLOW-UP

PATIENT MONITORING

Fluid, electrolyte, and acid-base balances; body weight; blood pressure; urine output; and clinical status; daily.

PREVENTION/AVOIDANCE

- Anticipate the potential for AKI in aged patients or those with systemic disease, sepsis, trauma, hemodynamic instability, receiving nephrotoxic drugs, multiple organ failure, or those undergoing prolonged anesthesia.
- Maintenance of hydration, mild saline volume expansion, and administration of mannitol may be preventive.
- Monitor urine production, SUN, and creatinine in high-risk patients.

POSSIBLE COMPLICATIONS

Seizures, coma, cardiac arrhythmias, hypertension, congestive heart failure,

(CONTINUED)

RENAL FAILURE, ACUTE

pulmonary edema, uremic pneumonitis, aspiration pneumonia, GI bleeding, hypovolemic shock, sepsis, cardiopulmonary arrest, and death.

EXPECTED COURSE AND PROGNOSIS

- Prognosis depends on underlying cause, extent of renal injury, concomitant disease or organ failure, age of patient and response to therapy.
- Survival rates average 50% overall for both cats and dogs, ranging from 20% for ethylene glycol toxicosis up to 80% for acute leptospirosis.
- Infectious and obstructive etiologies have a better prognosis for recovery than toxic causes.
- Non-oliguric AKI—typically milder than oliguric; recovery may occur over 2–6 weeks, but the prognosis remains guarded.
- Oliguric AKI—extensive kidney injury, difficult to manage, and has a poor prognosis for recovery without dialysis; recovery signaled by a sudden (and often excessive) polyuria and a sluggish and possibly incomplete return of renal function over 4–12 weeks; dialysis extends the potential for renal regeneration and repair.
- Anuric AKI—poor prognosis without dialysis; often incomplete recovery of renal function.

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

Leptospirosis—avoid contact with infective urine.

PREGNANCY/FERTILITY/BREEDING

A rare complication of pregnancy in animals; promoted by acute metritis, pyometra, and postpartum sepsis or hemorrhage.

SYNONYMS

Acute renal failure, acute tubular necrosis, acute uremia

SEE ALSO

- Azotemia and Uremia
- Hyperkalemia
- Hypertension, Systemic
- Leptospirosis
- Urerterolithiasis

ABBREVIATIONS

- ACEI = angiotensin converting enzyme inhibitors
- AKI = acute kidney injury

- CKD = chronic kidney disease

- CRI = constant rate infusion

- CT = computed tomography

- DIC = disseminated intravascular coagulation

- GI = gastrointestinal

- NSAID = nonsteroidal anti-inflammatory drug

- PCV = packed cell volume

- RBC = red blood cell

- SUN = serum urea nitrogen

- USG = urine specific gravity

- WBC = white blood cell

Suggested Reading

Cowgill LD, Langston C. Acute kidney injury. In: Bartges J, Polzin DJ, eds., *Nephrology and Urology of Small Animals*. Ames, IA: Wiley-Blackwell, 2011.

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**Client Education Handout
available online**

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RENAL FAILURE, CHRONIC



BASICS

DEFINITION

Kidney disease encompasses functional or structural lesions in one or both kidneys as detected by blood or urine tests, imaging studies, or kidney biopsy. Chronic kidney disease has been present for > 3 months. This definition includes all cases previously described by the terms renal insufficiency or renal failure, as well as less advanced forms of kidney disease. Patients are categorized into stages along a continuum of progressive CKD (IRIS CKD stages 1–4) based on two or more serum creatinine values obtained over several weeks when the patient is fasted and well hydrated. The IRIS system uses the term “kidney” rather than “renal” because it is more universally recognized by pet owners.

PATHOPHYSIOLOGY

More than approximately 75% reduction in renal function results in impaired urine-concentrating ability (leading to PU/PD) and retention of nitrogenous waste products of protein catabolism (leading to azotemia). More advanced CKD results in uremia. Decreased erythropoietin and calcitriol production by the kidneys results in hypoproliferative anemia and renal secondary hyperparathyroidism, respectively.

SYSTEMS AFFECTED

- Cardiovascular—hypertension; uremic pericarditis; cardiomegaly.
- Endocrine/Metabolic—renal secondary hyperparathyroidism, activation of the renin-angiotensin-aldosterone system, erythropoietin deficiency.
- Gastrointestinal—uremic stomatitis, uremic halitosis, enhanced dental calculus, nausea, vomiting, anorexia, gastrointestinal bleeding, diarrhea (may be hemorrhagic).
- Hemic/Lymphatic/Immune—anemia; hemorrhagic diathesis.
- Musculoskeletal—renal osteodystrophy; sarcopenia.
- Neuromuscular—seizures and other neurologic signs due to hypertension and/or uremia; muscle tremors, muscle wasting.
- Ophthalmic—retinal detachment, hemorrhage or edema due to hypertension.
- Reproductive—impaired reproductive capacity.
- Respiratory—uremic pneumonitis.
- Skin/Exocrine—calcinoses cutis.

GENETICS

• Inherited in the following breeds (mode of inheritance, known or suspected, indicated in parentheses):

- Abyssinian cats (autosomal dominant with incomplete penetrance)
- Persian cats (autosomal dominant)
- Bull terrier (autosomal dominant)
- Cairn terrier (autosomal recessive)

- German shepherd (autosomal dominant)
- Samoyed (X-linked dominant)
- English cocker spaniel (autosomal recessive)
- Renal dysplasia (mode of inheritance unresolved): shih tzu, Lhasa apso, golden retriever, Norwegian elkhound, chow chow, standard poodle, soft-coated Wheaten terrier, Alaskan malamute, miniature schnauzer, Dutch kooiker, and sporadically in many other breeds).

INCIDENCE/PREVALENCE

- 9 cases per 1,000 dogs examined and 16 cases per 1,000 cats examined.
- Prevalence increases with age—age > 15 years, reportedly 57 cases per 1,000 dogs examined and 153 cases per 1,000 cats examined.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog and cat

Breed Predilections

See “Genetics”

Mean Age and Range

Mean age at diagnosis is approximately 7 years in dogs and 9 years in cats. Animals of any age can be affected, but prevalence increases with increasing age.

Predominant Sex

None

General Comments

Clinical signs are related to the stage of CKD and the presence of complications such as proteinuria and hypertension. Cats and dogs with CKD stages 1 and 2 may be asymptomatic; overt clinical signs typically become apparent in stages 3 and 4. An animal with stable CKD (particularly stages 3 and 4) may decompensate, resulting in a uremic crisis.

Historical Findings

- PU/PD (less frequent in cats than dogs); litter box more wet; less color to urine
- Anorexia
- Lethargy
- Vomiting
- Weight loss
- Nocturia
- Constipation
- Diarrhea
- Acute blindness—due to hypertension
- Seizures or coma—late
- Cats may have ptalism and muscle weakness with cervical ventroflexion (because of hypokalemic myopathy).

Physical Examination Findings

- Small, irregular kidneys, or enlarged kidneys secondary to polycystic kidney disease or lymphoma
- Dehydration
- Cachexia

- Lethargy, weakness
- Mucous membrane pallor
- Oral ulceration
- Uremic halitosis
- Constipation
- Hypertensive retinopathy
- Renal osteodystrophy (may manifest as bone pain, particularly in the skull)
- Reduced body temperature

CAUSES

- Origin unknown in most cases due to late diagnosis.
- Include familial and congenital renal disease, nephrotoxins, hypercalcemia, hypokalemic nephropathy, glomerulopathies, amyloidosis, pyelonephritis, polycystic kidney disease, nephroliths, chronic urinary obstruction, drugs, lymphoma, leptospirosis (following acute renal failure), and FIP.

RISK FACTORS

Age, proteinuria, hypercalcemia, hypokalemia (cats), hypertension, urinary tract infection.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- See Polyuria and Polydipsia chapter for differential diagnosis.
- Azotemia—includes causes of prerenal and post-renal azotemia, acute renal failure, and hypoadrenocorticism.
 - Prerenal azotemia—azotemia with urine specific gravity > 1.030 in dogs and > 1.035 in cats; Rapid reduction in azotemia after correcting fluid volume/perfusion issues indicates prerenal azotemia. Prerenal azotemia commonly occurs concurrent with primary renal azotemia when gastrointestinal signs of uremia are present.
 - Post-renal azotemia—azotemia with obstruction or rupture of the excretory system; rapid correction of azotemia following elimination of obstruction or resolution of leakage from the urinary tract supports post-renal azotemia.
- Acute renal failure—differentiated by normal to large renal size, cylindruria, lack of indications of chronicity, (absence of small kidneys, hypoproliferative anemia and renal osteodystrophy), and a history of recent nephrotoxin exposure or hypotensive episode.
- Hypoadrenocorticism—characterized by hyponatremia and hyperkalemia with resting cortisol value < 1 µg/dL or decreased adrenal response to ACTH stimulation.

CBC/BIOCHEMISTRY/URINALYSIS

- Hypoproliferative anemia
- High BUN and creatinine
- Hyperphosphatemia
- Metabolic acidosis (normal or high anion gap)
- Hypokalemia or hyperkalemia
- Hypercalcemia or hypocalcemia

(CONTINUED)

- Urine specific gravity < 1.030 in dogs and < 1.035 in cats
- Proteinuria

OTHER LABORATORY TESTS

- Urinary protein:creatinine ratio to assess proteinuria
- Microalbuminuria assay to screen for early evidence of glomerular injury

IMAGING

- Abdominal radiographs may demonstrate small kidneys, or large kidneys secondary to polycystic kidney disease or lymphoma.
- Ultrasound demonstrates small kidneys and hyperechoic renal parenchyma with less apparent distinction between the cortex and medulla in some animals. Animals with lymphoma often have renomegaly with hypoechoic renal parenchyma.
- See also Congenital and Developmental Renal Diseases; Pyelonephritis; Nephrolithiasis; Hydronephrosis; Polycystic Kidney Disease.

DIAGNOSTIC PROCEDURES

- Blood pressure measurement to detect hypertension.
- Measurement of glomerular filtration rate may be useful for detection of loss of kidney function before the onset of azotemia.
- Renal biopsy is not indicated in patients with small kidneys; it may be indicated in proteinuric patients with normal to large kidneys.

PATHOLOGIC FINDINGS

- Gross—small kidneys with a lumpy or granular surface; renal capsule frequently adheres to the renal parenchyma.
- Histopathologic—variable. Patients with proteinuric stage 1 CKD may have changes consistent with various forms of glomerulopathy. Depending on the cause for kidney disease, complete evaluation of biopsy material from these patients may require light, immunofluorescent, and electron microscopy. In patients with more advanced CKD, nonspecific changes including interstitial fibrosis and foci of interstitial mononuclear cells; chronic generalized nephropathy or “end-stage” kidneys.
- Findings may be specific for diseases causing CKD in some patients with less advanced disease.

**TREATMENT****APPROPRIATE HEALTH CARE**

Patients with compensated CKD may be managed as outpatients; patients in uremic crisis should generally be managed as inpatients.

NURSING CARE

- Patients in uremic crisis—correct fluid and electrolyte deficits with intravenous fluid

therapy (e.g., lactated Ringer's solution). Generally provide 25% of calculated fluid deficit in the first hour. Thereafter, serially monitor perfusion (capillary refill time, pulse pressure, heart rate, and temperature of feet), blood pressure and urine output to assess adequacy of fluid therapy. If perfusion has not improved, additional fluid should cautiously be administered. Provide the remaining fluid deficit over the next 12–24 hours.; Avoid excessive fluid administration.

- Subcutaneous fluid therapy (q24–48h) may benefit patients (especially cats) with moderate-to-severe CKD. Continue therapy only if clinical improvement is noted.

ACTIVITY

Unrestricted

DIET

- Diets designed for dogs and cats with CKD delay the onset of uremic crisis and extend survival in dogs and cats with CKD stages 2–4. They are a standard of care for these patients.
- Foods containing reduced protein and n-3 fatty acids may be beneficial for proteinuric patients with stage 1 CKD.
- Important components of renal foods include: reduced protein, phosphorus, sodium and net acid content and supplementation of n-3 fatty acids and antioxidants.
- Free access to fresh water at all times.

CLIENT EDUCATION

- Dogs and many cats—CKD typically progresses to terminal kidney failure over months to years.
- CKD may not be progressive in some cats.
- Higher levels of proteinuria associated with shorter survival times. This effect may be mitigated by therapy for proteinuria.
- Heritability of familial renal diseases.

SURGICAL CONSIDERATIONS

- Avoid hypotension during anesthesia to prevent additional renal injury.
- Renal transplantation has been successfully performed in cats with CKD.

**MEDICATIONS****DRUG(S) OF CHOICE*****Uremic Crisis***

- Famotidine (0.5–1 mg/kg PO, IM, IV q12–24h) to minimize nausea and vomiting (primarily dogs).
- Antiemetics (maropitant 1 mg/kg q24h up to 5 days; or ondansetron 0.1–0.2 mg/kg slow IV q12h) to minimize vomiting and impaired appetite due to nausea.
- Potassium chloride in IV fluids or potassium gluconate PO (2–6 mEq/cat/day) as needed to correct hypokalemia.
- Sodium bicarbonate to correct metabolic acidosis (IV to raise blood pH > 7.1).

RENAL FAILURE, CHRONIC**Compensated CKD**

- Famotidine (dogs, 0.5–1 mg/kg PO q24h) to minimize uremic gastritis and possible nausea and inappetence.
- Antiemetic (maropitant) and potassium gluconate as above.
- Intestinal phosphate binders (e.g., aluminum carbonate, 30–100 mg/kg/day PO with meals) as needed to correct hyperphosphatemia (see Hyperparathyroidism, Renal Secondary).
- Calcitriol (start at 2 ng/kg PO q 24h and monitor effect on PTH and ionized calcium—avoid inducing hypercalcemia) (see Hyperparathyroidism, Renal Secondary).
- Darbepoetin (see Anemia of Chronic Kidney Disease).
- Amlodipine (dogs, 0.1–0.6 mg/kg PO q24h; cats, 0.625–1.25mg/cat PO q24h) or ACE inhibitors (e.g., enalapril or benazepril, 0.5 mg/kg PO q24h) as needed for hypertension. Amlodipine is more effective than ACE inhibitors in cats with CKD-induced hypertension. If refractory to monotherapy, consider combination of amlodipine and ACE inhibitor with frequent monitoring of blood pressure.
- ACE inhibitor (benazepril or enalapril) for proteinuria (start at 0.5 mg/kg PO q24 h; may increase to 1 mg/kg PO q12h if needed to reduce proteinuria).

CONTRAINDICATIONS

Avoid nephrotoxic drugs (aminoglycosides, cisplatin, amphotericin B) and corticosteroids.

PRECAUTIONS

- Drug dosage or dosing interval may need to be modified for some drugs eliminated by the kidneys.
- Use ACE inhibitors with caution; monitor for worsening of azotemia.
- Generally avoid NSAIDs.

POSSIBLE INTERACTIONS

Cimetidine or trimethoprim may cause artifactual increases in the serum creatinine concentration by reducing tubular secretion in dogs with CKD.

ALTERNATIVE DRUG(S)

- Metoclopramide (0.2–0.4 mg PO or SC q6–8h) can be used in addition to H₂-receptor antagonists to treat uremic vomiting.
- Ranitidine (0.5–2 mg/kg PO or IV q12h) or cimetidine (5 mg/kg q8–12h for dogs; 2.5–5 mg/kg q8–12h for cats) may be used instead of famotidine.
- Hemodialysis and renal transplantation are available at selected referral hospitals.

**FOLLOW-UP****PATIENT MONITORING**

- Dogs and cats with CKD—monitor at regular intervals; initially weekly for patients

RENAL FAILURE, CHRONIC

(CONTINUED)

receiving calcitriol or erythropoietin; every 1–3 months for stable patients with CKD stages 3 and 4 (minimum: chemistry profile and PCV).

- Proteinuric patients—monitor at least every 3–4 months (minimum: serum creatinine and urine protein:creatinine ratio).

PREVENTION/AVOIDANCE

- Do not breed animals with familial renal disease.
- Include urinalysis and serum creatinine in yearly examination for older dogs and cats.

POSSIBLE COMPLICATIONS

- Systemic hypertension
- Uremia
- Anemia
- Urinary tract infection
- Nephrolithiasis and uretrolithiasis
- Exuberant dental calculus

EXPECTED COURSE AND PROGNOSIS

- Short-term—depends on severity.
- Long-term—guarded to poor in dogs (CKD tends to be progressive over months to years); poor to good in cats (CKD does not progress in some cats).



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Hyperthyroidism in cats
- Urinary tract infection

- Systemic hypertension
- Nephrolithiasis and ureterolithiasis

AGE-RELATED FACTORS

Renal function may decrease with aging.

ZOONOTIC POTENTIAL

Leptospirosis

PREGNANCY/FERTILITY/BREEDING

Patients with mild CKD may maintain pregnancy; those with moderate-to-severe disease may be infertile or have spontaneous abortions; breeding of female patients not recommended.

SYNOMYS

- Chronic kidney failure
- Chronic renal disease
- Chronic renal failure

SEE ALSO

- Anemia of Chronic Kidney Disease
- Azotemia and Uremia
- Congenital and Developmental Renal Diseases
- Hydronephrosis
- Hyperparathyroidism, Renal Secondary
- Hypertension, Systemic
- Nephrolithiasis
- Polycystic Kidney Disease
- Polyuria and Polydipsia
- Proteinuria
- Pyelonephritis
- Renal Failure, Acute
- Urinary Tract Obstruction

ABBREVIATIONS

- ACE = angiotensin-converting enzyme
- ACTH = adrenocorticotropic hormone
- CKD = chronic kidney disease
- FIP = feline infectious peritonitis
- IRIS = International Renal Interest Society
- NSAID = nonsteroidal anti-inflammatory drug
- PCV = packed cell volume
- PU/PD = polyuria/polydipsia

INTERNET RESOURCES

www.iris-kidney.com.

Suggested Reading

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Author David J. Polzin

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Client Education Handout
available online

RENAL TUBULAR ACIDOSIS



BASICS

OVERVIEW

- A syndrome characterized by hyperchloremic metabolic acidosis due either to decreased bicarbonate reabsorption from the proximal renal tubule (proximal or type 2 RTA) or decreased hydrogen ion secretion in the distal tubule (distal, classic or type 1 RTA) in patients with normal or near normal glomerular filtration rate and absence of diarrhea.
- Aldosterone deficiency or resistance can cause type 4 distal RTA leading to hyperkalemia. Proximal RTA has not been documented as an isolated entity in dogs but has been observed as part of Fanconi syndrome.
- The following discussion is limited to classic distal RTA. In distal RTA, the urine cannot be maximally acidified despite moderately to markedly decreased plasma bicarbonate concentration as a consequence of impaired hydrogen secretion in the collecting ducts. Urine pH typically is above 6.0 (normally urine pH should be 4.5–5.0 in the presence of systemic acidosis).

SIGNALMENT

- Reported in 8 dogs and 4 cats • No apparent breed or sex predilection • Age range at time of diagnosis, 1–12 years

SIGNS

- Associated with acidemia and may include lethargy, muscle weakness (may be related to hypokalemia), inappetence, nausea, weight loss, stunted growth, and neurologic signs.
- Other signs depend on the associated diseases (e.g., pyelonephritis). • Panting.
- Polyuria and polydipsia (usually associated with hypokalemia or calcuiresis). • Vomiting.
- Hematuria and dysuria (secondary to urolithiasis). • Osteomalacia associated with chronic metabolic acidosis (not yet reported in dogs and cats).

CAUSES & RISK FACTORS

- May be primary (i.e., inherited), or secondary to hypercalcuria, toxins, drugs (e.g., amphotericin B), altered calcium metabolism causing nephrocalcinosis (e.g., hypervitaminosis D, primary hyperparathyroidism), autoimmune (e.g., immune-mediated hemolytic anemia, systemic lupus erythematosus, renal transplant rejection), hypergammaglobulinemic disorders (e.g., multiple myeloma, systemic lupus erythematosus), and tubulointerstitial nephropathies. • In cats, distal RTA has been associated with pyelonephritis (2 cases), hepatic lipidosis (1 case), and idiopathic with secondary hyperaldosteronism (1 case). • In

dogs, clinical cases were idiopathic or associated with immune-mediated hemolytic anemia (3 cases), leptospirosis (1 case), or experimentally-induced renal ischemia.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Consider other causes of hyperchloremic (normal anion gap) metabolic acidosis (e.g., diarrhea, carbonic anhydrase inhibitors, ammonium chloride, cationic amino acids, post-hypocapnic metabolic acidosis, dilutional acidosis, hypoadrenocorticism). Small bowel diarrhea is the most important differential diagnosis.

CBC/BIOCHEMISTRY/URINALYSIS

- Results vary depending on associated diseases. • Hypokalemia (due to increased renal excretion) in some animals; may be severe enough to cause muscle weakness.
- Alkaline urine ($\text{pH} > 6.0$); rule out urease-positive urinary tract infection (e.g., *Staphylococcus aureus*, *Proteus* spp.) as a cause of alkaline urine.

OTHER LABORATORY TESTS

Evaluation of blood gases and serum electrolytes indicates hyperchloremic (normal anion gap) metabolic acidosis. Urine pH is > 6.0 in distal RTA versus < 5.5 in proximal RTA.

IMAGING

Radiography—may detect uroliths or osteomalacia (uncommon).

DIAGNOSTIC PROCEDURES

- The key diagnostic feature is normal anion gap metabolic acidosis accompanied by an inappropriately alkaline urine pH (> 6.0).
- Ammonium chloride tolerance test—administer 200 mg/kg PO in dogs; measure urine pH before and at hourly intervals for 5 hours; empty the bladder hourly. Urine pH in normal dogs decreases to < 5.5 within 4 hours. Avoid this test if severe acidosis is present.
- Type 1 and 2 RTA can be differentiated based on response to NaHCO_3 infused at 0.5–1.0 mEq/kg/h. Fractional excretion of bicarbonate will increase markedly in type 2 RTA.



TREATMENT

- Individualize depending on the nature and severity of associated conditions. • Typically, less bicarbonate is needed to resolve metabolic acidosis associated with distal RTA than is

needed to resolve acidosis associated with proximal RTA. • Hypokalemia may resolve with bicarbonate or citrate administration alone, or additional potassium supplementation may be required.



MEDICATIONS

DRUG(S)

- Potassium citrate alone or in combination with sodium citrate (depending on the serum potassium concentration) at a total dosage of 1–5 mEq/kg/day PO, divided into two doses, or sodium bicarbonate at 10–50 mg/kg q8–12h PO (1–3 mEq/kg/day).
- Potassium supplementation—potassium gluconate; cats, 2–8 mEq/day divided q12h PO; dogs (depending on body size), 2–44 mEq/day divided q12h PO, if required.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Citrate should be avoided in patients with renal failure receiving aluminum hydroxide because citrate increases intestinal permeability and can lead to excessive aluminum absorption.



FOLLOW-UP

- Serial blood gas analyses (e.g., every 3–5 days) until acid-base status has normalized.
- Monitor serum electrolytes, especially potassium, as needed.
- Long-term prognosis depends on the nature and severity of associated conditions; may be reasonably good in patients without other diseases, but little information exists on the long-term course of this disease in dogs and cats.



MISCELLANEOUS

SEE ALSO

- Acidosis, Metabolic • Fanconi Syndrome
- Hypokalemia

ABBREVIATIONS

- NaHCO_3 = sodium bicarbonate • RTA = renal tubular acidosis

Suggested Reading

Riordan L, Schaer M. Renal tubular acidosis. Comp Cont Ed Pract Vet 2005, 27(7):513–529.

Authors Joao Felipe de Brito Galvao and Stephen P. DiBartola

Consulting Editor Carl A. Osborne

RENOMEGLY



BASICS

DEFINITION

One or both kidneys are abnormally large as detected by abdominal palpation or diagnostic imaging.

PATHOPHYSIOLOGY

The kidneys may become abnormally large because of abnormal cellular infiltration (e.g., inflammation, infection, and neoplasia), urinary tract obstruction, acute tubular necrosis, or development of renal cysts or pseudocysts.

SYSTEMS AFFECTED

- Endocrine/Metabolic—metabolic acidosis due to decreased elimination of acid by kidneys and inability to reclaim bicarbonate
- Gastrointestinal—inappetence, vomiting, diarrhea, or melena due to gastrointestinal irritation or ulceration in patients with uremia
- Hemic/Lymphatic/Immune—anemia due to blood loss or decreased red blood cell survival in patients with uremia; increased susceptibility to infections due to immune dysfunction in patients with uremia, and impaired production of erythropoietin
- Hepatobiliary—bilateral renomegaly may occur in patients with portosystemic shunts.
- Nervous—depression and lethargy associated with effect of uremic toxins on central nervous system.
- Renal/Urologic—one or both kidneys are abnormally large.
- Respiratory—tachypnea or respiratory distress due to uremic pneumonitis or compensatory response for metabolic acidosis

SIGNALMENT

- Cat and dog
- Polycystic kidney disease, a cause of renomegaly, occurs in several breeds of dogs (bulldog, cairn terrier, and West Highland white terrier) and cats (Persian, longhaired cats, others)
- Mode of inheritance is autosomal dominant in Bulldogs and Persian cats and autosomal recessive in cairn terriers and West Highland white terriers.

SIGNS

Historical Findings

- May be asymptomatic, especially if only one kidney is affected
- Lethargy
- Loss of appetite
- Weight loss
- Vomiting
- Diarrhea
- Polyuria and polydipsia
- Discolored urine
- Abdominal enlargement
- Lameness (rarely) because of hypertrophic osteopathy associated with renal neoplasia

Physical Examination Findings

- Abdominal mass
- Abdominal pain
- One or both kidneys palpably large
- Abdominal enlargement
- One kidney enlarged; one kidney abnormally small
- Dehydration
- Pale mucous membranes
- Oral ulcers
- Uremic halitosis

CAUSES & RISK FACTORS

Developmental/Acquired Disorders

- Hydronephrosis—can cause unilateral or bilateral renomegaly in dogs and cats; develops secondary to ureteral obstruction (e.g., urolithiasis, ureteral strictures, and neoplasia at trigone of urinary bladder) and ectopic ureters.
- Polycystic kidney disease—causes bilateral renomegaly in cats and often leads to chronic kidney disease; more common in Persians and domestic longhair cats.
- Hematoma—occurs secondarily to trauma; infrequent cause of renomegaly.
- Compensatory hypertrophy—causes unilateral renomegaly and occurs secondary to abnormality of the other kidney (e.g., renal hypoplasia, renal dysplasia, previous damage or nephrectomy).
- Perinephric pseudocyst—causes apparent unilateral or bilateral enlargement. Kidney size may be normal, but the subcapsular fluid accumulation makes the kidney appear large on palpation and radiography.

Metabolic

- Portosystemic shunt, acromegaly
- Males have larger kidneys than females

Neoplastic

- Lymphoma—most often occurs in cats and causes bilateral renomegaly; some patients have unilateral renomegaly.
- Renal carcinoma—most common renal tumor of dogs; often causes unilateral renomegaly; very malignant and rapidly metastatic to distant sites such as lungs.
- Nephroblastoma—also called Wilms' tumor; a congenital renal tumor that affects young dogs, although it may not be diagnosed until the patient is much older; biologic behavior varies; usually unilateral.
- Sarcomas—usually cause unilateral renomegaly and behave malignantly.
- Cystadenocarcinoma—bilateral renal tumor that occurs in German shepherd dogs; often associated with skin lesions (i.e., nodular dermatofibrosis).

Infectious/Inflammatory

- Amyloidosis.
- Leptospirosis (dogs).
- Feline infectious peritonitis.
- Feline leukemia virus infection predisposes cats to development of renal lymphoma.

- Acute kidney injury.
- Renal abscess—localized abscess within renal parenchyma usually causes unilateral renomegaly in dogs and cats.

Toxic

- Ethylene glycol toxicosis—can cause bilateral renomegaly secondary to renal tubular swelling and renal infiltration by calcium oxalate crystals.
- Other toxins that cause acute renal injury (e.g., grapes/raisins, lilies).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Must distinguish from other abdominal masses.
- Confirmation may require diagnostic imaging procedures or exploratory celiotomy.

CBC/BIOCHEMISTRY/URINALYSIS

- Azotemia, hyperphosphatemia, and inappropriately low urine-concentrating capacity.
- Leukocytosis—infectious, inflammatory, and neoplastic causes of renomegaly.
- Nonregenerative anemia—chronic kidney disease or inflammatory disorders.
- Hyperglobulinemia—infectious or inflammatory disorders (e.g., feline infectious peritonitis).
- Hematuria and proteinuria—renal neoplasia.
- Polycythemia and extreme leukocytosis rarely accompany some renal neoplasms.
- Neoplastic cells rarely observed in urine of patients with renal neoplasia.

OTHER LABORATORY TESTS

- Test cats for feline leukemia virus infection if renal lymphoma is suspected.
- Perform serum protein electrophoresis to distinguish between polyclonal and monoclonal hyperglobulinemia.
- Evaluate paired titers for *Leptospira* spp. 2–3 weeks apart in dogs with suspected leptospirosis.

IMAGING

Radiographic Findings

- Survey abdominal radiographs indicated to confirm renomegaly and identify potential causes of ureteral obstruction (e.g., radiopaque ureteroliths).
- Enlarged kidneys on the ventrodorsal view are > 3 or 3.5 times the length of the second lumbar vertebra in cats or dogs, respectively.
- Excretory urography or CT to confirm presence of renomegaly, hydronephrosis, and space-occupying masses of the kidneys.
- Antegrade pyelography may be needed to exclude ureteral obstruction in some cats.
- Thoracic radiography indicated to detect metastases in patients with renal neoplasia.

(CONTINUED)

RENOMEGLY***Ultrasonographic Findings***

- Helps distinguish between causes of renomegaly including polycystic kidney disease, perinephric pseudocysts, hydronephrosis, neoplasia, abscess, and subcapsular hematoma.
- Acute inflammation (e.g., leptospirosis, ethylene glycol toxicosis) may be associated with increased cortical echogenicity, perinephric effusion, or a medullary band of increased echogenicity.

DIAGNOSTIC PROCEDURES

- Cytologic examination of fine-needle aspirate can confirm presence of renal cyst, abscess, and/or neoplasia (lymphoma). Due to potential for “seeding” of neoplastic cells in the abdominal wall, fine-needle aspiration should be avoided if other renal tumors (e.g., renal carcinoma) are suspected.
- If no definitive diagnosis is made by cytologic evaluation of renal aspirates, renal biopsy may be indicated.

**TREATMENT**

- Diagnose and treat underlying cause of renomegaly.
- Usually treat as an outpatient unless dehydration or decompensated renal failure exist.
- Therapeutic renal diet is indicated to prolong survival time for dogs and cats with chronic kidney disease when serum creatinine exceeds 2 mg/dL.
- If patient is healthy otherwise, feed normal diet and allow normal exercise.

- If the patient cannot maintain hydration, administer balanced electrolyte solution either intravenously or subcutaneously.

- If the patient has dehydration or continuing fluid losses such as vomiting or diarrhea, administer fluids intravenously to correct hydration deficits, maintain daily fluid requirements, and replace ongoing losses.

**MEDICATIONS****DRUG(S)**

Vary with the cause

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Avoid nephrotoxic drugs.

**FOLLOW-UP****PATIENT MONITORING**

- Perform physical examination and weigh patient to assess hydration status.
- Other tests (CBC, serum chemistries, urinalysis, blood pressure measurements) are indicated depending on the underlying cause and presence of other conditions (e.g., anemia, azotemia, hypertension, proteinuria).

POSSIBLE COMPLICATIONS

- Chronic kidney disease, depending on underlying cause of renomegaly.

- Paraneoplastic syndromes associated with renal tumors that produce hormone-like substances.

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

Leptospirosis can be spread by contact with infected urine.

SEE ALSO

- Ethylene Glycol Toxicosis
- Feline Infectious Peritonitis
- Hydronephrosis
- Leptospirosis
- Lymphoma—Cats
- Polycystic Kidney Disease
- Urinary Tract Obstruction
- Perirenal Pseudocysts

Suggested Reading

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Authors Cathy E. Langston and Allyson C. Berent

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REOVIRUS INFECTIONS



BASICS

OVERVIEW

- Respiratory enteric orphan virus (reovirus)—genus in the family Reovirus; non-enveloped, double-stranded RNA virus; isolated from respiratory and enteric tracts; not associated with any known disease (hence orphan).
- Ubiquitous in geographic distribution and host range, virtually every species of mammal, including humans.
- Virus—infests mature epithelial cells on luminal tips of the intestinal villi; causes cellular destruction, resulting in villous atrophy (similar to rotavirus and coronavirus).
- Loss of absorptive capability and loss of brush border enzymes (e.g., disaccharidases) leads to osmotic diarrhea.

SIGNALMENT

Dogs and cats

SIGNS

Dogs

- Conjunctivitis
- Rhinitis
- Tracheobronchitis—minor role
- Pneumonia
- Diarrhea
- Encephalitis—rare

Cats

- Generally mild disease
- Respiratory illness
- Conjunctivitis
- Gingivitis
- Ataxia
- Diarrhea

CAUSES & RISK FACTORS

- Predominantly excreted from respiratory and digestive tract; acquired by inhalation and oral ingestion.
- Infection is common; specific disease has not been reproduced.
- Other viral pathogens— infections observed repeatedly; speculated that reovirus may have an immunosuppressive effect that aggravates such infections.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Canine viral enteritis—canine parvovirus; canine coronavirus; canine astrovirus; canine calicivirus; canine herpesvirus; canine distemper virus; canine rotavirus.
- Canine infectious tracheobronchitis—canine parainfluenza; *Bordetella bronchiseptica*; *Mycoplasma*; canine adenovirus types 1 and 2; canine herpesvirus; canine distemper virus; canine influenza virus; canine respiratory coronavirus.
- Feline upper respiratory disease—feline rhinotracheitis virus; feline calicivirus; *Chlamydia*; *Mycoplasma*; bacterial infection.

CBC/BIOCHEMISTRY/URINALYSIS

Non-contributory

OTHER LABORATORY TESTS

- Virus isolation—cytopathic effect slow to develop.
- Histopathology—large intracytoplasmic inclusion body EM.
- Immunohistochemistry.
- RT-PCR.
- EM.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Doubtful that reovirus is an important pathogen.
- No vaccines developed.
- Other control measures ignored.



MEDICATIONS

DRUG(S)

N/A

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

N/A



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Infection can spread among individuals of the same or different species.
- The role (if any) that animals serve as a reservoir for virus or as a possible source of human infection is unknown.
- Humans—by early childhood, the vast majority demonstrate serologic evidence of past reovirus infection; difficult to link to disease; majority of infections must be asymptomatic or blend imperceptibly with minor respiratory and gastrointestinal illness of infancy and early childhood.
- Candidate virus for oncolytic therapy of cancer (e.g., malignant glioma).

ABBREVIATIONS

- EM = electron microscopy
- RT-PCR = reverse transcription polymerase chain reaction

Suggested Reading

Decaro N, Campolo M, Desario C, et al. Virological and molecular characterization of a mammalian orthoreovirus type 3 strain isolated from a dog in Italy. *Vet Microbiology* 2005; 109:19–27.

Hwang CC, Umeki S, Kubo, M, et al. Oncolytic reovirus in canine mast cell tumor. *PLoS One* 2013; 8:e73555.

Saif LJ. Reoviridae. In: MacLachlan NJ, Dubovi EJ, eds., *Fenner's Veterinary Virology*, 4th ed. London: Elsevier, 2011, pp. 275–291.

Author J. Paul Woods

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RESPIRATORY PARASITES



BASICS

DEFINITION

Helminths, arthropods, and protozoa that reside in the respiratory tract or pulmonary vessels of dogs and cats.

PATHOPHYSIOLOGY

Infestation with parasites causes rhinitis, bronchitis, pneumonitis, or arteritis, depending on the location of the organism within the respiratory system. Eosinophilic inflammation usually results from invasion of the parasite.

SYSTEMS AFFECTED

- Respiratory.
- Cardiovascular.
- Hepatic—with hepatopulmonary migration of some parasites (*Toxocara* spp.).
- Neurologic—with migration of parasites to the brain (*Cuterebra*) or cerebral hemorrhage (*Angiostrongylus*).

GENETICS

There is no genetic basis.

INCIDENCE/PREVALENCE

Depends on parasite

GEOGRAPHIC DISTRIBUTION

- *Pneumonyssoides caninum*, *Aelurostrongylus abstrusus*, *Linguatula serrata*, *Oslerus (Filaroides) osleri*, *Crenosoma vulpis*, *Eucoleus (Capillaria) aerophilus*, *Toxoplasma gondii*, *Toxocara* spp.—worldwide.
- *Eucoleus boehmi*, *Cuterebra* spp., *Filaroides hirthi*, *Paragonimus kellicotti*—primarily North America.
- *Andersonstrongylus (Filaroides) milksi*—North America; Europe.
- *Angiostrongylus vasorum*—various countries of Europe, Africa, South America, North America.

SIGNALMENT

Species

Dog and cat

SIGNS

General Comments

- Four basic categories—upper airway (nasal cavity and sinuses), lower respiratory (trachea and bronchi), pulmonary parenchyma, and vascular; based on location and lifestyle of parasite.
- Often insidious and chronic, with few clinical signs.
- Respiratory compromise often not severe.

Historical Findings

- Upper respiratory—sneezing; nasal discharge (serous, sanguinous); reverse sneezing; nasal irritation or rubbing; neurologic signs with *Cuterebra* spp.
- Lower respiratory and parenchyma—may have no clinical signs, variable coughing, tachypnea, or altered respiratory pattern.
- Vascular—can have weight loss, lethargy, coughing, exercise intolerance. Acute onset of respiratory distress if embolization or hemorrhage occurs.

Physical Examination Findings

- Upper respiratory—similar to historical findings; variable.
- Lower respiratory and parenchyma—cough elicited on tracheal palpation; occasionally harsh lung sounds.
- Vascular—may present with signs of pulmonary disease, right-sided heart failure, anemia, coagulopathy, neurologic signs.

CAUSES

- Upper respiratory (nasal cavity and sinuses)—*Pneumonyssoides caninum*, *Eucoleus boehmi*, *Linguatula serrata*, *Cuterebra* spp.
- Lower airway (trachea and bronchi)—dogs and cats: *Eucoleus (Capillaria) aerophilus* (rare in cats); dogs: *Oslerus osleri*, *Filaroides hirthi*, *Andersonstrongylus milksi*, *Crenosoma vulpis*, *Cuterebra* spp. in the trachea.
- Pulmonary parenchyma—dogs and cats: *Paragonimus kellicotti*, *Toxoplasma gondii*; dogs: *Filaroides hirthi*, *Andersonstrongylus milksi*; cats: *Aelurostrongylus abstrusus*, *Troglotrypanosoma brevior*, *Troglotrypanosoma subcrenatus*.
- Vascular—dogs and cats: *Dirofilaria immitis*, larval migration of *Toxocara canis* and *cati*; dogs: *Angiostrongylus vasorum*.

RISK FACTORS

- Depends on the specific parasite—some have intermediate or paratenic hosts that must be ingested by the definitive host, putting hunting or scavenging animals at higher risk.
- *Crenosoma vulpis*—snails.
- *Paragonimus kellicotti*—snails; crabs; shellfish.
- *Aelurostrongylus abstrusus*—snails and slugs; transport hosts: rodents, frogs, lizards, birds.
- *Linguatula serrata*—ingestion of sheep offal.
- *Toxoplasma gondii*—ingestion of infected small mammals and birds or less commonly by ingesting sporulated oocysts in soil or water.
- Multi-animal households with unhygienic living conditions—allows fecal-oral or direct-contact transmission.
- *Angiostrongylus vasorum*—gastropod (slug/snail) or frogs are the intermediate host. Frogs can also serve as paratenic hosts.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Upper respiratory—other causes of epistaxis, rhinitis, or sinusitis (see specific chapters).
- Lower respiratory—acute bronchitis (non-parasitic); chronic bronchitis; infectious tracheobronchitis.
- Pulmonary parenchyma—eosinophilic lung disease; bronchopneumonia; granulomatous pneumonia; pulmonary granulomatosis.
- Vascular—other causes of coagulopathy, right-sided heart failure, or pulmonary artery disease.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—variable; may note eosinophilia, basophilia, neutrophilia, and monocytosis;

can see anemia with *Angiostrongylus vasorum*.

- Biochemistry—often normal; high liver enzyme activity with some parasites during early stages as a result of hepatic migration if burden is substantial.
- Urinalysis—normal.

OTHER LABORATORY TESTS

Coagulopathy with *Angiostrongylus vasorum* or severe cases of heartworm disease (DIC).

IMAGING

Thoracic Radiography

- Often nonspecific findings—generalized interstitial pattern; peribronchiolar infiltrates, nodular to alveolar pattern.
- *Oslerus*—soft tissue nodular densities within the trachea at the level of the carina.
- *Paragonimus*—can see bullae, cystic lesions or pneumothorax due to bulla or cyst rupture.
- *Dirofilaria*—right-sided heart enlargement, tortuous and truncated pulmonary arteries, pulmonary infiltrates (dogs). Few cardiac changes in cats, large pulmonary arteries possible.

DIAGNOSTIC PROCEDURES

Sputum examination

May reveal eggs or larvae (L-1).

Fecal Examination

- Multiple examinations often necessary; negative results do not rule out infection.
- Direct fecal smear: *Angiostrongylus* (larvae).
- Standard fecal flotation: *Eucoleus aerophilus* (eggs), *Eucoleus boehmi* (eggs).
- Zinc sulfate centrifugation: *Aelurostrongylus* (larvae), *Oslerus osleri*, *Andersonstrongylus milksi*, *Filaroides hirthi* (larvae, larvated eggs), *Angiostrongylus vasorum* (larvae).
- Baermann: *Aelurostrongylus* (larvae), *Oslerus osleri*, *Andersonstrongylus milksi*, *Filaroides hirthi* (larvae, eggs), *Crenosoma* (larvae, larvated eggs), *Angiostrongylus* (larvae).
- Sedimentation: *Paragonimus* (eggs).

Rhinoscopy

- Upper respiratory—examination via retrograde pharyngoscopy or rhinoscopy with antegrade flushing of anesthetic gas can allow visualization of nasal mites; retrograde nasal lavage and cytologic examination of fluid can be helpful.
- *Eucoleus boehmi*—histopathology can reveal eggs deep within the epithelium.
- *Linguatula serrata*—diagnosis made by observation of eggs in nasal secretions or around the nares.

Bronchoscopy

- Lower respiratory and parenchyma—rarely can see tracheal and bronchial parasites and parasitic nodules; occasionally can be removed for definitive identification.
- Tracheal wash or bronchoalveolar lavage can allow identification of larvae (*Oslerus osleri*, *Aelurostrongylus*, *Crenosoma*, *Filaroides hirthi*, *Andersonstrongylus milksi*, *Angiostrongylus*); eggs (*Eucoleus aerophilus*, *Paragonimus*); organisms (*Toxoplasma*).
- *Oslerus osleri*—can also be diagnosed by brushings or histopathology of nodules at the carina.

RESPIRATORY PARASITES

(CONTINUED)

PATHOLOGIC FINDINGS

- Upper respiratory—may find nasal mites or worms in epithelium of sinuses and nasal cavity.
- Lower respiratory and parenchyma—can see pulmonary nodules containing parasites throughout the parenchyma or within bronchi.
- Vascular—changes include thrombi and intimal proliferation of the vascular walls.
- *Cuterebra* spp. can be found in brain sections when associated with neurologic signs.



TREATMENT

APPROPRIATE HEALTH CARE

Most commonly outpatient—upper and lower respiratory parasites; may need repeated examinations to monitor response.

NURSING CARE

Supportive care and oxygen therapy can be needed depending on the severity of disease.

ACTIVITY

Strict cage rest if severe pulmonary dysfunction occurs with upper or lower respiratory parasites; also with vascular parasite infection or bullous lung disease associated with *Paragonimus*.

DIET

No special restrictions

CLIENT EDUCATION

- Explain that treatment duration and response depend on the type of parasite.
- Warn client of the risk of recurrence in animals that maintain lifestyles conducive to transmission of the parasites (e.g., hunting, sporting dogs, multidog households, outdoor cats).

SURGICAL CONSIDERATIONS

Ruptured *Paragonimus* cysts generally require surgical excision.

R



MEDICATIONS

DRUG(S) OF CHOICE

- Anthelmintics—few studies confirm efficacy; most data anecdotal. For treatment of *Dirofilaria*, see chapters on Heartworm Disease.
- *Pneumonyssoides caninum*—selamectin at 6–24 mg/kg applied every 2 weeks for three treatments, milbemycin oxime at 0.5–1 mg/kg PO weekly for 3 weeks, ivermectin at 200 µg/kg SC or PO for two treatments 3 weeks apart; note: not labeled for use in dogs at this dosage.
- *Cuterebra*—ivermectin at 300 µg/kg SC or PO every other day for three doses combined with a tapering dose of corticosteroids.
- *Linguatula serrata*—physical removal of organisms from the sinuses.
- *Eucoleus aerophilus*, *Eucoleus boehmi*—ivermectin 200 µg/kg PO once;

fenbendazole 25–50 mg/kg q12h for 10–14 days, very difficult to clear.

- *Oslerus osleri*—efficacious therapy not fully determined. Consider ivermectin at 400 µg/kg SC or PO q3 weeks for four doses.
- *Crenosoma vulpis*—levamisole 7.5 mg/kg SC q48h (two doses); fenbendazole at 50 mg/kg PO q24h for 7 days; milbemycin oxime 0.5 mg/kg PO once.
- *Aelurostrongylus abstrusus*—fenbendazole at 25–50 mg/kg PO q24h for 10 days; ivermectin 400 µg/kg SC, selamectin spot-on formula 45 mg/cat, two doses, 23 days apart.
- *Filaroides hirthi*, *Andersonstrongylus milksi*—fenbendazole 50 mg/kg PO q24h for 14 days; albendazole 50 mg/kg PO q12h for 5 days, repeat in 3 weeks.
- *Paragonimus kellicotti*—praziquantel at 25 mg/kg PO, SC q8h for 3 days; fenbendazole at 25–50 mg/kg PO q12h for 14 days.
- *Toxoplasma*—clindamycin 12.5 mg/kg PO q12h for 28 days.
- *Angiostrongylus vasorum*—fenbendazole at 20–50 mg/kg PO q24h for 5–21 days; milbemycin oxime 0.5 mg/kg PO weekly for 4 weeks; single topical application of moxidectin at 2.5 mL/kg.
- *Toxocara* spp. larval migration—fenbendazole 50 mg/kg PO q24h for 10 days.
- Anti-inflammatory agents—recommendations for concurrent use of steroids vary.

CONTRAINdications

Ivermectin—not labeled for use in dogs or cats other than for heartworm prophylaxis; contraindicated at dosages > 100 µg/kg in breeds with known sensitivity (collies, collie breeds, and Australian shepherds).

PRECAUTIONS

None

ALTERNATIVE DRUGS

None



FOLLOW-UP

PATIENT MONITORING

• Serial fecal Baermann larval extractions or examination for eggs—some anthelmintics can suppress egg or larval production in some species and intermittent shedding reduces value of repeated fecal exams.

- Resolution of clinical signs—suggests response to treatment; does not indicate complete clearance of parasites.
- Peripheral eosinophilia, if noted initially, may subside with treatment.
- Repeat bronchoscopic examination—can help assess efficacy of treatment for *Oslerus osleri*.

PREVENTION/AVOIDANCE

- Avoid activity that predisposes to infestations (often not practical).
- Avoid contact with wildlife reservoirs (especially wild canids and felids).
- Consider prophylactic treatment for heartworm.

POSSIBLE COMPLICATIONS

- Chronic pulmonary damage—possible with persistent and heavy lower respiratory parasite burdens.
- Infestations generally not fatal; however, severe pulmonary damage can result with some species; *Cuterebra* spp. and *Angiostrongylus* can cause fatal neurologic complications.
- *Pneumonyssoides caninum* has been associated with gastric dilation and volvulus.

EXPECTED COURSE AND PROGNOSIS

- With aggressive management—prognosis usually fair to excellent; variable.
- Return to performance—depends on chronicity of disease and level of chronic pulmonary damage by lower respiratory parasites.
- Recurrence possible.



MISCELLANEOUS

ZONOTIC POTENTIAL

None

SYNOMYMS

- Lungworm infestation—*Aelurostrongylus*, *Eucoleus (Capillaria) aerophilus*, *Crenosoma*, *Oslerus osleri*, *Filaroides hirthi*, *Andersonstrongylus milksi*.
- Nasal mite infestation—*Pneumonyssoides caninum*, *Pneumonyssus caninum*.
- French heartworm—*Angiostrongylus vasorum*.

SEE ALSO

- Heartworm Disease—Cats
- Heartworm Disease—Dogs
- Pneumonia, Eosinophilic

INTERNET RESOURCES

- Bowman DD. Respiratory System Parasites of the Dog and Cat (Part I): Nasal Mucosa and Sinuses, and Respiratory Parenchyma: http://www.ivis.org/advances/Parasit_Bowman/ddb_resp/ivis.pdf.
- Bowman DD. Respiratory System Parasites of the Dog and Cat (Part II): Trachea and Bronchi, and Pulmonary Vessels: http://www.ivis.org/advances/Parasit_Bowman/ddb_resp2/ivis.pdf.

Suggested Reading

- Lacorgia L, Gaser R, Anderson BA, Beveridge I. Comparison of bronchoalveolar lavage fluid examination and other diagnostic techniques with the Baermann technique for detection of naturally occurring *Aelurostrongylus abstrusus* infection in cats. J Am Vet Med Assoc 2009, 235(1):43–49.
- Marks SL, Moore MP, Rishniw M. *Pneumonyssus caninum*: The canine nasal mite. Compend Contin Educ Pract Vet 1994, 16:577–582.

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Client Education Handout
available online

RETAINED PLACENTA



BASICS

OVERVIEW

- Dogs—placenta retained beyond the immediate postpartum period; placentas usually passed within 15 minutes of birth of a puppy; may develop acute metritis secondary to retained placenta.
- Cats—may retain placentas for days without signs of illness.
- Extremely uncommon.

SIGNALMENT

- Dog—rare, most common in toy dog breeds
- Cat—rare

SIGNS

Historical Findings

- Recent parturition.
- Continued vulvar discharge of lochia.
- Owner may note number of placentas passed, although this information is frequently unreliable.

Physical Examination Findings

- Green lochia vulvar discharge
- Palpation of firm mass in uterus—not always possible
- Concurrent clinical signs of postpartum metritis

CAUSES & RISK FACTORS

- Toy breed
- Large litter size
- Dystocia



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Postpartum metritis—physical examination and vaginal cytologic examination show no signs of infection with uncomplicated retained placenta; metritis may develop concurrently.
- Retained fetus—differentiated by radiography or ultrasonography.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal when uncomplicated

OTHER LABORATORY TESTS

Vaginal cytologic examination—parabasal epithelial cells; may note erythrocytes; biliverdin clumps.

IMAGING

Ultrasonography—echogenic but non-fetal mass within the uterus.

DIAGNOSTIC PROCEDURES

Celiotomy or hysterotomy—may be required for diagnosis.



TREATMENT

- Outpatient for healthy bitch or queen.
- Instruct owner to monitor temperature and observe for signs of systemic illness.
- Ovariohysterectomy—curative; recommended if future breeding is not a consideration.
- Surgical removal—indicated if medical treatment is unsuccessful and the bitch develops metritis.



MEDICATIONS

DRUG(S)

- Oxytocin—known or suspected condition in otherwise healthy cats and dogs; dogs, 0.5 IU/kg IM up to 5 IU; cats, 0.5–1 IU IM. Oxytocin may be ineffective after 48 hours postpartum.
- May precede oxytocin treatment with calcium gluconate (10%); dogs and cats, 0.5–1.5 mL/kg IV slow over 15 minutes; monitor for arrhythmia during injection.
- Metritis—treat accordingly (see Metritis).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Do not give progestational drugs.



FOLLOW-UP

- Monitor temperature and physical condition.
- Acute metritis (dogs)—may develop if the placenta is not passed; fair to good prognosis for recovery with treatment.
- Prognosis for future reproduction—good without metritis; fair to poor with metritis.



MISCELLANEOUS

SEE ALSO

Metritis

Suggested Reading

Feldman EC, Nelson RW. Periparturient diseases. In: Feldman EC, Nelson RW, eds., Canine and Feline Endocrinology and Reproduction, 3rd ed. Philadelphia: Saunders, 2004, pp. 808–834.

Grundy SG, Davidson AP. Theriogenology question of the month. Acute metritis secondary to retained fetal membranes and a retained nonviable fetus. J Am Vet Med Assoc 2004, 224(6):844–847.

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RETINAL DEGENERATION



BASICS

DEFINITION

- Degeneration of the retina from any cause, inherited or acquired.
- Inherited—generalized PRA; a group of progressive retinal diseases; may be subdivided into photoreceptor dysplasias (begin before the retina fully develops, < 12 weeks) and photoreceptor degenerations (begin after the retina matures).

PATHOPHYSIOLOGY

- A number of genetic defects in photoreceptor metabolism have been identified.
- May be secondary to retinal pigment epithelial or choroidal disease; amino acid metabolic disorders, and storage diseases.
- Central PRA: genetic defect in vitamin E metabolism, can be acquired with vitamin E deficiency.
- Also may be idiopathic, secondary to diffuse or focal inflammation and scarring (e.g., chorioretinitis), toxin exposure, nutritional deficiency, or previous retinal detachment.
- SARDS.

SYSTEMS AFFECTED

- Nervous system with lysosome storage diseases
- Ophthalmic

GENETICS

Dogs

- PRA—autosomal recessive most breeds (see breed predilection).
- Neuronal ceroid lipofuscinosis—autosomal recessive in most breeds.
- Hemeralopia—cone degeneration, autosomal recessive.
- Inheritance in many breeds not determined.

Cats

- Early onset—mixed breed and Abyssinian retinal dysplasia (rod-cone dysplasia), autosomal dominant. Persians (autosomal recessive). Clinical signs at 4 months; may be blind by 2 years.
- Late onset—Abyssinian autosomal recessive rod cone degeneration: blind by 4 years of age.

INCIDENCE/PREVALENCE

- Hereditary—prevalence greater in dogs than in cats.
- Taurine deficiency—uncommon now that cat foods are appropriately supplemented.

GEOGRAPHIC DISTRIBUTION

Central PRA—more common in dogs from Europe than from the United States.

SIGNALMENT

Species

Dog and cat

Breed Predilections

Hereditary—Dogs

- Retinal dysplasia—Bedlington terrier, Sealyham terrier, English springer spaniel, cocker spaniel, and others.
- Early-onset PRA—Irish setter, collie, Norwegian elkhound, miniature schnauzer, Belgian

shepherd, mastiff, Cardigan Welsh corgi, American Staffordshire terrier, pit bull terrier, and Briard (congenital stationary night blindness); late-onset PRA—miniature and toy poodle, American and English cocker spaniel, Basenji, Labrador retriever, Tibetan terrier, miniature longhaired dachshund, Akita, Samoyed, Siberian huskie.

- Central PRA—Labrador, golden retriever, border collie, collie, Shetland sheepdog, Briard, others.
- Cone degeneration disease—German shorthaired pointer, Alaskan malamute, and Australian shepherd.

- Neuronal ceroid lipofuscinosis—English setter, border collie, American bulldog, Dalmatian, Tibetan terrier, collie.
- SARDS—Brittany spaniel, miniature schnauzer, dachshund, any breed.

Hereditary—Cats

- Abyssinian and Somali (longhaired Abyssinian)
- Siamese
- Persians—autosomal recessive

Mean Age and Range

- Early PRA and dystrophies—3–4 months–2 years
- Late PRA—clinical signs > 4–6 years
- Cone degeneration disease—3–4 months
- SARDS—middle-aged to old

Predominant Sex

- PRA—X-linked recessive condition in Siberian huskie and Samoyed, therefore more likely to be present in males.
- SARDS—70% are females.

SIGNS

Historical Findings

- PRA (dog)—a gradually progressing nyctalopia that ultimately affects vision in bright light; may note dilated pupils or brighter tapetal reflex; may appear to be acutely blind (when patient becomes totally blind or is moved to unfamiliar surroundings). Dysplasias will have early onset and may be blind by 2 years. Degenerations are later onset and blind in later life.
- Hemeralopia or cone degeneration disease—rare. Between 8 and 12 weeks of age puppies show photophobia and trouble navigating in bright light. Progresses to total day blindness. Night vision remains normal.
- Central PRA (dogs)—rare in the United States; central vision lost; may never become completely blind.
- SARDS—vision lost in 1–4 weeks; polyuria, polydipsia, and polyphagia common.

Physical Examination Findings

- If severe—direct and consensual pupillary light reflexes impaired or nearly abolished.
- Tapetal hyperreflectivity and non-tapetal depigmentation or mottled hyperpigmentation; retinal blood vessel attenuation and optic nerve atrophy.
- PRA (dogs)—cataracts and vitreous degeneration can occur.
- SARDS (dogs)—obesity; may note slow or absent pupillary light reflexes. Chromatic PLR testing (melan 100), reduce red PLR with escape, normal blue PLR.
- Borzoi chorioretinopathy—multifocal

chorioretinal lesions (hyperpigmented and hyperreflective).

- Taurine-deficient retinopathy (cats)—begins as a spot in area centralis; then horizontal band forms superior to the optic nerve; finally, diffuse degeneration and hyperreflectivity.
- Post-inflammatory retinal scars—focal or multifocal lesions manifest as areas of tapetal hyperreflectivity or altered pigmentation.
- Skeletal dysplasia may be associated with Samoyed and Labrador retriever, i.e., dwarfism.
- Retinal dysplasia may also be associated with multiple other ocular anomalies in Akita, Doberman pinscher, or any breed.
- Storage diseases—may have cloudy corneas and possibly neurologic signs.
- Neuronal ceroid lipofuscinosis—mental deterioration, CNS signs, paralysis, and death.

CAUSES

Degenerative

- PRA—affects both eyes symmetrically; most forms of PRA are recessively inherited except for dominant PRA in mastiffs.
- Chronic or uncontrolled glaucoma—retinal and optic nerve atrophy.
- Secondary to scarring from previous multifocal or diffuse retinal detachment or inflammation.

Anomalous

- Rod-cone dysplasias—affect both eyes.
- Other dysplasias—may be multifocal and non-blinding (e.g., in English springer spaniel and Labrador retriever).
- Oculoskeletal dysplasia in Labrador and Samoyed.

Metabolic

- Storage disease—mucopolysaccharidosis, gangliosidosis, mannosidosis, fucosidosis (English springer spaniel).
- Ornithine aminotransferase deficiency—progressive and total atrophy of the choroid and retina, manifests in older cats.

Neoplastic

Neoplastic cell infiltrate may lead to scars from previous retinal detachment if treated.

Nutritional

- Severe deficiency of vitamin E or A (dogs and cats)—dogs fed poor diets (high in polyunsaturated fats) may cause partial or complete degeneration.
- Taurine deficiency (cats)—causes retinal degeneration and dilated cardiomyopathy.

Infectious/Immune

Retina will degenerate from inflammation; may be focal, multifocal, or generalized.

Idiopathic

SARDS—dogs; post-inflammatory—dogs and cats.).

Toxic

- Idiosyncratic reaction to griseofulvin or enrofloxacin (cats).
- Radiation—dogs or cats treated for nasal or CNS neoplasia.
- Phototoxicity—operating microscopes, welding light exposure.

(CONTINUED)

RETINAL DEGENERATION**RISK FACTORS**

- Ocular disease—cataracts; panuveitis; chorioretinitis; retinal detachment; glaucoma.
- Cats—enrofloxacin dose should not exceed 5 mg/kg/day. Toxicity noted at lower doses especially in compromised animals, i.e., renal disease.

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- Acute vision loss—pupillary light reflex slow or absent: SARDs, optic neuritis, retinal detachment, unrecognized PRA, or glaucoma; pupillary light reflex normal: rapidly developing diabetic cataracts or visual cortex disease.
- Slowly progressive visual loss—PRA; cataracts; severe corneal disease (e.g., pigmentation, scarring, or edema); chronic retinitis; chorioretinitis; vitreal inflammation.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal, unless systemic disease.
- SARDs (dogs)—results may be suggestive of hyperadrenocorticism, which patient may have.

OTHER LABORATORY TESTS

- Test for Cushing's disease, evaluate sex hormone levels, check blood pressure, evaluate for proteinuria—with SARDs.
- Taurine concentration (cats)—especially with dilated cardiomyopathy.
- Serum and urine ornithine concentrations (cats)—elevated with ornithine aminotransferase deficiency.
- Genetic testing—OptiGen, VetGen or Michigan State University. New tests for a variety of breeds are steadily being developed. Details on tests available, samples needed, and how to interpret test results may be found at testing center websites. Test results often allow identification of affected, non-affected, and probable carriers with good confidence.

IMAGING

- Thoracic radiographs and cardiac ultrasound—may be indicated in cats with suspected taurine-deficient condition.
- Abdominal radiographs and ultrasound (dogs)—with SARDs if Cushing's disease is suspected.
- CT or MRI—used to rule out causes of central blindness (e.g., optic nerve damage, cortical blindness).

DIAGNOSTIC PROCEDURES

- Ophthalmic examination.
- Electroretinography—localizes cause of blindness (when retina not visible or appears normal).
- Chromatic PLR (Melan 100)—can help screen for outer retinal layer problems (red reduced) vs. inner retina layers (absent blue). Definitive diagnosis requires electroretinogram as assessment of PLR is subjective and interpretation can be confounded by iris atrophy and stress-induced mydriasis.
- CSF tap—may be performed for cases of suspected optic neuritis.

PATHOLOGIC FINDINGS

- Thin retina.
- Edges of focal retinal scars—sharply delineated.
- Hyperpigmented areas—associated with post-inflammatory scars or central PRA.
- End-stage degenerations—marked photoreceptor atrophy and reduction in retinal cell density.
- Lipopigment accumulated in the neuroepithelium—central PRA, ceroid lipofuscinosis, congenital stationary night blindness.
- Lysosome storage diseases—accumulation in neuronal/retinal layers/cornea.

**TREATMENT****DIET**

- Cats—food should contain 500–750 ppm taurine.
- Dogs—balanced diet, avoid all meat high in polyunsaturated fats.

CLIENT EDUCATION

- Inform client that most blind animals function well in stable environment.
- Advise client that blind dogs should be supervised if they are outside, not in fenced yards or in an area with a pool.
- Suggest playing with toys that make sounds.
- Some old blind animals with other problems such as hearing loss or senility may not adapt well.
- Some blind animals experience behavioral changes such as increased aggression or reduced activity.
- Animals with only one blind eye can function normally.
- Blind cats should be kept indoors.

SURGICAL CONSIDERATIONS
Not indicated unless painful eye.**MEDICATIONS****DRUG(S)**

- None currently effective.
- Pyridoxine supplementation (cats)—for ornithine aminotransferase deficiency.
- Adequate dietary taurine—may halt the progression of the taurine-deficient retinopathy.

GENE THERAPY

Experimental—RPE dystrophy in the Briard.

CONTRAINdicATIONS

N/A

PRECAUTIONS

Cataract surgery—not recommended if retinal degeneration is severe; perform preoperative electroretinogram.

**FOLLOW-UP****PATIENT MONITORING**

- Serial fundic examinations—will note signs of degeneration over weeks with SARDs; months PRA.
- Cataract formation—with PRA or SARDs.

PREVENTION/AVOIDANCE

- Do not breed animals suspected of having PRA.
- Do not breed known carriers (e.g., offspring of affected).
- Do genetic testing on breeding animals.

POSSIBLE COMPLICATIONS

- Cataracts
- Glaucoma
- Uveitis
- Ocular trauma as a result of visual impairment
- Obesity—secondary to reduced activity

EXPECTED COURSE AND PROGNOSIS

- Inherited PRA—progresses to blindness; progression often slow enough for patient to adapt to visual loss; non-painful.
- Degeneration from previous inflammation—usually does not progress unless a systemic disease or autoimmune etiology causes persistent or recurrent inflammation.
- SARDs—irreversible blindness.
- Transient taurine deficiency (cats)—degeneration may halt at any stage.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

SARDs—hyperadrenocorticism, proteinuria, hypertension, elevated sex hormones

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- PRA—progressive rod-cone degeneration; retinal atrophy
- Taurine-deficient retinopathy—previously called feline central retinal degeneration

SEE ALSO

- Blind Quiet Eye
- Chorioretinitis
- Lysosomal Storage Diseases
- Retinal Detachment

R

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- MRI = magnetic resonance imaging
- PLR = pupillary light reflex
- PRA = progressive retinal atrophy
- RPE = retinal pigment epithelium
- SARDs = sudden acquired retinal degeneration syndrome

Suggested Reading

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Author Patricia J. Smith

Consulting Editor Paul E. Miller

**Client Education Handout
available online**

RETINAL DETACHMENT



BASICS

DEFINITION

Any separation of the neural retina from the retinal pigment epithelium.

PATHOPHYSIOLOGY

- Subretinal space—a potential space between the RPE and neural retina in which fluid or exudates accumulate.
- Characterized by its etiopathogenesis—one or a combination of rhegmatogenous (retinal tear), subretinal exudation, or traction.

Rhegmatogenous

A tear or hole in the retina that may be related to age, cataracts, traction from inflammatory debris or vitreal degeneration, trauma, or retinal degeneration. Vitreous fluid moves into the subretinal space, which results in detachment. Probably the predominant type that occurs in association with cataracts and after cataract or lens surgery. Requires some vitreous abnormality (e.g., liquefaction, traction).

Exudative

Fluid accumulates in the subretinal space because of breakdown of the blood-retinal barrier. Subretinal fluid—may be serous, hemorrhagic, or exudative (e.g., granulomatous in patients with blastomycosis). Hematogenous/systemic pathogenetic factors—common. Vasculitis, hypertension, and hyperviscosity—may cause serous detachment with or without hemorrhage.

Traction

Usually by fibrous or fibrovascular tissue; detaches retina and/or may cause retina hole or tear. May be associated with trauma, intraocular foreign bodies, or any cause of severe vitreal inflammation.

SYSTEMS AFFECTED

- Nervous—dogs with GME will often develop neurologic symptoms.
- Ophthalmic—retina, uvea. May be manifestation of a systemic disease or neoplasia.

GENETICS

Depends on cause—dogs with hereditary cataracts or lens luxations may develop rhegmatogenous detachment. Some breeds may have retinal tears and detachment from primary vitreous abnormalities.

INCIDENCE/PREVALENCE

- Exudative—most common in dogs and cats.
- Rhegmatogenous—more common in dogs because of the greater prevalence of cataracts and cataract surgery.

SIGNALMENT

Species

Dog and cat

Breed Predispositions

- Depends on cause.
- Terrier breeds—predisposed to primary lens luxation, which may contribute to retinal tear and detachment with or without surgery.
- Breeds that develop cataracts.
- Shih-Tzu, Boston terrier, Italian greyhound, Chihuahua—appear to be predisposed to spontaneous rhegmatogenous detachments owing to abnormal liquefied vitreous.
- Dogs with merle coat color; Australian shepherd, Shetland sheepdog, harlequin Great Dane, collie.
- Breeds that may have severe retinal dysplasia: springer spaniel, Labrador, Bedlington terrier.
- Breeds with serous retinopathy (also known as RPE dysplasia, canine multifocal retinopathy): Great Pyrenees, mastiff, Coton de Tulear.

Mean Age and Range

- Depends on cause.
- Older patients—cataracts and systemic diseases (e.g., hypertension, neoplasia, and immune-mediated disease).
- Young dogs: affected with severe retinal dysplasia, canine multifocal retinopathy.

SIGNS

- Blindness or reduced vision in affected eye.
- Dilated pupil with slow or no PLR. PLR may be near normal if detachment is acute.
- Blood vessels or a “membrane” may be observed easily through the pupil just behind the lens.
- Vitreous abnormalities—floaters, hemorrhage, or syneresis (liquefaction); common.
- Interruption or alteration of the course of blood vessels owing to retinal elevation.
- With clear subretinal fluid—vessels may cast shadows.
- With exudative fluid or blood, tapetum may not be visible.
- Other symptoms will depend on any underlying systemic diseases.
- See chapter, Chorioretinitis, for signs of inflammation.
- Canine multifocal retinopathy: multifocal gray to tan elevated lesions (focal detachments) of various size. Starts around 11 weeks, progresses with time.

CAUSES

Bilateral—suggests a systemic problem led to disruption of blood-retinal barrier unless severe vitreal degeneration is present in breed known to have predisposition e.g., Shih Tzu.

Degenerative

- End-stage progressive retinal degeneration—may lead to retinal hole formation and detachment: see Retinal Degeneration.

Anomalous

- Colobomas—collie eye anomaly: abnormal retina around colobomatous optic nerve or large choroidal staphylomas may lead to rhegmatogenous detachments; border collies, Australian shepherds, and other breeds in which dogs have merle coats (merle ocular dysgenesis).
- Multiple ocular anomalies—Akitas, any breed.
- Severe retinal dysplasia—oculoskeletal dysplasia in Labrador retrievers and Samoyeds; retinal dysplasia; English springer spaniels and Bedlington terriers.

- Canine multifocal retinopathy—suspect RPE dysplasia; Great Pyrenees, mastiffs, Coton de Tulear.

Metabolic

- Hyperviscosity.
- Polycythemia.
- Hypoxia with hemorrhagic complications.
- Dogs—systemic hypertension (any cause such as renal failure or pheochromocytoma), hypothyroidism, hypercholesterolemia, and hyperproteinemia (e.g., with multiple myeloma).
- Cats—most often caused by systemic hypertension either as a primary condition or secondary to renal failure or hyperthyroidism. Multiple myeloma, adrenal tumors also can cause RD due to hyperviscosity or hypertension.

Neoplastic

- Any primary or metastatic neoplasm.
- Commonly associated with multiple myeloma, lymphoma, granulomatous meningoencephalitis, and intraocular masses—ciliary body adenocarcinoma or melanoma.
- Hypertension secondary to adrenal tumors like pheochromocytoma; rare.

Infectious

- Infectious retinitis or chorioretinitis—may cause focal or diffuse detachment.
- Infection may extend from or to the CNS.
- See Chorioretinitis.

Immune Mediated/Inflammatory

- Immune complex disease—may cause vasculitis or inflammation resulting in exudative detachment.
- Dogs—SLE; uveodermatologic syndrome.
- Cats—periarteritis nodosa; SLE.

Idiopathic

- If all other causes are ruled out, including retinal tears.
- Idiopathic steroid-responsive detachment—reported in giant-breed dogs but may occur in any breed.

Trauma and Toxic

- Bilateral—traumatic probably never occurs.
- Penetrating injury or foreign body.
- Severe blunt trauma with inflammation or hemorrhage.
- Surgical trauma—may contribute to retinal tearing.
- Toxic—idiosyncratic reactions to drugs (e.g., trimethoprim-sulfa, ethylene glycol in dogs, griseofulvin in cats).

RISK FACTORS

- Systemic hypertension.
- Old age: retinal thinning, severe vitreal degeneration.
- Hypermature cataracts.
- Luxated lenses.
- Lens extraction.
- Hereditary: young dogs that have more severe retinal dysplasia and/or multiple ocular anomalies.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Blindness or impaired vision—optic neuritis; glaucoma; cataracts; progressive

(CONTINUED)

- retinal atrophy; SARDs (see Retinal Degeneration); CNS disease.
- Dilated pupil with slow or absent pupillary light reflexes—glaucoma; oculomotor nerve lesion; optic neuritis; progressive retinal atrophy; SARDs.
- Membrane or vessels associated with or behind lens—persistent tunica vasculosa lentis; persistent pupillary membranes; fibrovascular membrane secondary to intraocular neoplasia or inflammation.

CBC/BIOCHEMISTRY/URINALYSIS

- Typically normal if the problem is confined to the eye.
- Abnormalities consistent with an associated systemic disease process.

OTHER LABORATORY TESTS

- Depends on suspected systemic problem.
- Protein electrophoresis.
- Documentation of Bence-Jones protein in urine.
- Coagulation profile.
- Bacterial culture of ocular or body fluids.
- Thyroid hormone measurement.
- Serologic or PCR testing for infectious diseases—see Chorioretinitis.

IMAGING

- Thoracic radiograph, abdominal X-rays, and abdominal ultrasound—search for lymphadenopathy, primary neoplasia, metastatic disease, or infiltrates consistent with infectious agents.
- Radiographs of the spine—may reveal bony changes consistent with multiple myeloma.
- Ocular ultrasound—identify retinal detachments, intraocular masses; helpful if the ocular media is not clear.
- Cardiac ultrasound—cats with hypertensive retinopathy.

DIAGNOSTIC PROCEDURES

- Ophthalmic examination.
- Single or repeated blood pressure measurement—may reveal hypertension; normal mean arterial pressure in dogs and cats usually $< 160 \text{ mmHg}$.
- CSF tap—indicated with signs of CNS disease or optic neuritis.
- Vitreocentesis or subretinal fluid aspirate—may be performed if other diagnostic tests failed to yield a cause and an infectious agent or neoplasia is suspected; may aggravate the inflammation or induce hemorrhage.

PATHOLOGIC FINDINGS

- Retina separated from the RPE and underlying choroid.
- May note masses or subretinal exudate or etiologic infectious organism.
- Chronic—results in retinal atrophy and a tombstone appearance to the RPE.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Depends on the physical condition of the patient.
- Usually outpatient.
- Acute blindness—vision may be restored if the underlying cause is rapidly identified and treated; make every attempt to determine the

cause.

- Degeneration occurs rapidly—provide therapy as soon as possible after diagnosis.

CLIENT EDUCATION

- Explain that RD may be a sign of systemic disease, so diagnostic testing is important.
- Inform client that RD associated with vitreal degeneration, lens luxation or cataract surgery has a bilateral potential, minimize head shaking.
- Inform client that with short-duration RD return of vision may occur if the underlying cause is treated.
- Advise client that blind pets can adapt remarkably well and live a good-quality life (see Retinal Degeneration).

SURGICAL CONSIDERATIONS

- Rhegmatogenous—may be surgically repaired by an ophthalmologist.
- Laser retinopexy—may reverse detachments associated with optic disk colobomas with collie eye anomaly; may stabilize partial/small detachments. May prevent detachment in predisposed fellow eye.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Depends on underlying systemic cause, which should be identified and treated.
- Systemic prednisone 2 mg/kg divided q12h for 3–10 days, then taper; if systemic mycosis is ruled out and the detachment is believed to be immune mediated; may facilitate retinal reattachment; for immune-mediated disease, taper medications very slowly over months.
- Anti-inflammatory doses of prednisone 0.5 mg/kg, then taper; may be useful for exudative detachments of an infectious nature as long as the underlying disease is being definitively treated.
- Antihypertensive agents—amlodipine 0.5–1 mg/kg PO q24h in dogs; cats 0.625–1.25 mg. Propranolol and/or enalapril (0.25–0.5 mg/kg q12–24h) or benazapril (0.25–0.5 mg/kg q24h) for cats with hypertension not responsive to amlodipine alone. Calcium channel blockers may be important in cats that have renal failure and proteinuria. Consult with internist. See Renal Failure chapters.

CONTRAINDICATIONS

Systemic corticosteroids—do not use unless systemic mycosis is ruled out or is being definitively treated.

ALTERNATIVE DRUG(S)

- Chemotherapeutic agents—suggested for treatment of neoplastic conditions.
- Other immunosuppressive drugs may be needed in some immune-mediated RD if prednisone not effective long term at safe dose, i.e., uveodermatologic syndrome.
- Azathioprine: dogs, 2 mg/kg PO q24h initially, then 0.5–1 mg/kg q48h; to control inflammation.

RETINAL DETACHMENT

- Oral cyclosporine: dogs, 5 mg/kg/day then taper.
- Leflunomide, mycophenolate; also can be used if prednisone is not effective at a safe dose; consult with internist.

**FOLLOW-UP****PATIENT MONITORING**

- Immunosuppressive drugs such as azathioprine—obtain an initial CBC, chemistry panel, then every 1–2 weeks to monthly (depending on which medication) to monitor for bone marrow suppression, liver, renal, or pancreas toxicity.
- Monitor blood pressure in hypertensive cases.

POSSIBLE COMPLICATIONS

- Permanent blindness.
- Cataracts.
- Glaucoma.
- Chronic ocular pain.
- Death if secondary to a systemic disease/neoplastic process.

EXPECTED COURSE AND PROGNOSIS

- Prognosis for vision with complete detachment—guarded. The exception is hypertensive retinopathy that is diagnosed and treated promptly.
- Vision may return if the underlying cause is removed and reattachment occurs.
- Blindness—may develop in days to weeks even if reattachment occurs (more likely and rapid with exudative than with serous detachments).
- Focal or multifocal chorioretinitis—does not markedly impair vision; will leave scars.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Exudative—systemic disease.
- Cataracts.
- Trauma.
- Vitreous abnormalities.
- CNS signs with GME or systemic disease affecting CNS.

R

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- GME = granulomatous meningoencephalomyelitis
- PLR = pupillary light reflex
- RD = retinal detachment
- RPE = retinal pigment epithelium
- SARDs = sudden acquired retinal degeneration syndrome
- SLE = systemic lupus erythematosus

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Author Patricia J. Smith

Consulting Editor Paul E. Miller



Client Education Handout
available online

RETINAL HEMORRHAGE



BASICS

DEFINITION

- Focal or generalized areas of bleeding into part or all layers of the retina.
- May be acute or chronic.

PATHOPHYSIOLOGY

- Depends on cause.
 - Trauma-induced retinal detachments—may tear retinal blood vessels.
 - Often involved in congenital malformations, concurrent vascular abnormalities, and neovascularization syndromes.
 - Intoxications, vasculitis, systemic clotting, neoplastic disorders, systemic infectious disease—may cause focal or more widespread hemorrhage.
 - Systemic hypertension and immune-mediated diseases (e.g., those causing anemia)—may cause local hemorrhage in conjunction with vascular abnormalities and/or complete or partial retinal detachments.
 - May note a retinopathy in conjunction with diabetes mellitus—includes the formation of vascular microaneurysms with accompanying hemorrhage or exudation.

SYSTEMS AFFECTED

Ophthalmic

GENETICS

- Collie eye anomaly—autosomal recessive trait.
- Retinal dysplasia—suspected to be autosomal recessive inheritance.
- Retinal detachment—depends on causative factor, hereditary type when observed in conjunction with collie eye anomaly or retinal dysplasia.

INCIDENCE/PREVALENCE

- Common in hypertensive retinopathy of elderly cats.
- Low incidence in collie eye anomaly.

SIGNALMENT

Species

Dog and cat: any breed, age, or sex

Breed Predilections

- Cause may have a genetic basis and be highly breed- and age-specific—young collies with collie eye anomaly; Labrador retrievers with congenital vitreoretinal dysplasia.
- Hereditary breed-specific congenital defects that might cause detachment or severe retinal dysplasia—collies and shelties with collie eye anomaly; Australian shepherds with merle ocular dysgenesis; Labradors, Sealyhams, Bedlington terriers, and springer spaniels with retinal dysplasia; and miniature schnauzers with retinal dysplasia and persistent hyperplastic primary vitreous.

Mean Age and Range

- Old cats of both sexes—often affected by systemic hypertension.
- Collie eye anomaly and retinal dysplasia are congenital defects and can be observed in 5- to 7-week-old dogs.

Predominant Sex

No sex predilection

SIGNS

General Comments

Signs depend on underlying causes such as inflammatory disease in the posterior segment, systemic disease, or ocular malformations.

Historical Findings

- Often none
- Vision loss
- Bumping into objects

Physical Examination Findings

- Depends on underlying cause
 - Light or dark red appearance of the posterior segment
 - Blood-filled anterior chamber (hyphema)
 - Evidence of bleeding elsewhere—petechia, ecchymoses, melena, hematuria
 - Leukocoria (whitish-appearing pupil) with or without reddish coloration behind the lens
 - Absence of menace response
 - Abnormal pupillary responses

CAUSES

Congenital

- Retinal detachment secondary to severe congenital malformations in the eye.
- Vitreoretinal defects; e.g., in PHTVL/PHPV.
- Retinal defects in geographic or complete retinal dysplasia or in partial or complete retinal detachment.

Acquired

- Trauma.
- Systemic hypertension (especially old cats)—renal disease; cardiac disease; hyperthyroidism; hyperadrenocorticism; idiopathic.
- Intoxication—dicumarol; paracetamol; sulfonamide; estradurin.
- Rickettsia—*Rickettsia rickettsiae*, *Ehrlichia* spp. associated.
- Systemic mycosis—cryptococcosis.
- Neoplasia—lymphosarcoma.
- Plasma cell myeloma.
- Hematologic disorders—blood-clotting disorder (von Willebrand disease); severe anemia; thrombocytopenia; monoclonal gammopathy and hyperviscosity syndrome.
- Diabetic retinopathy.
- Retinal detachment.
- Immune-mediated vasculitis.

RISK FACTORS

- Systemic hypertension or clotting disorders
- Hematologic such as anemia and polycythemia
- Vascular membranes



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Normal choroidal vessel pattern in a subalbinotic fundus. Lightly pigmented eyes. Blood is contained in vascular channels and not outside of the vessel lumen.

- Vitreal opacities (blood or inflammation).
- Vitreal hemorrhage—reddish coloration of the pupil, impossible to rule out concurrent retinal hemorrhage.
- Vitreal inflammation—

generalized or local blurring or lack of fundus detail—usually no reddish coloration. Vitreal opacities can be caused by persistent hyaloid arteries, neoplasia—especially lymphoma or ciliary body tumors; uveitis; glaucoma; lens luxation; blunt or sharp trauma, foreign bodies, and spread from local or systemic diseases (e.g., rickettsial or systemic mycosis).

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal unless secondary to a systemic disease.
- Hyperglycemia and/or glucosuria—may note with diabetic retinopathy.
- High BUN or serum creatinine and proteinuria—common in cats with retinal detachment and hemorrhage secondary to systemic hypertension.
- Thrombocytopenia or other changes consistent with systemic hematologic disorders.

OTHER LABORATORY TESTS

Complete workup—suspected systemic disease; includes thyroid and adrenal endocrine tests, serologic tests for infectious agents, and immune studies.

IMAGING

- Ocular ultrasound to evaluate position of lens and retina in cases with blood-filled posterior segment.
- If neoplasia is possible consider chest radiographs.
- Abdominal ultrasound may be considered if systemic disease is suspected.

DIAGNOSTIC PROCEDURES

- Ophthalmic examination with a penlight—usually permits diagnosis of complete retinal detachment with partial retinal hemorrhage; detached neuroretina may often be visualized through the pupil as a whitish veil of tissue.
- Indirect ophthalmoscopy—diagnosis of funduscopic and vitreal changes.
- Vitreous paracentesis and cytologic examination—aid in the diagnosis for suspected neoplasia or mycotic disease.
- Blood pressure measurement—indicated in all patients with severe retinal and vitreal hemorrhage.

PATHOLOGIC FINDINGS

- Depends on the cause.
- Findings include preretinal, intraretinal, or subretinal hemorrhage that may be focal or involve large areas.
- Secondary morphologic changes include fibrotic areas with proliferation of cellular extensions into the subretinal space, intraretinal, and thickening of the external limiting membrane.



TREATMENT

APPROPRIATE HEALTH CARE

- Infections and intoxications—often require specific treatment. Systemic hypertension should be treated in a timely fashion to improve chances of retinal reattachment.
- Consider referral for a more detailed ophthalmic examination, including

(CONTINUED)

RETINAL HEMORRHAGE

ultrasound, before attempting empirical therapy.

NURSING CARE

- Depends on the cause.
- Supportive care often needed with well-trained veterinary technicians to monitor progress several times daily.

ACTIVITY

Retinal detachment—cage rest until the retina is reattached in trauma cases.

DIET

Depends on underlying cause; there may be dietary restrictions if the primary disorder is due to hepatic or renal disease.

CLIENT EDUCATION

- Discuss living with a blind dog or euthanasia of young puppies with severe bilateral hemorrhage due to congenital abnormalities (of the breeds listed under "Signalment").
- Advise client that unilaterally affected dogs can function as pets but should not be used for breeding, a fact not always obvious to the owner.

SURGICAL CONSIDERATIONS

Surgery—refer patient to an ophthalmologist for vitrectomy and/or reattachment surgery.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Depends on underlying cause.
- Systemic corticosteroids—if workup is declined and infectious disease is unlikely; prednisolone (1–2 mg/kg/day for 7–14 days, then taper; long-term treatment up to 4–6 weeks); especially for retinal detachment as a sequela to trauma in dogs and cats. Doxycycline (4 mg/kg PO q12h for 14–21 days) or other appropriate systemic antibiotic based on infectious disease testing; may be administered concurrently with corticosteroids.
- Primary systemic hypertension—treat as required; often combined with diuretics (e.g., furosemide, 3–4 mg/kg/day for 5–7 days), and calcium channel blockers.
- Oral azathioprine 1–2 mg/kg/day up to a week, then taper; for immune-mediated retinal detachments; combine with systemic corticosteroids; perform a CBC, platelet count, and liver enzyme analysis every 2 weeks for the first 2 months, then periodically.
- Itraconazole—for cryptococcosis or other deep fungal infection; see Cryptococcosis or appropriate systemic mycosis.

CONTRAINDICATIONS

- Systemic corticosteroids and other immunosuppressive drugs—use with extreme caution in patients with systemic infection.
- Systemic NSAIDs—contraindicated with bleeding disorders, impaired renal function, or preexisting hypersensitivities; predispose patient (especially cats) to gastrointestinal ulceration.

PRECAUTIONS

NSAIDS—carprofen and meloxicam commonly used but may exacerbate bleeding; either may be administered to control intraocular inflammation in dogs. Use with caution in cats.

ALTERNATIVE DRUG(S)

Oral azathioprine—may be used in immune-mediated fundus disease; see "Drug(s) of Choice."

**FOLLOW-UP****PATIENT MONITORING**

- Repeated monitoring—required to ensure that condition subsides and retinal morphology normalizes.
- Preretinal hemorrhages—usually absorbed within a few weeks to several months if localized.
- Larger or repeated hemorrhages—may be followed by fibroplastic processes; may lead to the formation of fibrous preretinal membranes and vitreoretinal adhesions, which may cause vitreoretinal traction and retinal detachment.
- Intraretinal hemorrhage—reabsorbed within several weeks to months; may produce retinal scarring.

POSSIBLE COMPLICATIONS

- Retinal detachment
- Blindness
- Impaired vision
- Chronic uveitis
- Glucoma

EXPECTED COURSE AND PROGNOSIS

- Depends on underlying cause.
- Most retinal hemorrhagic lesions are small, observed during routine ophthalmoscopic examination, usually heal rapidly, and cause no visual problems.
- Retinal hemorrhage due to systemic diseases or retinal malformations is usually more serious, and most have an uncertain prognosis.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Trauma—may often note concurrent lesions in other parts of the eye or body.

- Hypertension—cardiac, renal disease, hyperthyroidism, or hyperadrenocorticism—common; may cause systemic medical problems that must be monitored.

- Intoxication—often a generalized bleeding disorder affecting other organs.
- Cryptococcus infection—often causes concurrent leptomeningitis and pneumonitis.
- Lymphoma—may affect several parts of the body; fatal disease.
- Hematologic disorders—cause systemic disease; symptoms depend on pathophysiology; anemia and recurrent bleeding common.
- Secondary cataracts—may develop within weeks after the onset of diabetes mellitus in dogs.

AGE-RELATED FACTORS

- May occur at any age.
- Often due to congenital diseases (usually have a hereditary background) or to developmental disease processes (see "Causes").

PREGNANCY/FERTILITY/BREEDING

- Dogs affected with hereditary retinal disease causing retinal hemorrhage should not be used in the breeding program.
- Corticosteroids and immunosuppressive drugs may cause complications in regards to pregnancy.

SEE ALSO

- Chorioretinitis
- Hypertension, Systemic
- Hyphema
- Retinal Detachment

ABBREVIATIONS

- NSAID = nonsteroidal anti-inflammatory drug
- PHPV = persistent hyperplastic primary vitreous
- PHTVL = persistent hyperplastic tunica vasculosa lentis

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Client Education Handout available online

RHINITIS AND SINUSITIS



BASICS

DEFINITION

- Rhinitis—inflammation of nasal epithelium.
- Sinusitis—inflammation of paranasal sinuses. Includes frontal sinus and maxillary recess in dogs, frontal and sphenopalatine sinuses in cats.
- The nasal cavity communicates directly with the sinuses; thus rhinitis and sinusitis often occur together (rhinosinusitis).

PATOPHYSIOLOGY

Inflammation and irritation stimulate serous glandular secretion in the nasal mucosa. With chronicity, opportunistic bacterial infections develop in the compromised nasal mucosa causing discharge to become mucoid or mucopurulent. The inflammatory process can lead to turbinate destruction and erosion of the vasculature that results in epistaxis.

SYSTEMS AFFECTED

- Respiratory—sneezing and nasal discharge usually indicate upper respiratory tract disease. Nasal discharge may occasionally be seen with lower airway disease or chronic vomiting disorders.
- Nervous—fungal and neoplastic disease can destroy the cribriform plate and invade the brain.
- Ocular—epiphora with inflammation or obstruction of the nasolacrimal ducts. Conjunctivitis, keratitis, and/or corneal ulcerations with FHV-1 related disease. Chorioretinitis with canine distemper or *Cryptococcus*.
- Oral Cavity—calicivirus, FeLV, FIV are associated with stomatitis, glossitis, faulitis. Tooth root abscess, oronasal fistula or cleft palate possible.

INCIDENCE/PREVALENCE

- Primary bacterial rhinosinusitis is rare, secondary infection associated with dental-related disease common.
- Cats—chronic rhinosinusitis common.
- Dogs—neoplasia, inflammatory rhinitis (lymphoplasmacytic rhinitis), fungal disease common. Nasal foreign body a cause for acute sneezing.

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Brachycephalic cats more prone to chronic rhinitis and *Aspergillus* infection.
- Dolichocephalic dogs more prone to *Aspergillus* infection and nasal tumors.

Mean Age and Range

- Cats—acute viral rhinosinusitis and nasopharyngeal polyps more common in young kittens (6–12 weeks).
- Congenital diseases (cleft palate, ciliary dyskinesia) more common in young animals.
- Neoplasia and dental disease—older animals.
- Foreign bodies more common in young dogs.

Predominant Sex

No sex predilection

SIGNS

Historical Findings

- Sneezing, nasal discharge, epistaxis.
- Discharge usually is serous initially and becomes mucoid, mucopurulent, serosanguinous, or hemorrhagic.
- Unilateral discharge suggests foreign body, tooth root abscess, early neoplasia, or early fungal infection. Idiopathic inflammatory rhinitis can also present with unilateral signs.
- Bilateral discharge more common with viral or bacterial rhinosinusitis, inflammatory rhinitis, pharyngeal disease, or congenital abnormalities. Chronic presentation of neoplasia or fungal rhinitis is often bilateral.
- Facial deformity or facial pain—usually with fungal or neoplastic disease.
- Reverse sneezing more common in dogs, inappetence more common in cats.

Physical Examination Findings

- Check for decreased nasal air flow, bilateral or unilateral, which would suggest an obstructive mass lesion.
- Evaluate oral cavity for tooth root abscess, oronasal fistula, cleft palate or ulcers.
- Increased tracheal sensitivity or cough possible with lower airway causes of nasal signs.
- Look for epiphora, conjunctivitis. Horner's syndrome can be seen with middle ear disease.
- Fundic examination—chorioretinitis possible with infectious diseases; hypertension can result in tortuous retinal vessels or hemorrhage, platelet abnormalities can be associated with retinal hemorrhage or petechiation.

CAUSES

Dogs

Primary Inciting Causes

- Fungal disease—*Aspergillus fumigatus* most common. *Penicillium* spp., *Rhinosporidium seeberi*, *Blastomycoses dermatitidis*, *Cryptococcus neoformans* are rare causes.
- Tooth root abscess.
- Foreign body.
- Congenital abnormalities such as cleft palate or primary ciliary dyskinesia.
- Parasitic causes—nasal mites (*Pneumonyssoides caninum*), *Capillaria aerophila*, *Eucoleus boehmii*.
- Intranasal neoplasia—adenocarcinoma most common (31.5%). Others include lymphoma, chondrosarcomas, or osteosarcomas.
- Immune-mediated rhinitis—allergic rhinitis rare, idiopathic lymphoplasmacytic rhinitis more common.
- Other infectious diseases include canine distemper or *Bordetella bronchiseptica*; *Bartonella* not associated with rhinitis.
- Local trauma can cause bone or turbinate deformity and predispose to chronic rhinitis or *Aspergillus* infection.

Secondary Causes

- Lower airway disease (bronchopneumonia) or vomiting can result in nasal signs through nasopharyngeal regurgitation.
- Nasal discharge can occur with eosinophilic bronchopneumopathy.
- Epistaxis can be related to hypertension, thrombocytopenia, thrombocytopathia, or rarely other

coagulopathies; trauma or foreign body also possible.

Cats

Primary Inciting Causes

- Viral infections—feline herpesvirus-1 and calicivirus account for 90% of acute infections in kittens.
- Bacteria—*Bordetella bronchiseptica* can be a primary pathogen in cats but its significance is uncertain.
- Bartonella* not associated.
- Neoplasia—adenocarcinoma and lymphoma most common.
- Fungal disease—*Cryptococcus neoformans* most common, *Aspergillus felis*, *Penicillium* (rare).
- Nasopharyngeal polyps in young cats > dogs.
- Nasopharyngeal webbing/stenosis—congenital or secondary to chronic infection or inflammation.
- Tooth root abscess or oronasal fistula.
- Foreign bodies.
- Congenital abnormalities include cleft palate.

Secondary Causes

- Epistaxis due to coagulopathy or hypertension.
- Aspiration of vomitus into the nasopharynx

RISK FACTORS

- Dolichocephalic breeds—fungal disease
- Brachycephalic cats—rhinosinusitis



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Rule-out secondary causes of rhinitis including coagulopathy, hypertension, lower airway disease, chronic vomiting.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram is nonspecific—may show leukocytosis (neutrophilia or eosinophilia) with infectious agents. Regenerative anemia with severe blood loss from coagulopathy. Nonregenerative anemia with chronic disease or neoplasia. Thrombocytopenia seen with coagulopathies or severe blood loss.
- Serum biochemistry and urinalysis typically normal.

OTHER LABORATORY TESTS

- FeLV and FIV serologic tests
- Latex agglutination test for cryptococcal capsular antigen
- *Aspergillus* titers: AGID in dogs—false negatives possible, false positives uncommon. ELISA in cats (research tool currently)—high sensitivity and specificity for disease
- Coagulation profile—if epistaxis present

IMAGING

- Radiography—chest radiographs if lower airway disease or neoplasia suspected.
- Dental radiographs highly sensitive for detecting periodontal disease.
- Skull radiographs are useful but do not differentiate among inflammatory rhinitis, fungal infection, and neoplastic disease. Loss of turbinate structures can be seen with all causes. Open-mouth or intraoral ventrodorsal

(CONTINUED)

views provide superior evaluation of the nasal cavity and avoid superimposition of the mandible. • Nasopharyngeal polyps occasionally seen within the nasopharynx. • CT/MRI—superior to plain radiography in evaluating the extent of disease and assessing the integrity of the cribriform plate. Also useful in evaluating disease of the palate, nasopharyngeal meatus, maxillary sinus, periorbital tissues, middle ear canal.

DIAGNOSTIC PROCEDURES

Arterial Blood Pressure

- Evaluate for hypertension if epistaxis.

Lymph Node Aspirate

- Can be diagnostic for neoplasia or *Cryptococcus*.

Cytology

- Nasal swab may reveal *Cryptococcus*.

Culture

- Usefulness of culture is controversial—most animals have secondary bacterial infection. Potential bacterial pathogens are more commonly isolated in cats with rhinosinusitis than healthy cats. • Fungal culture of a plaque lesion visualized on endoscopy aids in diagnosis of aspergillosis. Blindly collected specimen less likely to be useful.
- Asymptomatic intranasal carriage of *Cryptococcus* possible.

Endoscopy

- An otoscope evaluates only the rostral nasal cavity. A rigid endoscope can be guided to the ethmoid turbinates; flexible endoscope provides good visualization rostrally, and can be retroflexed in the nasopharynx to visualize the caudal choanae. • Guided biopsy is possible with rigid and flexible endoscopy. Other techniques include core or blind pinch biopsies. Excessive hemorrhage can be controlled with topical epinephrine at 1:100,000.

Surgery

- Exploratory rhinotomy most invasive diagnostic tool, can be required for difficult foreign body or mass removal, if endoscopy is unsuccessful. Rarely required to obtain a definitive biopsy sample.

PATHOLOGIC FINDINGS

Chronic inflammation causes turbinate resorption, mucosal ulceration and necrosis. Lymphoplasmacytic infiltrate indicates chronicity; neutrophilic usually signifies acute component. Neoplasia and fungus also cause bony lysis or destruction.



TREATMENT

NURSING CARE

Humidification can aid in moistening and mobilizing nasal secretions. Saline intranasal drops helpful if tolerated. Keep nares clean of obstructive mucus.

CLIENT EDUCATION

Signs of chronic rhinitis can be variably controlled but are rarely eliminated.

SURGICAL CONSIDERATIONS

- Rhinotomy is reserved for obtaining a biopsy or foreign body/mass removal when endoscopic intervention is unsuccessful. Rarely provides an advantage over endoscopy.
- Surgery useful for polyp removal, dental-related nasal disease (tooth root abscess, oronasal fistula, cleft palate).



MEDICATIONS

DRUG(S)

Antibiotics

Antibiotics help control secondary bacterial rhinitis; however, they will not resolve disease. Selection of antibiotic is mainly empirical (common isolates include *Staphylococcus*, *Streptococcus*, *Bacillus*, *E. coli*, and *Pasturella multocida*). Long-term use often needed.

Antifungals

See Cryptococcosis and Aspergillosis chapters for detailed treatment discussion.

L-lysine

Inhibits FHV-1 replication; may be useful—250 (kitten)–500 (cat) mg PO q12h.

Anti-inflammatory Agents

Piroxicam (nonsteroidal anti-inflammatory agent) used for palliation of nasal tumors (via COX-2 inhibition), either as sole agent or in conjunction with chemotherapy. Sometimes helpful in animals with rhinitis.

Steroids

Consider use with chronic rhinosinusitis in cats or lymphoplasmacytic rhinitis in dogs at anti-inflammatory doses when mucus obstruction limits appetite.

Antihistamines

Efficacy is debated

Anti-parasitics

Ivermectin 300 µg/kg PO or SC once weekly for 3–4 treatments or milbemycin oxime 1 mg/kg PO once weekly for 3 weeks for treatment of nasal mites.

CONTRAINDICATIONS

Avoid chronic steroid use owing to danger of immunosuppression.

PRECAUTIONS

- NSAIDs can cause GI ulceration.
- Tetracycline may stain teeth of young animals.

POSSIBLE INTERACTIONS

Use of NSAIDs and corticosteroids together is contraindicated.

RHINITIS AND SINUSITIS



FOLLOW-UP

PREVENTION/AVOIDANCE

Vaccinations in kittens can lessen severity and duration of viral infection.

POSSIBLE COMPLICATIONS

- Extension of fungal or neoplastic invasion into brain. • Seizures and other neurologic signs are possible if topical antifungal therapy is used when the cribriform plate is not intact.

EXPECTED COURSE AND PROGNOSIS

- Dependent on etiology and extent of disease. • Acute viral/bacterial rhinitis—good prognosis, chronic rhinitis—guarded for control of signs. • Fungal—fair to guarded prognosis depending on invasiveness and response to therapy. • Neoplastic—3–5 months with no treatment. Life expectancy can be extended up to 9–23 months with radiation therapy.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Cryptococcus, *Aspergillus*, *Penicillium* are transmissible to humans via shared environment. No direct transmission.

SEE ALSO

- Aspergillosis • Cryptococcosis • Epistaxis
- Nasal and Nasopharyngeal Polyps • Nasal Discharge • Respiratory Parasites • Stertor and Stridor

ABBREVIATIONS

- CT = computed tomography • FeLV = feline leukemia virus • FHV = feline herpesvirus • FIV = feline immunodeficiency virus • GI = gastrointestinal • MRI = magnetic resonance imaging • NSAID = nonsteroidal anti-inflammatory drug

R

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Client Education Handout
available online

RHINOSPORIDIOSIS



BASICS

OVERVIEW

- A rare chronic infection of the mucous membranes of dogs, resulting in a fibromyxoid reaction that develops into polypoid growths that may be single or multiple and often protrude from the nostril. Reported in two cats; horses, cows, and humans reported rarely.
- Respiratory system affected.
- Worldwide distribution.
- Endemic areas—Argentina, Venezuela, Uganda, Cuba, Brazil, Iran, Sri Lanka, and India.
- United States—most infections have been reported in the southeastern states.

SIGNALMENT

- Reported in 13 dogs, 7 of which were males.
- No apparent breed predilection.
- Reported in 2 cats.

SIGNS

- Anterior nasal cavity—most common site.
- Sneezing, epistaxis, and stertorous breathing—most prominent.
- Mass—often seen protruding from the nostril; usually single and polypoid; may be lobulated or sessile; surface may have white or yellowish superficial flecks.
- Humans—reported sites: vagina, penis, conjunctival sac, and ears.

CAUSES & RISK FACTORS

- *Rhinosporidium seeberi* now classified as one of five protists in the DRIPS clade.
- Suspected that stagnant fresh water, standing water, and arid (dusty) environment increase likelihood of occurrence.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Nasal neoplasia
- Nasal inflammatory polyp

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

None

IMAGING

Radiographs of nasal cavity—generally normal; mass located in the anterior nasal cavity and does not invade turbinates.

DIAGNOSTIC PROCEDURES

- Impression smears—reveal organisms from nasal mass; use new methylene blue stain, H&E, or periodic acid-Schiff stains. The organisms are 6–8 μm in size and round to oval. A large nucleus is seen in many organisms.
- Histopathology—spores and sporangia (the sac in which spores are produced) can usually be seen with H&E, PAS, Gridley's toluidine blue, and Grocott's stains. In areas where sporangia have ruptured, a purulent neutrophilic inflammation is common.

PATHOLOGIC FINDINGS

Histopathology

- Examination of mass—papillomatous hyperplasia; ulceration of the epithelium; fibrovascular stroma.
- Identification of the organism is diagnostic.
- An intense inflammatory reaction will be seen if organisms are released into the surrounding tissues.



TREATMENT

- Good nursing care—important; anorexia and dehydration not typically reported.
- Cage confinement or other means of exercise restriction—helpful if epistaxis occurs.
- Surgical excision of the mass—treatment of choice; approach through the external nares or rhinotomy; failure to remove the entire mass will likely result in regrowth.



MEDICATIONS

DRUG(S)

- Ketoconazole and itraconazole have been used, but they have been consistently ineffective because this is not a fungal disease.
- Dapsone—used to treat humans; report of use in one dog (1.1 mg/kg PO q8–12h) with favorable response but no cure; however, it has severe side effects.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Dapsone (dogs)—hepatotoxicity; anemia; neutropenia; thrombocytopenia; gastrointestinal signs; skin reactions.



FOLLOW-UP

If surgical approach was through the external nasal orifice, monitor patient closely for mass regrowth; difficult to remove the entire mass.



MISCELLANEOUS

ZOONOTIC POTENTIAL

The organism is infectious to humans, but there is no known risk of direct transmission to humans by handling of infected dogs. The organism may be acquired in humans from the same source as dogs.

ABBREVIATIONS

- DRIPS = *Dermatocystidium*, rosette agent (*Sphaerotilus deservens*), *Ichthyophonus*, *Psorospermium*, *Rhinosporidium seeberi*
- H&E = hematoxylin and eosin
- PAS = periodic acid-Schiff

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Authors Gary D. Norsworthy and Lisa Restine

Consulting Editor Stephen C. Barr

RIGHT BUNDLE BRANCH BLOCK



BASICS

DEFINITION

Conduction delay or block in the right bundle branch resulting in late activation of the right ventricle; the block can be complete or incomplete.

ECG Features

- A right axis deviation and wide QRS (≥ 0.08 second in dogs; ≥ 0.06 in cats) in most patients.
- Large, wide S waves in leads I, II, III, and aVF.
- Incomplete right bundle branch block has right axis deviation with normal width QRS complexes.

PATHOPHYSIOLOGY

- The right bundle branch is anatomically vulnerable to injury because it is a thin strand of tissue and has a long undivided course.
- No hemodynamic compromise.

SYSTEMS AFFECTED

Cardiovascular

GENETICS

N/A

INCIDENCE/PREVALENCE

- Dog—most frequent form of intraventricular conduction defect.
- Cat—not as frequent as left anterior fascicular block.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat

Breed Predilections

In beagles, incomplete right bundle branch block can result from a genetically determined localized variation in right ventricular wall thickness.

Predominant Sex

N/A

SIGNS

Historical Findings

- Usually an incidental ECG finding—does not cause hemodynamic abnormalities.
- Observed signs are usually associated with the underlying condition.

Physical Examination Findings

- Splitting of heart sounds because of asynchronous activation of ventricles in some patients.
- Does not cause signs of hemodynamic compromise.

CAUSES

- Occasionally seen in normal and healthy dogs and cats.
- Congenital heart disease.
- Chronic valvular fibrosis.
- After surgical correction of a cardiac defect.
- Trauma caused by cardiac needle puncture to obtain blood sample.
- Trauma from other causes.
- Chronic infection with *Trypanosoma cruzi* (Chagas' disease).
- Neoplasia.
- Heartworm disease.
- Acute thromboembolism.
- Cardiomyopathy.
- Hyperkalemia (most commonly in cats with urethral obstruction).

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Right ventricular enlargement—absence of right ventricular enlargement on thoracic radiographs or echocardiogram supports a diagnosis of right bundle branch block.
- Can also be confused with ventricular ectopic beats (especially if the block is intermittent), but consistent PR intervals and no pulse deficits with right bundle branch block.

CBC/BIOCHEMISTRY/URINALYSIS

- None specific.
- Serum potassium may be extremely high in cats with urethral obstruction.

OTHER LABORATORY TESTS

- Occult heartworm test may be positive in dogs or cats.
- Chagas' indirect fluorescent antibody test, direct hemagglutination, and complement fixation test may be positive in dogs.

IMAGING

- Echocardiogram may show structural heart disease; absence of right heart enlargement supports the diagnosis.
- Thoracic and abdominal radiographs may show masses or pulmonary metastatic lesions; traumatic injuries could cause localized or diffuse pulmonary densities.

DIAGNOSTIC PROCEDURES

- Electrocardiography
- Echocardiography

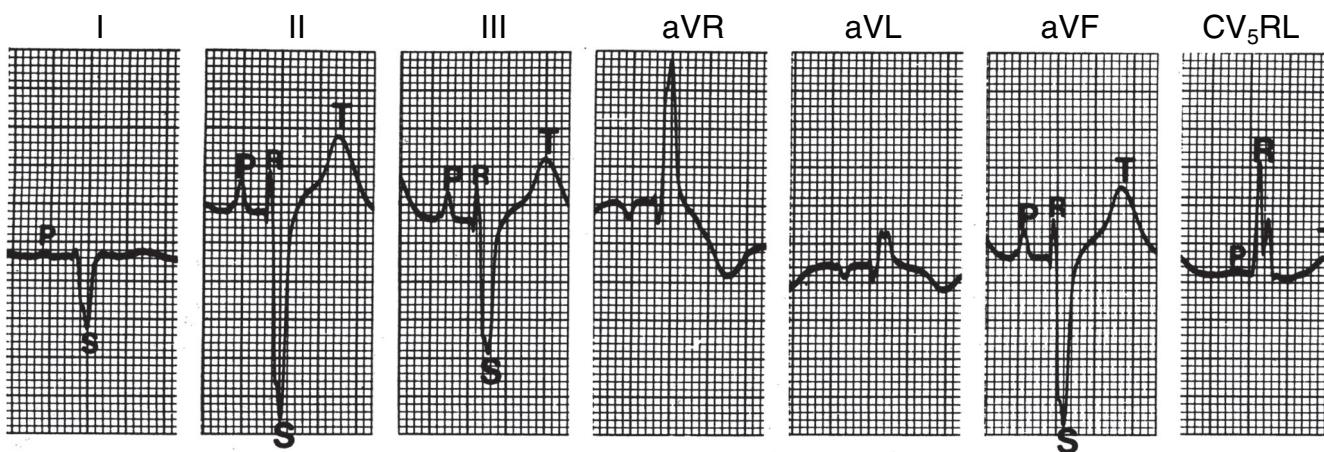


Figure 1.

Right bundle branch block in a dog. The electrocardiographic features include QRS duration of 0.08 second; positive QRS complex in aVR, aVL, and CV₅RL (M-shaped); and large wide S waves in leads I, II, III, and aVF. There is a right axis deviation (approximately -110°) (50 mm/second, 1 cm = 1 mV). (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

RIGHT BUNDLE BRANCH BLOCK

(CONTINUED)

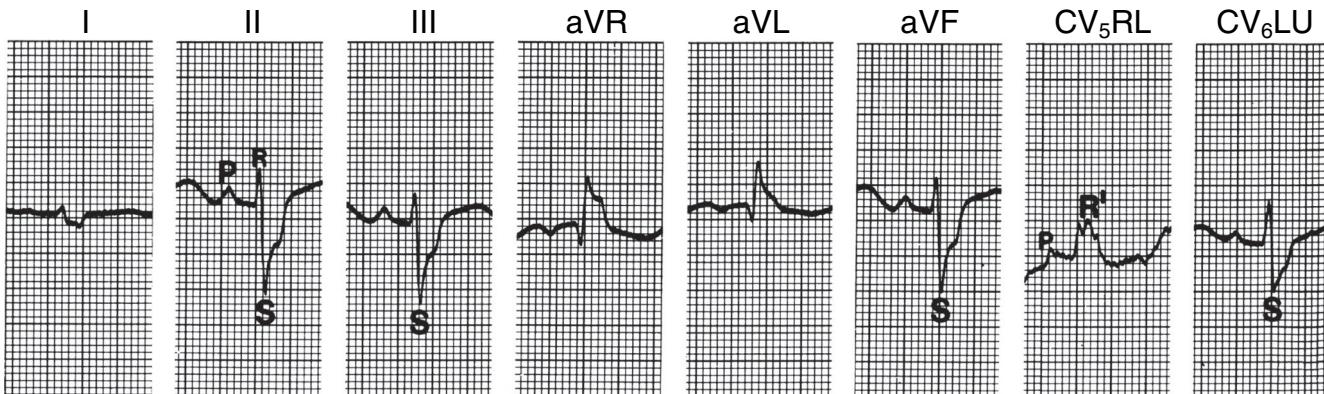


Figure 2.

Right bundle branch block in a cat with the dilated form of cardiomyopathy. The QRS duration is 0.08 second (4 boxes). Large and wide S waves are present in leads I, II, III, aVF, and CV_6 LU. The QRS in CV_5 RL has a wide R wave (M-shaped). There is a marked axis deviation (approximately -90°). (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

PATHOLOGIC FINDINGS

Possible lesions or scarring on endocardial surface in the path of the bundle branches; applying Lugol's iodine to the endocardial surface within 2 hours post-mortem gives clear visualization of the conduction system.

**TREATMENT****APPROPRIATE HEALTH CARE**

Direct treatment toward the underlying cause

NURSING CARE

N/A

ACTIVITY

Unrestricted

DIET

No modifications unless required to manage underlying condition

R

CLIENT EDUCATION

- Does not cause hemodynamic abnormalities itself.
- The lesion causing the block could progress, leading to more serious arrhythmias or complete heart block.

SURGICAL CONSIDERATIONS

N/A

**MEDICATIONS****DRUG(S) OF CHOICE**

Not required unless needed to manage underlying condition

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

Serial ECG may show resolution of the lesion or progression to complete heart block.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- The causative lesion could progress, leading to a more serious arrhythmia or complete heart block.
- First- or second-degree AV block may indicate involvement of the left bundle branch.

EXPECTED COURSE AND PROGNOSIS

No hemodynamic compromise

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Atrioventricular Block, Complete (Third Degree)
- Atrioventricular Block, First Degree
- Atrioventricular Block, Second Degree—Mobitz I
- Atrioventricular Block, Second Degree—Mobitz II
- Left Anterior Fascicular Block
- Left Bundle Branch Block

ABBREVIATIONS

- AV = atrioventricular
- ECG = electrocardiogram

INTERNET RESOURCES

www.vetgo.com/cardio.

Suggested Reading

Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992.

Tilley LP, Smith FW. Essentials of Electrocardiography. Interpretation and Treatment, 4th ed. Ames, IA: Wiley Blackwell Publishing, 2016 (in preparation).

Tilley LP, Smith FWK, Jr.

Electrocardiography. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., Manual of Canine and Feline Cardiology, 5th ed. St. Louis, MO: Saunders Elsevier, 2015 (in press).

Author Larry P. Tilley

Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

ROCKY MOUNTAIN SPOTTED FEVER



BASICS

DEFINITION

A tick-borne rickettsial disease, caused by *Rickettsia rickettsii*, that affects dogs and is considered the most important rickettsial disease in humans.

PATHOPHYSIOLOGY

- Vector—American dog tick (*Dermacentor variabilis*), found east of the Great Plains; wood tick (*D. andersoni*), found from the Cascades to the Rocky Mountains. • Novel vectors (*Rhipicephalus sanguineus*) might explain the expansion of the disease into other regions of North America. • Transmission—via the saliva of the vector or blood transfusion; tick must be attached for 5–20 hours to infect host (humans, dogs, cats) or reservoir host (rodents and dogs).
- Incubation period—2 days–2 weeks.
- Infection—organism invades and multiplies in vascular endothelium; causes microvascular hemorrhage; platelet aggregation and antiplatelet antibodies cause thrombocytopenia, vasoconstriction, increased vascular permeability, increased plasma loss into the interstitial space (organ swelling), hypotension, and eventually DIC and shock; leads to widespread vasculitis in organs with endarterial circulation (cause of clinical signs).

SYSTEMS AFFECTED

- Multisystemic involvement.
- Cardiovascular—vasculitis, hypotension, shock. • Hemic/Lymphatic/Immune—bleeding tendency from thrombocytopenia, vasculitis, lymphadenopathy, splenomegaly.
- Musculoskeletal—joint pain. • Nervous—stupor, seizures, vestibular deficits, coma, cervical pain. • Ophthalmic—conjunctivitis, scleral injection. • Respiratory—dyspnea, cough. • Skin/Exocrine—edema of extremities, face.

GENETICS

N/A

INCIDENCE/PREVALENCE

- Tick season—late March to the end of September. • Prevalence—overall infections in ticks < 2%; varies by geographic locality.

GEOGRAPHIC DISTRIBUTION

- North and South America. • United States—no accurate data for dogs; similar distribution as for humans: eastern seaboard states (especially the Carolinas), Mississippi River valley, and south-central states.

SIGNALMENT

Species

Dog

Breed Predilections

- Purebred dogs seem more prone to developing clinical illness than mixed-breed dogs. • German shepherds—more common.

Mean Age and Range

Any age

Predominant Sex

None

SIGNS

Historical Findings

- Fever—within 2–3 days of tick attachment.
- Lethargy. • Depression. • Anorexia.
- Swelling (edema)—lips, scrotum, prepuce, ears, extremities. • Stiff gait—especially with scrotal or preputial swelling. • Spontaneous bleeding—sneezing, epistaxis. • Respiratory distress. • Neurologic—ataxia, head tilt.
- Ocular pain.

Physical Examination Findings

- Both clinical and subclinical illness occurs.
- Clinical—variable in severity; lasts 2–4 weeks untreated. • Ticks may still be present in acute cases. • Pyrexia. • Cutaneous lesions—edema of face, limbs, prepuce, scrotum. • Extremities—necrosis.
- Conjunctivitis. • Scleral injection.
- Respiratory—dyspnea, exercise intolerance resulting from pneumonitis, increased bronchovascular sounds. • Generalized lymphadenopathy. • Neurologic—vestibular dysfunction, altered mental status, seizures.
- Myalgia/arthritis. • Petechia.
- Ecchymoses—ocular, oral, genital regions; 20% of patients. • Hemorrhagic diathesis—epistaxis, melena, hematuria; in severe cases.
- Cardiac arrhythmias—sudden death. • DIC and death from shock—in severe acute cases.

CAUSES

R. rickettsii

RISK FACTORS

- Exposure to ticks • Co-infection with other pathogens (tick-borne)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Canine ehrlichiosis—*Ehrlichia canis*; not seasonal; can be clinically indistinguishable from Rocky Mountain spotted fever (especially acute cases); differentiate with serologic testing; both respond to same treatment. • Immune-mediated thrombocytopenia—not usually associated with fever or lymphadenopathy; differentiate with serologic testing; may treat for both until results are known. • Systemic lupus erythematosus—antinear antibody titer usually negative with Rocky Mountain spotted fever; serologic testing diagnostic.
- Brucellosis—scrotal edema; serologic testing diagnostic.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Thrombocytopenia (~ 40% of cases)—partly due to antiplatelet antibody.
- Megathrombocytosis mild anemia (normochromic, normocytic), mild leukopenia (early in infection), leukocytosis occasionally with toxic changes in neutrophils (and monocytosis)—as disease becomes more chronic.

Biochemistry

- Usually nonspecific. • Mild increases in ALT, ALP, BUN, creatinine, and total bilirubin (rare). • Hypercholesterolemia—consistently found; cause unknown.
- Hypoalbuminemia—from vascular endothelial damage. • Azotemia, hyponatremia, hypochloremia, and metabolic acidosis have all been reported.

Urinalysis

- Proteinuria—with or without azotemia; from glomerular/tubular damage.
- Hematuria—coagulation defects.

OTHER LABORATORY TESTS

- Several serologic tests available including the micro-IF, ELISA, and latex agglutination tests. Micro-IF test—most commonly used in diagnostic laboratories; measures IgG; serum titers take 2–3 weeks to rise; may be negative in very acute cases; paired titers—perform 3 weeks apart; four-fold increase between acute and convalescent titers; avoid misdiagnosis because of considerable cross-reactivity with other rickettsial organisms; high titers can be detected for up to 1 year after treatment. • ELISA—high sensitivity as can measure both IgG and IgM; detect infection earlier than tests measuring IgG alone. • Latex agglutination test—higher specificity, lower sensitivity than the micro-IF test (false-negative results occur), single increased titer is diagnostic. • PCR on whole blood and tissue specimens—more sensitive than culture, although might be detecting non-viable DNA. May detect DNA before sero-conversion in some dogs. Available from North Carolina State University.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Direct immunofluorescence—skin biopsies obtained by local anesthesia and punch biopsies from affected lesions; detect rickettsial antigens as early as 3–4 days post-infection. • CSF—often normal; may show an increase in protein and nucleated cells.

PATHOLOGIC FINDINGS

- Widespread petechia, splenomegaly, and generalized hemorrhagic lymphadenopathy.
- Necrotizing vasculitis with perivascular cell infiltration (mononuclear and neutrophilic).
- Vascular lesions—most prominent in the skin, kidneys, myocardium, meninges, retina,

R

ROCKY MOUNTAIN SPOTTED FEVER

(CONTINUED)

pancreas, gastrointestinal tract, and urinary bladder. • Hepatic and focal myocardial necrosis, nodular gliosis in the brain, and interstitial pneumonia common. • Special stains—to identify organisms.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient until stable and showing response to treatment.

NURSING CARE

- Dehydration—balanced electrolyte solution; use cautiously because of increased vascular permeability and expanded extracellular fluid volume (exacerbating cerebral and pulmonary edema). • Anemia—blood transfusion. • Hemorrhage from thrombocytopenia—platelet-rich plasma or a blood transfusion.

ACTIVITY

Restricted

DIET

N/A

CLIENT EDUCATION

- Prognosis—good in acute cases with appropriate and prompt therapy. • Response occurs within hours of treatment. • If treatment is not instituted until CNS signs occur or later in the disease process, mortality is high; patient with CNS signs may die within hours.

SURGICAL CONSIDERATIONS

If surgery is required for other reasons, blood transfusion may be needed to correct anemia and/or thrombocytopenia.



MEDICATIONS

DRUG(S) OF CHOICE

- Doxycycline—synthetic derivative of tetracycline, 10 mg/kg PO q12h for 10 days; or IV for 5 days if patient is vomiting.
- Prednisone—concurrent use; anti-inflammatory or immunosuppressive dose; given early in course of disease does not seem to be detrimental to the clinical recovery. May alleviate immune-mediated thrombocytopenia and cerebral edema but is not generally recommended as antibiotic therapy is curative.

CONTRAINDICATIONS

- Tetracycline (or derivatives)—do not use in patients < 6 months because of permanent yellowing of the teeth. • Renal

insufficiency—do not use tetracycline; doxycycline may be given (also excreted via the gastrointestinal tract). • Enrofloxacin—avoid in young dogs because articular cartilage damage can occur (preceded by lameness); gastrointestinal upset (vomiting, anorexia).

PRECAUTIONS

Chloramphenicol

- Avoid if serologic confirmation will be conducted after treatment has started; reduces titers to a greater extent than will tetracyclines.
- Warn client of public health risks; directly interferes with heme and bone marrow synthesis. • Avoid use in dogs with thrombocytopenia, pancytopenia, or anemia.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

- Tetracycline, chloramphenicol, and enrofloxacin—equally efficacious if used early.
- Oxytetracycline and tetracycline—22 mg/kg PO q8h for 14 days; effective and less expensive. • Chloramphenicol—puppies < 6 months of age; 20 mg/kg PO q8h for 14 days; recommended to avoid yellow discoloration of erupting teeth or in pregnant patients. • Enrofloxacin—3 mg/kg PO q12h for 7 days.



FOLLOW-UP

PATIENT MONITORING

Monitor platelet count every 3 days until normal.

PREVENTION/AVOIDANCE

- Control tick infestation on dogs—use dips or sprays containing dichlorvos, chlорfenvinphos, dioxathion, propoxur, or carbaryl. • Flea and tick collars—may reduce reinfestation; reliability is unproven. • Avoid tick-infested areas. • Environment—tick eradication impossible; organism maintained in rodents and other reservoir hosts.
- Removing ticks by hand—use gloves (see “Zoonotic Potential”); ensure mouth parts are removed because a foreign body reaction is likely to result if they are left in place.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

- Early antibiotic treatment—reduces fever and albumin extravasation and improves patient's attitude within 24–48 hours.
- Platelet counts—repeat every 3 days after initiating treatment until within normal

range; should return to normal within 2–4 days after initiating treatment.

- Serologic titers—lower in treated than in untreated dogs; titers remain positive during convalescence. • Naturally infected dogs never seem to become reinfected. • Acute cases—excellent prognosis with appropriate treatment. • With CNS disease—poor prognosis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

None

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

- Incidence (humans)—dropping in the United States; mid-1992–mid-1993: 300 cases; earlier incidence: up to 1,000 cases/year. • Mainly young adults and children infected. • Source of infection (humans)—from ticks that are transferred from dogs; not from dogs directly; when removing infected ticks from dogs. • Major clinical signs (humans)—mimic those in dogs; mainly fever and headache; neurologic signs occur later; skin rash appreciated in only 50% of patients. • Treatment with tetracycline results in a rapid recovery.

PREGNANCY/FERTILITY/BREEDING

N/A

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- CNS = central nervous system
- CSF = cerebrospinal fluid
- DIC = disseminated intravascular coagulation
- ELISA = enzyme-linked immunosorbent assay
- micro-IF = microscopic immunofluorescence
- PCR = polymerase chain reaction

Suggested Reading

Allison RW, Little SE. Diagnosis of rickettsial diseases in dogs and cats. *Vet Clin Pathol* 2013; 42:127–144.

Greene CE, Kidd L, Breitschwerdt EB. Rocky Mountain spotted fever. In: Greene CE, ed., *Infectious Diseases of the Dog and Cat*, 4th ed. St. Louis, MO: Saunders Elsevier, 2012, pp. 259–267.

Author Stephen C. Barr

Consulting Editor Stephen C. Barr



Client Education Handout
available online

RODENTICIDE TOXICOSIS—ANTICOAGULANTS



BASICS

DEFINITION

- Anticoagulant rodenticide intoxication results in a delayed onset (3–5 days) coagulopathy caused by the reduction of vitamin K₁–dependent clotting factors (II, VII, IX, X).
- There are two primary types of anticoagulant rodenticides, first- and second-generation. First-generation anticoagulants, such as warfarin, are generally less toxic and shorter acting than second-generation which tend to persist longer in the liver and require 3–4 weeks of antidote therapy.

PATHOPHYSIOLOGY

- Anticoagulant rodenticides inhibit vitamin K₁ epoxide reductase, DT diaphorase, and possibly other enzymes involved in the reduction of vitamin K₁ epoxide to vitamin K₁.
- Vitamin K₁ is required for carboxylation of clotting factors II, VI, IX, and X; uncarboxylated clotting factors do not bind calcium sufficiently to participate in clot formation.

SYSTEMS AFFECTED

- Hemic/Lymphatic/Immune
- Respiratory

INCIDENCE/PREVALENCE

Common. Anticoagulant rodenticide exposures are the most frequently reported type of rodenticide exposure to animal poison control centers. Traditionally, most rodenticides sold for in-home use contained anticoagulant baits. In 2011, the United States Environmental Protection Agency banned the use of second-generation anticoagulants (i.e., brodifacoum, bromadiolone, difenacoum, and difethialone) for residential use unless placed by a pest control operator. Although first-generation anticoagulants (e.g., warfarin, chlorophacinone, and diphacinone) are still allowed, some manufacturers switched to non-anticoagulant baits such as bromethalin. Between 2011 and 2014, Pet Poison Helpline reported a 65% increase in bromethalin exposures in cats and dogs.

SIGNALMENT

- No breed or gender predilections; younger animals may ingest bait more readily.

SIGNS

General Comments

- May be slightly more prevalent in the spring and fall when rodenticide products are used.
- Clinical signs typically begin 3–5 days after ingestion.

Historical Findings

- Use of anticoagulant rodenticides.

- Evidence of rodenticide dye in vomitus or feces.
- Coughing, dyspnea, tachypnea, or exercise intolerance are often the first clinical signs.
- Bleeding from body orifices; subcutaneous or joint swelling may also be observed.

Physical Examination Findings

- Evidence of hemorrhagic shock (i.e., tachycardia, hypovolemia, hypotension, poor pulse quality, pallor).
- Coughing, dyspnea, tachypnea, pale mucous membranes.
- Hematomas—often ventral and at venipuncture sites; subcutaneous hematomas.
- Bleeding from body orifices, periorbital bleeding, scleral hemorrhage.
- Hemarthrosis, lameness.
- Exercise intolerance, lethargy, depression.
- Muffled heart or lung sounds.
- Distended abdomen (hemoabdomen).

CAUSES

Ingestion of anticoagulant rodenticides or, rarely, ingestion of prey that have been exposed to anticoagulant rodenticides (see “Risk Factors”).

RISK FACTORS

- Dogs are much more sensitive to anticoagulant rodenticides than cats.
- Small doses over several days may add up to a toxic dose.
- Secondary or relay toxicosis by consumption of poisoned rodents is possible but unlikely.
- There is a wide range of toxicity between anticoagulant rodenticides. In general, if the ingestion exceeds 1/5–1/10 the LD₅₀, decontamination and monitoring for coagulopathy are indicated.
 - Dogs
 - Brodifacoum, LD₅₀ 0.25–2.5 mg/kg
 - Bromadiolone, LD₅₀ 11–20 mg/kg
 - Chlorophacinone, LD₅₀ 50–100 mg/kg
 - Difethialone, LD₅₀ 4 mg/kg
 - Diphacinone, LD₅₀ 3–7.5 mg/kg
 - Warfarin, LD₅₀ 20–50 mg/kg
 - Cats
 - Brodifacoum, LD₅₀ 25 mg/kg
 - Bromadiolone, LD₅₀ > 25 mg/kg
 - Difethiolone, LD₅₀ > 16 mg/kg



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Congenital clotting factor deficiencies.
- Immune-mediated thrombocytopenia: platelet count will reveal severe thrombocytopenia.
- Coagulation factor deficiency secondary to hepatic disease: assay for factor deficiencies (e.g., factor VII), liver function, bile acids.
- Disseminated intravascular coagulopathy which is typically associated with neoplasia, sepsis, pancreatitis, or concurrent disease. Lab evidence includes prolonged PT, PTT,

- elevated fibrin degradation products, d-dimer with thrombocytopenia.
- Fat malabsorption.
- Hemorrhagic shock from trauma, neoplasia, bone marrow suppression, immune mediated hemolytic anemia.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia with marked hemorrhage, often acute and nonregenerative.
- Thrombocytopenia, mild. Typically 50,000–150,000 × 10³/µL.

OTHER LABORATORY TESTS

- Activated clotting time > 150 seconds supports coagulopathy but is not specific for anticoagulant rodenticide poisoning.
- Prolonged PT and PTT support exposure to anticoagulant rodenticide; PT will be prolonged 6–18 hours earlier than PTT. These values will normalize with vitamin K₁ therapy.
- PIVKA assay, although this is rarely used.
- Anticoagulant rodenticide detection in the blood or liver will confirm exposure to a specific product.
- Anticoagulant rodenticide detection in the stomach or intestinal contents is not reliable due to the delay between consumption of bait and appearance of clinical signs.

IMAGING

- Thoracic radiography may reveal pleural effusion (i.e., hemothorax); multilobular, alveolar infiltration (i.e., pulmonary hemorrhage), or an enlarged cardiac silhouette (i.e., hemopericardium).
- Ultrasound of both the pleural and peritoneal cavities may reveal effusion consistent with hemorrhage.

DIAGNOSTIC PROCEDURES

Thoracentesis may confirm hemothorax.

PATHOLOGIC FINDINGS

- Free blood in the thoracic cavity, lungs, and abdominal cavity is a common post mortem finding.
- Hemorrhage into the cranial vault, gastrointestinal tract, subcutaneous space, intramuscular space, and urinary tract is less common.



TREATMENT

APPROPRIATE HEALTH CARE

- Patients in acute crisis should be hospitalized.
- Patients without active hemorrhaging or a stabilized coagulopathy may be treated on an outpatient basis.
- Vitamin K₁ is antidotal at 2.5–5 mg/kg q24h or divided q12h. The preferred route of administration is oral; however, in case of a coagulopathic patient, the subcutaneous route is preferred due to the potential for limited GI absorption. Use a small needle in multiple locations, if needed.

RODENTICIDE TOXICOSIS—ANTICOAGULANTS

(CONTINUED)

- Treat acute hemorrhagic shock with IV crystalloids, colloids, or blood products as needed. Initial crystalloid boluses of 10–20 mL/kg can be given over 15–20 min during stabilization. Repeat 2–3 times as needed to increase blood pressure.
- The use of packed RBCs, whole blood, fresh frozen plasma (FFP), or frozen plasma (FP) may be necessary to replace coagulation factors.
- Treat life-threatening cardiac tamponade or hemothorax with pericardiocentesis or thoracocentesis as indicated. If the patient is stable and responding to treatment, these procedures should be avoided. With time, the blood will reabsorb.

NURSING CARE

Provide supportive care as needed.

ACTIVITY

Confine the patient until the coagulopathy is stabilized as activity enhances blood loss.

DIET

Feed a nutritious, high-quality protein diet to support coagulation factor synthesis.

CLIENT EDUCATION

- Warn client that re-exposure, even months to years later, could be a serious problem due to persistence of second-generation anticoagulants in the liver.
- Encourage the owner to pick up all loose/unprotected bait on the property.
- Do not discontinue vitamin K₁ therapy early, even if the patient is asymptomatic.

SURGICAL CONSIDERATIONS

- Thoracentesis may be important for removing free thoracic blood, which causes dyspnea and respiratory failure (see "Appropriate Health Care").
- The coagulopathy must be corrected before surgery.

**MEDICATIONS****DRUG(S) OF CHOICE**

Vitamin K₁, 2.5–5.0 mg/kg PO q12h for 5–7 days for most first-generation anticoagulants and PO q24h for 4–6 weeks for most second-generation anticoagulants; bioavailability may be enhanced by the concurrent feeding of a small amount of fat, such as canned dog food.

CONTRAINDICATIONS

- Vitamin K₃ is not efficacious in the treatment of anticoagulant rodenticide toxicosis and should not be used.
- Intravenous vitamin K₁ has been reported to cause anaphylactoid reactions. Avoid this route of administration.
- Minimize stress, trauma, jugular venipuncture, and cystocentesis due to the risk of acute and catastrophic hemorrhage.

PRECAUTIONS

- Avoid large-bore hypodermic needles, unnecessary surgical procedures, and parenteral injections.
- Use the smallest possible needle when giving an injection or collecting samples.

POSSIBLE INTERACTIONS

Sulfonamides and phenylbutazone may displace anticoagulant rodenticides from plasma binding sites, leading to more free toxicant and increased risk of toxicosis.

**FOLLOW-UP****PATIENT MONITORING**

Use PT (preferred) 2–3 days following the last dose of vitamin K₁ to assess proper duration of therapy. If the PT is prolonged, administer another 1–3 weeks of vitamin K₁ and retest.

PREVENTION/AVOIDANCE

Prevent pet's access to anticoagulant rodenticides by using bait stations and keeping stored bait in a secure location.

POSSIBLE COMPLICATIONS

- Secondary bacterial pneumonia may occur following intrapulmonary hemorrhage.
- Intracranial and intra-articular hemorrhage may occur.
- Pregnant animals can abort due to placental hemorrhage and detachment.

EXPECTED COURSE AND PROGNOSIS

If the patient survives the first 48–72 hours of acute coagulopathy, the prognosis improves.

**MISCELLANEOUS****PREGNANCY/FERTILITY/BREEDING**

- Warfarin, diphacinone, and perhaps other anticoagulant rodenticides may pass into amniotic fluid and to the fetuses of an exposed pregnant animal. These toxicants may also pass via the milk and present concerns for nursing offspring. In general, antidotal treatment of the pregnant or nursing patient is recommended. Alternatively, nursing young should be weaned.
- Pregnant animals can abort due to placental hemorrhage and detachment.

ABBREVIATIONS

- ACT = activated clotting time
- DIC = disseminated intravascular coagulation
- PT = prothrombin time
- PTT = partial thromboplastin time

INTERNET RESOURCES

- www.petpoisonhelpline.com
- www.aspca.org/pet-care/animal-poison-control

Suggested Reading

Murphy MJ. Anticoagulants. In: Osweiler GD, et al., eds., Blackwell's Five-Minute Veterinary Consult Clinical Companion Small Animal Toxicology. Ames, IA: Wiley-Blackwell, 2011, pp. 759–768.

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Consulting Editor Lynn R. Hovda



Client Education Handout
available online

RODENTICIDE TOXICOSIS—BROMETHALIN



BASICS

OVERVIEW

- Bromethalin produces marked CNS effects.
- Bromethalin uncouples oxidative phosphorylation resulting in cerebral edema and elevated CSF pressure.
- Toxic doses are approximately 0.3 and 2.5 mg/kg in cats and dogs, respectively.
- The reported oral LD₅₀ of bromethalin bait is 0.54 and 3.7 mg/kg in cats and dogs, respectively.
- Trade names include Vengeance, Assault, Trounce, No Pest Rat & Mice Killer, CyKill, Fastrac, and others.
- Chemical name: N-methyl-2,4-dinitro-N-[2,4,6-tribromophenyl]-6-[trifluoromethyl] benzeneamine.

SIGNALMENT

- Dogs and cats. Other species may be affected.
- No breed predilections have been noted.
- Any age may be affected.

SIGNS

- Ingestion of supralethal doses of bromethalin (\geq LD₅₀) may result in an acute onset of CNS excitation, muscle tremors, and seizures.
- Ingestion of lower doses of bromethalin ($<$ LD₅₀) results in a delayed syndrome that develops within 2–7 days of ingestion; however, delays of up to 2 weeks may occur.
- Common clinical signs seen include anorexia, progressive ataxia, paresis, and hind limb paralysis, moderate to severe central nervous system depression, fine muscle tremors, and focal motor or generalized seizures.
- Forelimb extensor rigidity and decerebrate postures are often seen.
- With mild poisoning, clinical signs may resolve within 1–2 weeks of onset of clinical signs, although signs can persist for up to 4–6 weeks in some animals. Prognosis is very guarded in severely affected animals.

CAUSES & RISK FACTORS

Ingestion of rodenticides containing bromethalin occurs most often in animals $<$ 1 year of age.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Neurologic syndromes produced by trauma, neoplasia, cerebral vascular disorders, as well as infectious and other toxic agents.

CBC/BIOCHEMISTRY/URINALYSIS

Alterations in routine serum electrolytes and chemistries are not anticipated.

OTHER LABORATORY TESTS

- Diagnosis dependent upon (1) the presence of an exposure history to a potentially toxic dose of a bromethalin-based rodenticide, (2) the development of appropriate clinical

signs, (3) the presence of diffuse white matter vacuolization, and (4) analytical confirmation of bromethalin residues in tissues.

- EEG abnormalities may include spike and spike-and-wave activity, marked voltage depression, and abnormal high voltage slow wave activities.
- CSF from bromethalin-poisoned dogs generally reveals normal cytology, protein concentration, specific gravity, and cell count.

IMAGING

Neuroimaging (MRI) may reveal generalized brain edema.

PATHOLOGIC FINDINGS

- Lesions are generally confined to the CNS.
- Gross evidence of cerebral edema may occur but is relatively mild.
- Histopathologic changes include spongy degeneration (white matter vacuolization) in the cerebrum, cerebellum, brain stem, spinal cord, and optic nerve white matter due to myelin edema.
- Analytical chemical confirmation of bromethalin residues in fresh frozen fat, liver, kidney, and brain tissue.
- Bromethalin has been detected in formalin-fixed human liver and brain samples by gas chromatography with mass spectrometry detection.



TREATMENT

- Aggressive early treatment with oral activated charcoal and a cathartic to reduce gastrointestinal absorption is warranted.
- Animal Poison Control Centers have recommended the judicious use of intravenous lipid emulsions (ILE) in cases of severe intoxication.
- Many animals recovering from bromethalin toxicosis exhibit prolonged anorexia and may require supplemental feeding to maintain caloric intake.
- Use cage padding to reduce the risk of decubitus ulcer formation in recumbent animals.



MEDICATIONS

DRUG(S)

- Gastrointestinal tract decontamination including early induction of emesis followed by repeated administration of activated charcoal (0.5–1 mg/kg PO) and an osmotic cathartic (sodium sulfate, 125 mg/kg PO) should be given every 4–8 hours for at least 2–3 days.
- Control of cerebral edema with mannitol (250 mg/kg, q6h IV), dexamethasone (2 mg/kg, q6h IV), and furosemide (1–2 mg/kg, q6h IV) has been recommended but shown to have limited clinical efficacy.
- Diazepam (1–2 mg/kg, as needed, IV) and/or phenobarbital

(5–15 mg/kg, as needed, IV) may be given to abolish severe muscle tremors and seizures.

- 20% intravenous lipid emulsions: Bolus dose 1.5 mL/kg over 2–3 min; continuous rate infusion of 0.25 mL/kg/min for 30–60 min. Check serum q2h until it becomes clear; repeat as needed; if no clinical improvement after 3 doses, discontinue.

CONTRAINdications/POSSIBLE INTERACTIONS

- Contraindications for the use of mannitol include renal disease, pulmonary edema, dehydration, and intracranial hemorrhage.
- Animals receiving mannitol therapy may become dehydrated during treatment.
- Rehydration of some animals is associated with a worsening of clinical signs, possibly due to rebound cerebral and pulmonary edema. Maintenance of hydration is important and can be more safely accomplished through the administration of oral fluids.
- Adverse effects of ILE may relate to contamination of the lipid product or direct reaction to the emulsion.



FOLLOW-UP

- May require several weeks to recover from mild poisoning.
- Prognosis is poor for the severely affected animals.
- Prevent ongoing rodenticide ingestion.



MISCELLANEOUS

Relay toxicity arising from the consumption of animals poisoned with bromethalin has been reported.

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- EEG = electroencephalogram
- ILE = intravenous lipid emulsion
- MRI = magnetic resonance imaging

Suggested Reading

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Dunayer E. Bromethalin – the other rodenticide. Vet Med 2003, 98(9):732–736.

Gwaltney-Brant S, Meadows I. Use of intravenous lipid emulsions for treating certain poisoning cases in small animals. Vet Clin North Am Small Anim Pract 2012, 42:251–262.

Author David C. Dorman

Consulting Editor Lynn R. Hovda

RODENTICIDE TOXICOSIS—PHOSPHIDES



BASICS

OVERVIEW

- Used as a rodenticide since the early 1930s at various concentrations (2–10%) in a powder, pellet, or paste formulation. Available as zinc, aluminum, and magnesium salts.
- Most have a distinctive odor, often described as acetylene, rotten fish, or garlic.
- Most common route of exposure is ingestion; however, toxicosis can occur via inhalation and absorption through broken skin.
- Hydrolysis leads to phosphine gas production. Phosphine gas has corrosive and irritant effects on the GI mucosa, which leads to vomiting, hematemesis, or melena. The gas is rapidly absorbed and systemically distributed leading to effects on other organ systems.
- Phosphine leads to the production of free radicals and oxidative stress causing direct cellular damage and may inhibit cellular respiration.
- Toxic exposure is reported to be 20–40 mg/kg; however, the gastric pH is reported to affect toxicity.

SIGNALMENT

No known age, breed, or sex predilection

SIGNS

- Clinical signs generally occur within 15 minutes to 4 hours, but can be delayed up to 18 hours.
- Gastrointestinal—anorexia, vomiting, and melena.
- Cardiovascular—direct myocardial damage, arrhythmias, decreased inotropy, hypotension.
- Pulmonary—pulmonary edema, pleural effusion.
- Hemic/lymphatic/immune—methemoglobinemia, Heinz body production.
- Nervous—ataxia, weakness, tremors, hyperesthesia, and seizures.
- Renal/urologic—azotemia, acute renal failure.
- Hepatobiliary—increased ALT, AST, and total bilirubin.
- Endocrine/metabolic—metabolic acidosis, electrolyte imbalance.
- Musculoskeletal—weakness, ataxia.

CAUSES & RISK FACTORS

- Increased hydrolysis in a moist, acidic environment; thus recent food ingestion lowers gastric pH and increases hydrolysis. Owner should be told not to feed their pet.
- Owners and veterinary staff are at risk for inhalation exposure if the animal vomits in a poorly ventilated area. Owners should be told to lower their windows on the way to the clinic.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Organophosphate • Metaldehyde
- Serotonin syndrome • NSAID toxicosis
- Tremogenic mycotoxins • Acute GI disease (HGE, gastroenteritis, parvovirus)

- Congestive heart failure • Respiratory disease (non-cardiogenic pulmonary edema—secondary to electrocution, near drowning, seizures, or ARDS) • Metabolic disease (renal, hepatic, pancreatitis)

CBC/BIOCHEMISTRY/URINALYSIS

- May see increased liver enzymes (ALT, AST, and total bilirubin); can be delayed 3–5 days.
- Electrolyte alterations (decreased potassium or magnesium). • Methemoglobinemia, Heinz body formation, and subsequent hemolysis on a CBC.

OTHER LABORATORY TESTS

Confirmation through gas chromatography or a Dräger detection tube (referral laboratory testing). The Dräger detection tube test was validated using canine stomach contents and vomitus. • Post-mortem samples from the liver, kidney.

IMAGING

If respiratory signs, thoracic radiographs to assess for pulmonary edema.

PATHOLOGIC FINDINGS

Are nonspecific



TREATMENT

- There is no antidote.
- The goal of treatment with recent, asymptomatic patients is to safely decontaminate. Administration of a liquid antacid such as magnesium hydroxide, aluminum hydroxide, calcium carbonate, or even a 5% sodium bicarbonate solution may help to increase the gastric pH and thus decrease phosphine gas production.
- Emesis induction with apomorphine, or gastric lavage and hydrogen peroxide may also be considered for gastric emptying.
- Activated charcoal may help decrease toxicity, but should be given only if the patient's clinical status allows.
- The patient should be placed on IV fluid therapy and monitored for any clinical signs or progression of clinical signs for at least 18 hours.
- Supplemental oxygen for hypoxemia.



MEDICATIONS

- GI protectants such as famotidine 0.5–1 mg/kg IV/PO q12–24h, omeprazole 0.5–1 mg/kg PO q24h, sucralfate 0.25–1 g PO q8–12h, and possibly misoprostol 2–5 µg/kg PO q8h.
- Tremors, methocarbamol (50–220 mg/kg IV or to effect; do not exceed 330 mg/kg/day).
- Seizures may require anticonvulsants (diazepam 0.5 mg/kg IV, phenobarbital 4–16 mg/kg IV/to effect, levetiracetam 30–60 mg/kg IV, or propofol 1–8 mg/kg or to effect, followed by a CRI at 0.1–0.6 mg/kg/h).
- If liver effects give hepatoprotectants

(S-adenosyl-methionine 18 mg/kg PO q24h, silymarin/milk thistle 50–250 mg/day PO q24h, and Vit K₁ 2–3 mg/kg PO q12–24h).

- Oxidative damage or for methemoglobinemia, N-acetylcysteine. • If painful consider analgesics, opioids (hydromorphone 0.05–0.1 mg/kg IV) or tramadol 2–4 mg/kg PO q8–12h. Avoid NSAIDs.



FOLLOW-UP

Varies on a case basis

PATIENT MONITORING

Several organ systems may be affected; vitals, heart rhythm, blood pressure, and CNS should be monitored for 18 hours.

PREVENTION/AVOIDANCE

Have owners remove all baits from environment.

POSSIBLE COMPLICATIONS

Liver or renal failure

EXPECTED COURSE AND PROGNOSIS

- Asymptomatic patients should be monitored for up to 12–18 hours.
- Symptomatic patients should be monitored for at least 48 hours or until life-threatening signs have resolved.



MISCELLANEOUS

ABBREVIATIONS

- ALT = alanine transaminase • ARDS = acute respiratory distress syndrome • AST = aspartate transferase • CNS = central nervous system • GI = gastrointestinal • HGE = hemorrhagic gastroenteritis • NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

Easterwood L, Chaffin MK, Marsh PS, et al. Phosphine intoxication following oral exposure of horses to aluminum phosphide-treated feed. J Am Vet Med Assoc 2010, 236:446–450.

Gray SL, Lee JA, Hovda LR, et al. Potential zinc phosphide rodenticide toxicosis in dogs: 362 cases (2004–2009). J Am Vet Med Assoc 2011, 239:646–651.

Knight MW. Zinc phosphide. In: Peterson ME, Talcott PA, eds., Small Animal Toxicology, 3rd ed. St. Louis, MO: Elsevier Saunders, 2013, pp.853–864.

Author Sarah L. Gray

Consulting Editor Lynn R. Hovda



Client Education Handout
available online

ROTAVIRUS INFECTIONS



BASICS

OVERVIEW

- Non-enveloped, double-stranded RNA virus; *rota* (Latin; “wheel”) for shape of the capsid; genus within the family Reoviridae; relatively resistant to environmental destruction (acid and lipid solvents); unique double capsid protects virus from inactivation in the upper gastrointestinal tract.
- Wide host range, identified in almost every species investigated.
- Most significant cause of severe gastroenteritis in young children (< 2 years) and animals throughout the world.
- Transmission—fecal-oral contamination.
- Infection—affects mature epithelial cells on luminal tips of the intestinal villi; causes swelling, degeneration, and desquamation; denuded villi contract; results in villous atrophy with loss of absorptive capability and loss of brush border enzymes (e.g., disaccharidases); leads to osmotic diarrhea.

SIGNALMENT

- Dogs and cats.
- Pups < 12 weeks old and more often < 2 weeks old—diarrhea.
- Kittens and young cats (< 6 months of age)—more susceptible to infection.

SIGNS

- Dogs—most infections subclinical or limited to relatively mild, nonspecific, watery to mucoid diarrhea, anorexia, and lethargy; rare fatalities reported.
- Cats—primarily subclinical or mild diarrhea; more severe clinical disease may occur with co-infections or in stressed conditions.

CAUSES & RISK FACTORS

- Rotavirus.
- Young animals with immature immune systems at increased risk.
- Presence of other enteric pathogens.
- Overcrowding (virus stable in environment).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Canine viral enteritis—canine parvovirus; canine coronavirus; canine astrovirus; canine calicivirus; canine herpesvirus; canine distemper virus; canine reovirus.
- Feline viral enteritis—feline parvovirus (feline panleukopenia virus); FeLV; feline coronavirus; feline astrovirus; feline calicivirus.

- Other causes of enteritis—bacteria (e.g., *Salmonella*, *Campylobacter*, *Clostridium*); fungi; protozoa; parasites; foreign bodies; intussusception; allergies; toxicants.

CBC/BIOCHEMISTRY/URINALYSIS

Non-contributory

OTHER LABORATORY TESTS

- Serology—not recommended; most animals (e.g., 85% of dogs) carry antibodies owing to previous exposure or from passive antibody immunization transfer from the bitch or queen; must demonstrate four-fold difference in acute and convalescent serum samples.
- Direct electron microscopy—detects virus in feces; rapid; lack of sensitivity.
- Immunoelectron microscopy—more sensitive and specific than direct electron microscopy; not commonly available.
- ELISA—detect common group rotavirus antigen in feces (Remel Xpect Rotavirus test, Oxoid Company, Nepean, ON, Canada).
- Latex agglutination; Virogen Rotatest (Wampole Laboratories, Cranbury, NJ).
- Immunochemical assay (ImmunoCard STAT! Rotavirus Meridian Bioscience, Inc. Cincinnati, OH).
- Immunofluorescence.
- Virus isolation.
- PCR.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Histology—swollen small intestinal villi; mild infiltration by macrophages and neutrophils; virus detected by fluorescent antibody test.



TREATMENT

- Symptomatic for diarrhea—fluids, electrolytes, and dietary restriction.
- Antibiotic therapy not indicated.
- Principal protection—probably antibodies in milk of immune bitch or queen.



MEDICATIONS

DRUG(S)

N/A

CONTRAINdications/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

N/A



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Rotaviruses are not host-specific; thus, affected puppy or kitten may pose a potential human health hazard, particularly for infants.
- Exercise care when handling fecal material from pets with diarrhea.
- Humans—diarrhea; infants in developed countries: high morbidity and low mortality (attributed to fluid therapy); infants and young children in developing countries: leading cause of life-threatening diarrhea (more than 600,000 deaths per year in children < 5 years old); in United States, prior to routine vaccination of infants which began in 2006, more than 3 million episodes of diarrhea, ~500,000 clinic visits, ~60,000 hospitalizations but only 20–40 deaths per year. In US, pentavalent rotavirus oral vaccine has reduced hospitalizations by 60–75%.

ABBREVIATIONS

- ELISA = enzyme-linked immunosorbent assay
- FeLV = feline leukemia virus
- PCR = polymerase chain reaction

Suggested Reading

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Author J. Paul Woods

Consulting Editor Stephen C. Barr

R

ROUNDWORMS (ASCARIASIS)



BASICS

OVERVIEW

- Ascariasis caused by *Toxocara canis* (dogs), *T. cati* (cats), and *Toxascaris leonina* (dogs and cats); *Baylisascaris* (raccoons) can infect dogs and causes neurocysticercosis in people.
- Transplacental transmission of *T. canis* larvae from bitch's tissues to pups causes prenatal infection; transmammary transmission of larvae occurs with both *Toxocara* spp.; no transplacental or transmammary transmission occurs with *Toxascaris*. • In first month of life, infected neonatal pups may develop abdominal pain and rapidly deteriorate before eggs appear in feces.
- Older pups and kittens can acquire infection by ingesting eggs disseminated on premises by dams with post-gestational infection; dams can be infected by ingesting immature stages in pups' feces or vomitus, or by predation on vertebrate transport hosts.
- Adult ascarids occur in lumen of small intestine; larval stages of *Toxocara* spp. may migrate in liver and lungs. • If very numerous, ascarids (up to 10–12 cm long) can distend intestine leading to colic, interference with gut motility, inability to utilize food, and, intestinal rupture.

SIGNALMENT

- Dog and cat. • Important clinically in pups and kittens due to transmission *in utero* and/or in colostrum/milk.

SIGNS

- Abdominal distension ("pot belly"); often with palpable intestinal distension. • Colic.
- Weakness, loss of condition, cachexia; poor nursing or appetite; scant feces. • Coughing due to larval lung migration. • Entire litter may be affected.

CAUSES & RISK FACTORS

- *Toxocara* infection of bitch with dormant larvae in tissues or infection of queen during late pregnancy or early lactation. • Access to infected transport hosts. • Concurrent enteric infections. • Larvae undergo extensive migrations throughout the body and can cause granulomatous inflammation (visceral larva migrans). Visceral larva migrans caused by a variety of ascarids is a major cause of morbidity in humans throughout the world.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Transmammary perinatal infection of neonates with hookworms (anemia, melena, weakness, lethargy, pale mucus membranes, enteritis) or *Strongyloides* (diarrhea); coccidiosis, giardiasis also cause enteritis in pups and kittens; examine feces to identify

eggs or larvae. • *Physaloptera* can also occur in vomitus.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Fecal flotation to detect eggs; *Toxocara* eggs spherical pitted outer shell membrane, single dark cell filling interior, 80–85 µm (*T. canis*), ~75 µm (*T. cati*). • *Baylisascaris* eggs similar to *T. canis* eggs but smaller (~76 × 60 µm), more finely pitted shell. • *Toxascaris* eggs ovoid, smooth exterior shell membrane, 1–2 cells with light-colored cytoplasm; cells do not fill interior of egg; 80 × 70 µm in diameter. • Necropsy of siblings that died of similar signs. • Identify ascarids in feces, vomitus, or small intestine by size, presence of three lips, and cervical alae.



TREATMENT

- Anthelmintic treatment as outpatient.
- Acute severe cases treated as inpatients; supplement with intravenous fluids.
- Milbemycin or other anthelmintic effective against *T. canis* suggested for treatment (extra-label) of *Baylisascaris* in dog. • Alert client to possibility of sudden death or chronic debilitation. • Treat bitch or queen with adulticide/larvicide anthelmintic to remove intestinal stages and to limit transmission to subsequent litters.



MEDICATIONS

DRUG(S)

Adulticide/Larvicide Anthelmintics

- Fenbendazole 50 mg/kg PO q24h for 3 days. • Milbemycin oxime 0.5 mg/kg (dogs) or 2 mg/kg (cats) PO q30 days. • Emodepside (3 mg/kg) or praziquantel (12 mg/kg) topically once for cats ≥ 8 weeks old; repeat in 30 days if cat is reinfected.

Adulticide Anthelmintics

- Pyrantel, 5 mg/kg (dogs) or 10–20 mg/kg (cats, extra-label) PO.
- Pyrantel/praziquantel, label dose for cats.
- Febantel/ praziquantel/pyrantel, label dose for dogs. • Ivermectin/pyrantel, label dose for dogs. • Pyrantel pamoate 5 mg/kg (dogs) or 10–20 mg/kg (cats, extra-label). • Selamectin 6 mg/kg topically once (*T. cati*, cats), extra-label in dogs. • Milbemycin oxime, label dosages for dogs and cats. • Moxidectin/ imidacloprid, label dosages topically for dogs and cats.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

Repeat post-treatment fecal exams on pups/kittens and/or repeat anthelmintic treatment every 2–3 weeks until old enough for monthly anthelmintic product because migrating larvae acquired from bitch or dam will continue to mature.

PREVENTION/AVOIDANCE

- To minimize environmental contamination with infective eggs, treat infected dogs/cats with anthelmintic and promptly dispose of feces. • Prevent dogs/cats from hunting or ingesting transport hosts. • Extra-label treatment of bitch or queen with adulticide/larvicide anthelmintic to remove intestinal stages and decrease vertical transmission to offspring.

POSSIBLE COMPLICATIONS

- Transplacental transmission of large numbers of larvae can result in fetal death or birth of weak, non-viable pups. • Infection with large numbers of ascarids can cause blockage, possible rupture of small intestine.

EXPECTED COURSE AND PROGNOSIS

Prognosis good after anthelmintic treatment; guarded with severe prenatal *T. canis* infection.



MISCELLANEOUS

AGE-RELATED FACTORS

Greater clinical concern in neonates

ZOONOTIC POTENTIAL

- Visceral larva migrans, ocular larva migrans, neural larva migrans, chronic abdominal or cutaneous problems may follow ingestion of infective *Toxocara* spp. or *Baylisascaris* eggs by humans. • Most likely cause of neural larva migrans is *Baylisascaris*. Virtually all raccoons become infected with *Baylisascaris* and therefore extreme caution should be exercised with clients having raccoons as "pets."

INTERNET RESOURCES

- <http://www.capcvet.org>
- <http://www.cdc.gov>

Suggested Reading

Bowman DD. Georgis' Parasitology for Veterinarians, 9th ed. St. Louis: Saunders, 2009, pp. 197–198, 201–208.

Author Matt Brewer

Consulting Editor Stephen C. Barr

SAGO PALM TOXICOSIS



BASICS

OVERVIEW

- Cycad palms, also called sago palms, belong in the family Cycadaceae.
- Are native to tropical and subtropical regions but have become popular ornamental plants in the US.
- *Cycas revoluta*, *Cycas circinalis*, and *Zamia floridana* are the most common species.
- Contain the toxins, cycasin, beta-methylamino-L-alanine, and an unidentified high molecular weight compound.
- Toxins present in all parts of the plant; highest concentrations in seeds.
- Cycasin is metabolized by the intestinal flora to the active hepatotoxic, carcinogenic, mutagenic, teratogenic, and neurotoxic compound, methylazoxymethanol (MAM).
- Cycad toxicosis has been documented in several animal species (dogs and ruminants) and humans.
- In dogs, gastrointestinal disturbances and hepatic damage predominate; nervous system involvement is less common.

SIGNALMENT

- Dogs—no breed, sex, or age predilection
- Cats—no cases reported.

SIGNS

- Gastrointestinal disturbances such as vomiting, diarrhea, and abdominal pain.
- Signs associated with hepatic damage (ecchymoses, petechiae, hemorrhage, edema, etc.).
- Gait abnormalities; paresis/paralysis; tremors.
- Depression, coma, and death.

CAUSES & RISK FACTORS

Access to and ingestion of cycad palm



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other Causes of Acute Gastrointestinal Upset

- Infectious • Metabolic • Toxic • Dietary

Other Causes of Acute Liver Failure

- Microcystins (hepatotoxic blue-green algal toxins)—access to water with algal bloom, algal material on legs or in stomach contents, detection of microcystins in stomach contents.
- Amanitin—access to mushrooms (*Amanita*, *Galerina*, and *Lepiota* spp.), gastrointestinal signs between 6 and 24 hours after ingestion.
- Cocklebur (*Xanthium* spp.)—access to cocklebur (only seeds and two-leaf cotyledon stage are toxic).
- Aflatoxins—access to moldy food.
- Acetaminophen overdose.
- Xylitol—access to xylitol-containing products (sugar-free gum, chewable vitamins, baked goods); initial hypoglycemia.
- Severe acute pancreatitis.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia • Elevated serum liver enzymes (ALT, AST, ALP, bilirubin)
- Hypoalbuminemia • Hypoglycemia
- Glucosuria, hemoglobinuria, myoglobinuria, bilirubinuria, proteinuria, and increased urine specific gravity

OTHER LABORATORY TESTS

- Ammonia tolerance test—hyperammonemia • Prolonged PT/PTT

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- History of cycad palm ingestion and presence of appropriate clinical signs.
- Identification of plant in ingesta or feces.
- Biopsy and histopathology of liver—hepatocellular necrosis.
- Necropsy—hepatocellular necrosis.

PATHOLOGIC FINDINGS

- Detection of cycad palm material in GI tract and/or in feces.
- Gross detection of liver enlargement.
- Histologic detection of centrilobular and midzonal coagulative hepatocellular necrosis.



TREATMENT

- No antidote available.
- GI decontamination with activated charcoal can be attempted but efficacy is unknown.
- Supportive care including close monitoring and, depending on the severity of clinical signs, intravenous fluids, correction of electrolyte imbalances and hypoglycemia, vitamin K1, and plasma transfusions.



MEDICATIONS

DRUG(S)

- Activated charcoal: Multi-dose activated charcoal at 1–4 g/kg PO q4–6h until 2–3 days post-ingestion. Mix activated charcoal in water at 1 g/5–10 mL of water.
- Intravenous fluids: maintain hydration, induce diuresis, correct hypoglycemia.
- Dextrose: 50% dextrose 1 mL/kg IV slow bolus (1–3 minutes).
- Vitamin K1: 0.5–1.5 mg/kg SC or IM q12h; 1 mg/kg PO q24h.
- Blood products: dependent on hemostatic test results.

ALTERNATIVE DRUGS

- S-adenosylmethionine (SAMe): antioxidant and hepatoprotectant; no data on efficacy in sago palm toxicosis available. Dose 20 mg/kg PO q24h.
- Ascorbic acid and cimetidine: hepatocyte protectors; no data on efficacy in sago palm toxicosis available. Can be given for supportive therapy.
- N-Acetylcysteine

(NAC): antioxidant; no data on efficacy in sago palm toxicosis available. A glutathione precursor that can be included in the treatment regimen for acute fulminant hepatic failure at 140 mg/kg IV load, followed by 70 mg/kg IV q6h for 7 treatments.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Liver enzymes/function • Coagulation status

PREVENTION/AVOIDANCE

Deny access to sago palms.

POSSIBLE COMPLICATIONS

- Hepatic encephalopathy • DIC • Renal failure

EXPECTED COURSE AND PROGNOSIS

- Dogs develop vomiting within minutes, followed by further GI upset.
- Changes in clinical laboratory values occur after 24–48 hours.
- Liver failure within a few days.
- Prognosis is poor to guarded.



MISCELLANEOUS

ABBREVIATIONS

- AC = activated charcoal • ALP = alkaline phosphatase • ALT = alanine transaminase
- AST = aspartate transaminase • DIC = disseminated intravascular coagulation
- GGT = γ -glutamyltransferase • GI = gastrointestinal • PT = prothrombin time
- PTT = partial thromboplastin time

INTERNET RESOURCES

- <http://www.petpoisonhelpline.com/poison/sago-palm/>
- <http://www.aspca.org/pet-care/animal-poison-control/toxic-and-non-toxic-plants/fern-palm>

Suggested Reading

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Authors Adrienne C. Bautista and Birgit Puschner

Consulting Editor Lynn R. Hovda

SALIVARY MUCOCELE



BASICS

OVERVIEW

- Salivary mucoceles are non-epithelial-lined cavities filled with saliva that has leaked from a damaged salivary gland or duct; they are surrounded by granulation tissue that forms secondary to inflammation caused by the free saliva.
- There are four major pairs of salivary glands: parotid, mandibular, sublingual, zygomatic. Smaller buccal salivary glands are located in the soft palate, lips, tongue, and cheeks.
- Types of mucoceles are listed in Table 1. The most common type occurs with rupture of the sublingual duct.

SYSTEMS AFFECTED

Gastrointestinal

SIGNALMENT

- Three times more frequent in dog than in cat.
- All breeds are susceptible. Commonly affected breeds include miniature poodle (pharyngeal mucoceles), German shepherd, dachshund, and Australian silky terrier.
- Slight predisposition of males compared to females.
- No age predisposition.

SIGNS

Cervical Mucocele

- Soft, fluctuant, minimal, or nonpainful gradually developing cervical mass.
- Pain is usually manifested only during the acute-manifestation phase of the mucocele.

Ranula

- Sublingual, soft, frog-like swelling (Latin *rana*, frog).
- Often blood-tinged saliva secondary to self-trauma while eating.

Zygomatic Mucocele

- Periorbital facial swelling
- Exophthalmos and protrusion of third eyelid
- Divergent strabismus
- Periorcular pain
- Pressure-related neuropathy of the optic nerve

Pharyngeal Mucocele

- Respiratory distress
- Dysphagia
- Abnormal tongue movement

CAUSES & RISK FACTORS

- Cause is rarely identified. Suspected causes:
 - Blunt trauma to the head and neck (choke chains)
 - Bite wound
 - Penetrating foreign body
 - Ear canal surgery, parotid duct transposition, hemimaxillectomy
 - Sialoliths
 - Dirofilariasis



DIAGNOSIS

- Diagnosis is based on history, visual examination, and paracentesis of the mass.
- Determine the site of origin with help of oral examination, palpation, sialography, or exploration of the mucocele.

DIFFERENTIAL DIAGNOSIS

- Sialadenitis (second most common salivary disease, usually involving the mandibular gland, often concurrent with sialoceles).
- Sialadenosis.
- Salivary neoplasia (rare; mandibular and parotid glands most commonly involved; usually carcinomas or adenocarcinomas in dogs; benign neoplasms exclusively found in cats).
- Sialoliths (calcium phosphate or carbonate).
- Cervical abscess.
- Salivary gland infarction (95% occur in mandibular gland).
- Foreign body.
- Hematoma.
- Cystic or neoplastic lymph nodes.
- Orbital myxoma and myxosarcoma.
- Tonsil cysts.
- Thyroglossal cysts (rare, congenital).
- Cystic Rathke's pouch and branchial cysts (rare congenital).

CBC/BIOCHEMISTRY/URINALYSIS

Laboratory abnormalities are rarely seen.

OTHER LABORATORY TESTS

N/A

IMAGING

- Rarely needed.
- Plain cervical radiographs only to identify sialoliths, foreign bodies, or neoplasia.
- Skull radiographs sometimes helpful to differentiate neoplastic disease from zygomatic mucocele, if cytologic evaluation is indeterminate.
- Sialography (injection of iodinated, water-soluble contrast agent into the salivary duct) is in general reserved for patients with trauma, previous surgeries, or fistulous draining tracts and can be helpful to determine the side and source of mucoceles.
- Retrobulbar ultrasound shows a cavitary lesion in 75% of zygomatic mucoceles and 50% of retrobulbar abscesses.
- Cross-sectional imaging can be valuable to differentiate neoplastic from non-neoplastic disease.

DIAGNOSTIC PROCEDURES

Aseptic Paracentesis

- Differentiates mucoceles from neoplasia, abscesses, and sialadenitis.
- Aspirated fluid is viscous, yellowish, clear, or blood-tinged with a low cell count. Inflamed sialoceles are characterized by low-grade chronic plasmacytic-lymphocytic inflammation.
- Cytologic evaluation (Wright's stain) reveals diffuse or irregular clumps of pink to violet staining mucin, large phagocytic cells with small, round nuclei and foamy cytoplasm, intermixed salivary gland epithelial cells, and non-degenerate neutrophils in small numbers.
- Stain with a mucus-specific stain (e.g., periodic acid-Schiff) for definitive diagnosis.



TREATMENT

- Patients with acute respiratory distress (pharyngeal mucoceles) might need to be intubated or have a temporary tracheostomy performed. Transoral drainage via stab incision may be required prior to intubation.
- Complete surgical excision of the involved gland-duct complex and drainage of the mucocele is the treatment of choice. Prolonged drainage can be achieved with

Table 1

Types of mucoceles.		
Salivary Mucocele Type	Location	Gland/Duct Involved
Cervical mucocele	Intermandibular space, jaw angle, upper cervical region	Sublingual
Ranula	Sublingual tissues	Mandibular or sublingual
Pharyngeal mucocele	Pharyngeal wall	Sublingual
Zygomatic mucocele	Ventral to the globe	Zygomatic
Parotid mucocele	Angle of the jaw, ventral to ear	Parotid
Complex mucoceles	Depending on gland/duct involvement (see above)	Two or more glands/ducts

(CONTINUED)

SALIVARY MUCOCELE

marsupialization of ranulas and pharyngeal mucoceles and with placement of Penrose drains in cervical mucoceles.

**MEDICATIONS****DRUG(S)**

Antibiotics based on bacteriologic evaluation, if concurrent abscess or sialadenitis.

CONTRAINDICATIONS

Nonsurgical treatment of salivary mucoceles with repeated drainage or injection of cauterizing or anti-inflammatory agents is not curative and will complicate subsequent surgery by causing abscessation or fibrosis.

**FOLLOW-UP****PATIENT MONITORING**

- Daily bandage changes with Penrose drain placement.

- Penrose drains are usually removed 24–72 hours following surgery.
- Drain site should heal by second intention and contraction following marsupialization.

POSSIBLE COMPLICATIONS

- Seroma formation (17% for resection of mandibular and sublingual mucoceles).
- Infection.
- Mucocele recurrence (< 5% with complete resection).

EXPECTED COURSE AND PROGNOSIS

- Excellent prognosis with complete surgical excision.
- Previous infection or injection complicates successful surgical excision.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Sialoadenitis

SYNONYMS

- Honey cyst
- Salivary cyst
- Sialocele

Suggested Reading

Radlinsky MG. Salivary mucoceles. In: Fossum TW, ed., Small Animal Surgery, 3rd ed. St. Louis, MO: Mosby, 2012, pp. 417–422.

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Author Susanne Lauer

Consulting Editor Stanley L. Marks

Salmon Poisoning Disease



BASICS

OVERVIEW

- Infection with the rickettsial organism *Neorickettsia helminthoeca*, an obligate intracellular pathogen that resides within a trematode (fluke) vector, *Nanophyetus salmincola*, for the course of the trematode's life cycle.
- Organism—invades small intestinal epithelium and associated lymphoid tissue after ingestion of uncooked or under-cooked fluke-infected salmonid fish by dogs; an acute systemic illness with high fever and gastrointestinal signs develops.
- Geographically restricted to coastal regions of northern California, Oregon, Washington and southern British Columbia as a result of the distribution of an aquatic snail intermediate host (*Oxytrema silicula*) for the trematode.

SIGNALMENT

- Dogs of all ages; median age is 3 years.
- Dogs of all breeds and sexes may develop illness, but intact male dogs and Labrador retrievers may be overrepresented because of their popularity among individuals engaged in fishing activities.

SIGNS

- Inappetence • Lethargy • Fever (up to 107.6°F); terminally hypothermia may develop
- Lymphadenopathy • Splenomegaly
- Vomiting • Diarrhea, which may contain melena or frank blood • Weight loss
- Uncommonly, neurologic signs including mental obtundation, cervical pain, twitches, and seizures.

CAUSES & RISK FACTORS

- Residence in an endemic area.
- Ingestion of uncooked or undercooked fish containing the fluke metacercariae that in turn harbor *Neorickettsia helminthoeca*. Salmonid fish (salmon and trout) are most often implicated, but other freshwater fish can occasionally be involved.
- Any part of the fish can be infected (skin, entrails, muscle).
- Supermarket-bought fish have been implicated in some cases.
- Occasionally dogs from areas not endemic for salmon poisoning disease develop disease after ingesting fish that has been transported from endemic areas.
- Infection has also been reported after swimming, without apparent exposure to fish.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Lymphoma • Poisoning • Canine parvovirus type 2 infection • *Ehrlichia canis* infection • *Anaplasma phagocytophilum* infection • Canine distemper virus infection

- Rocky Mountain spotted fever
- Salmonellosis • Whipworm infestation
- Pancreatitis • Hypoadrenocorticism
- Disseminated cryptococcosis

CBC/BIOCHEMISTRY/URINALYSIS

- Common hematologic findings are thrombocytopenia (90% of dogs), neutrophilia with a left shift, and lymphopenia.
- Serum chemistry findings are nonspecific and include electrolyte abnormalities secondary to gastrointestinal losses, hypoalbuminemia, increased activity of alkaline phosphatase, hypoglobulinemia and hypocholesterolemia.
- Urinalysis may reveal proteinuria and bilirubinuria.

OTHER LABORATORY TESTS

Some dogs have laboratory findings suggestive of disseminated intravascular coagulation

IMAGING

- Abdominal ultrasound may reveal splenomegaly with a mottled echotexture and abdominal lymphadenomegaly.
- Fluid-distended intestinal loops with wall thickening, corrugation, hypermotility or hypomotility may also be seen using ultrasonographic examination.

DIAGNOSTIC PROCEDURES

- Aspirate of enlarged lymph nodes; reveals increased numbers of histiocytes that contain basophilic granular material in their cytoplasm (rickettsial inclusions).
- Fecal examination—reveals operculated eggs of the trematode *Nanophyetus salmincola*. Use of a combination of centrifugal fecal flotation and fecal sedimentation maximizes the sensitivity of this test (sensitivity 93%).
- Where available, PCR assays for *Neorickettsia helminthoeca* DNA can also be performed on lymph node aspirates or fecal material.

PATHOLOGIC FINDINGS

- Lymphoid tissue enlargement—tissues are often yellowish with prominent white foci.
- Petechial hemorrhages.
- Gastrointestinal tract thickening with white nodules.
- Intestinal contents—frequently contain free blood. Flukes may not be visible grossly.
- Histopathology reveals depletion of lymph node follicles and infiltration of lymphoid tissues and the intestinal submucosa by histiocytes, the cytoplasm of which contains numerous lymphoid follicles. Flukes may also be found embedded in the gastrointestinal mucosa.



TREATMENT

- Inpatient—acutely ill patients.
- Supportive therapy—intravenous fluids with electrolytes; colloids or packed red blood cell transfusions may also be needed. Consider antiemetics and parenteral nutrition.



MEDICATIONS

DRUG(S)

- Oxytetracycline 7.5–10 mg/kg IV q12h for 7–14 days
- Doxycycline 5 mg/kg PO or IV q12h for 7–14 days
- Praziquantel 10–30 mg/kg PO q24h for 1–2 days to kill flukes.



FOLLOW-UP

PATIENT MONITORING

Monitor hydration, electrolytes, acid-base balance, and body temperature.

PREVENTION/AVOIDANCE

- Prevent animals from eating improperly cooked fish.
- Inform client of necessity to act quickly and consider other dogs that may have eaten the same raw fish.

EXPECTED COURSE AND PROGNOSIS

- Animals likely to succumb within 5–10 days of infection unless treated with appropriate antimicrobial drugs and supportive care.
- With early diagnosis and treatment—prognosis excellent. Animals without severe gastrointestinal signs show a rapid clinical response to oral doxycycline (within 24–48 hours). Dogs with severe gastrointestinal signs may require hospitalization and aggressive treatment for more than a week.
- Untreated—often fatal.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Infection with *Nanophyetus salmincola* does not itself cause severe clinical disease.

ZOONOTIC POTENTIAL

Nanophyetus salmincola can cause gastrointestinal disturbances and eosinophilia in humans, but *Neorickettsia helminthoeca* does not cause human disease.

ABBREVIATION

- PCR = polymerase chain reaction

INTERNET RESOURCES

- <http://www.vetmed.wsu.edu/ClientED/salmon.asp>

Suggested Reading

Sykes JE. Salmon poisoning disease. In: Sykes JE, ed., *Canine and Feline Infectious Diseases*. St. Louis, MO: Elsevier Saunders, 2014, pp. 311–319.

Author Jane E. Sykes

Consulting Editor Stephen C. Barr



BASICS

DEFINITION

A bacterial disease that causes enteritis, septicemia, and abortions and is caused by many different serotypes of *Salmonella*.

PATHOPHYSIOLOGY

- *Salmonella*—a Gram-negative bacterium; colonizes the small intestine (ileum); adheres to and invades the enterocytes; eventually enters and multiplies in the lamina propria and local mesenteric lymph nodes; cytotoxin (cell death) and enterotoxin (increases cAMP) are produced; inflammation occurs; and prostaglandin synthesis ensues; results in secretory diarrhea and mucosal sloughing.
- Uncomplicated gastroenteritis—organisms are stopped at the mesenteric lymph node stage; patient has only diarrhea, vomiting, and dehydration.
- Bacteremia and septicemia following gastroenteritis—more serious disease; focal extra-intestinal infections (abortion, joint disease) or endotoxemia may result; may lead to organ infarction, generalized thrombosis, DIC, and death.
- Some patients recover from the septicemic form but suffer prolonged recovery as a result of their debilitated state.

SYSTEMS AFFECTED

- Gastrointestinal—enterocolitis; inflammation, mucosal sloughing, secretory diarrhea.
- Systemic disease (e.g., bacteremia, focal infections, septicemia)—multiorgan infarction, thrombosis, abscesses, meningitis, osteomyelitis, abortion.

GENETICS

Genetic susceptibility not well known

INCIDENCE/PREVALENCE

• True incidence unknown. • Most infections subclinical. • Dogs—clinical disease most often seen in the young and pregnant bitches. Common in racing greyhounds and racing sled dogs due to raw meat diets; presence of *Salmonella* does not necessarily imply infection but could reflect transient pass-through. • Cats—have a high natural resistance; stressed hospitalized animals at high risk especially when treated with an oral antimicrobial drug prior to spay-neuter surgery or dentistry or declaw surgery. Shelter cats more likely to have *Salmonella* in feces; pandemics of salmonellosis in migrating songbirds (usually *S. typhimurium*) in spring create epidemics in bird-hunting cats. • New dangers noted in the trend of feeding commercial raw meat diets (especially chicken) to dogs and to cats; *Campylobacter* spp. in addition to *Salmonella* spp. and *Clostridium perfringens* often found in raw diets. Outbreaks linked to pet foods/treats are now common.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dogs and cats

Mean Age and Range

- Dogs—clinical disease manifests in neonatal/immature puppies and in pregnant bitches; most adult carrier dogs clinically normal.
- Cats—adults highly resistant.

SIGNS

General Comments

Disease severity—subclinical (carrier state: *Salmonella* shed in stool) to mild, moderate, and severe clinical cases in neonatal and stressed adult dogs and cats; subclinical infection more common than clinical disease (rare).

Historical Findings

- Diarrhea.
- Vomiting.
- Fever.
- Malaise.
- Anorexia.
- Vaginal discharge/abortion—dogs.
- Chronic febrile illness—persistent fever, anorexia, malaise without diarrhea.

Physical Examination Findings

- Asymptomatic carrier states—no clinical signs.
- Gastroenteritis—anorexia; malaise/lethargy; depression; fever (39–40°C; 102–104°F); diarrhea with mucus and/or blood; progressive dehydration; abdominal pain; tenesmus; pale mucous membranes; mesenteric lymphadenopathy; weight loss.
- Gastroenteritis with bacteremia and septicemia, septic shock, or endotoxemia—pale mucous membranes; weakness; cardiovascular collapse; tachycardia; tachypnea.
- Focal extra-intestinal infections—conjunctivitis; uterus/abortion; cellulitis; pyothorax.
- Cats—may exhibit syndrome of a chronic febrile illness (without gastrointestinal signs); persistent fever; prolonged illness with vague, nonspecific clinical signs; and left shift on leukogram.
- Recovering patients—may exhibit chronic intermittent diarrhea for 3–4 weeks; may shed *Salmonella* in stool for 6 weeks or longer.

CAUSES

- Any one of more than 2,000 serotypes of salmonellae.
- Two or more simultaneous serotypes in a host animal not uncommon.

RISK FACTORS

Disease Agent

- *Salmonella* serotype—virulence factors, infectious dose, and route of exposure.
- Host factors that increase susceptibility.
- Age—neonatal/young dogs and cats; immature immune system.
- Overall health status—debilitated young animals or adults; other concurrent disease, parasitism; young animals: immature gastrointestinal tract, poorly developed normal microbial flora.
- Disrupted gastrointestinal bacteria flora (adult cats)—antimicrobial treatment;

subsequent exposure to salmonellae during hospitalization.

Environmental Factors

- Coprophagy spreads infection.
- Dehydrated (dry) pet food—known to harbor salmonellae; semi-moist foods (e.g., kibble and dog biscuits) usually not as risky.
- Pig ear dog treats contaminated by *Salmonella*.
- Horse and cattle meat fed to exotic felids.
- New dangers noted in the trend of feeding commercial raw meat diets (especially chicken), plus contaminated pet foods and treats.
- Grooming habits—may result in *Salmonella*-contaminated hair coat, which contaminates cage or run environment, feed and water dishes.
- Dense population—research colony, boarded animals, shelter/pound animals; overcrowded housing; unsanitary conditions; exposure to other infected (or carrier) animals—buildup of *Salmonella* in the environment; more efficient fecal-oral cycling; high opportunity for fecal exposure; stress factors.

Hunting/Stray Animals

- Scavenging for food—exposure to garbage, contaminated food/water, dead animals.
- Exposure to other infected (or carrier) animals.

Hospitalized Animals

Nosocomial exposure (plus stress) or activation (by stress) of preexisting asymptomatic (carrier) *Salmonella* infection, especially in animals treated with antimicrobial drugs.

Vaccinated Cats

Death in kittens (likely to be infected by *Salmonella* subclinically) post-vaccination, with high titers of modified live panleukopenia vaccine.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute gastroenteritis—vomiting, diarrhea, infectious enteritis; differentiate by serology and/or culture.
- Viral gastroenteritis—feline panleukopenia, FeLV, FIV, feline enteric coronavirus, canine enteric coronavirus, canine parvovirus, rotavirus, canine distemper.
- Bacterial gastroenteritis—*E. coli*, *Campylobacter jejuni*, *Yersinia enterocolitica*.
- Bacterial overgrowth syndrome—*Clostridium difficile*, *Clostridium perfringens*.
- Parasites—helminths (hookworms, ascarids, whipworms, *Strongyloides*); protozoa (*Giardia*, *Coccidia*, *Cryptosporidium*); *Rickettsiae*; salmon poisoning.
- Acute gastritis—erosions or ulcers.
- Dietary-induced distress—overeating, abrupt changes, starvation, thirst, allergy or food intolerance, indiscretions (foreign material, garbage).
- Drug- or toxin-induced distress.
- Extra-intestinal disorders/metabolic disease.

SALMONELLOSIS

(CONTINUED)

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—variable; depends on stage of illness
- Neutropenia initially • Left shift with toxic neutrophils
- Nonregenerative anemia
- Lymphopenia • Thrombocytopenia
- Hypoalbuminemia • Electrolyte imbalances

DIAGNOSTIC PROCEDURES

- Fecal/rectal bacterial culture—positive; special media needed.
- Fecal leukocytes—positive.
- Blood cultures—positive in patients with bacteremia.
- Joint fluid—may be culture-positive.
- Subclinical carrier states—chronic; intermittent fecal culture positive (> 6 weeks).
- Note: use of antimicrobials in a patient before sampling may produce false-negative cultures.

PATHOLOGIC FINDINGS

- Gross lesions—only in severely affected patients.
- Cultures of ileum, mesenteric lymph node, liver/spleen, and bone marrow—positive.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—uncomplicated gastroenteritis (without bacteremia) and carrier states.
- Inpatient—with bacteremia/septicemia and for gastroenteritis in neonatal/immature animals that are rapidly debilitated by diarrhea.

NURSING CARE

Varies according to severity of illness—assess percentages of dehydration, body weight, ongoing fluid loss, shock, PCV/total protein, electrolytes, acid-base status.

Uncomplicated Gastroenteritis

- Supportive care—fluid and electrolyte replacement.
- Parenteral, balanced, polyionic isotonic solution (lactated Ringer's).
- Oral fluids—hypertonic glucose solutions; for secretory diarrhea.
- Plasma transfusions—if serum albumin < 2 g/dL.

Neonates, Aged, and Debilitated Animals

- Plasma transfusions.
- Supportive care—as outlined above.

ACTIVITY

- Isolate inpatients—all patients in acute stages may shed large numbers of salmonellae in the stool.
- Restrict activity with cage rest, monitor, and provide warmth—acutely ill, bacteremic/septicemic, and chronically ill animals.

DIET

Restrict food 24–48 hours; gradually introduce a highly digestible, low-fat diet.

CLIENT EDUCATION

Instruct client to wash hands frequently and to restrict access to patient in acute stages of the disease; large numbers of salmonellae may be shed in the stool.



MEDICATIONS

DRUG(S) OF CHOICE

Asymptomatic Carrier State

- Antimicrobials—contraindicated.
- Quinolone drugs—demonstrated clearing of carrier states in humans; more controlled trials in animals needed.

Uncomplicated Gastroenteritis

- Antimicrobials not indicated.
- Locally acting intestinal adsorbents and protectants.

Neonates, Aged, and Debilitated Animals

- Glucocorticoids—shown to reduce mortality in endotoxic shock.
- Antimicrobial therapy—indicated; culture and susceptibility testing/MIC necessary to assess drug-resistance problems.
- Trimethoprim-sulfa 15 mg/kg PO or SC q12h.
- Enrofloxacin 5 mg/kg PO or IM q12h; norfloxacin 22 mg/kg PO q12h.
- Chloramphenicol: dogs, 50 mg/kg PO, IV, IM, or SC q8h; cats, 50 mg/kg total PO, IV, IM, or SC q12h.
- Recent strains of *Salmonella* are multidrug resistant; adjust empirical therapy based on later antimicrobial susceptibility testing results.

PRECAUTIONS

- Chloramphenicol and trimethoprim-sulfa—use cautiously in neonatal and pregnant patients.
- Fluoroquinolones—avoid use in pregnant, neonatal, or growing animals (medium-sized dogs < 8 months of age; large or giant breeds < 12–18 months of age) because of adverse effect of arthropathy in dogs 4–28 weeks of age; do not administer to cats at doses higher than 5 mg/kg and do not administer to cats IV.



FOLLOW-UP

PATIENT MONITORING

- Fecal culture—repeat monthly for few months to assess development of carrier state.
- Other animals—monitor for secondary spread of infection.
- Advise client to contact veterinarian if patient shows signs of recurring disease.

PREVENTION/AVOIDANCE

- Keep animals healthy—proper nutrition; avoid raw meat diets; vaccinate for other infectious diseases; clean and disinfect cages, runs, and food and water dishes frequently; store food and feeding utensils properly.
- Reduce overcrowding—pounds, shelters, kennels, catteries, and research colonies.
- New arrivals—isolate and screen; monitor for sickness before mixing with other animals.

- Experimental live attenuated vaccine shows promise, especially for racing dogs.
- Important to protect animals being treated with antimicrobial drugs from exposure to a *Salmonella*-contaminated environment (e.g., animal hospital).

POSSIBLE COMPLICATIONS

- Spread of infection not uncommon within household to other animals or humans.
- Development of chronic infection with diarrhea.
- Recurrence of disease with stress.

EXPECTED COURSE AND PROGNOSIS

- Uncomplicated gastroenteritis—prognosis excellent; frequently self-limited; patients recover with good nursing care.
- Recovered animals may shed *Salmonella* intermittently for months or longer as a recovered carrier.
- Neonatal, aged, pregnant, and stressed animals—can develop septicemia/systemic disease and/or abortion; can be severe and debilitating; may lead to death if untreated.



MISCELLANEOUS

AGE-RELATED FACTORS

Clinical disease is frequently seen in neonatal, pregnant, aged animals.

ZOONOTIC POTENTIAL

- High potential, especially in children, elderly, immunosuppressed, and antimicrobial drug users.
- Multidrug resistant *Salmonella* isolated from kittens with enteritis.
- Acutely ill animals shed large numbers of salmonellae in stool.
- Grooming habits allow rapid contamination of animal's fur and environment.
- Isolation is needed.

PREGNANCY/FERTILITY/BREEDING

- May complicate disease.
- Abortion—may be a sequela to infection.
- Antimicrobial therapy—consider the effect on the fetus.

ABBREVIATIONS

- DIC = disseminated intravascular coagulation
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- MIC = minimal inhibitory concentration
- PCV = packed cell volume

INTERNET RESOURCES

- <http://www.cfph.iastate.edu/DiseaseInfo/disease.php?name=salmonella-nontyphoidal&lang=en>
- <http://www.cdc.gov/healthypets>

Suggested Reading

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Author Patrick L. McDonough

Consulting Editor Stephen C. Barr



BASICS

OVERVIEW

A non-seasonal, intensely pruritic, highly contagious parasitic skin disease of dogs and other mammalian species caused by *Sarcoptes scabiei* mites. In dogs, the causative parasite is *Sarcoptes scabiei* var *canis*.

PATHOPHYSIOLOGY

Mites burrow through the stratum corneum, induce hypersensitivity, and cause intense pruritus.

SYSTEMS AFFECTED

Skin/Exocrine

SIGNALMENT

- No age/breed predisposition
- All in-contact dogs usually affected.
- Transient pruritus of in-contact other species: cats, humans.

SIGNS

- Non-seasonal, intense pruritus
- Incubation period is variable; pruritus typically develops within 30 days of exposure due to a hypersensitivity response.
- Seroconversion 3 weeks after clinical signs develop
- Rare individuals do not seroconvert and therefore may not develop severe pruritus
- Following exposure, initial pruritus is mild but progresses to severe
- Elbows, pinnal margins, ventrum, and hocks affected first
- Crusted papules leading to generalized alopecia, crusting, and excoriations
- Poor response to antihistamines and anti-inflammatory doses of steroids
- If untreated skin becomes thickened, lichenified, alopecic, and crusted
- Mite numbers often low in most affected cases
- Immunocompromised individuals may harbor larger numbers of mites
- Peripheral lymphadenopathy develops with chronicity.

CAUSES & RISK FACTORS

- Exposure to infected dogs weeks before the development of symptoms
- Close contact with other dogs in animal shelters, boarding kennels, groomers, dog parks, and veterinary offices
- Living in fox- or coyote-endemic areas.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Atopy
- food allergy
- Bacterial folliculitis
- Demodicosis
- Dermatophytosis
- *Malassezia* dermatitis
- *Cheyletiella*
- Trombiculosis (chiggers)
- Contact dermatitis
- *Pelodera* dermatitis
- Otodectic dermatitis
- Dirofilariasis
- Zinc-responsive dermatosis
- Ear margin seborrhea
- Pemphigus foliaceus

OTHER LABORATORY TESTS

- ELISA—available in some countries to identify *Sarcoptes*-infested dogs.
- False

positives due to cross-reactivity with other mites; false negatives due to glucocorticoids.

DIAGNOSTIC PROCEDURES

- Positive pinnal-pedal reflex—rubbing the ear margin between the thumb and forefinger induces the dog to scratch with its hind leg.
- Superficial skin scrapings—positive in 20%–50% of scabies cases; false-negative results are common.
- Fecal flotation—may reveal mites or ova.
- Response to scabicidal treatment—most common method for diagnosing scabies.



TREATMENT

- Dogs with non-seasonal pruritus should be treated with a scabicide to definitively rule-out sarcoptic mange.
- When scabicidal dips are used, the entire dog must be treated including face and ears.
- All in-contact dogs must be treated.
- Resolution of pruritus may take several weeks due to hypersensitivity reaction to the mite.
- *Sarcoptes* mites usually die quickly in the environment; however, mites have been reported to survive for up to 3 weeks. Thorough cleaning of the dog's environment is recommended in crowded conditions.



MEDICATIONS

DRUG(S) OF CHOICE

- Selamectin—labeled for treatment of scabies when applied every 30 days; application every 2 weeks for at least three treatments may be more effective.
- Ivermectin—0.2–0.4 mg/kg SC or PO every 1–2 weeks; Milbemycin—2 mg/kg PO every 1–2 weeks.
- Doramectin 0.2–0.6 mg/kg SC or PO weekly.
- Moxidectin 0.2–0.3 mg/kg SC or PO weekly.
- Injectable and oral medications are administered for 3–6 treatments.
- Imidacloprid/moxidectin—applied twice 4 weeks apart.
- Amitraz rinse 0.025–0.03% effective when used weekly for 4–6 treatments.
- Lime-sulfur 2–4% applied weekly for 4–6 weeks.
- Fipronil spray applied to entire skin surface every 2 weeks for three treatments.
- Topical antiseborrheic therapy in conjunction with scabicidal therapy—helps speed clinical resolution of the scaling, crusting lesions.
- Systemic antibiotics—may be needed to resolve secondary pyoderma.
- Prednisone or prednisolone 1 mg/kg for 5–7 days or longer if necessary to relieve pruritus and self-mutilation.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Do not use extra-label macrocyclic lactone medications in heartworm-positive dogs, with spinosad-containing flea preventatives, or in collies, Shetland sheepdogs, Old English

SARCOPTIC MANGE

sheepdogs, Australian shepherds, and their crossbreeds—increased risk of avermectin toxicity in herding breeds (*ABCB1* [formerly *MDR1*] gene mutation). • Amitraz rinses may cause excessive sedation in small dogs.

- Potential increased risk of neurotoxicosis with concurrent use of macrocyclic lactone medications and systemic azole medications.



FOLLOW-UP

- Response to therapy may require 4–6 weeks.
- Topical scabicidal treatments are more prone to failure because of incomplete application of the treatment solution.
- Reinfection may occur if contact with infected animals continues.
- Approximately 30% of dogs with *Sarcoptes* infections will also react to house dust mite antigens on intradermal tests, suggesting that house dust mite allergy may be a possible sequela to scabies infection.



MISCELLANEOUS

ZOONOTIC POTENTIAL

• Sarcoptic mange is zoonotic. People in close contact with an affected dog may develop a pruritic, papular rash on body areas in frequent contact with dogs.

• Lesions resolve spontaneously when the affected animals are treated.

ABBREVIATION

ELISA = enzyme-linked immunosorbent assay

Suggested Reading

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Author Liora Waldman

Consulting Editor Alexander H. Werner

Acknowledgment The author and editor acknowledge the prior contribution of Alexander H. Werner as co-author.



Client Education Handout
available online

SCHIFF-SHERRINGTON PHENOMENON



BASICS

OVERVIEW

- Thoracic limb extension associated with hindlimb paralysis or paresis after acute and usually severe spinal cord lesion caudal to the cervical intumescence, best observed when the patient is in lateral recumbency.
- Posture—caused by damage to the border cells or their ascending processes, which are interneurons located in the lumbar spinal cord (mainly L2–4) and normally inhibiting the extensor motor neurons of the cervical intumescence.

SIGNALMENT

Any dog suffering from thoracolumbar spinal cord injury.

SIGNS

- Forelimbs—rigidly extended; normal gait and postural reactions (because the lesion is caudal to the cervical intumescence).
- Hind limbs—depends on the severity and location of the lesion; usually upper motor neuron in type, but may be lower motor neuron.
- In severe, acute thoracolumbar myelopathies, spinal shock may be present in addition to the Schiff-Sherrington phenomenon: there is an initial flaccid paralysis caudal to the level of the lesion, with loss of myotatic and flexor reflexes. In dogs and cats, spinal shock is uncommon and usually resolves within an hour, with more typical signs of upper motor neuron disease subsequently developing caudal to the spinal cord lesion.

CAUSES & RISK FACTORS

- Trauma (especially road accident) and intervertebral disc disease—most common.
- Vascular myelopathies (e.g., fibrocartilaginous embolism, coagulopathies, etc.).

S



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Decerebrate rigidity—observed with brainstem disease in which all four limbs are rigid and have upper motor neuron dysfunction; opisthotonus present; patient is unconscious.
- Decerebellate rigidity—observed with cerebellar disease in which the forelimbs are rigid but the hind limbs are flexed; consciousness is usually altered.
- Cervical spinal cord injury—may have extensor hypertonia in the forelimbs; upper motor neuron and proprioceptive deficits of all four limbs are also seen.
- The key feature in differential diagnosis is that in the Schiff-Sherrington phenomenon, function and postural reactions in the forelimbs are normal despite their extensor rigidity, while they are abnormal in the rear limbs.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

IMAGING

Radiology (radiography, myelography, computed tomography, magnetic resonance imaging)—demonstrate the thoracolumbar spinal lesion.



TREATMENT

- Directed toward the underlying thoracolumbar spinal cord lesion.
- No specific treatment available.
- Condition resolves if adequate spinal cord function is restored.
- Schiff-Sherrington phenomenon is not a prognostic indicator: prognosis is determined by the severity of signs caudal to the spinal cord lesion.



MEDICATIONS

DRUG(S)

As indicated for underlying spinal cord disease

CONTRAINDICATIONS/POSSIBLE

INTERACTIONS

N/A



FOLLOW-UP

- Posture may persist for days to weeks; not an indication of a hopeless prognosis.
- With rapid and aggressive treatment, the patient may recover, especially if there is pain perception caudal to the lesion.



MISCELLANEOUS

Suggested Reading

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Author Stephanie Kube

Consulting Editor Joane M. Parent

Acknowledgment The author and editors acknowledge the prior contribution of Mary O. Smith.

SCHWANNOMA



BASICS

OVERVIEW

Schwannomas are tumors of nerve sheath origin, arising from Schwann cells. The term peripheral nerve sheath tumor (PNST) has been proposed to include schwannomas, neurofibromas, and neurofibrosarcomas, as these tumors arise from the same cell.

Importantly, schwannomas are grouped with several other soft tissue sarcomas (e.g., hemangiopericytoma and fibrosarcoma) for therapeutic and prognostic purposes, as the biologic behaviors of this group of tumors are similar.

SIGNALMENT

- Dogs—median of 10 years, no sex predisposition, no known breed predilection.
- Cats rarely affected.

SIGNS

Vary depending on tumor location, which can be peripheral (e.g., skin or tongue) or more central (e.g., axillary region).

CAUSES & RISK FACTORS

None identified



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other neoplasia that can involve the connective tissues
- Orthopedic disease
- Other neurologic disease (e.g., intervertebral disc disease)

CBC/BIOCHEMISTRY/URINALYSIS

Results usually normal

OTHER LABORATORY TESTS

None

IMAGING

- Myelography may be helpful in cases with dorsal or ventral nerve root involvement.
- Contrast computed tomography or, ideally, magnetic resonance imaging provides the most information regarding extent and location of disease.

DIAGNOSTIC PROCEDURES

Electromyography consistently reveals abnormal, spontaneous electrical activity in muscles of the affected limb.



TREATMENT

- Surgical excision is the treatment of choice.
- Radiotherapy following incomplete surgical resection is likely to result in excellent long-term outcome.
- Excision of a distal mass may still result in a functional limb; amputation is required in most cases.
- Laminectomy is necessary in cases of nerve root involvement; local recurrence is common if the primary extends into the spinal canal.



MEDICATIONS

DRUG(S)

- Chemotherapy—no successful chemotherapeutic management has been described.
- Corticosteroid therapy—may help to reduce peritumoral edema and temporarily relieve clinical signs.
- Gabapentin for neuropathic pain alleviation.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS

- Recurrence common following incomplete surgical excision (up to 72% of cases).
- The more distal the tumor, the better the possibility of a surgical cure.
- For tumors involving the brachial or lumbosacral plexus, median disease-free interval is 7.5 months.
- For tumors involving dorsal or ventral nerve roots, median disease-free interval is 1 month.
- High histologic-grade tumors (e.g., grade 3) may metastasize to regional lymph nodes or lung.



MISCELLANEOUS

Suggested Reading

Chase D, Bray J, Ide A, Polton G. Outcome Following Removal of Canine Spindle Cell Tumours in First Opinion Practice: 104 Cases. J Small Anim Pract 2009, 50:568–574.

Author Ruthanne Chun

Consulting Editor Timothy M. Fan

SEBACEOUS ADENITIS, GRANULOMATOUS



BASICS

OVERVIEW

- A destructive inflammatory disease process directed against cutaneous adnexal structures (sebaceous glands).
- May be genetically inherited, immune-mediated, or metabolic.
- Initial defect—a keratinization disorder or an abnormality in lipid metabolism (accumulation of toxic intermediate metabolites).

SYSTEMS AFFECTED

Skin/Exocrine

SIGNALMENT

- Young adult to middle-aged dogs; very rare in cats.
- Two forms—long- and short-coated breeds (short-coated form now called “idiopathic pyogranulomatous periadnexal dermatitis”).
- Predisposed—standard poodle, Akita, Samoyed, German shepherd, Havanese, and Vizsla.

SIGNS

Long-Coated Breeds

- Symmetrical, partial alopecia.
- Dull, brittle hair.
- Tightly adherent silver-white scale.
- Follicular casts around hair shaft (“keratin-collaring”).
- Small tufts of matted hair.
- Lesions—often first observed along dorsal midline and dorsum of the head.
- Severe—secondary bacterial folliculitis, pruritus, and malodor.
- Akitas—often relatively severely affected; morbidity associated with deep secondary bacterial infections.
- Standard poodles—affected dogs frequently described as having excellent hair coats prior to developing lesions; secondary bacterial folliculitis rare; most patients do not exhibit systemic illness.

Short-Coated Breeds

- Alopecia—moth-eaten, circular, or diffuse.
- Mild scaling.
- Lesions often plaque-like.
- Affects the trunk, head, and pinnae.
- Secondary bacterial folliculitis rare.
- Lesions can produce significant scarring.

CAUSES & RISK FACTORS

- Mode of inheritance is being studied/an autosomal recessive mode of inheritance is documented in the standard poodle and suspected in Akitas.

• Multiple pathophysiologic causes theorized including auto-immunity against sebaceous glands and/or leakage of sebaceous gland contents into surrounding dermis causing an inflammatory reaction and eventual destruction of glands.

- Destruction of sebaceous glands may be secondary—“innocent bystander” from other inflammatory conditions.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Primary seborrhea—keratinization disorder
- Bacterial folliculitis
- Demodexis
- Dermatophytosis
- Pemphigus foliaceus
- Endocrine skin disease

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Skin scrapings—normal
- Dermatophyte culture—negative
- Endocrine function tests—normal
- Skin biopsy

PATHOLOGIC FINDINGS

- Nodular granulomatous to pyogranulomatous inflammatory reaction at the level of the sebaceous glands.
- Orthokeratotic hyperkeratosis and follicular cast formation; more prominent in long-coated breeds.
- Advanced—complete loss of sebaceous glands; periadnexal fibrosis.
- Destruction of entire hair follicle and adnexal unit rare.



TREATMENT

- Clinical signs may wax and wane irrespective of treatment.
- Controlled studies have not been done to document efficacy of any therapy.
- Results extremely variable; response may depend on severity of disease at the time of diagnosis.
- Akita—breed most refractory to treatment.



MEDICATIONS

DRUG(S)

- Propylene glycol and water—50–75% mixture; spray every 24 hours to affected areas.
- Baby oil—soak affected areas for 1 hour; follow with multiple shampoos to remove oil and scales; used monthly or as needed to reduce severe accumulations of crusts.
- Frequent bathing with keratolytic shampoos (twice weekly).
- EFA supplementation and evening primrose oil (500 mg PO q12h); possible side effects include vomiting, diarrhea, and flatulence.
- Isotretinoin (Accutane) 1 mg/kg PO q12h; reduce to 1 mg/kg q24h after 1 month and to 1 mg/kg q48h after 2 months; continue as needed for maintenance; rarely used.
- Cyclosporine 5 mg/kg PO q12–24h; side effects include vomiting, diarrhea, gingival hyperplasia, hirsutism, papillomatous skin lesions, increased incidence of infections, nephrotoxicity, and hepatotoxicity.
- Doxycycline (5 mg/kg PO q12h) and niacinamide (250 mg PO q8h, < 10 kg; 500 mg PO q8h > 10 kg) with vitamin E.
- Bactericidal antibiotics for secondary bacterial folliculitis.

CONTRAINdications/POSSible INTERACTIONS

Isotretinoin (Accutane)—known teratogen; do not use in pregnant dogs; advise owners of risk.



FOLLOW-UP

Urge owners to register affected dogs so that mode of inheritance can be determined.



MISCELLANEOUS

Suggested Reading

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Rosser EJ. Sebaceous adenitis. In: Griffin CE, Kwochka KW, MacDonald JM, eds., Current Veterinary Dermatology. St. Louis, MO: Mosby, 1993, pp. 211–214.

Author Karen Helton Rhodes

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SEIZURES (CONVULSIONS, STATUS EPILEPTICUS)—CATS



BASICS

DEFINITION

- Epilepsy—recurrence of seizures from primary brain origin.
- Genetic epilepsy—syndrome that is only epilepsy, with no demonstrable underlying brain lesion or other neurologic signs; the genetic origin must be proven through family studies, gene isolation or other specific forms of evidence (ILAE).
- Rare in cats.
- Structural epilepsy—syndrome in which the epileptic seizures are the result of identifiable structural brain lesions; frequent in cats.
- Epilepsy of unknown cause—structural epilepsy suspected but a lesion cannot be demonstrated; frequent in cats.
- Cluster seizures—> 1 seizure/24 hours.
- Status epilepticus—continuous seizure activity, or seizures repeated at brief intervals without complete recovery between seizures. Can be nonconvulsive.
- Convulsive SE—life-threatening medical emergency.

PATHOPHYSIOLOGY

- Paroxysmal disorganization of one or several brain functions originating from the thalamocortex. Any thalamocortical disturbance or disease process may lead to seizure activity.
- Not all cortical regions have the same propensity to seize; from the most to the least likely to cause seizures—temporal, frontal, parietal, and occipital lobes.
- As more seizures occur, the tendency for neuronal damage and propensity for more seizures or SE increases; this kindling effect does not occur in all cortical regions.
- The clinical appearance of the seizure is directly related to the location of the neuronal hyperactivity. If the electrical abnormality remains regional, the seizure is focal. If there is recruitment of both hemispheres, the seizure is generalized.
- The great majority of seizures and SE in cats are secondary to structural brain lesions.

SYSTEMS AFFECTED

Nervous

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Cats of any breed, age, or sex

SIGNS

General Comments

- Nonconvulsive generalized seizures—frequent in cats; movements of facial musculature predominate, such as bilateral twitches of eyelids, whiskers and ears, salivation, lip smacking; may be associated with whole body trembling/shaking, piloerection, dilated pupils. Nonconvulsive SE frequent in cats.
- Focal seizure—when

limited to one hemisphere; frantic running and colliding with objects (aura), unilateral facial twitches or eyelid blinks, unilateral limb motions or head/neck turning to one side. Focal seizures often generalize.

- Generalized convulsive seizures—bilateral symmetrical tonic-clonic contractions of limb muscles and dorsiflexion of the head, often associated with autonomic signs such as salivation, urination, defecation. At time of admission, the gross motor activity may have stopped, but there may still be twitching of the lids and body/limb jerks.
- Mutilation frequent—biting of tongue, nail avulsion.

Historical Findings

- Confirm that seizure activity has indeed occurred.
- Pattern of seizures (age at seizure onset, type and frequency of seizures)—most important factor in listing the possible causes.
- Metabolic diseases may cause GS.
- With most seizurogenic toxins, there is a crescendo of hyperexcitability, shaking, trembling, with ultimately GS and death.
- Asymmetry in the signs (eyelid twitches, limb movements primarily on one side, circling) before, during or after the seizure suggests focal cortical lesion.
- Overdose of insulin, post-renal transplant, bilateral thyroidectomy lead to GS shortly after the fact.
- Presence of abnormal behavior in the days/weeks preceding the seizure activity indicates structural brain disease.
- Presence of concomitant gastrointestinal, respiratory, or other systemic signs indicates multisystem disease.

Physical Examination Findings

- If chorioretinitis present, look for infectious diseases.
- Dark red mucous membranes suggest polycythemia vera.

Neurologic Examination Findings

- Mental status, menace responses, responses to nasal septum stimulation, and proprioceptive positioning are neurologic tests that evaluate the cerebral cortex. Asymmetry indicates structural brain lesion on the contralateral side of the deficits.
- In most cases of structural epilepsy, neurologic deficits are present at presentation.

CAUSES

Extracranial

Metabolic—hypoglycemia from insulin overdose, hypocalcemia from bilateral thyroidectomy, severe hyperthyroidism, hypertension secondary to renal transplant, hepatic encephalopathy, uremia, polycythemia vera, severe hypertriglyceridemia.

Toxins; Intracranial

- Anatomic—congenital malformation.
- Metabolic—cell storage disease (e.g., neuronal ceroid-lipofuscinosis reported in one cat with myoclonus and seizure activity).
- Neoplastic—meningioma, astrocytoma, lymphoma.
- Inflammatory infectious—viral non-FIP, FIP, toxoplasmosis, cryptococcosis.
- Toxicity—organochlorines, pyrethrins, and

pyrethroids; seizures usually observed at end stage; chlorambucil in lymphoma treatment.

- Vascular—polycythemia vera secondary to hyperviscosity, feline ischemic encephalopathy secondary to *Cuterebra* larva.
- Trauma has not been linked to seizures in cats.

RISK FACTORS

- Any forebrain lesion
- Diabetes mellitus
- Treatment with chlorambucil
- Renal failure



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Sleep disorders—the cat does not wake up, or has a normal waking behavior following the episode.
- Syncope—the body is limp with a rapid recovery phase, with no abnormal behavior.
- When seizures are preceded by 2–3 weeks of vague transient systemic illness (decreased appetite, GI signs) in an otherwise healthy cat—viral non-FIP encephalitis or epilepsy of unknown cause.
- When seizures are preceded by systemic signs that persist (> 3 weeks)—FIP, cryptococcosis.
- Insidious abnormal behavior with/without circling in a cat > 10 years old presented for seizure activity suggests meningioma.
- Cats with hepatic encephalopathy drool excessively.
- Cats with polycythemia vera have GI signs and dark mucous membranes.

CBC/BIOCHEMISTRY/URINALYSIS

- Extracranial metabolic causes are diagnosed on history, physical examination, and blood test results.
- High PCV (> 60%) in polycythemia vera.
- Low blood glucose in insulin overdose.
- Low calcium in bilateral post-thyroidectomy.
- High BUN and creatinine with low specific gravity in acute renal failure.
- Creatine kinase—mild to markedly elevated in cats with SE, even nonconvulsive; with or without myoglobinuria; indicates muscle necrosis.

OTHER LABORATORY TESTS

- Serologic testing—FIV, FeLV titers often non-contributory to diagnosis; FIP and *Toxoplasma gondii* titers non-reliable by themselves.
- Bile acid testing—in cats with suspected hepatic encephalopathy.

S

IMAGING

- Thoracic radiographs and abdominal ultrasound—if infectious disease suspected; to evaluate lung pathology if SE; to look for neoplasia if tumor suspected.
- MRI—best to define location, extent, and nature of lesion.

DIAGNOSTIC PROCEDURES

CSF—sensitive to detect structural disease; unspecific in itself to reach diagnosis except when organism is seen (e.g., cryptococcosis).

PATHOLOGIC FINDINGS

- Findings reflect etiology.
- It is unknown if hippocampal necrosis is a cause or the consequence of seizures.
- Small lesions may

SEIZURES (CONVULSIONS, STATUS EPILEPTICUS)—CATS (CONTINUED)

be easily missed in cats diagnosed with epilepsy of unknown cause.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—isolated recurrent seizures in an otherwise healthy cat.
- Inpatient—cluster seizures and SE. Isolated recurrent seizures in an ill cat.

NURSING AND SUPPORTIVE CARE

- Constant supervision.
- Install IV line for drug and fluid administration.
- Draw blood for rapid measurement of blood gases, glucose, calcium, and antiepileptic drug levels if pertinent.
- Cool if hyperthermia.

CLIENT EDUCATION

Antiepileptic treatment in structural epilepsy may not help until the primary cause is addressed. Seizures can be difficult to stop in cases of SE, especially with nonconvulsive status.

SURGICAL CONSIDERATIONS

Craniotomy—tumor excision with meningioma or other accessible mass.



MEDICATIONS

DRUG(S) OF CHOICE

Seizure type and frequency determine therapeutic approach.

Isolated Recurrent Generalized Seizures

- First line—phenobarbital 7.5–15 mg/cat q12h; optimal therapeutic serum levels 100–130 µmol/L (23–30 µg/L).
- Second line— gabapentin 3–8 mg/cat q8–12h.
- Levetiracetam—20 mg/kg q8h (serum levels humans 10–40 µg/mL).
- Initiate gradually to avoid overt sedation.

Convulsive Cluster and Status Epilepticus

- S**
- Treat cluster and GSE early—the more seizures in a given time, and the more drugs for seizure control, time for recovery, and cost for treatment.
 - No ongoing seizure activity at presentation and patient naïve to the drug—phenobarbital IV bolus 10 mg/kg to a maximum of 60 mg/cat over 15 minutes, continued with phenobarbital maintenance dosage PO 12 hours later.
 - Ongoing seizure activity at presentation—diazepam IV bolus 0.5–1 mg/kg, continuing with CRI at 0.25–0.5 mg/cat/h in an in-line burette using a fluid pump; IV bolus of diazepam can be repeated 5 minutes after the first bolus if gross seizure activity persists; in this case, add phenobarbital to CRI at 4 mg/cat/hour.
 - Start oral phenobarbital at maintenance dose as soon as patient can swallow.
 - After

6 hours seizures-free, wean CRI gradually over 4–6 hours.

Persistent Seizures

Sub-anesthetic doses of IV propofol (1–3.5 mg/kg) bolus and 0.01–0.25 mg/kg/minute CRI titrated to effect.

Non-antiepileptic Drug Treatment

- Dexamethasone 0.25 mg/kg IV q24h for 1–3 days, to improve edema secondary to SE and treat the primary cause if systemic infectious disease is not suspected; dexamethasone alters CSF results.
- Thiamin—5–50 mg/cat in any cat presented with acute neurologic signs, including seizures.

CONTRAINdications

- Do not use KBr in cats; side effects include life-threatening respiratory disease.
- Avoid giving aminophylline, theophylline, ketamine, and fentanyl to epileptic cats.

PRECAUTIONS

- Prolonged use of propofol (> 24 hours) may cause Heinz body anemia in cats.
- Cats on CRI of antiepileptic drug(s) are often overtly sedated; cardiovascular and respiratory depression may occur; close monitoring necessary; lubricate eyes, express bladder manually, correct hypothermia.
- Close monitoring necessary to observe if mild ongoing seizure activity persists.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

- Zonisamide—5–10 mg/kg PO q24h (serum levels humans 15–45 µg/mL).
- Diazepam—0.5–2.0 mg/kg/day PO divided q12h.



FOLLOW-UP

PATIENT MONITORING

- CBC, biochemistry, urinalysis prior to initiating AED.
- Phenobarbital-induced hepatotoxicity is not a problem in the cat.
- CK to evaluate muscular necrosis and indirectly subtle ongoing seizure activity in cats presented in SE.
- Measure phenobarbital serum level 2 weeks after initiation; correct dosage accordingly; it is difficult to titrate phenobarbital in cats, i.e., a mild increase in dosage often leads to a major increment of the serum levels.
- CBC and biochemistry—repeat every 6–12 months.
- If structural epileptic patient has recovered from primary disease and remains seizure-free for 6 months—seizures may recur when drug is weaned off.

POSSIBLE COMPLICATIONS

- SE—seizure control may not be reached despite polypharmacy.
- Rare hypersensitivity to phenobarbital—thrombocytopenia, neutropenia, pruritus, swollen feet; do CBC

4–6 weeks after onset of phenobarbital.

- Diazepam rarely may cause acute hepatic necrosis and death.
- Cardiovascular and respiratory collapse from overdose during SE treatment.

EXPECTED COURSE AND PROGNOSIS

- Depends on the underlying cause and response to treatment.
- Cats with epilepsy of unknown cause have good long-term prognosis.
- Cats can recover despite episode of severe cluster-seizures and GSE.



MISCELLANEOUS

AGE-RELATED FACTORS

Cats with seizure onset prior to < 1 year of age and diagnosed with epilepsy of unknown cause have guarded prognosis for seizure control.

SEE ALSO

- Feline Ischemic Encephalopathy
- Meningioma

ABBREVIATIONS

- AED = antiepileptic drug
- CK = creatine kinase
- CRI = constant rate infusion
- CSF = cerebrospinal fluid
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- GI = gastrointestinal
- GS = generalized seizures
- GSE = generalized status epilepticus
- ILAE = International League Against Epilepsy
- MRI = magnetic resonance imaging
- PCV = packed cell volume
- SE = status epilepticus

Suggested Reading

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Wähle AM, Brühschwein A, Matiasek K, et al. Clinical characterisation of epilepsy of unknown cause in cats. J Vet Intern Med 2014, 28:182–188.

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Client Education Handout
available online

SEIZURES (CONVULSIONS, STATUS EPILEPTICUS)—DOGS



BASICS

DEFINITION

- Epilepsy—recurrence of seizures from primary brain origin.
- Genetic epilepsy—epilepsy with no observable underlying brain lesion or other neurologic signs or symptoms.
- Structural epilepsy—seizures are the result of identifiable structural brain lesions.
- Epilepsy of unknown cause—structural epilepsy is suspected but a lesion cannot be demonstrated.
- Cluster seizures—> 1 seizure/24 hours.
- Status epilepticus—continuous seizure activity or seizures repeated at brief intervals without complete recovery between seizures.
- Status epilepticus can be convulsive or nonconvulsive.
- Seizures are classified as focal (limited to one hemisphere), generalized (involve both hemispheres), and focal with secondary generalization.

PATOPHYSIOLOGY

- Any thalamocortical disturbance may lead to seizure activity.
- Not all cortical regions have equal propensity to seize; from the most to the least likely to cause seizures—temporal, frontal, parietal, and occipital lobes.
- As more seizures occur, the tendency for neuronal damage and propensity for more seizures or SE increases; this kindling effect does not occur in all cortical regions.
- The clinical appearance of a seizure is related to the location of the neuronal hyperactivity.

SIGNALMENT

- Dogs of any breed, age, or sex.
- SE—overrepresentation of German shepherd dog, English foxhound, Pug, teacup poodle, Boston terrier, Lakeland terrier.

Mean Age and Range

SE—4.2–5 years (0.15–15 years)

SIGNS

General Comments

- Prodrome—hours to days prior to the seizure; no EEG changes.
- Aura—short period (seconds) prior to generalization of a seizure where the dog seeks help, looks lost, frightened or has a glazed look. Focal seizure. If it precedes the tonic-clonic generalized seizure, the seizure has a focal onset.
- Ictus—may start with an aura and progress to GS; lateral recumbence with bilateral symmetrical tonic-clonic contractions of limb muscles; often with autonomic signs, e.g., salivation, urination, defecation.
- GS—may be mild, the animal remaining sternal or even standing during the event; may be long-lasting, 20 minutes or more. Convulsive or nonconvulsive.
- Post-ictal phase—disorientation, confusion, aimless pacing, blindness, polydipsia, polyphagia.
- A seizure lasts < 2 minutes.
- Most seizures occur when dog is resting or sleeping.

Historical Findings

- Confirm that seizure has occurred.
- Seizure pattern (age at onset of seizure, seizure type and frequency)—most important factor in establishing list of possible causes.
- Metabolic diseases usually cause generalized seizures.
- Asymmetric neurologic signs before, during, or after the seizure suggest structural brain lesion.
- Presence of behavioral changes in the days/weeks preceding seizure onset indicates structural brain disease.

Neurologic Examination Findings

- Mental status, menace responses, responses to nasal septum stimulation, and proprioceptive positioning—neurologic tests that evaluate the cerebral cortex. Asymmetry indicates structural brain lesion contralateral to deficits.
- Compensated SE, first 30 minutes—salivation, hyperthermia, tachycardia, arrhythmia, increased blood pressure.
- Decompensated SE—difficulty breathing, weak pulse, low blood pressure, poor capillary refill.

CAUSES

Extracranial

- Metabolic—electrolyte disturbances, hypoglycemia (insulinoma); hypocalcemia; acute renal failure; hepatic encephalopathy.
- Toxicities—metaldehyde, pyrethrins/pyrethroids, lead, hexachlorophene, chlorinated hydrocarbons, organophosphates, bromethalin, mycotoxins, macadamia nut, theobromine (chocolate), 5-fluorouracil.

Intracranial

- Degenerative—encephalopathy.
- Malformations—cortical dysplasia.
- Genetic epilepsy.
- Metabolic—cell storage diseases.
- Neoplasia—primary (meningioma, gliomas); secondary (metastatic).
- Inflammatory infectious—viral (e.g., canine distemper); fungal; protozoal (*Neospora*, *Toxoplasma*); rickettsial (ehrlichiosis, Rocky Mountain spotted fever).
- Inflammatory non-infectious—meningoencephalomyelitis of unknown origin, eosinophilic meningoencephalomyelitis; breed-related encephalitis (pug, Maltese, Yorkshire terriers, etc.).
- Trauma.
- Vascular—cerebrovascular accident.
- Epilepsy of unknown cause—post-encephalitic glial scar.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Syncope—body is limp, rapid recovery with no abnormal behavior; occurs at exercise, cough, excitement.
- Insulinoma—seizures occur at exercise, excitement.
- Obsessive-compulsive behaviors or stereotypies—complex and goal-directed behaviors; behavior can be stopped.
- Seizurogenic toxins—progression from whole body tremor to SE and death if left untreated.
- Metabolic

encephalopathy—seizures unusual and accompanied with obtunded mental state and abnormal behavior; no lateralizing signs.

- Structural brain disease likely—if acute onset of > 2 GS within first week of onset, acute onset of focal seizures with gradual progression to GS, or presence of interictal neurologic deficits including behavioral changes.
- Genetic epilepsy—differentiated on age, breed, and seizure pattern; progressive onset of GS with/without aura.
- Cervical pain/spasms—may be mistaken for focal seizures.
- Head bobbing or idiopathic head tremor—dog remains active; can eat, drink, walk.

CBC/BIOCHEMISTRY/URINALYSIS

- Infectious CNS diseases—may reflect multisystem involvement.
- Hypoglycemia—small/toy breeds during SE; insulinoma.
- Hepatic and renal dysfunction—advanced SE.
- Urinalysis—rule out myoglobinuria.

OTHER LABORATORY TESTS

- Blood gases—metabolic acidosis frequent with SE. Respiratory acidosis needs immediate treatment.
- Coagulation profile—DIC in advanced SE.
- Bile acids—suspected hepatic encephalopathy.
- Fasting blood glucose and amended insulin:glucose ratio—dogs > 5 years with occasional seizures during exercise.
- Serology (infectious diseases)—as suggested by systemic signs and laboratory abnormalities.
- Toxicity screen—cholinesterase levels.

IMAGING

- Thoracic radiographs and abdominal ultrasound—to identify metastatic or systemic illness, or lung pathology from SE.
- MRI—best to define location, extent, and nature of lesion.

DIAGNOSTIC PROCEDURES

ECG—arrhythmias can occur in SE due to myocardial damage. CSF—if intracranial structural cause is suspected; CSF and serum titers and PCR for diagnosing infectious diseases. EEG—to document ongoing seizure activity once physical manifestations have ceased.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—isolated seizures in an otherwise healthy dog.
- Inpatient—cluster seizures and SE.

NURSING AND SUPPORTIVE CARE

- SE and cluster-seizures—constant supervision.
- Ensure airway patency. May need to be suctioned due to excessive salivation.
- Administer 100% oxygen via non-rebreathing mask.
- Cool down if hyperthermia.
- Install IV line for drug and fluid administration.
- Draw blood for rapid measurement of blood gases, glucose,

SEIZURES (CONVULSIONS, STATUS EPILEPTICUS)—DOGS (CONTINUED)

calcium, renal and hepatic function, and AED levels if pertinent. • Monitor urine output with indwelling urinary catheter.

CLIENT EDUCATION

- Treat cluster of GS and GSE early—the more seizures in a given time, and the more drugs for seizure control, time for recovery, and cost for treatment.
- Antiepileptic treatment in structural epilepsy may not help until the primary cause is addressed.
- Client to keep a seizure calendar noting date, time, severity, and length of seizures to objectively evaluate response to treatment.
- Outline an in-home treatment emergency plan for cluster-seizures.



MEDICATIONS

- Electrolytes imbalance—treat immediately with fluid therapy.
- Low glucose—50% dextrose diluted to 25% (500 mg/kg IV) over 15 minutes or treat with oral glucose syrup.

DRUG(S) OF CHOICE

Seizure type and frequency determine the therapeutic approach. Important to seek and treat primary cause.

Convulsive Cluster Seizures or Status Epilepticus

Diazepam

- Administer 0.5–1 mg/kg IV bolus; repeat 5 minutes later if gross motor activity has not subsided; follow with CRI of 0.5–1 mg/kg/h added to hourly maintenance fluids in an in-line burette or through syringe pump.
- Rectal—only where IV access cannot be obtained; may diminish or stop gross motor seizure activity to allow IV catheter placement.
- Refractoriness may rapidly develop, necessitating the addition of phenobarbital CRI.

Phenobarbital

- Add if seizures persist after second diazepam bolus or during diazepam CRI; administer CRI phenobarbital (2–6 mg/dog/h added to diazepam infusion) if patient already treated with PB, or loading dose if patient naïve to PB.
- Loading dose—12–24 mg/kg given as boluses of 4 mg/kg IV, 20 minutes apart until desired effect is reached, to a maximum of 24 mg/kg. Optimal therapeutic range: 100–120 µmol/L (23–28 mg/L).
- If patient already on PB, obtain serum level prior to initiating PB CRI. IV bolus 2–6 mg/kg can be administered once while waiting results if serum levels believed inadequate.
- Once seizures have been controlled for 4–6 hours, gradually wean the patient off CRI over as many hours.
- Start/resume oral maintenance AED using PB and/or other GS AED as soon as patient can swallow.

Other

- If seizures continue, propofol at 1–2 mg/kg IV slowly over 60 sec, followed with CRI at 0.1–0.6 mg/kg/min to effect; monitor

anesthetized patient with EEG to evaluate treatment response.

- Ketamine is also used occasionally at 5 mg/kg IV bolus followed with CRI at 5 mg/kg/h.
- Dexamethasone—0.2 mg/kg q24h for 1–3 days; reduce cerebral edema.
- Dexamethasone—for acute treatment of cerebral edema secondary to severe inflammatory CNS disease, even if infectious.

Acute Focal Status Epilepticus

- Often harbors brain lesion.
- Diazepam and PB CRI—effective for focal and GS.
- Frequently difficult to reach seizure control.
- Instances of chronic nonconvulsive generalized or focal SE—owner unaware it is occurring (e.g., senile encephalopathy); if seizures remain focal and patient's quality of life not significantly altered, no treatment necessary.
- Long-term antiepileptic treatment if necessary—PB (3–5 mg/kg q12h PO), levetiracetam (20 mg/kg q8h PO), or zonisamide (5 mg/kg q12h PO).

CONTRAINdications

- Potassium bromide—do not use to treat SE; too long half-life; loading dose not recommended.
- Aminophylline, theophylline—CNS excitement; may cause seizure.
- Steroids—alter CSF parameters; avoid if considering CSF analysis.

PRECAUTIONS

- Phenobarbital—liver disease, lower dose; monitor levels closely; for SE, add cautiously to diazepam because the drugs potentiate each other, cardiac/respiratory depression may ensue.
- Steroids—contraindicated in infectious diseases, but one dose of dexamethasone (0.2 mg/kg IV) may decrease brain edema when impending brain herniation or life-threatening edema is suspected.

POSSIBLE INTERACTIONS

- Cimetidine, ranitidine, and chloramphenicol—interfere with PB metabolism; may lead to PB toxic level.
- Phenobarbital decreases zonisamide serum levels. Dosage recommended when drugs are used simultaneously—10 mg/kg q12h.
- If levetiracetam used concomitantly with PB—measure serum levels (humans 10–40 µg/mL).

ALTERNATIVE DRUG(S)

Levetiracetam—20–60 mg/kg IV; use upper end dosage if patient already on oral phenobarbital. Good alternative in liver disease or portosystemic shunts, as the drug is not metabolized in the liver. Use with caution in patients with renal disease.



FOLLOW-UP

PATIENT MONITORING

- Inpatients—constant supervision for seizure monitoring.
- Eyelid or lip twitching in a heavily sedated patient is sign of ongoing

seizure activity.

- Monitor heart rate, respiratory rate, oxygenation/ventilation, body temperature, blood pressure, urine production, neurologic examination.
- EEG monitoring for ongoing seizure activity.
- Patient may need 7–10 days before returning to normal after SE.

POSSIBLE COMPLICATIONS

- Phenobarbital—hepatotoxicity after long-term treatment with serum levels > 140 µmol/L (> 33 µg/L); acute neutropenia (rare) in the first few weeks of use requires permanent withdrawal.
- Paradoxical hyperexcitability.
- Permanent neurologic deficits (e.g., blindness, abnormal behavior, cerebellar signs) may follow severe SE.
- GSE may lead to hyperthermia, acid-base and electrolyte imbalances, pulmonary edema, cardiovascular collapse and death.

EXPECTED COURSE AND PROGNOSIS

- Genetic epilepsy or epilepsy of unknown cause represents a large proportion of dogs with GSE or cluster-seizures. In-home emergency measure using diazepam rectal/nasal should be provided.
- Dogs with encephalitis and GSE—poor outcome.
- Structural epileptic dogs recovered from primary disease (e.g., *Ehrlichia canis*)—slowly (over months) wean patient off AEDs after 6 months seizure-free; if seizures recur, reinstate AED.



MISCELLANEOUS

AGE-RELATED FACTORS

- The immature brain has a higher propensity to seize.
- Genetic epilepsy—6 months–5 years; often epilepsy refractory when onset at < 2 years.
- Phenobarbital—higher dose needed in puppies (< 5 months) to reach therapeutic range.

ABBREVIATIONS

- AED = antiepileptic drug
- CNS = central nervous system
- CRI = constant rate infusion
- CSF = cerebrospinal fluid
- CVA = cerebrovascular accident
- DIC = disseminated intravascular coagulation
- ECG = electrocardiogram
- EEG = electroencephalogram
- GS = generalized seizure
- GSE = generalized status epilepticus
- KBr = potassium bromide
- MRI = magnetic resonance imaging
- PB = phenobarbital
- PCR = polymerase chain reaction
- SE = status epilepticus

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Client Education Handout
available online

SEMINOMA**BASICS****OVERVIEW**

Sex cord stromal tumor of the testicle arising from the spermatogenic epithelium.

SIGNALMENT

- Median age, 10 years.
- Boxer, German Shepherd, Afghan hound, Weimaraner, Shetland sheepdog, Collie, and Maltese may be at increased risk.
- 33–52% of all testicular tumors in dogs, extremely rare in cats.

SIGNS

- Usually none.
- Fertility issues in breeding dogs.
- 4–20% of dogs will have more than one type of testicular tumor.
- Up to 50% of dogs will have bilateral tumors, only 12% of contralateral tumors will be palpable.

CAUSES & RISK FACTORS

Cryptorchidism

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- Sertoli cell tumor
- Interstitial (Leydig cell) cell tumor

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal unless hormone productive and consequent male feminization syndrome.

IMAGING

- Testicular sonography may aid in differential diagnosis.
- Abdominal sonography for retained testicles and to evaluate for concurrent malignancies.

DIAGNOSTIC PROCEDURES

N/A

**TREATMENT**

- Bilateral orchiectomy and scrotal ablation is the treatment of choice.
- Exploratory laparotomy for retained testicles.
- Histopathologic examination of appropriate tissue.
- Immunohistochemistry may be necessary to identify cell of origin in some cases.
- Radiotherapy—reported effective in patients with regional metastasis.

**MEDICATIONS****DRUG(S)**

None reported in dogs.

**FOLLOW-UP****PREVENTION/AVOIDANCE**

Castration at a young age

POSSIBLE COMPLICATIONS

None likely

EXPECTED COURSE AND PROGNOSIS

Bilateral orchiectomy and scrotal ablation are often curative. Reported rate of regional or distant metastasis < 15%.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Prostate disease
- Perianal adenoma
- Perineal hernia

SEE ALSO

- Interstitial Cell Tumor, Testicle
- Sertoli Cell Tumor

Suggested Reading

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SEPARATION DISTRESS SYNDROME



BASICS

DEFINITION

A distress response of dogs (occasionally cats) separated from the person or persons to whom they are most attached, usually their owner(s). The separation may be real (the owner is gone) or perceived (the pet is just separated from the owner). In other cases the pet may be distressed because some fear-inducing event has occurred while home alone such as thunderstorms or loud noises resulting in distress responses during other departures. The resulting distress may be evident by episodes of destruction, vocalization, and elimination. Separation anxiety is a subset of separation-related problems that may have different underlying motivations including fear, anxiety, overattachment to owner(s), and lack of appropriate stimulation or interactions.

PATHOPHYSIOLOGY

Unknown

SYSTEMS AFFECTED

- Behavioral—escape attempts, howling, whining, depression, hyperactivity.
- Cardiovascular—tachycardia.
- Endocrine/Metabolic—increased cortisol levels, stress-induced hyperglycemia.
- Gastrointestinal—inappetence, gastrointestinal upset.
- Musculoskeletal—self-induced trauma resulting from escape attempts.
- Nervous—adrenergic/noradrenergic overstimulation.
- Respiratory—tachypnea.
- Skin/Exocrine—acral lick dermatitis.
- Oral—dental damage during escape attempts.

GENETICS

None known

INCIDENCE/PREVALENCE

Speculated that 7–28% of companion dogs experience some degree of separation distress syndrome. May be different entities with younger dogs and senior dogs experiencing different underlying pathology.

S

SIGNALMENT

Species

Primarily dogs; possible in cats

Mean Age and Range

Any age, most commonly in dogs > 6 months; may be another increase in prevalence in dogs > 8 years.

SIGNS

General Comments

Destruction, vocalization, and elimination in the absence of the owner alone are not diagnostic for separation anxiety or separation distress.

Historical Findings

- Destruction, vocalization (whining, howling, barking), and indoor elimination are

commonly reported. Destruction targets windows and doors and/or owner possessions.

- Other signs include behavioral depression, anorexia, drooling, hiding, shaking, panting, pacing, attempts to prevent owner departure, and self-trauma from lick lesions. Diarrhea and vomiting are occasionally noted.
- Signs of strong pet-owner attachment may be present: excessive attention-seeking behaviors and following behaviors but not necessary for diagnosis.
- Frequently owners report excessive, excited, and prolonged greeting behavior upon return.
- Separation distress behavior(s) usually occurs regardless of the length of owner absence, often within 30 minutes of owner departure.
- Specific triggers that are predictive of possible departure may initiate the anxiety response: getting keys, putting on outer garments, or packing the car.
- May occur on every departure and absence or only with atypical departures or after-work, evening, or weekend departures; the reverse pattern may also be seen.
- May also occur when fear-inducing stimuli are present such as noises or storms.
- In cats, elimination problems in the owner's absence may be linked to separation-related anxiety.
- Some animals initially show signs in the presence of acute fear or anxiety inducing events such as thunderstorms or fireworks when home alone but may recur with future departures even in the absence of stimuli.
- Distress may also be initiated by a change in daily routine or in the household (e.g., moving).

Physical Examination Findings

- Usually normal.
- Injuries incurred in escape attempts or destructive activities.
- Skin lesions from excessive licking.
- Rare cases of dehydration from drooling or diarrhea due to stress.

CAUSES

Specific causes are unknown. Speculated causal factors include:

- In owner departure and absence.
- Lack of appropriate pet-owner interactions.
- Prolonged contact with humans without learning to be alone.
- Improper or incomplete early separation from the bitch (French behavior school).
- Traumatic episodes during owner absence.
- Change in household routine.
- Medical issues contributing to anxiety including endocrine dysfunction, pain, sensory decline or cognitive decline.

RISK FACTORS

- Suspected but not proven risk factors: adoption from humane shelters, extended time with preferred person such as during vacation or illness, boarding, lack of detachment when young.
- Geriatric animals seem to be overrepresented.
- Possible correlation between separation anxiety and other anxiety disorders including noise phobias.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Vocalization: response to outdoor influences, territorial displays, play with other pets in the home or fears.
- Destructive behaviors: occur both when the owner is present and absent (e.g., territorial destructive displays at windows and doors; destruction due to fear-producing stimuli such as noises and thunderstorms).
- Housesoiling: inadequate housetraining, illness, endocrine dysfunction, cognitive decline.
- Licking due to primary dermatologic conditions.
- Fear-based conditions that mimic separation anxiety behaviors.
- Barrier frustration: dogs unable to be confined in crates or behind barriers but who are fine if not confined.
- Underlying medical conditions including endocrinopathies, sensory decline, pain and cognitive dysfunction syndrome.

CBC/BIOCHEMISTRY/URINALYSIS

Abnormalities, if present, suggest alternate diagnosis or concurrent medical disease.

OTHER LABORATORY TESTS

Endocrine testing if indicated based on history and results of CBC and biochemistry panel

IMAGING

MRI or CT if neurologic disorders are suspected

DIAGNOSTIC PROCEDURES

- Behavioral history • Video recordings of the pet when home alone to verify diagnosis.
- Questionnaires targeting cognitive decline are advisable for geriatric dogs.
- Skin biopsies if a dermatologic condition is suspected.
- CSF tap if neurologic disorders are suspected.
- Endoscopy with biopsies if gastrointestinal signs are persistent.



TREATMENT

ACTIVITY

Regular, scheduled daily exercise and playtime are beneficial.

DIET

No dietary changes are necessary unless diarrhea is also present.

CLIENT EDUCATION

General Comments

Set realistic expectations of the time course of treatment and the need for behavior modification to have successful resolution of the problem. Problem behavior may take weeks or months to resolve depending on severity and duration of the problem. Treatment components include the following.

(CONTINUED)

SEPARATION DISTRESS SYNDROME***Independence Training***

- Teach the dog to be more independent of the owner(s). • All attention is at owner initiation—owner begins and ends attention sessions. • No attention on pet demand.
- Have the pet earn attention and food, treat or toy rewards, by performing a task such as “sit.” • Decrease following behavior while the owner is home. Owner must not ignore the dog, but give attention in a predictable and calm manner—requesting a sit or other calm behavior before petting, throwing a ball etc. If the dog is jumping, whining, pawing at the owner they should not receive attention for that excited behavior but the owner should wait until the dog is calm before interaction.
- Teach the dog to calmly stay in another location away from the owner and create a safe haven for the dog to settle and relax on command. The dog must be able to be calm and relaxed when the owner is home for gradually longer times and gradually increasing separation to be calm and relaxed when they are gone.

Changing the Predictive Value of Pre-departure Cues

- Presentation of pre-departure cues (picking up keys, walking to the door) without leaving.
- Repeated 2–4 times daily until the dog does not respond to cues with anxious behaviors (panting, pacing, following, or increased vigilance). • Goal is to disassociate the cues with departures and diminish the anxious response. If the dog becomes more anxious, this step is discontinued.

Counter-Conditioning

- Teach the dog to sit/stay near the typical exit door. • Owner gradually increases the distance between the dog and the exit door. • Owner slowly progresses toward the door, increasing the time away on each trial. • Eventually elements of departure, such as opening and closing the door, are added. • Finally, the owner steps outside the door and returns.

Classical Counter-Conditioning

- Leaving the dog a delectable food treat or food-stuffed toy on departure. • Associating departure with something pleasant.

Changing Departure and Return Routine

- Ignore the pet for 15–30 minutes prior to departure and upon return. • On return, attend to the dog only when it is calm and quiet. • May allow the dog outside to eliminate.

Graduated Planned Departures and Absences

- Begun after dog is not responding to pre-departure cues. • Use short absences to teach the dog how to be home alone.
- Departures must be short enough not to elicit a separation distress response; the pet must be calm when owners depart and calm when they return. • Goal—animal learns consistency of owner return and to experience

departure and absence without anxiety.

- Departures must be just like real departures (owner must do all components of departure, including leaving in the car if that is how he or she usually departs). Owner will leave a safety cue (radio or television on, ring a bell) on planned departures only (must not be used on departures where length of absence is not controlled, such as work departures). • Initial departures must be very short, 1–5 minutes.
- Length of absence is slowly increased at 3–5 minute intervals if no signs of distress were evident at the shorter interval (excited greetings, barking etc.). • Increase in interval must be variable; intersperse short (1–3 minute) with longer (5–20 minute) departures. • If destruction, elimination, or vocalization occur, departure was too long. Use video recordings to assess pet anxiety. • If departures and absences are continued even though distress behaviors are present, the dog will get worse. • Audio recordings for vocalization can help monitor progress.
- Once the pet can be left for 2–3 hours on a planned departure, it often can be left all day.
- Cue is slowly phased out over time or can be used indefinitely.

Arrangements for the Pet During Retraining and Owner Absence

- If possible, allow no more destructive activity. • Mixing up or eliminating triggering departure cues may help diminish the anxious responses. • Doggie daycare arrangements or pet sitters. • Gradual conditioning to a crate.
- Crates must be used cautiously if at all and only in dogs that are calm when left in a crate as they may increase anxiety and result in pet injury.

SURGICAL CONSIDERATIONS

If the animal is on medication, care should be exercised prior to administering anesthesia.

**MEDICATIONS****DRUG(S) OF CHOICE*****Drugs for Chronic Therapy******Clomipramine***

- TCA—approved for use in the treatment of separation anxiety in dogs.
- Approved for dogs older than 6 months of age.
- Dosage: 2–4 mg/kg total daily dose (canine). Administered as one dose or divided twice daily; dogs may do better with dividing the dose and administering twice daily. Must be given daily, not on an “as needed” basis, and in conjunction with a behavior modification plan.
- May take 2–4 weeks before behavioral effect is evident.
- Side effects: vomiting, diarrhea, and lethargy.

Fluoxetine

- SSRI—approved for use in the treatment of separation anxiety in dogs.
- Dosage: 1–2 mg/kg PO q24h.
- Administer in conjunction with a behavior modification plan.
- Side effects: lethargy, decreased appetite, weight loss, and vomiting.

Drugs For Acute Anxiety At Departure

- While waiting for an SSRI or TCA to provide anxiety relief, the use of short-term anxiolytics and pheromones is advisable in many cases.
- Benzodiazepines: alprazolam for panic at owner departure (dog, 0.01–0.1 mg/kg) 30 minutes prior to departure. Some dogs experience paradoxical excitement with benzodiazepines, changing dosages or switching to another one may help. Polyphagia is also common with benzodiazepine administration.
- Trazodone: A serotonin receptor antagonist and reuptake inhibitor and can be used in conjunction with a TCA or SSRI to augment calming effects. Dosage recommendation (dog) is to begin with 2–3 mg/kg PO prior to departure and titrate up gradually to effect (up to 8–10 mg/kg). Dose should be increased cautiously, especially if using with an SSRI or TCA. Side effects include: vomiting, diarrhea, sedation, ataxia, hypotension, excitement or agitation and panting and rare reports of polyphagia.
- Adaptil: synthetic analogue of the natural appeasing pheromones of the nursing bitch that calms puppies; used to calm dogs in fearful, stressful, and anxiety situations such as separation anxiety and noise phobias; available as a plug-in diffuser for the area the dog is housed, a spray for the cage or mat, and collar.

CONTRAINDICATIONS

- Neither clomipramine nor fluoxetine should be used in conjunction with MAOIs such as amitriptyline and selegiline or within 14 days before or after an MAOI. • Use clomipramine with caution in patients showing cardiac conduction disturbances. • Caution advised using in conjunction with CNS active drugs including general anesthesia, neuroleptic, anticholinergic, and sympathomimetic drugs for dogs on either clomipramine or fluoxetine.
- A 6-week wash-out interval should be observed following discontinuation of therapy with fluoxetine prior to administration of any drug that may interact with fluoxetine.
- Fluoxetine should not be used in dogs with epilepsy or a history of seizures or with drugs that lower the seizure threshold (phenothiazines). • Practitioners are urged to read package insert for contraindications.

PRECAUTIONS

- Studies to determine effects of medication in patients less than 6 months of age have not been conducted. • Studies to assess the

SEPARATION DISTRESS SYNDROME

(CONTINUED)

interaction of fluoxetine with TCAs have not been conducted. • Improperly applied behavioral modification may actually increase anxiety. • Crating can result in serious physical damage to the pet if it attempts to escape; it should only be recommended cautiously for those animals that are already crate-trained. • Animals that do not respond may have other concurrent anxieties such as noise and storm phobias.

POSSIBLE INTERACTIONS

Serotonin syndrome with MAOI and SSRI or SSRI and TCA combinations.

ALTERNATIVE DRUG(S)

- TCA such as amitriptyline (dog, 1–2 mg/kg q12h) might be considered in place of clomipramine or fluoxetine. • Clonidine – An alpha agonist which acts as an antihypertensive agent which might be used in combination with a TCA or SSRI at a dose of 0.01–0.05 mg/kg. Begin at the lowest end of the dose range and increased cautiously.
- Nutraceutical preparations: L-theanine (Anxitane), alpha-casosopene (Zyken) alone or in combination with l-tryptophan (Royal Canine Calm diet), or Harmonease may be useful in milder cases or adjunctively.



FOLLOW-UP

PATIENT MONITORING

Good client follow-up is necessary to monitor both the behavioral treatment plan and medication if prescribed. Weekly follow-up is best in the early stages to assess efficacy of the treatment plan and owner compliance with instructions. Once the dog has become more independent, habituated to pre-departure

cues, and calmer on departures and returns, graduated planned departures may be implemented.

PREVENTION/AVOIDANCE

Teaching animals how to be left home alone, making animals independent.

POSSIBLE COMPLICATIONS

- Injuries during escape attempts. • Ongoing destruction and elimination disrupt the human-animal bond and result in pet relinquishment. • Other anxieties causing signs that mimic separation distress; if not identified and treated, the problem may worsen.

EXPECTED COURSE AND PROGNOSIS

Separation anxiety often responds well to behavioral modification with or without medication. Some severe cases can be very resistant to treatment. Other concurrent behavioral disorders may make resolution more difficult. Drug therapy alone is rarely curative for most behavioral disorders. Realistically, drug therapy can be expected to decrease the anxiety associated with owner departure, but the dog still must be taught how to be left alone during owner absences.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Other anxiety conditions including noise phobias, generalized anxiety, fears, and compulsive disorders.

AGE-RELATED FACTORS

Common behavior problem in senior dogs.

SYNOMYS

- Hyperattachment • Separation anxiety

SEE ALSO

- Cognitive Dysfunction Syndrome
- Excessive Vocalization and Waking at Nights • Thunderstorm and Noise Phobias

ABBREVIATIONS

- CNS = central nervous system • CSF = cerebrospinal fluid • CT = computerized tomography • MAOI = monoamine oxidase inhibitor • MRI = magnetic resonance imaging • SSRI = selective serotonin reuptake inhibitor • TCA = tricyclic antidepressant

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Consulting Editor Gary M. Landsberg



Client Education Handout
available online



BASICS

DEFINITION

- Bacteremia—the presence of viable bacterial organisms in the bloodstream.
- Sepsis—systemic inflammatory response to bacterial infection (e.g., fever, hypotension).
- Terms are not synonymous, although often used interchangeably.

PATHOPHYSIOLOGY

- Shedding of bacterial organisms into the bloodstream—may occur transiently, intermittently, or continually.
- The most critical host response for elimination of bacteremia—is provided by mononuclear phagocyte system of the spleen and liver; activation leads to release of numerous cellular mediators (cytokines), some of which are beneficial and others detrimental; may lead to death of the host.
- Neutrophils—relatively more important for defense against extravascular infection.
- Bacteremia—may occur as a transient, subclinical event or escalate to overt sepsis when the immune system is overwhelmed; generally of more pathologic significance when the bloodstream is invaded from venous or lymphatic drainage sites.

SYSTEMS AFFECTED

Cardiovascular

- With peracute development of septicemia—increased or decreased cardiac output, decreased systemic vascular resistance, and increased vascular permeability; ultimately, refractory hypotension develops, leading to multiorgan failure and death.
- Endocarditis—may develop; presence of bacteremia alone is not sufficient for induction; multiple factors involving both the host and the bacterial organism must be favorable for bacterial adherence to heart valves.

Hemic/Lymphatic/Immune

- Coagulation disorders and thromboembolism.
- Kidney and myocardium especially prone to septic embolization.
- With chronic bacteremia—antigenic stimulation of the immune system may lead to immune-complex deposition.

Endocrine

A syndrome of relative adrenal insufficiency has been reported in dogs with sepsis.

Other

- Respiratory
- Gastrointestinal
- Hepatobiliary

SIGNALMENT

Species

- Dog and cat.
- No age, sex, or breed predispositions reported.

- Large-breed male dogs—predisposed to bacterial endocarditis and discospondylitis.

SIGNS

General Comments

- Development may be acute or may occur in a vague or episodic fashion.
- Variable and may involve multiple organ systems.
- May be confused with those of immune-mediated disease.
- Clinical—more severe when gram-negative organisms are involved.
- Dogs—the earliest signs are usually referable to the gastrointestinal tract.
- Cats—respiratory system more commonly involved.

Historical Findings

A thorough history is essential; historical findings highly variable depending upon underlying cause.

Physical Examination Findings

- Intermittent or persistent fever; hypothermia more common than fever in cats in one study.
- Lameness.
- Depression.
- Tachycardia; bradycardia more common than tachycardia in cats in one study.
- Heart murmur.
- Weakness.

CAUSES

- Dogs—gram-negative organisms (especially *E. coli*) most common; Gram-positive cocci and obligate anaerobes also important; polymicrobial infection reported in about 20% of dogs with positive blood cultures.
- Cats—bloodstream pathogens usually Gram-negative bacteria from the *Enterobacteriaceae* family or obligate anaerobes; *E. coli* and *Salmonella* most common Gram-negative organisms cultured.
- *Pseudomonas aeruginosa*—uncommon isolate from animal blood cultures.

RISK FACTORS

- Peracute—pyometra and disruption of the gastrointestinal tract most often associated.
- More protracted onset— infections of the skin, upper urinary tract, oral cavity, and prostate.
- Hyperadrenocorticism, diabetes mellitus, liver or renal failure, splenectomy, malignancy, and burns—predisposing factors.
- Immunodeficient state—chemotherapy, FIV, splenectomy; particular risk.
- Glucocorticoids—considered an important risk factor for bacteremia; allows greater multiplication of bacteria in extravascular tissues.
- Intravenous catheter—provides rapid venous access for bacteria.
- Indwelling urinary catheters—may be a predisposing factor.
- Rectal exam.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Consider other causes of fever, heart murmur, joint or back pain, or hypotension.
- Clinical signs of more chronic bacteremia may be confused with immune-mediated disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilic leukocytosis with a left shift and an associated monocytosis—most common hematologic abnormalities.
- Neutropenia—may develop.
- Hypoalbuminemia and a high ALP (up to two times upper limit of normal)—up to 50% of affected dogs.
- Hypoglycemia—about 25% of affected dogs; hyperglycemia more common than hypoglycemia in cats in one study but another report found most cats with hypoglycemia.

OTHER LABORATORY TESTS

- With suspected catheter-induced sepsis—submit catheter tip for culture.
- Urine culture—may be useful; positive culture does not determine if urinary tract is primary or secondary source of infection.
- Coagulation parameters should be monitored in most cases.

IMAGING

May identify source of bacteremia (e.g., pyometra, prostate) or secondarily infected organs (e.g., discospondylitis).

DIAGNOSTIC PROCEDURES

Blood Culture Indications

- Any patient that develops fever (or hypothermia), leukocytosis (especially with a left shift), neutropenia, shifting leg lameness, recent onset or changing heart murmur, or any sign of sepsis that cannot be explained.
- Essential for confirming suspected bacteremia and for optimizing management of the patient; one study of critically ill animals reported approximately 75% of cats and 50% of dogs had positive blood cultures.
- Clinical findings—not reliable for discriminating between particular types of bacteria.

Guidelines

- Current antimicrobial therapy—does not preclude collection of blood cultures; advise laboratory that patient is receiving antibiotics; steps can be taken to inactivate certain medications.
- Anaerobic cultures—special bottles may not be necessary.
- Sets (pairs) of samples—inform laboratory that for each submitted pair of bottles, one is for aerobic culture and the other for anaerobic.
- Collect at least two (and preferably three) sets of samples—improves chance of

SEPSIS AND BACTEREMIA

(CONTINUED)

obtaining a positive culture and facilitates interpretation of results.

- Volume—the greater the volume of collected blood, the better the chances of obtaining positive cultures; often only a few organisms present per milliliter of blood; 10 mL of blood per culture recommended; may not be possible for cats and small dogs; have an assortment of culture bottles available (including 25, 50, and 100 mL); small bottles useful for small patients for maintaining appropriate blood-to-culture broth ratio.
- Timing—for most patients, sufficient to take three cultures over a 24-hour period; for critically ill patients, take three cultures over a 2-hour period.

Collection

- Bottles—warm to room temperature; apply alcohol or iodine to the rubber stopper.
- Patient—clip hair; thoroughly disinfect skin before venipuncture to avoid contamination; wipe with 70% alcohol, then apply an iodine-based disinfectant; allow a minimum of 1 minute of contact time with the skin.
- Withdrawing blood—wearing a sterile glove, palpate the vein; draw blood into a sterile syringe; evacuate all air from the syringe; attach a new needle before inoculating blood into the bottles.
- Samples—maintain culture bottles at room temperature for transport to the laboratory.

Media

- Commercial multipurpose nutrient broth media—recommended.
- A medium that supports growth of both aerobes and anaerobes—ideal.
- Often the laboratory that processes the culture will supply culture bottles.

Interpretation of Results

- Single positive culture—not possible to distinguish true bacteremia from sample contamination.
- Two or more positive cultures identified as the same organism desired.
- Coagulase-negative staphylococci, α -hemolytic streptococci, and *Acinetobacter*—probably contamination.
- *Enterobacteriaceae*, *Bacteroidaceae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Staphylococcus intermedius*, β -hemolytic streptococci, and yeasts—nearly always clinically significant bacteremia.
- Negative results from two or three successive cultures—generally eliminates bacteremia owing to common pathogens; some less common bacteria may take several weeks to grow.

PATHOLOGIC FINDINGS

Varies with the underlying cause.



TREATMENT

APPROPRIATE HEALTH CARE

- Success—requires early identification of the problem and aggressive intervention; careful monitoring essential, because the status of patient may change rapidly.
- Hypotension—intravenous fluids; isotonic fluids (e.g., lactated Ringer's) at a rate up to 90 mL/kg/h in dogs and 55 mL/kg/h in cats; use caution when hypoalbuminemia or increased vascular permeability is a concern.
- Volume expanders (e.g., hydroxyethyl starch)—may help maintain oncotic pressure.
- With hypoglycemia—may add dextrose to intravenous fluids.
- Electrolytes and acid-base balance—correct abnormalities.
- External sources of infection—give appropriate attention to wound care and bandage changes.
- Internal sources of infection (e.g., pyometra or disruption of the bowel)—surgical intervention essential.

NURSING CARE

As appropriate for each patient's situation.

DIET

Nutritional support—provide by assisted feeding or placement of a feeding tube.

CLIENT EDUCATION

Prognosis should be discussed with client.

SURGICAL CONSIDERATIONS

Any identifiable focus of infection such as an abscess should be located and removed where possible.



MEDICATIONS

DRUG(S) OF CHOICE

- Antibiotics—usually selected before culture and sensitivity results available; empiric therapy acceptable while waiting for results; do not delay treatment.
- Antimicrobials—give intravenously; direct therapy to cover all possible bacterial organisms (gram-positive and -negative; aerobic and anaerobic).
- If patient not in shock—a good choice is a first-generation cephalosporin; dogs and cats: administer cefazolin at 40 mg/kg IV as a loading dose; then 20–30 mg/kg IV q6–8h (dogs and cats).
- Aminoglycosides—add to protocol if more aggressive therapy is warranted; administer gentamicin at 2–4 mg/kg IV q8h (dogs and cats).

CONTRAINDICATIONS

Glucocorticoids and NSAIDs—value in treating septic shock; do not improve survival unless given within the first few hours of the

onset; may complicate the clinical picture in potentially ischemic organs (e.g., gastrointestinal tract and kidneys).

PRECAUTIONS

Aminoglycosides—use with caution with renal impairment.



FOLLOW-UP

PATIENT MONITORING

- Aminoglycoside therapy—monitor renal function.
- Blood pressure and ECG.

POSSIBLE COMPLICATIONS

Multiple organ failure

EXPECTED COURSE AND PROGNOSIS

Bacteremia is associated with a high rate of mortality; death owing to hypotension, electrolyte, and acid-base disturbances, and endotoxicemic shock.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Suspected discospondylitis (dogs)—may need to screen for *Brucella canis*.
- See "Risk Factors" for possible underlying diseases.

SYNOMYMS

- Septic shock
- Septicemia

SEE ALSO

- Abscessation
- Anaerobic Infections
- Endocarditis, Infective
- Shock, Septic

ABBREVIATIONS

- ALP = alkaline phosphatase
- ECG = electrocardiogram
- FIV = feline immunodeficiency virus
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

- Bellhorn TL, Macintire DK. Bacterial translocation: Clinical implications and prevention. Compend Contin Educ Pract Vet 2002, 32:1165–1178.
- Burkitt JM, Haskins SC, Nelson RW, et al. Relative adrenal insufficiency in dogs with sepsis. J Vet Intern Med 2007, 21:226–231.
- Morressey PR. Synthesis of proinflammatory mediators in endotoxemia. Compend Contin Educ Pract Vet 2001, 23:829–836.
- Author** Sharon Fooshee Grace
Consulting Editor Stephen C. Barr



Client Education Handout
available online

SERTOLI CELL TUMOR



BASICS

OVERVIEW

Sex cord stromal tumor of the testicle arising from the sustenacular cells of Sertoli.

SIGNALMENT

- Median age, 10 years.
- Boxer, German shepherd, Afghan hound, Weimaraner, Shetland sheepdog, Collie, and Maltese may be at increased risk.
- 8–33% of all testicular tumors in dogs, extremely rare in cats.

SIGNS

- Usually none. Fertility issues in breeding dogs.
- 4–20% of dogs will have more than one type of testicular tumor.
- Up to 50% of dogs will have bilateral tumors, only 12% of contralateral tumors will be palpable.
- > 50% of dogs will have hyperestrogenism. Most common clinical signs include: bilateral symmetric alopecia and hyperpigmentation, pendulous prepuce, gynecomastia, galactorrhea, atrophy of the penis, squamous metaplasia of the prostate.
- Clinical signs associated with severe pancytopenia include weakness, hemorrhage and febrile episodes.
- Abdominal mass—if patient is cryptorchid.

CAUSES & RISK FACTORS

- Cryptorchid testicles 12.7 per 1000 dog-years (versus 0 for scrotally located testicles).
- Cryptorchid and ≥ 6 years of age, 68.1 per 1000 dog-years.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Interstitial cell tumor
- Seminoma
- Hyperadrenocorticism
- Hypothyroidism

- More likely to have an abdominal location than other testicular tumors; high testicular temperature in the abdominal location may destroy spermatogenic cells and leave Sertoli cells unregulated.

CBC/BIOCHEMISTRY/URINALYSIS

Transient neutrophilia followed by progressive neutropenia, thrombocytopenia, and nonregenerative anemia.

OTHER LABORATORY TESTS

Low testosterone to estradiol ratio.

IMAGING

- Testicular sonography may aid in differential diagnosis.
- Abdominal sonography for retained testicles and to evaluate for concurrent malignancies.

DIAGNOSTIC PROCEDURES

- Histopathologic examination of testicular mass.
- Immunohistochemistry may be necessary to identify cell of origin in some cases.



TREATMENT

- Bilateral orchiectomy and scrotal ablation is the treatment of choice.
- Exploratory laparotomy for retained testicles.
- Blood products and/or antibiotics for dogs with bone marrow hypoplasia.



MEDICATIONS

DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Recurrence of feminization may be associated with metastasis.
- Serum hormone levels may be correlated with resolution of clinical signs.

POSSIBLE COMPLICATIONS

Irreversible bone marrow ablation resulting in life-threatening hemorrhage and recurrent infection.

EXPECTED COURSE AND PROGNOSIS

- Good in most patients.
- Guarded if cytopenias exist at diagnosis.
- Poor prognosis if aplastic anemia present.
- Clinical signs of hyperestrogenism expected to resolve within 1–3 months following castration; however, bone marrow hypoplasia might be irreversible.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- 50% of dogs with Sertoli cell tumor associated with hyperestrogenism and feminization.
- Hyperestrogenism can cause hematopoietic failure.

SEE ALSO

Hyperestrogenism (Estrogen Toxicity)

Suggested Reading

Grieco V, Riccardi E, Greppi GF, et al. Canine testicular tumours: A study on 232 dogs. J Comp Pathol 2008, 138(2–3): 86–89.

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SEXUAL DEVELOPMENT DISORDERS



BASICS

DEFINITION

- Errors in the establishment of chromosomal, gonadal, or phenotypic sex cause abnormal sexual differentiation.
- Variety of patterns from ambiguous genitalia to apparently normal genitalia with sterility.

PATHOPHYSIOLOGY

- Sexual differentiation is a sequential process—chromosomal sex established at fertilization (dog: 78,XX or 78,XY; cat: 38,XX or 38,XY), development of gonadal sex, and finally development of phenotypic sex.
- Testis differentiation normally determined by sex chromosome constitution; *SRY* (on the Y chromosome) and *SOX9* (autosomal gene), expressed by Sertoli cells, are critical for testis differentiation.
- Ovarian differentiation—an active process involving *WNT4/RSP01* and β -catenin.
- Phenotypic sex differentiation (tubular reproductive tract and external genitalia) depends on gonadal sex—basic embryonic plan is female; male phenotype results if testes are capable of secreting MIS and testosterone at the correct time during embryogenesis, and functional androgen receptors (X-linked gene) are present on genital tissues.
- Consensus terminology for categorizing Disorders of Sexual Development recently revised. Previous nomenclature also noted.

S Sex Chromosome DSD

- Defects in number or structure of sex chromosomes—chromosomal non-disjunction during meiosis causes trisomy, monosomy; mitotic non-disjunction of a single zygote causes mosaicism; fusion of zygotes leads to chimerism.
- XXY (Klinefelter) syndrome—79,XXY (dog); 39,XXY (cat); hypoplastic testes; phenotypic male (normal to hypoplastic genitalia); sterile; some tortoiseshell male cats.
- XO (Turner) syndrome—77,XO (dog); 37,XO (cat); dysgenetic ovaries; phenotypic female; infantile genitalia; sterile.
- XXX syndrome—79,XXX (dog); hypoplastic ovaries anestrus to irregular estrous cycles; female phenotype; high FSH and LH; somatic abnormalities common in XXX women.
- True hermaphrodite chimera—XX/XY or XX/XXY; ovarian and testicular tissue; phenotypic sex depends on amount of testicular tissue; dogs and cats.
- XX/XY chimera with testes and XY/XY chimera with testes—vary from phenotypic female with abnormal genitalia to male with possible fertility; dogs and cats (some tortoiseshell males).

XY DSD

Disorders of Testicular Development

- Complete or partial testicular dysgenesis—*SRY*-positive 78,XY dog; genitalia

incompletely-masculinized: (enlarged clitoris); testes undescended or perivulvar; Müllerian and Wolffian duct derivatives variably present.

- Ovotesticular DSD—(XY sex reversal, true hermaphrodite) • *SRY*-positive 38,XY true hermaphrodite cat (one report); ovotestes in ovarian position; Müllerian and Wolffian duct derivatives present; penis • 78,XY (*SRY* status unknown) dog; ambiguous female genitalia (enlarged clitoris, os clitoris); abdominal ovary (hypoplastic) and testis (Sertoli cell tumor, no spermatogenesis).

Disorders in Androgen Synthesis or Action

- Complete androgen insensitivity syndrome—38,XY cat; testes at caudal pole of kidneys; no Wolffian or Müllerian duct derivatives; blind-ended vagina; vulva.
- Partial androgen insensitivity syndrome—78,XY dog; vulva; perivulvar scrotal-like swellings at 6 months of age; blind vaginal pouch; hypoplastic testes; epididymides, partially developed vasa deferentia; vulvar fibroblasts unable to bind dihydrotestosterone.
- Persistent Müllerian duct syndrome (male pseudohermaphrodite)—XY; testes (50% are unilateral or bilateral cryptorchid); epididymides, vasa deferentia, prostate, oviducts, uterus, cervix, cranial vagina; penis, prepuce, and scrotum usually normal; dogs and cats.
- Isolated hypospadias—incomplete masculinization of urogenital sinus during urethral development causing abnormal location of urinary orifice from glans penis (mild) to perineum (severe); external genitalia unambiguous; testes (cryptorchid or scrotal) or bifid scrotum (cats) with spermatogenesis.

XX DSD

Ovotesticular DSD and Testicular DSD

- Canine XX DSD (sex reversal)—*SRY*-negative 78,XX reported in 28 dog breeds, not in cats; the autosomal gene causing testis induction presently unknown; not due to mutation of genes involved with sex reversal in polled goats and humans; two phenotypes:
- Ovotesticular DSD, XX true hermaphrodite (90% of cases)—ovotestis (at least one); masculinized female phenotype; varies from normal to abnormal vulva; normal or enlarged clitoris (os clitoris possible), uterus, oviducts, epididymides, and vasa deferentia; rarely fertile.
- Testicular DSD, XX males (10% of cases)—testes (usually cryptorchid); epididymides, vasa deferentia, prostate; bicornuate uterus, no oviducts; hypoplastic penis and prepuce; hypospadias common.

Androgen Excess

- Fetal origin—single report of congenital adrenal hyperplasia in a phenotypic male cat (38,XX, ovaries, oviducts, epididymides, vasa deferentia, bicornuate uterus); due to 11 β -hydroxylase deficiency; ACTH, testosterone, progesterone, 17-OH-progesterone, androstenedione, deoxycorticosterone, 11-dexoxycorticosterone elevated.
- Maternal origin (female pseudohermaphrodite)—XX; ovaries;

masculinized genitalia (mild clitoral enlargement to nearly normal male genitalia); oviducts, uterus, cranial vagina; prostate variable; caused by sex steroid administration during pregnancy; rare in dogs and cats.

SYSTEMS AFFECTED

- Reproductive—anomalies of the gonads, tubular tract, and external genitalia.
- Renal/Urologic—occasionally affected (e.g., agenesis, incontinence, hematuria, cystitis).
- Skin/Exocrine—perivulvar dermatitis (hypoplastic vulva); perineal or peri-preputial dermatitis (hypospadias); hyperpigmentation (Sertoli cell tumor).

GENETICS

- Chromosomal sex abnormalities—usually caused by random events during gamete formation or early embryonic development.
- XX DSD—autosomal recessive trait in American cocker spaniels and likely in beagles, German shorthaired pointers; familial in English cocker spaniels, Chinese pugs, Kerry blue terriers, Norwegian elkhounds, Weimaraners; other reported breeds include soft-coated Wheaten terriers, vizslas, Walker hounds, Doberman pinschers, basset hounds, American pit bull terriers, border collies, Afghan hounds.
- PMDS—autosomal recessive trait in miniature schnauzers in the US, Basset hounds in the Netherlands, and possibly Persian cats; expression limited to XY individuals.
- Hypospadias familial in Boston terriers.
- Failure of androgen-dependent masculinization (predominantly cats) probably X-linked.

INCIDENCE/PREVALENCE

- Generally rare.
- In affected breeds—may be common within families or within the breed as a whole.

SIGNALMENT

Species

Dog and cat

Breed Predilections

Dogs (see "Genetics").

Mean Age and Range

All are congenital disorders, but individuals with normal external genitalia may not be identified until breeding age or at routine gonadectomy.

Predominant Sex

Phenotypic females and males

SIGNS

General Comments

- Depends on type of disorder.
- Listed are possible findings for any of the conditions; not all occur with each specific disorder.

Historical Findings

- Failure to cycle.
- Infertility and sterility.
- Vulva, clitoris, prepuce, or penis—abnormal size, shape, or location.
- Urine stream—abnormal location.
- Affected phenotypic males attractive to other males.
- Urinary incontinence.
- Vulvar discharge.
- PU/PD.

(CONTINUED)

SEXUAL DEVELOPMENT DISORDERS**Physical Examination Findings**

- Vulva normal or hypoplastic.
- Clitoris normal or enlarged; os clitoris.
- Perivulvar dermatitis and vulvar discharge.
- Testes scrotal, unilateral or bilateral cryptorchid; bifid scrotum.
- Penis and prepuce normal or hypoplastic.
- Urethral meatus normal or abnormal location.
- Dermatologic signs of hyperestrogenism in males.
- Abdominal mass.

CAUSES

- Congenital—heritable or non-heritable
- Exogenous steroid hormone administration during gestation

RISK FACTORS

Androgen or progestagen administration during pregnancy (female pseudohermaphrodite).

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS***Individuals with Unambiguous Genitalia*

- Female infertility—male infertility; mistimed breeding; subclinical cystic endometrial hyperplasia/endometritis; hypothyroidism.
- Failure to cycle (female)—silent heat; hypothyroidism; hypercorticism; previous gonadectomy.
- Male infertility—female infertility; mistimed breeding; exogenous drug use affecting fertility; orchitis or epididymitis; testicular degeneration or hypoplasia; prostatitis.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal.
- Neutrophilia; normochromic, normocytic anemia; hyperglobulinemia, hyperproteinemia; azotemia; high ALT, ALP with pyometra (PMDS).
- Urinalysis—may reveal evidence of cystitis with anatomic abnormalities that affect the location of the urethral meatus.

OTHER LABORATORY TESTS

- Sex steroid hormones (progesterone, testosterone, and estradiol)—generally below the normal range; may be normal if disorder mild and patient not sterile.
- Detect testicular tissue—GnRH or hCG simulation test; resting serum AMH (see Cryptorchidism).
- Karyotyping—required to define chromosomal sex (Molecular Cytogenetics Laboratory, Texas A&M University, 979-458-0520; call first).
- Polymerase chain reaction test for SRY—not commercially available.
- Androgen-binding studies on genital fibroblasts—testicular feminization (not commercially available).

IMAGING

- Routine radiography and ultrasonography—may be of diagnostic value for suspected abdominal mass (e.g., testicular neoplasia with PMDS, testicular feminization, or XX DSD); males with signs referable to

pyometra (female pseudohermaphrodite or PMDS).

- Contrast studies of the lower urogenital tract—may be useful in diagnosing female pseudohermaphrodites.

PATHOLOGIC FINDINGS**Gross**

- Precisely describe the genitalia: size and location of the vulva or prepuce; presence and appearance of the clitoris, penis, scrotum, prostate, caudal vagina, or os clitoris; position of the urinary orifice (identifies the phallic structure as penis or clitoris).
- Most patients with no identified chromosomal abnormalities—exploratory laparotomy to determine the location and morphology of the gonads and internal genitalia.

Histopathologic

- Examination of all tissues removed—necessary to define the type of disorder.
- Gonads—vary from nearly normal architecture to dysgenetic or a combination of ovary and testis (ovotestis).
- Essential to describe the components of the Müllerian and/or Wolffian duct system, if found.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Usually outpatient • Inpatient—exploratory laparotomy

NURSING CARE

Phenotypic females with a hypoplastic vulva and perivulvar dermatitis and males with hypospadias—local therapy to improve dermatologic sequelae (see Dermatoses, Erosive or Ulcerative).

SURGICAL CONSIDERATIONS

- Gonadectomy and hysterectomy (if a uterus is found)—recommended.
- Amputation of an enlarged clitoris—recommended if the mucosal surface is repeatedly traumatized.
- Reconstructive surgery of the prepuce and malformed penis—dogs; may be necessary with testicular DSD, XX males, or hypospadias.

**MEDICATIONS****CONTRAINDICATIONS**

Avoid androgen or progestagen use during pregnancy.

**FOLLOW-UP****PREVENTION/AVOIDANCE**

- Sterilize individuals with heritable disorders.
- Remove carriers of heritable disorders from the breeding program.

POSSIBLE COMPLICATIONS

- Infertility • Sterility • Urinary tract problems—incontinence; cystitis • Testicular neoplasia • Pyometra

**MISCELLANEOUS****AGE-RELATED FACTORS**

Patients not diagnosed at an early age—pyometra (e.g., PMDS; female pseudohermaphrodite); testicular neoplasia (e.g., PMDS; any DSD with cryptorchidism).

SYNOMYMS

- Hermaphrodites • Intersexes • Klinefelter syndrome • Pseudohermaphrodites • Sex reversal • Turner syndrome

SEE ALSO

- Breeding, Timing • Cryptorchidism
- Infertility, Female—Dogs • Infertility, Male—Dogs

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- AMH = anti-müllerian hormone
- DSD = disorders of sexual development
- FSH = follicle-stimulating hormone
- GnRH = gonadotropin-releasing hormone
- hCG = human chorionic gonadotropin
- LH = luteinizing hormone
- MIS = Müllerian inhibiting substance
- PMDS = persistent Müllerian duct syndrome
- PU/PD = polyuria/polydipsia

INTERNET RESOURCES

Meyers-Wallen VN. Inherited abnormalities of sexual development in dogs and cats. In: Concannon PW, England G, Verstegen III J, Linde-Forsberg C, eds., Recent Advances in Small Animal Reproduction.

Suggested Reading

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SHAKER/TREMOR SYNDROME, CORTICOSTEROID RESPONSIVE



BASICS

OVERVIEW

Fine, rapid, whole-body tremor.

SYSTEMS AFFECTED

Nervous

SIGNALMENT

- Primarily dogs, but similar syndrome recently reported in 2 cats.
- Small to medium-size breed (< 15 kg), young adult dogs (< 5 years), regardless of coat color.
- Dogs with white hair coats (e.g., Maltese and West Highland white terriers) historically have been overrepresented.
- Both sexes affected.

SIGNS

- Acute onset, fine, rapid whole-body tremors.
- Clinical signs initially can be confused with signs of apprehension or hypothermia.
- Less commonly, signs can include abnormal nystagmus, hypermetria, head tilt, menace response deficits, and opsoclonus.

CAUSES & RISK FACTORS

Most often associated with mild inflammatory CNS disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Toxin ingestion—mycotoxins (penitrem A, roquefortine); metaldehyde (snail bait); pyrethrins/pyrethroids; organophosphates, many others
- Seizures
- Hypomyelination—seen in puppies; chow chow, springer spaniel, Samoyed, Weimaraner, and Dalmatian
- Metabolic disorder—hypoglycemia, hypoadrenocorticism, hypocalcemia, magnesium imbalance
- Behavioral—fear
- Hypothermia

S

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

IMAGING

N/A

OTHER DIAGNOSTIC PROCEDURES

Cerebellomedullary cistern CSF analysis—mild mononuclear pleocytosis; CSF can be normal.



TREATMENT

Inpatient or outpatient, depending on severity of clinical signs.



MEDICATIONS

DRUG(S)

- Steroid-responsive disease; prednisolone or prednisone (1–2 mg/kg PO q12h) for the first 1–2 weeks.
- Depending on clinical response, taper dosage slowly (usually over 4–6 months); assess periodically for clinical deterioration; if dosage reduced too rapidly, clinical signs may recur, necessitating reintroduction of initial dosage.
- Many patients do not require further treatment.

CONTRAINdications/POSSIBLE INTERACTIONS

Corticosteroids—may be contraindicated with infectious encephalitis.



FOLLOW-UP

PATIENT MONITORING

Weekly evaluations for approximately 1 month; then monthly until corticosteroids are discontinued.

PREVENTION/AVOIDANCE

N/A

EXPECTED COURSE AND PROGNOSIS

- Clinical signs usually subside in 3–7 days from onset of steroid treatment.
- In some patients, recurrence necessitates reinstitution of corticosteroids.
- A small percentage of patients require every-other-day, low-dose corticosteroids, indefinitely, to maintain remission.



MISCELLANEOUS

SYNOMYMS

- Idiopathic cerebellitis
- White shaker syndrome
- Idiopathic generalized tremor syndrome

SEE ALSO

- Movement Disorders
- Tremors

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid

INTERNET RESOURCES

N/A

Suggested Reading

- Bagley RS, Kornegay JN, Wheeler SJ, et al. Generalized tremors in Maltese terriers: Clinical findings in seven cases. *J Am Anim Hosp Assoc* 1993, 29:141–145.
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SHOCK, CARDIOGENIC



BASICS

DEFINITION

• A severe manifestation of forward heart failure. Profound impairment of cardiac function results in poor cardiac output, inadequate forward blood flow, and poor tissue perfusion in the presence of adequate intravascular volume. • Cardiac impairment may result from systolic dysfunction (dilated cardiomyopathy, sepsis, myocarditis, and ischemia), diastolic dysfunction (hypertrophic cardiomyopathy, restrictive cardiomyopathy, tension pneumothorax or mediastinum, restrictive pericarditis, and pericardial tamponade), conduction defects and arrhythmias, valvular diseases, obstructive diseases, pulmonary thromboembolism, and structural defects. Understanding the underlying defect and its hemodynamic consequences is imperative to institute appropriate therapy. • In congestive heart failure (CHF), sometimes referred to as backward heart failure, the ventricle cannot pump out all of the blood that comes into it resulting in systemic and/or pulmonary edema. This is in contrast to forward heart failure, when the heart is not pumping enough blood out to meet the needs of the body. Most, but not all, veterinary patients that present in cardiogenic shock will have concurrent CHF.

PATHOPHYSIOLOGY

- Decreased cardiac output leads to hypotension and systemic hypoperfusion.
- Hypotension decreases coronary perfusion pressure resulting in coronary ischemia that provokes further myocardial dysfunction.
- Peripheral vasoconstriction increases myocardial work and exacerbates tissue ischemia and energy depletion resulting in organ dysfunction.

SYSTEMS AFFECTED

- Cardiovascular—cardiac dysfunction is causative. Myocardial ischemia exacerbates cardiac dysfunction. • Endocrine—hyperglycemia and insulin resistance.
- Gastrointestinal—mucosal necrosis and sloughing, hemorrhage, and bacterial translocation. • Hemic—homeostatic imbalances lead to microvascular thrombosis.
- Hepatobiliary—hepatocellular enzyme leakage, cholestasis, reduced clearance of bacteria and bacterial by-products, and abnormal synthetic function. Hepatic congestion may result from right-sided CHF.
- Musculoskeletal—weakness. • Nervous—altered mental status. • Renal—ischemic tubular damage, oliguria and development of acute kidney injury. • Respiratory—as cardiac dysfunction progresses and ventricular end diastolic pressure increases, pulmonary edema and pleural effusion develop. Ultimately

pulmonary gas exchange is affected and hypoxemia results.

GENETICS

Many breeds are predisposed to specific cardiac diseases.

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

Unknown

SIGNALMENT

- Dogs and cats • Any breed, age, or sex

SIGNS

Historical Findings

- Cardiac decompensation may be associated with a history of previously compensated heart disease and cardiac drug administration.
- A suspicion of previously undiagnosed cardiac disease may result from a history of coughing, exercise intolerance, weakness, or syncope.

Physical Examination Findings

- Markers of poor perfusion: ° Pale mucous membranes ° Prolonged capillary refill time ° Weak femoral pulse quality ° Weakness ° Altered mental status ° Cool extremities and hypothermia ° Oliguria. • Muffled heart sounds if pericardial or pleural effusion is present. • Variable heart rate with possible cardiac arrhythmia, murmur or gallop rhythm. • Variable respiratory rate with possible increased bronchovesicular sounds, crackles, or moist cough (especially if concurrent CHF).

CAUSES

Primary Cardiac Disease

- All cardiomyopathies—dilated, hypertrophic, intermediate and restrictive
- Severe mitral insufficiency or other end-stage valvular disease • Tachy- or bradyarrhythmias • Myocarditis
- Endomyocarditis (cats) • Structural defects

Secondary Cardiac Dysfunction

- Pericardial tamponade • Sepsis • Severe electrolyte derangement (potassium, magnesium, and calcium) • Pulmonary thromboembolism • Tension pneumothorax/mediastinum • Caval syndrome

RISK FACTORS

- Underlying cardiac disease • Concurrent illness causing hypoxemia, acidosis, and electrolyte imbalances, or as in sepsis, the release of myocardial depressant factors.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiating Similar Signs

Cardiogenic shock is differentiated from other causes of circulatory shock when there is evidence of decreased cardiac output and

tissue hypoxia in the face of adequate intravascular volume.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Mature neutrophilia and lymphopenia secondary to stress

Biochemistry Panel

- Hyperglycemia (stress). • Elevated anion gap (accumulation of lactic and renal acids)
- Elevated hepatocellular enzyme activity (hepatic hypoxia) • Elevated phosphorus (decreased GFR) • Azotemia (decreased GFR or hypoxia induced renal injury)
- Hyponatremia and mild hypoalbuminemia (more common in patients with chronic heart failure)

Urinalysis

- Isosthenuria (concomitant diuretic therapy or acute tubular injury secondary to renal hypoxia)

OTHER LABORATORY TESTS

- Blood gas analysis may reveal metabolic acidosis, hypoxemia (if concurrent CHF), and evidence of increased oxygen extraction by tissues (a widened arteriovenous oxygen difference and or a decreased venous oxygen concentration in a patient that is not hypoxic or anemic). • Hyperlactatemia (tissue hypoperfusion). • Increased cardiac troponin I levels (sensitive and specific marker of myocardial injury). • NT-proBNP may be useful in ruling out significant intrinsic cardiac dysfunction.

IMAGING

Radiographic Findings

Thoracic radiography may reveal cardiomegaly, evidence of pulmonary edema (CHF), and or pleural effusion (CHF).

Echocardiography

To characterize cardiomyopathy, valvular disease, depressed myocardial contractility, structural disease, pericardial disease, or heartworm infection.

DIAGNOSTIC PROCEDURES

Thoracocentesis, abdominocentesis, and pericardiocentesis when indicated may provide insight to underlying etiology.

PATHOLOGIC FINDINGS

Cardiac abnormalities consistent with various underlying etiologies. Other abnormalities consistent with tissue hypoxia.



TREATMENT

APPROPRIATE HEALTH CARE

Emergency inpatient intensive care management

NURSING CARE

- Minimize stress as these patients are extremely fragile and at risk of cardiac arrest.

SHOCK, CARDIOGENIC

(CONTINUED)

- Oxygen supplementation is critical.
- Significant pleural effusion (CHF) should be relieved with thoracocentesis.
- Patients exhibiting respiratory failure may need to be mechanically ventilated.
- Most patients in cardiogenic shock should NOT receive ANY fluid therapy until the etiology of the underlying cardiac dysfunction is understood and cardiac function improved. The exceptions to this rule include patients in cardiogenic shock secondary to pericardial tamponade, tension pneumothorax/mediastinum, and pulmonary thromboembolism.
- Pericardial tamponade should be relieved with emergency pericardiocentesis.

ACTIVITY

Minimize patient exertion

DIET

Free choice access to water; withhold food until shock is resolved.

CLIENT EDUCATION

Warn of the danger of imminent cardiac arrest and discuss a "code status" in advance whenever possible.

SURGICAL CONSIDERATIONS

- Bradyarrhythmia may require implantation of a pacemaker device.
- Tension pneumothorax may require thoracostomy tube placement or exploratory thoracotomy.
- Caval syndrome secondary to *Dirofilaria immitis* infection will require worm extraction.



MEDICATIONS

DRUG(S) OF CHOICE

- Fast-acting positive inotropes to improve cardiac function and preserve end-organ perfusion in patients with reduced myocardial contractility (dobutamine 5–20 µg/kg/min CRI in dogs; 2.5–15 µg/kg/min CRI in cats; pimobendan 0.25 mg/kg PO q12h in dogs only).
- Arrhythmia and conduction abnormalities should be corrected promptly with antiarrhythmic therapy, cardioversion, or pacemaker implantation.
- Ventricular tachycardia:
 - Dogs may respond to lidocaine (2 mg/kg IV loading dose then 50 µg/kg/min CRI) or procainamide (10–15 mg/kg IV loading dose then 25–50 µg/kg/min CRI).
 - Boxers with arrhythmogenic right ventricular cardiomyopathy may respond favorably to sotalol (2 mg/kg PO q12h) alone, or combined with mexiletine (5–8 mg/kg PO q8h).
 - Supraventricular tachyarrhythmia:
 - Treatments to slow the heart rate in dogs with supraventricular tachyarrhythmia include vagal maneuvers, calcium channel blockers (diltiazem 0.125–0.35 mg/kg IV over 2–3 minutes or 0.125–0.35 mg/kg/h CRI),

beta-blockers (esmolol 0.5 mg/kg IV over 1 minute), and procainamide (6–8 mg/kg IV over 5–10 minutes then 20–40 µg/kg/min CRI).

- Patients that do not respond to vagal maneuvers or emergency drug therapy may require DC cardioversion or overdrive pacing.
- Bradyarrhythmia:
 - Treatment of choice for severe bradyarrhythmia is cardiac pacing. However, some patients may benefit from atropine (0.02–0.04 mg/kg IV) or isoproterenol (0.4 mg in 250 mL D5W slowly to effect).
 - Concurrent CHF:
 - Furosemide to treat pulmonary edema and enhance oxygenation in dogs and cats with CHF (2–8 mg/kg IV or IM; or 0.5–1.0 mg/kg/h CRI). The IV route is preferable, but IM is appropriate when IV access would require manual restraint.
 - Relief of pain or anxiety with morphine sulfate (0.1–0.5 mg/kg/h IV CRI, or 0.2–2 mg/kg IM) can reduce excessive sympathetic activity and decrease oxygen demand, preload, and afterload.

CONTRAINdications

- Avoid diuretic therapy in patients with pericardial effusion, tension pneumothorax/mediastinum, and pulmonary thromboembolism.
- Avoid beta-blockers and calcium channel blockers in patients with reduced myocardial contractility.

PRECAUTIONS

- Catecholamine infusions must be carefully titrated to maximize coronary perfusion pressure with the least possible increase in myocardial oxygen demand.
- Afterload reducers and vasodilators (angiotensin-converting enzyme inhibitors, nitroglycerin and nitroprusside) should be used with caution because of the risk for worsening hypotension and decreasing coronary blood flow.

ALTERNATIVE DRUG(S)

Dopamine may be used to improve systolic function as an alternative to dobutamine at a dose of 5–10 µg/kg/min (dogs and cats).



FOLLOW-UP

PATIENT MONITORING

- Serial subjective and objective assessment of perfusion (mentation, mucous membrane color, capillary refill time, pulse quality, muscle strength, temperature, serum lactate, urine output, heart rate, blood pressure, and oxygenation indices), respiratory rate and effort, and pulmonary auscultation is required to optimize therapy.
- Blood gas analysis and pulse oximetry to follow tissue oxygenation, ventilation, and acid-base balance.
- Packed cell volume, serum total protein, serum electrolytes, hepatocellular enzymes, blood urea nitrogen, and serum creatinine to

monitor effects of systemic tissue hypoxia.

- Daily monitoring of cardiac troponin I (cTn-I) to assess level of myocardial injury.
- Blood pressure measurement may document hypotension.
- Electrocardiography may aid in the detection and characterization of arrhythmias.
- Pulse oximetry may document low oxygen saturation in patients with concurrent CHF.
- Central venous pressure monitoring may aid in assessment of cardiac preload and central venous oxygen saturation.
- Hemodynamic monitoring to assess mixed venous oxygen saturation, cardiac output and systemic vascular resistance.

PREVENTION/AVOIDANCE

Prevention strategies aimed at the various underlying etiologies

POSSIBLE COMPLICATIONS

- CHF
- Cardiac arrhythmias
- Syncope
- Acid-base and electrolyte disturbances
- Renal dysfunction
- Cardiac arrest

EXPECTED COURSE AND PROGNOSIS

Dependent on underlying etiology. Patients with primary cardiac disease have generally worse prognosis (poor to grave) as compared to those with secondary cardiac dysfunction.



MISCELLANEOUS

SEE ALSO

- Atrioventricular Block
- Cardiomyopathy
- Congestive Heart Failure, Left-Sided
- Congestive Heart Failure, Right-Sided
- Endomyocardial Diseases—Cats
- Myocarditis
- Pericardial Effusion
- Pericarditis
- Pneumothorax
- Pulmonary Thromboembolism
- Sepsis and Bacteremia
- Shock, Hypovolemic
- Shock, Septic
- Sick Sinus Syndrome
- Supraventricular Tachycardia
- Ventricular Tachycardia

ABBREVIATIONS

- CHF = congestive heart failure
- GFR = glomerular filtration rate

Suggested Reading

- Brown AJ, Mandell DC. Cardiogenic shock. In: Silverstein D.C., Hopper K., ed., Small Animal Critical Care Medicine, 1st ed. St. Louis: Saunders, 2009, pp. 146–150.
- Hopper K, Silverstein D, Bateman S. Shock syndromes. In: Dibartola SP, ed., Fluid Therapy in Small Animal Practice. 4th ed. Philadelphia: Saunders, 2011, pp. 557–583.
- Author** Gretchen Lee Schoeffler
Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.
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SHOCK, HYPOVOLEMIC



BASICS

DEFINITION

Fluid loss that results in inadequate circulating volume and perfusion.

PATHOPHYSIOLOGY

- Hemorrhage or other fluid loss results in a critical decrease in intravascular volume, diminished venous return, and decreased cardiac output.
- Compensatory neuroendocrine responses lead to peripheral vasoconstriction thereby exacerbating tissue ischemia and energy depletion resulting in organ dysfunction.

SYSTEMS AFFECTED

- Cardiovascular—compensatory responses include increased heart rate, increased cardiac contractility, and peripheral vasoconstriction. Increased cardiac oxygen demand in the face of reduced oxygen delivery may result in arrhythmia.
- Endocrine—hyperglycemia and insulin resistance.
- Gastrointestinal—mucosal necrosis and sloughing, hemorrhage, and bacterial translocation.
- Hemic—homeostatic imbalances lead to microvascular thrombosis as well as hyper- and hypocoagulability.
- Hepatobiliary—hepatocellular enzyme leakage, cholestasis, reduced clearance of bacteria and bacterial by-products, and abnormal synthetic function.
- Musculoskeletal—weakness.
- Nervous—altered mental status.
- Renal—ischemic tubular damage, oliguria, and development of acute kidney injury.
- Respiratory—hyperventilation in an attempt to compensate for metabolic acidosis.

GENETICS

Unknown

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

Unknown

SIGNALMENT

- Dogs and cats
- Any breed, age, or sex

SIGNS

Historical Findings

May be associated with a history of trauma, weakness and collapse, surgery, vomiting and diarrhea, or polyuria and polydipsia.

Physical Examination Findings

- Compensated shock is also referred to as warm shock or preshock:
 - Compensatory mechanisms may allow an otherwise healthy pet to be relatively asymptomatic despite a 10% reduction in total effective blood volume. When homeostatic mechanisms can no longer compensate, patients will demonstrate signs of decompensated shock.
- Decompensated hypovolemic shock:
 - Markers of poor perfusion (pale mucous membranes [may be compounded by

anemia], prolonged capillary refill time, weak peripheral pulse quality, weakness, altered mental status, hypothermia and cool extremities, oliguria).

- Absent to minimal jugular vein distension.
- Tachycardia ± arrhythmia.
- Tachypnea.
- Clinical dehydration as evidenced by decreased skin turgor, tacky mucous membranes, and sunken eyes is more common in patients with fluid loss rather than hemorrhage.

CAUSES

Hemorrhage-Induced

- Blunt or penetrating trauma.
- Ruptured neoplasia.
- Gastrointestinal bleeding secondary to ulcerative disease, neoplasia, or severe thrombocytopenia.
- Coagulopathy resulting from anticoagulant rodenticide intoxication, synthetic liver failure, disseminated intravascular coagulation, hemophilia, and significant von Willebrand factor deficiency.

Fluid Loss-Induced

- Gastrointestinal (vomiting and diarrhea).
- Urinary (renal failure, diabetes mellitus, diabetes insipidus, hypercalcemia, Addison's, and Cushing's diseases).
- Burns.
- Third spacing (any disease that results in formation of significant volumes of effusion).

RISK FACTORS

Caused by another condition; as such it has no specific risk factors.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiating Similar Signs

Hypovolemic shock is differentiated from other causes of circulatory shock when inadequate circulating volume results in decreased cardiac output in the face of normal or increased cardiac function and normal or increased systemic vascular resistance.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Mature neutrophilia and lymphopenia secondary to stress.
- Hematocrit, total protein, and platelet count are variable (may be decreased with hemorrhage).

Biochemistry Panel

- Hyperglycemia secondary to stress.
- Total protein and albumin are variable (decreased with hemorrhage and increased in fluid loss).
- Elevated hepatocellular enzyme activity (ALT, AST).
- Electrolyte derangements are variable (more likely in fluid loss).
- Elevated anion gap (accumulation of lactic and renal acids).
- Azotemia due to decreased glomerular filtration rate.

Urinalysis

- Urine specific gravity may be increased; however, acute tubular injury secondary to renal hypoxia may result in isosthenuria.

OTHER LABORATORY TESTS

- Coagulation testing is indicated in critically ill patients and those with evidence of significant hemorrhage.
- Blood gas analysis may reveal metabolic acidosis and evidence of increased oxygen extraction by tissues (a widened arteriovenous oxygen difference and/or a decreased venous oxygen concentration in a patient that is not hypoxic or anemic).
- Hyperlactatemia reflects decreased clearance and increased production of lactate.

IMAGING

- Thoracic radiography may reveal microcardia and pulmonary vascular under-perfusion.
- Radiographic or ultrasonographic findings of pleural or abdominal effusion warrant timely sampling and evaluation of the fluid.

DIAGNOSTIC PROCEDURES

- Thoracocentesis, abdominocentesis, and pericardiocentesis when indicated may provide insight into underlying etiology.

PATHOLOGIC FINDINGS

Abnormalities consistent with various underlying etiologies. Other abnormalities consistent with tissue hypoxia.



TREATMENT

APPROPRIATE HEALTH CARE

- Emergency inpatient intensive care management.
- Resuscitation goals:
 - Maximize blood oxygen content by ensuring adequacy of ventilation and oxygen saturation of blood and correct anemia
 - Restore blood flow and control of further loss
 - Fluid therapy.
 - Traditional endpoints of resuscitation, including restoration of normal vital signs (mentation, capillary refill time, heart rate, peripheral pulse quality, and rectal temperature), blood pressure, and urine output remain the standard of care. However, it has been documented that critically ill patients have evidence of ongoing tissue hypoxia despite normalization of these parameters, suggestive of occult oxygen debt and the presence of compensated shock.
 - There is evidence that normalization of vital signs, blood lactate, base deficit, and oxygen transport indices such as cardiac index, oxygen delivery, oxygen consumption, and mixed venous oxygen and central venous oxygen saturation in concert are more sensitive markers for adequacy of tissue perfusion than any of these variables alone.
 - Until stronger support exists for preferential selection of one endpoint over the others, utilization of as many of these markers as are available on any given patient seems advisable.

NURSING CARE

- Maximize blood oxygen content:
 - Assess and stabilize the airway and breathing as

SHOCK, HYPOVOLEMIC

(CONTINUED)

necessary. • Administer high-flow supplemental oxygen and provide ventilatory support as needed. • Significant anemia (PCV < 25–30%) in a hypovolemic patient is concerning and should be corrected.

- Control further blood or fluid loss:
- External bleeding is frequently controlled with direct pressure; internal bleeding may require surgical intervention
- Control of fluid loss other than hemorrhage, centers on control of symptoms (e.g., antiemetics) and correction of the underlying disorder.
- Fluid resuscitation: ◦ Once IV or IO access is obtained, initial fluid resuscitation is performed with an isotonic crystalloid such as lactated Ringer's solution, normal saline, Plasmalyte-A, and Normosol-R (30 mL/kg, dog; 20 mL/kg, cat over 15 minutes). If the patient is not significantly dehydrated, addition of 7.5% hypertonic saline (4 mL/kg over 15 minutes) may expedite the resuscitation. ◦ After the initial bolus the patient's response is assessed. If vital signs and other resuscitation parameters return to normal, the patient must continue to be monitored to ensure stability. If vital signs and other resuscitation parameters transiently improve or if little or no improvement is seen, another crystalloid bolus should be infused and colloids such as hydroxyethylstarch (dose variable, dependent on type) or appropriate blood products (10–20 mL/kg) considered
- This process is repeated until the patient's resuscitation parameters normalize. When bolusing fluids to correct perfusion deficits, the clinician must monitor not only for response to therapy, but also for potential complications
- While fluid boluses are used to correct perfusion deficits, hydration deficits must be corrected more slowly. After perfusion has been normalized, the patient is reassessed and fluid therapy targeted to correct hydration deficits over 12–24 hours.

ACTIVITY

Minimize patient exertion.

DIET

Withhold oral intake until shock is resolved.

CLIENT EDUCATION

Warn of the danger of imminent cardiac arrest and discuss a "code status" in advance whenever possible.

SURGICAL CONSIDERATIONS

Identify and repair the source of fluid loss (most common in hemorrhage-induced).



MEDICATIONS

DRUG(S) OF CHOICE

- For patients with refractory hypovolemic shock it is important to rule in or out ongoing

losses (especially in the hemorrhage-induced category) and to administer blood products as needed. • If adequate circulating volume is assured and the patient is still demonstrating clinical signs of shock (not very common in patients with hypovolemic shock), consider:

- A pressor such as dopamine (5–20 µg/kg/minute), norepinephrine (0.05–2 µg/kg/minute), or vasopressin (0.5–2 mU/kg/minute). These can be used for vasopressor support in both dogs and cats. Monitor for tachyarrhythmia and excessive peripheral vasoconstriction
- A positive inotrope such as dobutamine (2–20 µg/kg/minute) may be beneficial in patients with decreased contractility or myocardial depression. Monitor for tachyarrhythmia. While dobutamine can generally be used safely in dogs, seizures have been observed in some cats at doses exceeding 5 µg/kg/minute.

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

ALTERNATIVE DRUGS

N/A



FOLLOW-UP

PATIENT MONITORING

- Serial assessment of perfusion: ◦ Physical exam including mentation, mucous membrane color, capillary refill time, pulse quality, muscle strength, temperature, and heart rate.
- Hemodynamic monitoring to include arterial blood pressure (frequently reveals a disproportionately low diastolic pressure), and in a subset of patients central venous pressure (decreased jugular and central venous pressure due to hypovolemia and decreased preload; catheter also allows for measurement of central venous oxygen saturation), cardiac output and tissue oxygenation.
- Laboratory data including serum lactate and base deficit.
- Serial assessment of respiratory rate and effort, and pulmonary auscultation is required to optimize therapy.
- Urine output as an indicator of glomerular filtration rate and renal blood flow.
- Electrocardiography may aid in the characterization of arrhythmias.
- A minimum of daily packed cell volume (PCV), serum total protein, blood glucose, blood gas, serum electrolytes, hepatocellular enzymes, blood urea nitrogen, and serum creatinine to monitor effects of systemic tissue hypoxia and to guide clinical management.
- Patients with hemorrhage-induced hypovolemic shock should have PCV and total protein assessed more frequently.
- Daily measurement of COP may help guide fluid therapy.

PREVENTION/AVOIDANCE

Prevention strategies aimed at the various underlying etiologies.

POSSIBLE COMPLICATIONS

- Dilutional coagulopathy and low colloid oncotic pressure (COP) can occur in patients receiving very large resuscitation volumes (more than 1–2 blood volumes). This is due to dilution of clotting factors and proteins respectively, but is rare within the first hour of resuscitation. Coagulation times should be used to guide the administration of fresh frozen plasma. Low COP is most common and effectively addressed with the administration of artificial colloid solutions.
- Volume overload with clinical signs of pulmonary and/or peripheral edema.
- Anemia and thrombocytopenia.
- Acid-base disturbances.
- Multiple organ dysfunction.
- Cardiac arrest.

EXPECTED COURSE AND PROGNOSIS

Dependent on underlying etiology and ability to institute appropriate therapy.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

SYNOMYS

N/A

SEE ALSO

Shock, Cardiogenic

ABBREVIATIONS

- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- COP = colloid oncotic pressure
- PCV = packed cell volume

Suggested Reading

Hopper K, Silverstein D, Bateman S. Shock syndromes. In: Dibartola SP, ed., *Fluid Therapy in Small Animal Practice*. 4th ed. Philadelphia: Saunders, 2011, pp. 557–583.

Young BC, Pritt JE, Fox P, Barton LJ. Decreased central venous oxygen saturation despite normalization of heart rate and blood pressure post shock resuscitation in sick dogs. *J Vet Emerg Crit Care* 2014, 24(2):154–161.

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BASICS

DEFINITION

Sepsis-induced hypotension that persists despite adequate intravascular volume and cardiac output, and is attributable to low systemic vascular resistance.

PATHOPHYSIOLOGY

- In sepsis, infectious agents trigger large-scale activation of monocytes, macrophages, and neutrophils that then interact with endothelial cells inducing a generalized inflammatory response.
- In the subset of septic patients described as having septic shock, the elaborate interaction of inflammatory cells and mediators decreases systemic vascular resistance and provokes maldistribution of blood flow (distributive effect). They also increase capillary permeability such that fluid shifts out of the intravascular space. To compensate for diminishing circulating volume, catecholamines increase cardiac output and myocardial contractility. In the face of severe arterial vasodilation, cardiac output is not sufficient to maintain oxygen delivery to tissues.
- Decreased oxygen delivery is compounded by the presence of interstitial edema and microvascular sludging. In due course, tissue hypoxia leads to organ failure and death.

SYSTEMS AFFECTED

- Cardiovascular**—increased cardiac output, arterial vasodilation, and maldistribution of blood flow with hypotension predominates; however, myocardial dysfunction secondary to circulating factors can be an important variable.
- Endocrine**—may manifest as hyperglycemia and insulin resistance or as insufficient production of either corticosteroids or vasopressin.
- Gastrointestinal**—mucosal necrosis, hemorrhage, and bacterial translocation.
- Hemic**—microvascular thrombosis as well as hyper- and hypocoagulopathy.
- Hepatobiliary**—hepatocellular enzyme leakage, cholestasis, reduced clearance of bacteria, and abnormal synthetic function.
- Nervous**—altered mental status.
- Renal**—ischemic tubular damage, oliguria, and development of acute kidney injury.
- Respiratory**—enhanced microvascular permeability results in interstitial and alveolar edema; hypercoagulopathy may result in pulmonary thromboembolism.

GENETICS

Unknown

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

Unknown

SIGNALMENT

- Dogs and cats
- Any breed, age, or sex

SIGNS

Historical Findings

Recent infection, injury, serious illness, surgery, or immunosuppression.

Physical Examination Findings

- Dogs may display a hyperdynamic form that is typified by altered mental status, weakness, hypotension, tachycardia, tachypnea, hyperemia, fast CRT, bounding pulse quality, and fever. Cats rarely demonstrate hyperdynamic signs.
- Patients with the hypodynamic form are more likely to exhibit altered mental status, weakness, hypotension, bradycardia, tachypnea, pale mucous membranes, prolonged CRT, weak pulse quality, and hypothermia.

CAUSES

- Septic peritonitis—gastrointestinal tract rupture, penetrating abdominal wound, infected urinary tract rupture.
- Respiratory and pleural space—pneumonia, pyothorax.
- Skin or soft tissue infections—infected wounds, foreign bodies.
- Urinary tract—pyelonephritis.
- Reproductive—prostatitis, pyometra.
- Cardiovascular—bacterial endocarditis.
- Musculoskeletal—septic arthritis, osteomyelitis.
- Iatrogenic sources of infection—catheters, implants, surgical sites.
- Central nervous system—meningitis, encephalitis.

RISK FACTORS

- Extremes of age
- Concurrent diseases such as diabetes mellitus, hyperadrenocorticism, and malignancy
- Immunosuppression
- Surgery, trauma, and burns
- Prior antibiotic therapy



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of distributive shock include drug or toxin reaction, anaphylaxis, and adrenal insufficiency.
- Hypovolemic shock.
- Cardiogenic shock.
- Heatstroke.

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilia or neutropenia, left-shift, and toxic change
- Lymphopenia
- Thrombocytopenia
- Hematocrit and blood glucose are variable
- Hypoalbuminemia
- Elevated bilirubin and liver enzymes
- Electrolyte derangements
- Azotemia
- Isosthenuria and variably active urine sediment

OTHER LABORATORY TESTS

- Prolongation of the activated partial thromboplastin and prothrombin times, increased D-dimers and fibrin degradation products, and decreased levels of antithrombin and protein C.
- Blood gas analysis may reveal hypoxemia and acid-base disturbances.
- Serum lactate elevation.
- Cytology, gram stain, and culture and

sensitivity on samples obtained from potential sites of infection may reveal etiologic organisms.

- Culture and sensitivity of urine and blood may be useful especially when the source of the sepsis is unknown.
- Low COP.
- ACTH stimulation test in patients not responding to standard therapy.

IMAGING

- Thoracic radiographs may reveal a septic focus or cause for respiratory dysfunction.
- Echocardiography may document a vegetative valvular lesion and/or characterize the adequacy of cardiac function.
- Abdominal ultrasonography may detect a septic focus.

DIAGNOSTIC PROCEDURES

Thoracocentesis, abdominocentesis, tissue aspirates, and arthrocentesis when indicated may provide insight into underlying etiology.

PATHOLOGIC FINDINGS

Abnormalities consistent with various underlying etiologies. Other abnormalities consistent with inflammation and tissue hypoxia.



TREATMENT

APPROPRIATE HEALTH CARE

- Emergency inpatient intensive care management.
- Resuscitation goals:
 - Maximize blood oxygen content by ensuring adequacy of ventilation and oxygen saturation of blood and correct anemia
 - Restore blood flow
 - Fluid therapy.
 - Traditional endpoints of resuscitation, including restoration of normal vital signs (mentation, CRT, heart rate, peripheral pulse quality, and rectal temperature), BP, and urine output remain the standard of care. However, it has been documented that critically ill patients have evidence of ongoing tissue hypoxia despite normalization of these parameters, suggestive of occult oxygen debt and presence of compensated shock. There is evidence that normalization of vital signs, blood lactate, base deficit, and oxygen transport indices are more sensitive markers for adequacy of tissue perfusion than any of these variables alone.
 - Until stronger support exists for preferential selection of one endpoint over the others, utilization of as many of these markers as are available on any given patient seems advisable.
- Identify and treat source of infection (antimicrobial therapy, surgery, or both).
- Maintain adequate organ function (guided by cardiovascular and laboratory monitoring).

NURSING CARE

- Maximize blood oxygen content:
 - Assess and stabilize the airway and breathing as necessary
 - Administer high-flow supplemental oxygen and provide ventilatory support as needed
 - Significant anemia (PCV < 25%) should be corrected.
 - Most septic

SHOCK, SEPTIC

(CONTINUED)

patients are hypovolemic and require initial fluid resuscitation with an isotonic crystalloid such as lactated Ringer's solution, normal saline, Plasmalyte-A, and Normosol-R (30 mL/kg, dog; 20 mL/kg, cat over 15 minutes). If the patient is not significantly dehydrated, addition of 7.5% hypertonic saline (4 mL/kg over 15 minutes) may expedite the resuscitation. • After the initial bolus the patient's response is assessed. If vital signs and other resuscitation parameters return to normal, the patient must continue to be monitored to ensure stability. If vital signs and other resuscitation parameters transiently improve or if little or no improvement is seen, another crystalloid bolus should be infused and colloids such as HES (dose variable, dependent on type) considered. • HES will help maintain adequate COP and may reduce the amount of crystalloid required to achieve effective resuscitation. HES at high doses may exacerbate coagulopathy. • Blood products should be administered based on patient need. Packed red blood cells are administered to anemic patients to improve oxygen carrying capacity. Plasma products are used to correct coagulation deficits and concentrated albumin products are most effective raising COP. • This process is repeated until the patient's resuscitation parameters normalize. • Septic patients that have received large volumes of fluids may achieve an adequate circulating volume without normalization of BP and other perfusion parameters. It is important to recognize that continued aggressive fluid therapy in these patients will result in volume overload and that vasopressors and or positive inotropes are indicated. Monitor closely since infusion of large volumes may precipitate pulmonary edema in patients with capillary leak or low COP.

ACTIVITY

Minimize patient exertion.

DIET

Withhold oral intake until shock is resolved.

CLIENT EDUCATION

Warn of the danger of imminent cardiac arrest and discuss a "code status" in advance whenever possible.

SURGICAL CONSIDERATIONS

Identify and remove the source of sepsis (e.g., septic peritonitis, abscess, pyothorax, pyometra, and soft tissue wounds).



MEDICATIONS

DRUG(S) OF CHOICE

- Once adequate circulating volume has been achieved, improvement in systemic BP and other clinical resuscitation parameters may

require the use of one or more vasopressors and or positive inotropic agents: • Dopamine (5–20 µg/kg/minute), norepinephrine (0.05–2 µg/kg/minute), and vasopressin (0.5–2 mU/kg/minute) can be used for vasopressor support (dogs and cats). Monitor for tachyarrhythmia and excessive peripheral vasoconstriction. • Dobutamine (2–20 µg/kg/minute) is primarily used as a positive inotrope in the subset of canine septic shock patients with decreased contractility or myocardial depression. Monitor for tachyarrhythmia. While dobutamine can be used safely in many feline patients, seizures have been observed in some cats at doses exceeding 5 µg/kg/minute. • It is essential that intravenous, empiric, broad-spectrum antibiotic therapy be instituted early in septic patients; the spectrum should be narrowed when culture results become available. Empiric selection is based on the patient's underlying immune status, the suspected source and organism(s) responsible, specific antibiotic properties (tissue penetration, cidal versus static activity), and considerations for resistance (previous antibiotic use, hospital- or community-acquired infection). • It is not unreasonable to empirically treat patients that are not responding adequately to standard therapy with 0.75–1.0 mg/kg q6h intravenous hydrocortisone after undergoing a standard ACTH stimulation test. Therapy should be continued in patients in whom relative adrenal insufficiency (hypoadrenocorticism) is documented.

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

ALTERNATIVE DRUGS

N/A



FOLLOW-UP

PATIENT MONITORING

• Serial assessment of perfusion to optimize titration of fluids and vasoactive therapy: • Exam—mentation, mucous membrane color, CRT, pulse quality, muscle strength, temperature, and heart rate. • Hemodynamic monitoring—BP (frequently reveals a disproportionately low diastolic pressure), CVP (decreased due to hypovolemia and decreased preload; also allows for measurement of central venous oxygen saturation), and cardiac output. • Laboratory data—serum lactate and base deficit. • Serial assessment of respiratory rate and effort, and pulmonary auscultation. • Urine output as an indicator of glomerular filtration rate and renal blood flow. • Continuous ECG to

detect arrhythmia. • Blood gas analysis and pulse oximetry to follow tissue oxygenation, ventilation, and acid-base balance. • A minimum of daily packed cell volume, serum total protein, COP, blood glucose, serum electrolytes, hepatocellular enzymes, blood urea nitrogen, and serum creatinine to monitor effects of systemic tissue hypoxia.

PREVENTION/AVOIDANCE

- Timely and effective treatment of wounds.
- Appropriate use of antimicrobial therapy.

POSSIBLE COMPLICATIONS

- Volume overload • Pulmonary edema
- Vasculitis and peripheral edema
- Hypoglycemia • Anemia and thrombocytopenia • Coagulopathy
- Multiple organ dysfunction (cardiac, respiratory, renal, hepatic, gastrointestinal, pancreatic, adrenal, and brain) • Cardiac arrest

EXPECTED COURSE AND PROGNOSIS

Dependent on underlying etiology and ability to institute appropriate therapy.



MISCELLANEOUS

SEE ALSO

- Disseminated Intravascular Coagulation
- Hypoadrenocorticism (Cushing's Disease)—Dogs • Hypoadrenocorticism (Cushing's Syndrome)—Cats • Shock, Cardiogenic • Shock, Hypovolemic

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone
- BP = blood pressure • COP = colloid oncotic pressure • CRT = capillary refill time
- CVP = central venous pressure • ECG = electrocardiogram • HES = hydroxyethylstarch

Suggested Reading

- Brady CA, Otto CM. Systemic inflammatory response syndrome, sepsis and multiple organ dysfunction. *Vet Clin North Am Small Anim Pract* 2001; 31(6):1147–1162.
Mittleman-Boller E, Otto CM. Septic shock. In: Silverstein DC, Hopper K, ed., *Small Animal Critical Care Medicine*. 1st ed. St. Louis: Saunders, 2009, pp. 459–463.

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Client Education Handout
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SHOULDER JOINT, LIGAMENT, AND TENDON CONDITIONS



BASICS

DEFINITION

Make up the majority of causes for lameness in the canine shoulder joint, excluding osteochondritis dissecans lesions.

PATHOPHYSIOLOGY

Bicipital Tenosynovitis

- Strain injury to the tendon of the biceps brachii. • Mechanism of injury—direct trauma; indirect trauma (more common).
- Pathologic changes—from partial disruption of the tendon to chronic inflammatory changes, including dystrophic calcification. • Proliferation of the fibrous connective tissue and adhesions between the tendon and the sheath—limit motion; cause pain.

Fibrotic Contracture of the Infraspinatus Muscle

- Primary muscle-tendon disorder—not a neuropathy. • Fibrous tissue replaces normal muscle. • Loss of elasticity and function.
- Degeneration and atrophy of affected muscle. • Partial muscle disruption—likely caused by repetitive strain injuries.

Other

- Rupture of the biceps brachii tendon of origin—strain injury or disruption of the tendinous fibers at or near the junction with the supraglenoid tubercle of the scapula.
- Mineralization of the supraspinatus tendon; granular deposits between the fibers of the tendon; unknown cause; probably repetitive strain injury. • Avulsion or fracture of the insertion of the supraspinatus tendon—bone is avulsed from the greater tubercle of the proximal humerus. • Strain injury to other muscles/tendons in the region.

SYSTEMS AFFECTED

Musculoskeletal

INCIDENCE/PREVALENCE

Common cause of forelimb lameness

SIGNALMENT

Species

Dog

Breed Predilections

Medium- to large-breed dogs

Mean Age and Range

- Skeletally mature dogs ≥ 1 year of age
- Usually 3–7 years of age

SIGNS

Historical Findings

- Bicipital tenosynovitis—onset usually insidious; often of several months in duration; may be a traumatic incident as the inciting cause; subtle, intermittent lameness that worsens with exercise. • Rupture of the biceps brachii tendon of origin—similar to bicipital tenosynovitis; may have acute onset due to a

known traumatic event; usually subtle, chronic lameness that worsens with exercise.

- Mineralization of the supraspinatus tendon—onset usually insidious; chronic lameness that worsens with activity.
- Avulsion/fracture of the supraspinatus tendon—similar to mineralization of supraspinatus tendon. • Fibrotic contracture of the infraspinatus muscle—usually sudden onset of lameness during a period of outdoor exercise (e.g., hunting); shoulder lameness and tenderness gradually disappears within 2 weeks; condition results in chronic, persistent lameness 3–4 weeks later, which is not particularly painful but has characteristic gait and limb carriage.

Physical Examination Findings

- Bicipital tenosynovitis—short and limited swing phase of gait owing to pain on extension and flexion of the shoulder; pain inconsistently demonstrated on manipulation of shoulder; *pain most evident by applying deep digital pressure over the tendon in the intertubercular groove region while simultaneously flexing the shoulder and extending the elbow.* • Rupture of the biceps brachii tendon—similar. • Mineralization of the supraspinatus tendon—similar; manipulations often do not produce pain; may palpate firm swelling over the greater tubercle. • Avulsion or fracture of the supraspinatus tendon—similar to mineralization of the supraspinatus tendon.
- Fibrotic contracture of the infraspinatus muscle—usually not painful on manipulation; not possible to internally rotate (pronate) the shoulder joint; when forced, the caudal aspect of the scapula elevates off the trunk, when standing—elbow adducted; paw abducted and outwardly rotated; when patient is walking—lower limb swings in a lateral arc (circumduction) as the paw is advanced; marked atrophy of the infraspinatus muscle on palpation.

CAUSES

- Indirect or direct trauma—likely
- Repetitive strain injury (indirect trauma)—most common

RISK FACTORS

- Overexertion and/or fatigue • Poor conditioning before performing athletic activities • Obesity



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Luxation or subluxation of the shoulder joint—history of trauma with an acute onset of lameness; often severe lameness with marked pain on manipulation of the shoulder joint. • Osteosarcoma of the proximal humerus—progressive lameness with varying degrees of pain on manipulation of the

shoulder; may note swelling and tenderness of the proximal humerus. • Brachial plexus nerve sheath tumor—slow, insidious, progressive lameness over a period of months; marked atrophy of the muscles with chronic disease; may feel a firm mass deep in the axillary region that is painful to digital pressure.

IMAGING

Radiology

- Required for differentiation. • Craniocaudal and mediolateral views necessary for all patients.

Bicipital Tenosynovitis

- Radiographs generally normal in recent injuries. • Mediolateral view (chronic disease)—may see bony reaction on the supraglenoid tubercle, dystrophic calcification of the bicipital tendon, sclerosis of the floor of the intertubercular groove, and osteophytes in the intertubercular groove.

Ruptured Origin of the Biceps Brachii Tendon

Chronic disease—may see bony, irregular reaction on the supraglenoid tubercle.

Mineralization of the Supraspinatus Tendon

- Mediolateral view—calcified foci in tendon cranial and immediately medial to the greater tubercle of the proximal humerus.

- Tangential or skyline view of the intertubercular region of the proximal humerus—eliminates superimposition; allows distinction from calcification of the biceps brachii tendon. • Often bilateral radiographically but rarely produces bilateral lameness.

Avulsion/Fracture of the Supraspinatus Tendon

- Similar to mineralization of the supraspinatus tendon. • Avulsion fragment—may be seen as a defect in the greater tubercle of the humerus; generally not as radiographically dense as that identified with mineralization of the supraspinatus tendon.

Fibrotic Contracture of the Infraspinatus Muscle

Radiographically normal.

Ultrasonography and MRI

- May help identify muscle injuries, bicipital tenosynovitis, and rupture of the biceps brachii tendon of origin. • Useful for determining the location of calcific densities near the intertubercular groove.

DIAGNOSTIC PROCEDURES

- Joint tap and analysis of synovial fluid—identify intra-articular disease; fluid should be straw-colored with normal to decreased viscosity; cytologic evaluation: < 10,000 nucleated cells/ μL (> 90% are mononuclear cells). • Arthroscopic exploration of the shoulder joint—diagnose bicipital tenosynovitis and rupture of the biceps brachii tendon of origin; confirm lack of intra-articular disease.

SHOULDER JOINT, LIGAMENT, AND TENDON CONDITIONS (CONTINUED)

PATHOLOGIC FINDINGS

- Bicipital tenosynovitis—mineralization of the biceps tendon; osteophytosis of the intertubercular groove; proliferative synovitis; and fibrous adhesions between the biceps tendon and its synovial sheath; histologically, synovial proliferation, edema, fibrosis, dystrophic mineralization, and lymphocytic-plasmacytic infiltration of the tendon and synovium.
- Ruptured origin of the biceps brachii tendon—partial to complete rupture of the biceps tendon at its insertion on the supraglenoid tubercle, proliferative synovitis, and fibrous adhesions between the biceps tendon and its synovial sheath; histologically, synovial proliferation, edema, fibrosis, and occasional dystrophic mineralization.
- Mineralization of the supraspinatus tendon—tendon often looks normal, but longitudinal incision reveals numerous pockets of mineralized debris within the fibers; histologically, chondromucinous stromal degeneration of the tendon with multiple foci of dystrophic mineralization.
- Avulsion of the supraspinatus tendon insertion—often looks normal, but longitudinal incision reveals bone fragment(s) surrounded by a fibrous tissue capsule; usually see a corresponding bony defect in the greater tubercle.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—early diagnosis.
- Inpatient—chronic, severe disease requires surgical intervention.
- Bicipital tenosynovitis—50–75% success with medical treatment; requires surgery with evidence of chronic changes and failure of medical management.
- Ruptured origin of the biceps brachii tendon generally requires surgery.
- Mineralization of the supraspinatus tendon—may be an incidental finding; requires surgery after excluding other causes of lameness and medical treatment.
- Avulsion or fracture of the supraspinatus tendon—often requires surgery because of persistent bone fragment irritation of the tendon.
- Fibrotic contracture of the infraspinatus muscle—requires surgery.

S

NURSING CARE

- Cryotherapy (ice packing)—immediately post-surgery; helps reduce inflammation and swelling at the surgery site; performed 5–10 minutes every 8 hours for 3–5 days.
- Regional massage and range-of-motion exercises—improve flexibility; decrease muscle atrophy.

ACTIVITY

- Medical treatment—requires strict confinement for 4–6 weeks; activity; premature return to normal likely exacerbates signs and induces a chronic state.

- Post-surgery—depends on procedure performed.

DIET

Weight control—decrease the load applied to the painful joint.

SURGICAL CONSIDERATIONS

- Bicipital tenosynovitis—recommended with poor response to medical treatment and chronic disease; goal: eliminate movement of the biceps tendon within the inflamed synovial sheath by performing a tenodesis or, more commonly, release of the bicipital tendon; either arthroscopic, or open, or percutaneous (\pm ultrasound guidance) tendon release.
- Rupture of the biceps brachii tendon of origin—reattach tendon to the proximal lateral aspect of the humerus with a screw and spiked washer or pass the tendon through a bone tunnel and suture it to the supraspinatus tendon.
- Mineralization of the supraspinatus tendon—longitudinally incise the tendon; remove the calcium deposits.
- Avulsion or fracture of the supraspinatus tendon—remove the bone fragment(s).
- Fibrotic contracture of the infraspinatus muscle—tenotomy and excision of part of the tendon of insertion; often feel a distinct pop after excision of the last adhesion, which allows complete range of motion of the shoulder joint.



MEDICATIONS

DRUG(S) OF CHOICE

Bicipital Tenosynovitis

- Intra-articular injection of a corticosteroid—initial treatment of choice.
- Systemic treatment (NSAIDs or steroids)—not as effective.
- Do not inject into a septic joint; perform complete synovial fluid analysis if any doubt.
- Prednisolone acetate 20–40 mg, depending on size.
- Lameness markedly improved but not eliminated—give a second injection in 3–6 weeks.
- Incomplete resolution—recommend surgery.

NSAIDs and Analgesics

- May be used for symptomatic treatment; minimize pain, decrease inflammation.
- Deracoxib (3–4 mg/kg PO q24h, chewable).
- Carprofen (2.2 mg/kg PO q12h or q24h).
- Etodolac (10–15 mg/kg PO q24h).
- Meloxicam (load 0.2 mg/kg PO, then 0.1 mg/kg PO q24h—liquid).
- Tepoxalin (load 20 mg/kg, then 10 mg/kg PO q24h).

CONTRAINDICATIONS

- Avoid prolonged use of corticosteroids because of the potential side effects and articular cartilage damage associated with long-term use.
- Direct injection of a corticosteroid into the biceps tendon—may promote further tendon disruption and eventual rupture.

PRECAUTIONS

NSAIDs—gastrointestinal irritation may preclude use.

ALTERNATIVE DRUG(S)

Chondroprotective drugs (e.g., polysulfated glycosaminoglycans, glucosamine, and chondroitin sulfate)—may help limit associated cartilage damage and degeneration.



FOLLOW-UP

PATIENT MONITORING

Most patients require a minimum of 1–2 months of rehabilitation after treatment.

EXPECTED COURSE AND PROGNOSIS

- Medically managed bicipital tenosynovitis—often successful after one or two treatments (50–75% of cases) with no chronic changes.
- Surgically treated bicipital tenosynovitis—good to excellent results (90% of cases); recovery to full function may take 2–8 months.
- Surgically treated release or tenodesis of the bicipital brachii tendon—good to excellent prognosis; > 85% of patients show improved return to function.
- Surgically treated mineralization of the supraspinatus tendon—good to excellent prognosis; recurrence possible but uncommon.
- Surgically treated avulsion or fracture of the supraspinatus tendon—good to excellent prognosis; recurrence possible but uncommon.
- Surgically treated fibrotic contracture of the infraspinatus muscle—good to excellent prognosis; patients uniformly return to normal limb function.



MISCELLANEOUS

ABBREVIATIONS

- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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**Client Education Handout
available online**

SICK SINUS SYNDROME



BASICS

DEFINITION

A disorder of impulse formation within, and conduction out of, the sinus node; dysfunction of subsidiary pacemakers and other segments of the cardiac conduction system frequently coexist with the sinus node dysfunction.

ECG Features

- Arrhythmias noted with SSS include any or all of the following: inappropriate sinus bradycardia, sinus pauses (representing sinus arrest or sinoatrial exit block), slow ectopic atrial rhythm, or alternating periods of sinus bradyarrhythmias and SVT (Figure 1).
- Paroxysms of SVT may alternate with prolonged periods of sinus node inertia and often AV nodal inertia as well, producing tachycardia-bradycardia syndrome, a variant of SSS.
- P waves and QRS complexes are usually normal.

- P waves may be abnormal or absent with slow atrial ectopic rhythm or junctional escape rhythm.

PATHOPHYSIOLOGY

- ECG manifestations may precede development of clinical signs.
- Clinical signs usually result from the failure of subsidiary pacemakers to generate escape rhythms when sinus node dysfunction occurs.
- The common clinical manifestations reflect transient decreases in organ perfusion, particularly reduced cerebral and skeletal muscle perfusion.
- Rarely, congestive heart failure develops.

SYSTEMS AFFECTED

- Cardiovascular.
- Nervous, musculoskeletal, and renal systems may be secondarily affected because of hypoperfusion.

GENETICS

- May be heritable in miniature schnauzers and West Highland white terriers.
- Doberman pinschers and boxers can have syncope associated with long sinus pauses, suggestive of sick sinus syndrome.

SIGNALMENT**Species**

Dog

Breed Predilections

- Miniature schnauzer (may be heritable).
- Noted commonly in cocker spaniel, dachshund, and West Highland white terrier.

Mean Age and Range

Most dogs > 6 years old

Predominant Sex

Female

SIGNS**Historical Findings**

- Clinical signs vary from asymptomatic to weakness, syncope, collapse, and/or seizures.
- Sudden death is infrequent.

Physical Examination Findings

- Heart rate may be abnormally rapid or abnormally slow.
- Pauses may be noted.
- Some patients appear normal.

CAUSES

- Idiopathic
- Familial in miniature schnauzers

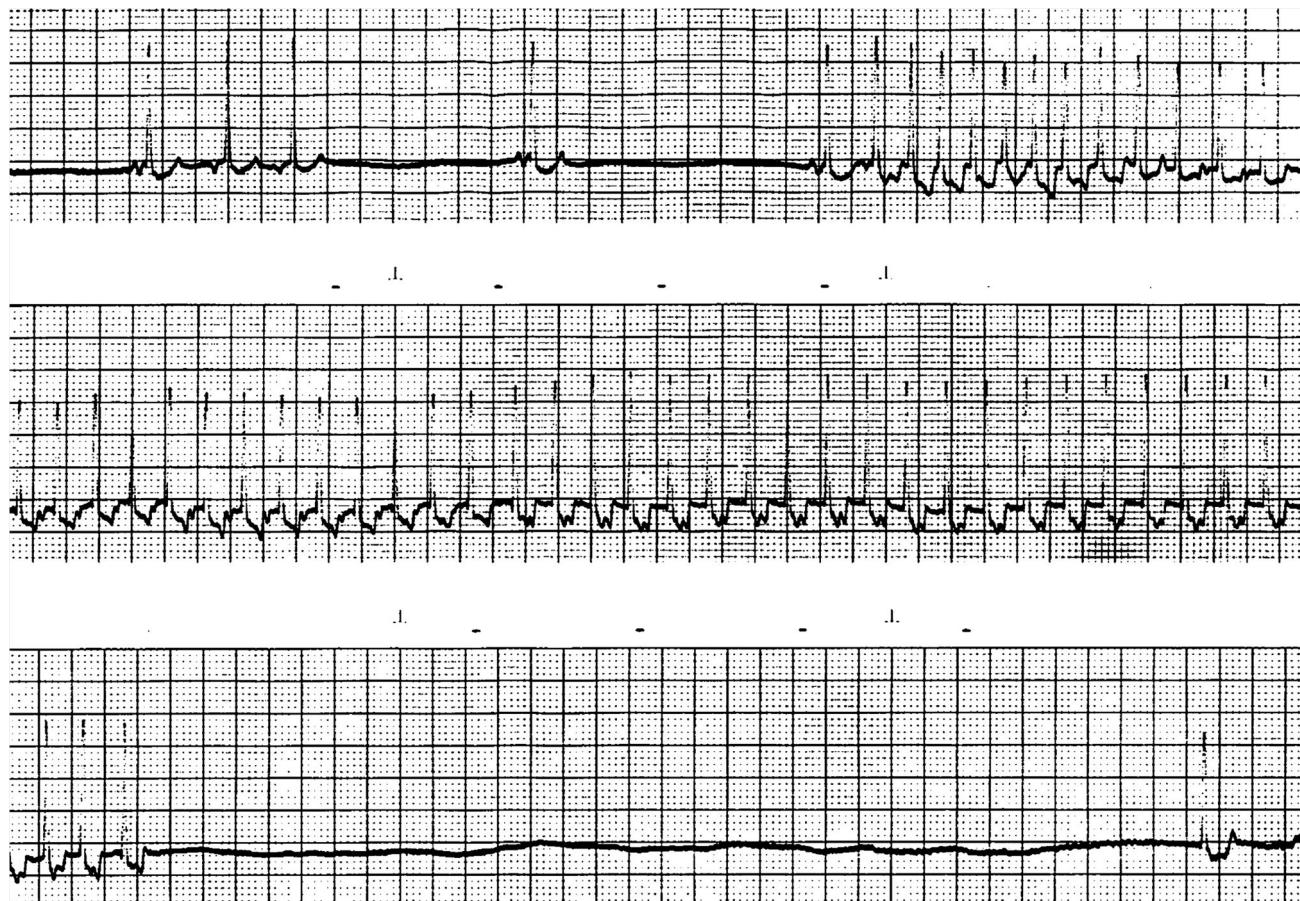


Figure 1.

A continuous lead II rhythm strip (25 mm/s) recorded from a dog with sick sinus syndrome showing an ectopic atrial rhythm interrupted by several short pauses. The third pause initiates a paroxysm of supraventricular tachycardia (250 beats/min) followed by asystole (6.6 s) terminated by a junctional escape complex.

SICK SINUS SYNDROME

(CONTINUED)

- Metastatic disease
- Ischemic disease



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Healthy dogs may exhibit sinus bradycardia (rate as low as 30 beats/minute) and sinus pauses (as long as 3.5 seconds) normally during sleep.
- Bradycardia and sinus arrest due to normal or enhanced vagal tone.
- Drug-induced (digitalis, α -adrenergic antagonists, α_2 -adrenergic agonists, calcium channel antagonists, cimetidine, opioids).
- Seizures or syncope due to non-cardiac disease.
- Atrial standstill secondary to hyperkalemia or atrial disease.
- Weakness due to neurologic, musculoskeletal, or metabolic diseases.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

IMAGING

Breeds predisposed to SSS are also predisposed to degenerative valvular disease; echocardiography is used to confirm presence of significant valvular disease when heart murmur is present.

DIAGNOSTIC PROCEDURES

- Atropine response testing—indicated in dogs with sinus bradycardia, sinus arrest, and sinoatrial exit block. Administer atropine (0.04 mg/kg IM), and evaluate the ECG 20–30 minutes later. A normal (positive) response is > 50% increase in heart rate with abolishment of pauses; dogs with SSS generally have no response or an incomplete response to atropine.
- Electrophysiologic testing of sinus node recovery time and sinoatrial conduction time.
- 24-hour ambulatory ECG (Holter) or event recording to correlate clinical signs with arrhythmia.

PATHOLOGIC FINDINGS

Vary with cause



TREATMENT

APPROPRIATE HEALTH CARE

- Hospitalization rarely necessary except for electrophysiologic testing or pacemaker implantation.
- Do not treat asymptomatic animals.

ACTIVITY

Avoid vigorous exercise and stressful situations

DIET

Modifications unnecessary

CLIENT EDUCATION

Owner should be aware that medical management is often ineffective.

SURGICAL CONSIDERATIONS

- Permanent artificial pacemaker necessary for dogs failing to respond to medical treatment and those exhibiting unacceptable medication side effects.
- Permanent artificial pacemaker usually required for dogs with bradycardia-tachycardia syndrome.
- Transvenous placement of a pacing lead in the right atrium or auricle may successfully abolish the sinus pauses.



MEDICATIONS DRUG(S)

- Do not treat asymptomatic animals.
- Symptomatic dogs are grouped into those showing primarily bradycardia, sinus arrest, and/or sinoatrial exit block and those with supraventricular tachycardia followed by sinus arrest.
- Atropine-responsive symptomatic dogs with bradycardia or sinus arrest—anticholinergic agents (propantheline: small dogs, 3.75–7.5 mg PO q8–12h; medium dogs, 15 mg PO q8h; large dogs, 30 mg PO q8h; hyoscyamine: 3–6 µg/kg q8h).
- Dogs with bradycardia and sinus arrest—may try theophylline (Theo-Dur, 20 mg/kg PO q12h), terbutaline (0.2 mg/kg PO q8–12h), or hydralazine (1–2 mg/kg PO q8–12h) if anticholinergic drugs are ineffective (avoid hydralazine if patient is hypotensive).
- Dogs with bradycardia-tachycardia whose clinical signs are due to tachycardia or tachycardia-induced sinus arrest—can give digoxin (5 µg/kg PO q12h) or atenolol (0.5–1 mg/kg PO q12–24h) in attempt to suppress the SVT (monitor closely for exacerbation of bradycardia).
- Therapy for tachycardias can only be considered, once pacing is established to avoid worsening of bradyarrhythmias.

CONTRAINDICATIONS

Avoid drugs that may worsen sinus node dysfunction (e.g., β -adrenergic antagonists, calcium channel blocking agents, phenothiazines, class I and III antiarrhythmic agents, opioids, cimetidine, α_2 -adrenergic agonists).

PRECAUTIONS

- Attempts to manage bradycardia-tachycardia syndrome medically without prior pacemaker implantation carry significant risk because drugs used to control SVT may worsen the bradyarrhythmias, and vice versa.
- Adverse effects of anticholinergic medication (constipation, difficulty voiding,

keratoconjunctivitis sicca, emesis, anxiety) occur commonly.



FOLLOW-UP

PATIENT MONITORING

- ECG in asymptomatic patients—to detect progression of disease.
- ECG in patients treated medically or with pacemaker implantation.

POSSIBLE COMPLICATIONS

- Rarely, reduced cerebral or renal perfusion results in chronic renal dysfunction or CNS damage.
- Presence of significant valvular disease has implications for type of permanent pacing mode selected.

EXPECTED COURSE AND PROGNOSIS

- Good, following pacemaker implantation in animals without congestive heart failure.
- Medical management—often ineffective; initial beneficial effects often not sustained.



MISCELLANEOUS

SYNONYMS

- Bradycardia-tachycardia syndrome
- Sinus node dysfunction
- Tachycardia-bradycardia syndrome

SEE ALSO

- Sinus Arrest and Sinoatrial Block
- Sinus Bradycardia
- Supraventricular Tachycardia

ABBREVIATIONS

- AV = atrioventricular
- CNS = central nervous system
- ECG = electrocardiogram
- SSS = sick sinus syndrome
- SVT = supraventricular tachycardia

Suggested Reading

Kraus MS, Gelzer ARM, Moise S. Treatment of cardiac arrhythmias and conduction disturbances. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., Manual of Canine and Feline Cardiology, 5th ed. St. Louis: Saunders Elsevier, 2015 (in press)

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Client Education Handout available online

SINUS ARREST AND SINOATRIAL BLOCK



BASICS

DEFINITION

- Sinus arrest—a disorder of impulse formation caused by slowing or cessation of spontaneous sinus nodal automaticity; failure of the SA node to initiate an impulse at the expected time. P-P interval does not equal a multiple of basic P-P interval.
- Sinoatrial block—a disorder of impulse conduction; an impulse formed within the sinus node fails to depolarize the atria or does so with delay; most commonly the basic rhythmicity of the sinus node is not disturbed and the duration of the pause is a multiple of the basic P-P interval. Classified into first-, second-, and third-degree SA block (similar to degrees of AV block). Difficult to diagnose first- and third-degree SA block from ECG. Second-degree SA block most common: Mobitz type I (Wenckebach) SA block—P-P interval progressively shortens prior to a pause; duration of pause is less than two P-P cycles; Mobitz type II SA block—duration of pause occurring after a sinus beat is exact multiple (two, three, or four times normal) of basic P-P interval.

ECG Features

- A normal P wave exists for each QRS complex with a pause equal to or greater than twice the normal P-P interval; rhythm is regularly irregular or irregular with pauses (Figure 1).
- Junctional or ventricular escape beats—occurs if pauses significantly prolonged. Subsidiary pacemaker takes over rhythm with escape beats normally from AV junctional tissue or Purkinje fibers; intermittent absence of P waves noted or P waves may be negative and precede, be superimposed on or follow the QRS complexes.
- Surface ECG cannot differentiate sinus arrest from block in the dog because of normal R-R interval variation (sinus arrhythmia).

PATHOPHYSIOLOGY

- Sympathetic and parasympathetic influences can alter spontaneous sinus node depolarization; vagal stimulation of acetylcholine, which binds to SA nodal receptor sites, can slow automaticity of the sinus node by reducing the slope of phase 4 depolarization; sympathetic stimulation releases norepinephrine that binds to β_1 receptors on the SA node, enhancing spontaneous SA nodal discharge rate.
- Post-drive inhibition phenomenon occurs when sinus arrest follows a run of ectopic beats. The sinus node requires a warming-up period until the usual rate of automaticity is reestablished.
- Intrinsic disease of the sinus node may affect the balance between the parasympathetic and sympathetic efferent traffic to the SA node and its spontaneous discharge rate.
- Duration of sinus arrest may be long and possibly irreversible when the sinus node is suppressed by an ectopic tachycardia, particularly with severe underlying heart disease. Persistent sinus arrest not due to any drug often indicates SSS.

SYSTEMS AFFECTED

Cardiovascular—clinical signs of weakness or syncope may appear if sinus arrest or block causes sufficiently long periods (generally 5 seconds or longer) of ventricular asystole with no escape beats initiated by latent pacemakers.

GENETICS

- Seen in purebred pugs with hereditary stenosis of the bundle of His.
- Seen in female miniature schnauzers predisposed to SSS. Is the most common arrhythmia in miniature schnauzers with SSS.
- Congenitally deaf Dalmatian coach hounds often have abnormal SA node and multiple atrial arteries. May be a genetic component to the cause of SSS in those breeds predisposed (see below).

INCIDENCE/PREVALENCE

- Normal incidental finding in brachycephalic breeds of dogs in which inspiration causes a reflex increase in vagal tone.

- Common in dog breeds predisposed to SSS.
- Uncommon in cats.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dogs and cats

Breed Predilections

- Brachycephalic breeds.
- Breeds predisposed to SSS (e.g., miniature schnauzers, dachshunds, cocker spaniels, pugs, boxers and West Highland white terriers).

Mean Age and Range

If associated with SSS, generally middle-aged to older animal

Predominant Sex

If associated with SSS, older females

SIGNS

General Comments

Generally no clinical significance by itself if terminated by sinus node depolarization, or latent pacemakers promptly escape to prevent ventricular asystole.

Historical Findings

- Usually none.
- Signs of low cardiac output (e.g., weakness and syncope) may occur with failure of the SA node to fire on time if no lower pacemaker focus takes over the rhythm.
- Sudden death is possible should prolonged periods of ventricular asystole occur.

Physical Examination Findings

- May be normal.
- Heart sounds following a pause may be louder because the ventricles had longer to fill and eject a larger amount of blood.
- Extremely slow heart rate if arrest or block is prolonged or frequent.
- With significant pathologic cardiac disease—may be findings consistent with poor cardiac output (e.g., prolonged perfusion time, pale mucous membranes, weak femoral pulses).

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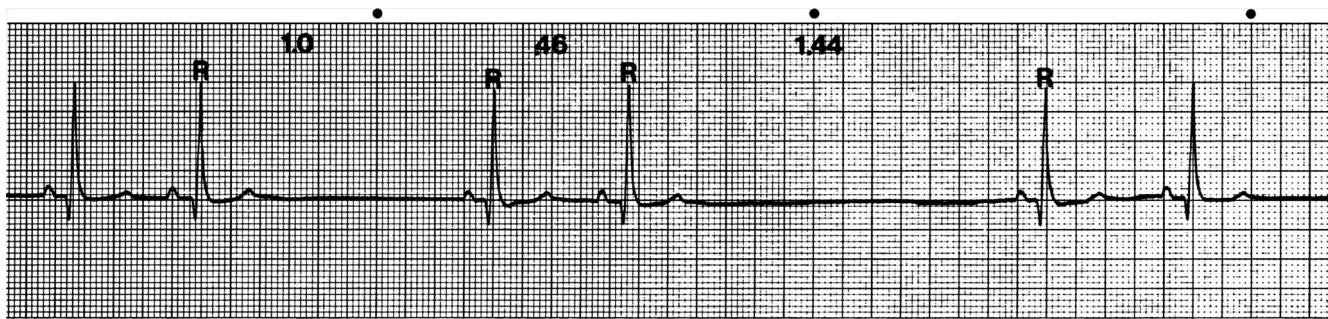


Figure 1.

Intermittent sinus arrest in a brachycephalic breed with an upper respiratory disorder. The pauses (1 and 1.44 seconds) are greater than twice the normal P-P interval (0.46). (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

SINUS ARREST AND SINOATRIAL BLOCK

(CONTINUED)

CAUSES

Physiologic

- Vagal stimulation secondary to coughing, pharyngeal irritation
- Ocular or carotid sinus pressure
- Surgical manipulation

Pathologic

- Degenerative heart disease (fibrosis)
- Dilatory heart disease
- Acute myocarditis
- Neoplastic heart disease
- SSS
- Irritation of vagus nerve secondary to thoracic or cervical neoplasia
- Electrolyte imbalance
- Drug toxicity (e.g., digoxin)

RISK FACTORS

- Certain drugs, including digitalis, quinidine, propranolol, xylazine, acepromazine, hydromorphone
- Respiratory tract disease
- Vagal maneuvers



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Marked sinus arrhythmia and sinus bradycardia.
- Not always possible to differentiate sinus arrest from SA block without direct recordings of sinus node discharge; pauses that are precise multiples of the dominant beat interval suggest sinus block.

CBC/BIOCHEMISTRY/URINALYSIS

Serum electrolyte abnormalities, especially hyperkalemia (serum K⁺ > 5.7 mEq/L).

OTHER LABORATORY TESTS

N/A

IMAGING

- Thoracic radiographs if neoplastic or cardiac disease suspected.
- Cardiac ultrasound if structural or neoplastic heart disease suspected.

DIAGNOSTIC PROCEDURES

- Provocative atropine response test to assess sinus node function. Administer 0.04 mg/kg IV atropine IM; evaluate ECG lead II rhythm strip 30 minutes later for response or administer 0.04 mg/kg atropine IV followed by ECG in 10 minutes. Resolution of the arrhythmia suggests high vagal tone as the underlying cause.
- Ambulatory monitoring may reveal prolonged periods of failure of impulses from the SA node if signs of weakness or syncope.
- In humans, a period of sinus arrest following right carotid massage that lasts longer than 3 seconds suggests inappropriate sinus responsiveness.
- Electrophysiologic studies of sinus node.
- Serum digoxin concentration, if applicable; trough level recommended (just before next

dose or at least 8 hours post pill); therapeutic serum concentrations are typically 0.5–1.5 ng/mL.

PATHOLOGIC FINDINGS

Histologic study of the SA node may reveal necrosis, fibrosis, and/or degenerative changes.



TREATMENT

APPROPRIATE HEALTH CARE

Asymptomatic sinus arrest or block does not require therapy. If clinical signs, therapeutic approach depends on cause, underlying cardiac status, and severity of symptoms. Any indicated treatment may be outpatient unless pacemaker implantation is necessary, which necessitates hospital management.

NURSING CARE

Correct any electrolyte abnormalities.

ACTIVITY

Unrestricted unless signs of weakness, syncope, or CHF develop.

CLIENT EDUCATION

An artificial pacemaker may be necessary when patient is symptomatic and non-responsive to medical management.

SURGICAL CONSIDERATIONS

Implantation of an artificial demand pacemaker in animals with clinical signs non-responsive to therapy.



MEDICATIONS

DRUG(S) OF CHOICE

- Only if patient is symptomatic, consider atropine (0.04 mg/kg IV, IM), glycopyrrolate (5–10 µg/kg IV, IM), or isoproterenol (10 µg/kg IM, SC q6h or dilute 1 mg in 500 mL of 5% dextrose or Ringer's solution, and infuse IV at 0.04–0.08 µg/kg/minute).
- If responsive to injectable anticholinergic drugs (e.g., atropine)—can prescribe parasympatholytic drug such as oral propantheline bromide (0.25–0.5 mg/kg q8–12h) or hyoscyamine (3–6 µg/kg q8h) for at-home management. Sympathomimetic agents including methylxanthine theophylline (10 mg/kg extended release formulation q12h) or terbutaline (0.14 mg/kg q8–12h PO in dogs and 0.1–0.2 mg/kg q12h in cats) could be considered for oral therapy.

CONTRAINDICATIONS

If patient is symptomatic secondary to prolonged pauses, discontinue any drugs that may be causative (e.g., digitalis, beta-blockers, calcium channel blockers).

PRECAUTIONS

Avoid drugs that depress SA node function.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

If medical therapy does not resolve signs, consider pacemaker implantation.



FOLLOW-UP

PATIENT MONITORING

When indicated, periodic serial ECG evaluation to assess therapeutic efficacy and possible progression to a more serious dysrhythmia.

POSSIBLE COMPLICATIONS

If associated with primary cardiac disease, CHF may develop and necessitate appropriate therapies.

EXPECTED COURSE AND PROGNOSIS

If cause is SSS, symptomatic patient may respond well to medical intervention; if poorly responsive, permanent pacemaker implantation would improve prognosis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Sick sinus syndrome
- Sinus arrhythmia
- Sinus bradycardia

SYNONYMS

- Sinus block
- Sinus pause

SEE ALSO

- Sick Sinus Syndrome
- Sinus Arrhythmia
- Sinus Bradycardia

ABBREVIATIONS

- AV = atrioventricular
- CHF = congestive heart failure
- ECG = electrocardiogram
- SA = sinoatrial
- SSS = sick sinus syndrome

INTERNET RESOURCES

The Calcium and Voltage Clocks in Sinoatrial Node Automaticity.
<http://dx.doi.org/10.4070/kcj.2009.39.6.217>

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Boyett MR, Honjo H, et al. The sinoatrial node: a heterogeneous pacemaker structure. *Cardiovasc Res* 2000, 47(4):658–687.

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SINUS ARRHYTHMIA



BASICS

DEFINITION

- Normal sinus impulse formation characterized by a phasic variation in sinus cycle length. An irregular R-R interval is present that has more than 10% variation in sinus cycle length (or variability of 0.12 seconds [dog], 0.10 seconds [cat], or more exists between successive P waves).
- Two basic forms exist—respiratory sinus arrhythmia (RSA): P-P interval cyclically shortens during inspiration due primarily to reflex inhibition of vagal tone and lengthens during expiration; non-respiratory sinus arrhythmia: phasic variation in P-P interval unrelated to the respiratory cycle.

ECG Features

- Other than the irregular rhythm, all other criteria for sinus rhythm are present.
- Normal heart rate.
- Positive P wave in leads, I, II, III, and aVF, unless a wandering pacemaker is present, where the P waves may be positive, diphasic, or negative temporarily.
- A P wave is present for every QRS complex.
- A QRS complex is present for every P wave.
- PR interval is relatively constant.

PATHOPHYSIOLOGY

Sinus node discharge rate depends on the two opposing influences of the autonomic nervous system. Vagal stimulation decreases spontaneous sinus nodal discharge rate and predominates over sympathetic stimulation. Negative intrathoracic pressure occurring with inspiration causes decreased pressure on the vagus nerves. Feedback from the cardioregulatory and vasomotor centers in the medulla produces cardiac acceleration by decreasing vagal restraint on the sinus node; the opposite occurs during exhalation. The genesis of sinus arrhythmia also depends on reflexes involving pulmonary stretch receptors (Hering-Breuer reflex), pressure-volume sensory receptors in the heart (Bainbridge—atrial stretch stimulates receptors in the atrial wall causing vagal inhibition and increase in heart rate, baroreceptor—receptors in the carotid sinus and aortic arch elicit inverse changes in heart rate with acute changes in arterial blood pressure), blood vessels, and chemical factors of the blood.

SYSTEMS AFFECTED

Cardiovascular—generally no hemodynamic consequence, but marked SA may produce a long enough sinus pause to produce syncope if not accompanied by an escape rhythm.

GENETICS

N/A

INCIDENCE/PREVALENCE

Most frequent form of arrhythmia in the dog

SIGNALMENT

Species

- Respiratory SA frequent normal finding in dogs.
- While common in cats asleep and in home environment, in a clinical setting sympathetic dominance occurs and RSA is rare without underlying pathology.

Breed Predilections

- Brachycephalic breeds predisposed.
- Dogs—bulldogs, Lhasa Apsos, Pekingese, pugs, Shar-Peis, Shih Tzus, boxers.
- Cats—Persians, Himalayans.

Mean Age and Range

N/A

Predominant Sex

N/A

SIGNS

General Comments

- Uncommon, but weakness may develop if pauses between beats are excessively long; syncope can occur when a marked sinus arrhythmia and sinus bradycardia develop.
- In general, symptoms more common in non-respiratory than in respiratory form.

Historical Findings

- Respiratory SA—none.
- Non-respiratory SA—may be findings related to underlying disease.

Physical Examination Findings

- May be normal.
- Irregular rhythm on auscultation.
- May be findings related to specific disease accentuating vagal tone (e.g., stertor and stridor in a patient with brachycephalic airway syndrome).

CAUSES

- Normal cyclic change in vagal tone associated with respiration in the dog; heart rate increases with inspiration and decreases with expiration.
- Underlying conditions that increase vagal tone—high intracranial pressure, gastrointestinal disease, respiratory disease, cerebral disorders, digitalis toxicity, organophosphates.
- Carotid sinus massage or ocular pressure (vagal maneuver) may accentuate.

RISK FACTORS

- Brachycephalic conformation
- Digoxin therapy
- Any disease that increases vagal tone



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Auscultation of SA is often confusing; ECG helps differentiate normal SA from true pathologic arrhythmia.

- Wandering sinus pacemaker frequently associated and a variant of sinus arrhythmia. Site of impulse formation shifts within the sinoatrial node or to an atrial focus or AV node, changing the configuration of the P wave.

- Important to differentiate normal SA from pathologic arrhythmias including atrial premature complexes, SSS, slow atrial fibrillation, and AV dissociation.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

Cats with chronic respiratory disease may be positive for feline leukemia or feline immunodeficiency virus.

IMAGING

Radiographs, CT, MRI of head and neck to assess for abnormal anatomic conformation that might predispose to airway problems.

DIAGNOSTIC PROCEDURES

- Pharyngoscopy/laryngoscopy if upper airway disease suspected.
- Atropine challenge test (administer atropine 0.04 mg/kg IM followed by ECG in 30 minutes or 0.04 mg/kg atropine IV followed by ECG in 10 minutes) if associated with sinus bradycardia and primary dysfunction of sinus node is suspected.

PATHOLOGIC FINDINGS

See specific disease



TREATMENT

APPROPRIATE HEALTH CARE

Generally, specific treatment required only when associated with symptomatic sinus bradycardia; if not related to respiration, underlying cause is treated. If patient is suffering respiratory distress, appropriate inpatient management indicated until patient is stable.

NURSING CARE

None unless associated with underlying disease (see also below).

ACTIVITY

Not restricted unless associated with specific disease (e.g., brachycephalic animals may need to limit exercise, especially in high ambient temperatures).

DIET

Caloric restriction for obese animals with airway compromise.

CLIENT EDUCATION

None unless associated with specific disease.

SURGICAL CONSIDERATIONS

None unless associated with specific disease.

SINUS ARRHYTHMIA

(CONTINUED)

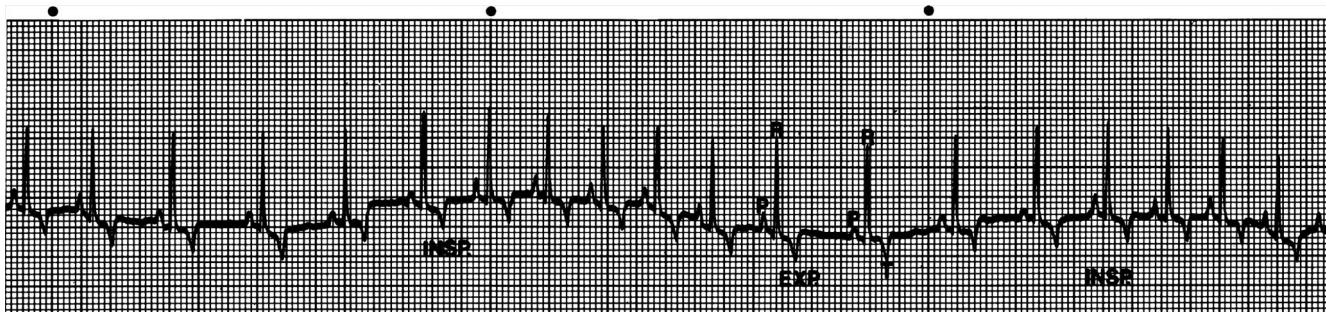


Figure 1.

Respiratory sinus arrhythmia with an average rate of 120/minute (paper speed, 25 mm/second; 6 complexes between 1 set of time lines \times 20). The rate increases during inspiration (INSP) and decreases during expiration (EXP). The fluctuation of the baseline correlates with the movement of the electrodes by the thoracic cavity. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

**MEDICATIONS****DRUG(S) OF CHOICE**

- Generally no therapy indicated; this is a normal rhythm.
- Infectious respiratory diseases require appropriate antibiotic therapy.
- If associated with symptomatic sinus bradycardia or sinus arrest or block, anticholinergics may be indicated—atropine (0.02–0.04 mg/kg IV, IM, SC) or glycopyrrolate 5–10 µg/kg IV, IM, SC).

CONTRAINdications

Discontinue digoxin if toxicity is a problem.

PRECAUTIONS

Avoid atropine in patients with respiratory disease; an adverse effect is drying of secretions.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

S

**FOLLOW-UP****PATIENT MONITORING**

Only if associated with specific disease.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

N/A

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- SSS
- Brachycephalic airway syndrome
- Asthma
- Chronic obstructive pulmonary disease

AGE-RELATED FACTORS

Generally more pronounced in young adult

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Increased incidence of arrhythmias

SYNOMYS

- Non-respiratory SA = non-phasic SA; sinus irregularity.
- Respiratory SA = phasic SA.
- Ventriculophasic SA—form of non-phasic SA in which atrial cycles containing ventricular complexes are shorter than those in which they are absent. That is, the P-P interval that includes the QRS complex is shorter than the P-P interval without a QRS complex. This can be seen with second-degree AV block, complete AV block or in the

presence of ventricular premature complexes with a full compensatory pause.

SEE ALSO

- Brachycephalic Airway Syndrome
- Sick Sinus Syndrome
- Sinus Arrest and Sinoatrial Block

ABBREVIATIONS

- AV = atrioventricular
- ECG = electrocardiogram
- RSA= respiratory sinus arrhythmia
- SA = sinus arrhythmia
- SSS = sick sinus syndrome

Suggested Reading

Bonow R, Mann D, Zipes D, Libby P. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, 9th ed. Ames, Iowa: Elsevier, 2012.

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SINUS BRADYCARDIA



BASICS

DEFINITION

Sinus rhythm in which impulses arise from the sinoatrial node at slower-than-normal rate for an animal's signalment and activity.

ECG Features

- Dogs—sinus rate < 60 bpm).
- Cats—sinus rate < 110 bpm at home or < 130 bpm at the clinic.
- Rhythm regular, often with a slight variation in R-R interval; may be irregular if bradycardia due to high vagal tone; often coexists with sinus arrhythmia.
- Normal P wave for each QRS complex.
- P-R interval constant.

PATHOPHYSIOLOGY

• Can be an incidental finding in healthy animals or during sleep.

- May represent normal physiologic response to athletic training; may result from enhanced cardiac parasympathetic tone or decreased sympathetic tone as well as from intrinsic changes in the sinus node.
- Automaticity of the heterogeneous sinus node is a very complex phenomenon invoking the calcium and voltage clock mechanisms. More than 16 autonomically influenced currents with the I_f (funny) channel predominating and Ca^{++} release from the sarcoplasmic reticulum are critical in maintaining autonomic balance and changes in heart rate.
- May represent pathophysiologic response due to high vagal tone, change in blood pH, PCO_2 , PO_2 , or serum electrolyte disorders, hypothyroidism, increased intracranial pressure, toxins and certain drugs.
- May be a result of SSS.

SYSTEMS AFFECTED

Cardiovascular—most instances benign arrhythmia and may be beneficial by producing a longer period of diastole and increased ventricular filling time; can be associated with syncope if due to abnormal reflex (neurocardiogenic) or intrinsic disease of sinus node.

GENETICS

Female miniature schnauzer, West Highland white terrier, boxer, cocker spaniel, dachshund, and pug predisposed to SSS with possible underlying heritable component—may cause bradycardia.

INCIDENCE/PREVALENCE

- Common in the dog, less common in cat.
- Interpretation of sinus node rate also depends on environment and type of patient. For example, a sinus rate can be as low as 20 beats/minute in a normal dog that is sleeping.

SIGNALMENT

Species

Dog and cat

Breed Predilections

Bradycardia associated with SSS—miniature schnauzer, cocker spaniel, dachshund, pug, and West Highland white terrier.

Mean Age and Range

- Decreased prevalence with advancing age unless associated with intrinsic disease of SA node.
- SSS typically seen in middle-aged to geriatric patients.

Predominant Sex

With SSS, older female miniature schnauzers

SIGNS

Historical Findings

- Often asymptomatic
- Lethargy
- Weakness
- Exercise intolerance
- Syncope
- Episodic ataxia

Physical Examination Findings

- Pulse rate slow
- Hypothermia may be present
- Poor perfusion
- Syncope
- Decrease level of consciousness

CAUSES

Physiologic

- Athletic conditioning
- Hypothermia
- Intubation with pharyngeal or soft palate tension
- Sleep
- Cushing's response with increased intracranial pressure
- Gastrointestinal distension
- Activation of baroreceptor reflex with increase in systemic BP

Pathophysiologic

- High vagal tone associated with gastrointestinal, respiratory, neurologic, and pharyngeal diseases.
- Reflex-mediated neurocardiogenic (vasovagal)—carotid sinus hyperactivity-situational (micturition, defecation, cough, swallowing).

Pathologic

- High intracranial pressure
- Hyperkalemia
- Hypercalcemia
- Hypocalcemia
- Hypermagnesemia
- Hypoxemia
- Hypothyroidism
- Hypoglycemia
- May precede cardiac arrest
- SSS (rare in the cat)
- Feline dilated cardiomyopathy
- Viral myocarditis
- Sinoatrial block
- In humans, mutations in the I_f channel and drugs which block I_f (such as ivabradine) have been associated with bradycardia.

Pharmacologic

- General anesthesia
- Any negative chronotrope including:
 - Phenothiazines
 - Beta-adrenergic blockers
 - Digitalis glycosides
 - Calcium channel blockers
 - α_2 -adrenergic agonists
 - Sotolol
 - Amiodarone
 - Centrally acting opioids: morphine, hydromorphone, butorphanol, fentanyl

RISK FACTORS

- Any situation or disease that may increase parasympathetic tone
- Oversedation
- Hypoventilation under anesthesia
- Breeds predisposed to SSS



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Persistent and marked SB should raise possibility of SSS.
- Clinical signs may mimic cerebral dysfunction.

CBC/BIOCHEMISTRY/URINALYSIS

- Hyperkalemia, hypercalcemia, hypocalcemia, or hypermagnesemia possible.
- CBC and serum chemistry profile may reveal changes associated with metabolic disease such as renal failure.

OTHER LABORATORY TESTS

- Serum T_4 , free T_4 (FT_4), and TSH assay if hypothyroidism suspected.
- Measure trough serum digoxin concentration, if applicable, 8 hours after last dose or close to next dosing; normal therapeutic serum concentration should be 0.5–1.5 ng/mL.
- Toxicologic screen.

DIAGNOSTIC PROCEDURES

- Provocative atropine response test to assess sinus node function—administer atropine 0.04 mg/kg IV, wait 10–15 minutes, then record ECG or administer same dose IM, wait 30 minutes, then record ECG; persistent sinus tachycardia at > 140 bpm is expected response. Lower doses of atropine have increased tendency to cause initial accentuation of sinus bradycardia and first- or second-degree AV block because of centrally mediated increase in vagal tone.
- 24-hour Holter monitoring or ECG event recorder, an owner triggered device, useful if transient bradycardia is suspected cause for clinical signs.



TREATMENT

APPROPRIATE HEALTH CARE

- Many animals exhibit no clinical signs and require no treatment. In dogs without structural heart disease, heart rates as low as 40–50 bpm generally provide normal cardiac output at rest.
- Therapeutic approaches—vary markedly; depend on the mechanism for SB, the ventricular rate, and severity of clinical signs.
- Inpatient or outpatient management—depends on underlying cause and clinical status of patient.

NURSING CARE

- Provide general supportive therapy including intravenous fluid therapy for hypothermic and hypovolemic patients.
- Discontinue any causative drug.
- Correct any serious electrolyte imbalance with appropriate fluid therapy.

CLIENT EDUCATION

- Discuss importance of complying with daily medical management when treating

SINUS BRADYCARDIA

(CONTINUED)

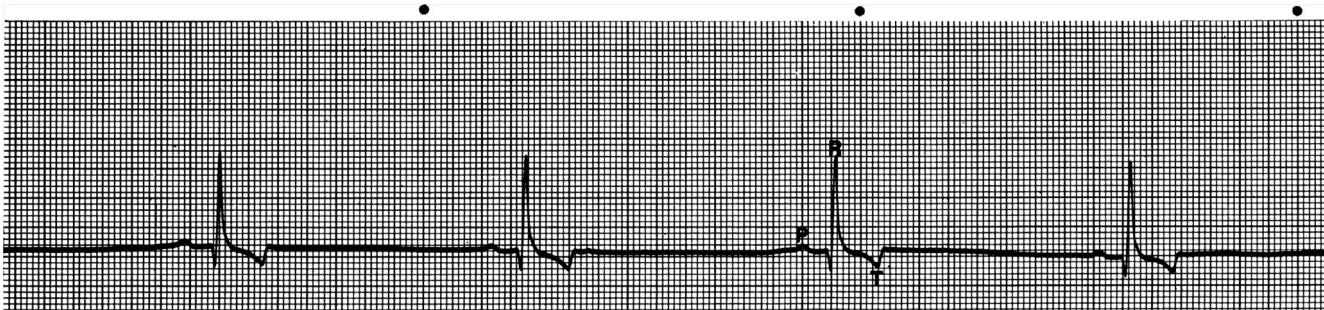


Figure 1.

Sinus bradycardia at a rate of 75 beats/minute in a cat from anesthetic complications during surgery. Note the tall R waves. (Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

underlying disease. • Advise that persistent symptomatic bradycardia may necessitate permanent pacemaker implantation for reliable long-term management.

SURGICAL CONSIDERATIONS

• If progressive bradycardia occurs during anesthesia and is attributed to hypoventilation, immediately discontinue inhalation anesthetics and provide adequate ventilation; atropine is generally ineffective in this situation. • If surgical manipulation triggering vagal reflexes (eye, vagus nerve, larynx) is anticipated, pretreatment with atropine (0.04 mg/kg IM, SC) or glycopyrrolate (5–10 µg/kg IM, SC) may prevent bradycardia. • Severe bradycardia may precipitate cardiopulmonary arrest; identify the causative agent or condition for effective management.

**MEDICATIONS****DRUG(S) OF CHOICE**

• If patient is hypothyroid, supplement with l-thyroxine. • For severe hypocalcemia (< 6 mg/dL) administer 10% calcium gluconate (0.5–1.5 mL/kg IV) slowly over 15–30 minutes; monitor with ECG. • For symptomatic drug-induced bradycardias, disorders causing excessive vagal tone, and initial management of bradycardia associated with SSS, administer atropine (0.04 mg/kg IV) or glycopyrrolate (5–10 µg/kg IV); anticholinergic therapy may be continued short-term using atropine (0.04 mg/kg IM, SC q6–8h) or glycopyrrolate (0.01 mg/kg IM, SC q6–8h). Consider propantheline bromide (0.25–0.5 mg/kg PO q8–12h) or hyoscymamine (3–6 µg/kg PO q8h), methylxanthine theophylline, an adenosine receptor antagonist (extended release formulation 10 mg/kg PO q12h, dogs; 12.5 mg PO q24h in the evening, cats), and/or terbutaline (0.14 mg/kg q8–12h PO, dogs; 0.625–1.25 mg/cat PO, cats) to manage symptomatic bradycardia associated with SA node disease. • For temporary management of symptomatic persistent bradycardia until pacing can be accomplished,

consider continuous IV infusion of isoproterenol (0.04–0.08 µg/kg/min IV). However, if temporary pacing is available this is initial procedure of choice.

CONTRAINDICATIONS

• For hypothermia-induced bradycardia with a pulse, rewarming and supportive measures should be mainstay of treatment. Parasympatholytics generally not recommended. • Parasympatholytic agents contraindicated for acidotic, hypercarbic patients under anesthesia (hypoventilation); bradycardia in this setting may protect the myocardium by decreasing oxygen consumption.

PRECAUTIONS

• Close ECG monitoring recommended when administering calcium solutions for treatment of hypocalcemia; if QT interval shortening or bradycardia, stop administration temporarily. • In patients with heart disease, a lower initial dose of l-thyroxine is advised to allow adaptation to higher metabolic rate. • Administer atropine selectively; rapid IV administration may predispose to ventricular arrhythmias by altering autonomic balance. • Caution when administering parasympatholytic agent to dogs with suspect SSS—could result in a tachycardia that overdrive suppress escape rhythms with potential consequence of asystole.

ALTERNATIVE DRUG(S)

• Bradycardia associated with structural heart disease is most reliably treated by permanent pacemaker implantation. • Glycopyrrolate may have longer vagal blocking effect and cause less frequent ventricular ectopic beats than atropine.

**FOLLOW-UP****PATIENT MONITORING**

• Assess total T₄ 6 hours post pill. • Addison's disease—assess electrolytes every 3–4 months after patient is stable. • ECG check of pacemaker function and pacing rate is

recommended during each follow-up examination.

PREVENTION/AVOIDANCE

• Maintain normal PaO₂ under anesthesia with proper ventilation; monitor with pulse oximetry or blood gases. • Avoid hypothermia intraoperatively.

EXPECTED COURSE AND PROGNOSIS

• Signs, if present, should resolve with correction of causative metabolic or endocrine problem. • Treatment of symptomatic SB with a permanent pacemaker generally offers a good prognosis for rhythm control.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

• Sick sinus syndrome • Heart block • Sinus arrhythmia

PREGNANCY/FERTILITY/BREEDING

Post-parturient hypocalcemia usually develops 1–4 weeks postpartum, but can occur at term, prepartum, or late lactation.

SEE ALSO

- Digoxin Toxicity • Eclampsia
- Hypercalcemia • Hyperkalemia
- Hypermagnesemia • Hypocalcemia
- Hypothermia • Hypothyroidism
- Organophosphate and Carbamate Toxicosis
- Sick Sinus Syndrome

ABBREVIATIONS

- AV = atrioventricular • ECG = electrocardiogram • SA = sinoatrial • SB = sinus bradycardia • SSS = sick sinus syndrome • T₄ = thyroxine • T₃ = triiodothyronine • TSH = thyroid stimulating hormone

Suggested Reading

Kornreich B, Moise S. Bradyarrhythmias. In: Bonagura J, Twedt D, eds. Current Veterinary Therapy XV. Elsevier Saunders, 2014, pp.731–737.

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SINUS TACHYCARDIA



BASICS

DEFINITION

Disturbance of sinus impulse formation; acceleration of the sinoatrial node beyond its normal discharge rate (Figure 1).

ECG Features

- Dogs—HR > 160 bpm (toy breeds HR > 180 bpm; giant breeds HR > 140 bpm; puppies HR > 220 bpm). • Cats—HR > 180 bpm; (kittens HR > 240 bpm). ECG shows a rapid regular rhythm with possible slight variation in R-R interval. • P wave of sinus origin for each QRS complex with constant P-R interval. • P waves may be partially or completely fused with preceding T waves. • Generally has a gradual onset and termination.

PATHOPHYSIOLOGY

- Accelerated phase 4 diastolic depolarization of sinus nodal cells (as a result of voltage and calcium-dependent mechanisms) generally responsible for ST. • Enhanced adrenergic effect or cholinergic inhibition results in high rate of sinus impulse formation; changes in heart rate usually involve a reciprocal action of the parasympathetic and sympathetic divisions of the autonomic nervous system.

SYSTEMS AFFECTED

Cardiovascular—cardiac output = heart rate × stroke volume. Changes in heart rate affect preload, afterload, and contractility, which determine stroke volume; severe tachycardia can compromise cardiac output. Rapid rates shorten diastolic filling time, and particularly in diseased hearts, the increased heart rate can fail to compensate for decreased stroke volume, resulting in decreased cardiac output and coronary blood flow. • Chronic tachycardias can cause cardiac dilation (tachycardiomyopathy) which often resolves with control of the tachycardia.

GENETICS

N/A

INCIDENCE/PREVALENCE

- Most common benign arrhythmia in the dog and cat. • Most common rhythm disturbance in the postoperative patient.

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dog and cat

Breed Predilections

None

SIGNS

General Comments

Often no clinical signs because ST is almost always a consequence of a variety of physiologic or pathophysiologic stresses.

Historical Findings

In general, ST itself does not produce any symptoms. • If associated with primary cardiac disease, weakness, exercise intolerance, or syncope may be reported. • If associated with other medical conditions, signs may be seen specific to the disease present.

Physical Examination Findings

- High HR • May otherwise be normal if not associated with a pathologic condition. • Pale mucous membranes if associated with anemia or CHF. • Fever may be present. • Signs of CHF (e.g., dyspnea, cough, cyanosis, ascites) if associated with primary cardiac disease.

CAUSES

Physiologic

- Exercise • Pain • Restraint • Excitement
- Any hyperadrenergic state

Pathologic

- Fever • CHF • Chronic lung disease
- Shock • Pericardial effusion • Anemia
- Pain • Infection • Hypoxia • Pulmonary thromboembolism • Hypotension
- Hypovolemia • Functional pheochromocytoma • Hyperthyroidism
- Pericarditis • Pneumothorax
- Hypoglycemia • Vestibulosympathetic hypovolemia

Pharmacologic

- Atropine • Epinephrine • Ketamine
- Telazol • Quinidine • Xanthine bronchodilators • β -agonists

RISK FACTORS

- Thyroid medications • Primary cardiac diseases • Inflammation • Pregnancy
- Anesthesia • Certain toxins (*Amanita muscaria*, scorpion venom, black widow spider venom), plants (Jimson weed, mandrake), and drugs (antihistamines, tricyclic antidepressants)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Must differentiate from supraventricular tachycardia including atrial tachycardia, atrial flutter with 2:1 AV block, and AV junctional tachycardia; as sinus rate increases, the P wave appears closer to the T wave of the previous beat. At very rapid rates, it becomes difficult to distinguish this condition from other pathologic SVT. Gradual slowing of the rate is more suggestive of ST.

CBC/BIOCHEMISTRY/URINALYSIS

- Low PCV if patient is anemic.
- Leukocytosis with left shift if inflammation or infection is causative.

OTHER LABORATORY TESTS

- High serum T_4 or free T_4 concentration (cats) if secondary to hyperthyroidism. • T_3 suppression test, TRH response test, or thyroid scintigraphy if T_4 values are normal and hyperthyroidism is suspected. • Plasma catecholamines (24-hour urine sample collection for catecholamine assay and their metabolites, low sensitivity) in diagnosis of pheochromocytoma; provocative testing to induce hypertension with histamine and glucagon or hypotension with phenolamine may be useful but is not practical. • 24-hour Holter monitoring. • Cardiac electrophysiologic studies. • Consider plasma

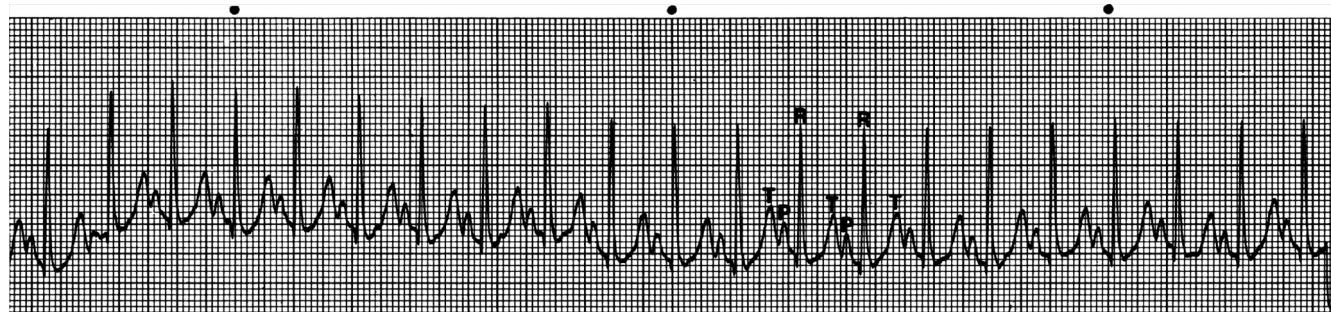


Figure 1.

Sinus tachycardia at a rate of 272 bpm/minute in a dog in shock. The rhythm is sinus because the P waves are normal, the P-R relationship is normal, and the rhythm is regular. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

SINUS TACHYCARDIA

(CONTINUED)

NT-proBNP assay if evaluating for cardiac disease.

IMAGING

- Thoracic radiographs and echocardiography to evaluate for evidence of primary cardiac disease
- Thyroid scan to evaluate for hyperthyroidism.
- Abdominal ultrasound and angiography to evaluate for adrenal mass.
- CT and MRI as well as functional imaging modalities very sensitive for detecting adrenal masses.

DIAGNOSTIC PROCEDURES

- Consider non-pharmacologic vagal maneuver to differentiate from other supraventricular tachyarrhythmias; carotid sinus or ocular pressure may terminate ectopic SVT. With ST, vagal maneuvers produce gradual, transient slowing of the HR if any. Less commonly, varying degrees of AV block (usually first-degree or Wenckebach) may occur transiently. ECG monitoring is recommended during these vagal maneuvers.
- A precordial thump may be used to differentiate ST from other SVT. ST will not be affected, whereas the SVT may stop for at least 1 or 2 beats.
- Serial arterial blood pressure measurement may document hypertension in patients with hyperthyroidism, pheochromocytoma, or renal disease.
- Pharmacologic cardioversion with IV diltiazem at 0.25 mg/kg administered over 2 minutes. If no response, can be repeated in 15 minutes.

PATHOLOGIC FINDINGS

- None if associated with physiologic or pharmacologic cause.
- Pathologic findings depend on the primary disease process.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Identify and correct underlying disorders whenever possible.
- Whether inpatient or outpatient depends on clinical status of patient and primary disease, if any (e.g., if CHF, treat as outpatient unless animal is dyspneic or severely hypotensive).

NURSING CARE

Depends on whether associated with a specific disease.

ACTIVITY

Exercise restriction recommended if symptomatic cardiac disease.

DIET

Sodium restriction generally advised with hypertension and CHF.

CLIENT EDUCATION

Discuss importance of managing any primary disease appropriately, with medical or surgical intervention.

SURGICAL CONSIDERATIONS

- Thyroidectomy—treatment option for hyperthyroidism (cats).
- Tumor removal is the definitive treatment for patients with pheochromocytoma.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Establish underlying cause and treat appropriately; specific antiarrhythmic therapy is generally limited to patients in CHF or those with secondary cardiac disease due to hyperthyroidism or hypertension.
- Dogs—if CHF is the cause, administer pimobendan along with appropriate diuretic therapy and angiotensin converting enzyme inhibitor. Digoxin may be indicated in some cases such as CHF with atrial fibrillation. If ST persists despite above management, consider adding a calcium channel blocker (e.g., diltiazem at 0.5–2.5 mg/kg PO q8h) or a beta-blocker (e.g., atenolol 0.25–1 mg/kg q12h, sotalol 1–2 mg/kg q12h PO) ONLY after congestion is controlled.
- Cats—if ST is associated with hyperthyroidism without CHF, a beta-blocker (e.g., atenolol 0.25–1 mg/kg PO q12–24h) may lower the HR. Consider digoxin (0.01875–0.03125 mg per average-size cat, equal to 1/8–1/4 of a 0.125 mg tablet—tablet preferred) if chronic hyperthyroidism with CHF or for treatment of primary dilated cardiomyopathy. If ST associated with hypertrophic cardiomyopathy, administer atenolol 6.25–12.5 mg/cat PO q12h or diltiazem (1.75–2.4 mg/kg PO q8h).

CONTRAINdications

Avoid drugs such as atropine or catecholamines (epinephrine) that may further increase the HR.

PRECAUTIONS

- Beta-blockers can potentially worsen signs of congestion and lower cardiac output in patients with systolic dysfunction
- Suppression of ST may be catastrophic if occurring as natural compensatory response to maintain cardiac output in a systemically ill patient.

POSSIBLE INTERACTIONS

See manufacturer's insert for specific drug.

ALTERNATIVE DRUG(S)

- If associated with pericardial effusion, avoid drug therapy and perform pericardiocentesis.
- If associated with a certain drug (e.g., hydralazine, bronchodilators), discontinue the medication or adjust the dose.
- If associated with hypovolemia, replace fluid volume.

**FOLLOW-UP****PATIENT MONITORING**

Depends on specific disease—for CHF, serial ECG, thoracic radiographs, BUN, creatinine, and serum electrolytes; for hyperthyroidism, serial serum T_4 , CBC, and biochemistry.

PREVENTION/AVOIDANCE

Minimize stress, exercise, and dietary sodium, if heart disease.

POSSIBLE COMPLICATIONS

- Weakness or syncope if associated with low cardiac output.
- Development of CHF if persistent ST associated with heart disease.

EXPECTED COURSE AND PROGNOSIS

- ST usually resolves with correction of the underlying cause.
- Poor despite treatment if ST is associated with CHF.
- Favorable for remission of ST when hyperthyroidism is controlled medically, surgically, or by radioactive iodine.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

See list of pathologic and physiologic causes.

PREGNANCY/FERTILITY/BREEDING

- Increase in cardiac output in late pregnancy (third trimester) largely due to an accelerated HR.

SYNOMYS

- Inappropriate sinus tachycardia
- Postural tachycardia syndrome

SEE ALSO

- Atrial Fibrillation and Atrial Flutter
- CHF—Left and Right-Sided
- Hyperthyroidism
- Pheochromocytoma
- Supraventricular Tachycardia

ABBREVIATIONS

- AV = atrioventricular
- CHF = congestive heart failure
- CT = computed tomography
- ECG = electrocardiogram
- HR = heart rate
- MRI = magnetic resonance imaging
- ST = sinus tachycardia
- SVT = supraventricular tachycardia
- T_4 = thyroxine
- T_3 = triiodothyronine
- TRH = thyrotropin-releasing hormone

Suggested Reading

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Author Deborah J. Hadlock

Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

SJÖGREN-LIKE SYNDROME



BASICS

OVERVIEW

- A systemic auto-immune disease characterized by keratoconjunctivitis sicca, xerostomia, and lymphoplasmacytic adenitis.
- Underlying mechanism unknown; however, auto-antibodies directed against glandular tissues have been identified.
- Associated with other auto-immune or immune-mediated diseases, such as rheumatoid arthritis and pemphigus.

SIGNALMENT

- Higher incidence in several canine breeds—English bulldogs, West Highland white terriers, and miniature schnauzers.
- Chronic disease of adult dogs.
- Cats unaffected.

SIGNS

Historical Findings

- Adult onset
- Conjunctivitis and keratitis
- Keratitis sicca most prominent clinical feature

Physical Examination Findings

- Blepharospasm
- Conjunctival hyperemia
- Corneal lesions (opacity to ulceration)
- Gingivitis
- Stomatitis

CAUSES & RISK FACTORS

- Possible genetic predisposition in breeds with high incidence.
- Develops concurrently with other immune-mediated and auto-immune diseases.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of keratoconjunctivitis sicca—canine distemper, trauma, and drug toxicities.

- Keratoconjunctivitis sicca associated with other immune-mediated diseases—atopy, lymphocytic thyroiditis, polymyositis, systemic lupus erythematosus, rheumatoid arthritis, and pemphigoid diseases.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

- Hypergammaglobulinemia revealed by serum protein electrophoresis.
- Positive antinuclear antibody test.
- Positive lupus erythematosus cell test.
- Positive rheumatoid factor test.
- Positive indirect fluorescent antibody test for auto-antibodies.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Schirmer tear test (0–5 mm/min)

PATHOLOGIC FINDINGS

- Histopathologic changes in salivary glands—lymphoplasmacytic adenitis
- Conjunctival biopsy—reveals conjunctivitis



TREATMENT

- Directed at controlling keratoconjunctivitis sicca.
- Any concurrent disease must be medically managed.
- May include administration of anti-inflammatory or immunosuppressive drugs.
- Surgical management of keratoconjunctivitis sicca indicated in animals that fail to respond to medical treatment.



MEDICATIONS

DRUG(S)

- Topical tear preparations.
- Appropriate topical antibiotics for secondary bacterial infection.

- Immunosuppressive or anti-inflammatory drugs.

- For more aggressive medical treatment and surgical intervention, see Keratoconjunctivitis Sicca.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Use of topical steroids in patients with acute keratoconjunctivitis sicca may cause corneal ulceration and is, therefore, not recommended.



FOLLOW-UP

- Reexamine patients weekly until keratoconjunctivitis sicca controlled.
- Additional monitoring may be indicated to manage underlying or concurrent disease.
- Immunosuppressive drugs—monitor patients every other week for possible side effects.
- Prognosis variable and depends on existence of concurrent disease.



MISCELLANEOUS

SEE ALSO

Keratoconjunctivitis Sicca

Suggested Reading

Quimby FW, Schwartz RS, Poskitt T, et al. A disorder of dogs resembling Sjögren's syndrome. Clin Immunol Immunopathol 1979, 12:471–476.

Author Paul W. Snyder

Consulting Editor Alan H. Rebar

Skin Fragility Syndrome, Feline



BASICS

OVERVIEW

- A disorder of multifactorial causes characterized by extremely fragile skin.
- Tends to occur in old cats that may have concurrent hyperadrenocorticism, diabetes mellitus, excessive use of megestrol acetate or other progesterone compounds, or as a paraneoplastic syndrome.
- A small number of cats have no biochemical alterations.

SYSTEMS AFFECTED

- Skin/Exocrine
- Endocrine/Metabolic

SIGNALMENT

- Naturally occurring disease tends to be recognized in old cats.
- Iatrogenic cases have no age predilection.
- No breed or sex predilection.

SIGNS

Historical Findings

- Gradual onset of clinical signs.
- Progressive alopecia (not always present).
- Often associated with weight loss, lusterless coat, poor appetite, and lack of energy.

Physical Examination Findings

- Skin becomes markedly thin and tears with normal handling.
- Skin rarely bleeds upon tearing.
- Multiple lacerations (both old and new) may be noted on close examination.
- Partial to complete alopecia of the truncal region may be noted.
- Sometimes associated with "rat tail," pinnal folding, pot-belly appearance.

CAUSES & RISK FACTORS

- Hyperadrenocorticism—pituitary or adrenal dependent.
- Iatrogenic—secondary to excessive corticosteroid or progesterone drug administration.
- Diabetes mellitus—rare, unless associated with hyperadrenocorticism.
- Possibly idiopathic or paraneoplastic syndrome.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cutaneous asthenia.
- Feline paraneoplastic syndrome—pancreatic neoplasia, hepatic lipidosis, cholangiocarcinoma.

CBC/BIOCHEMISTRY/URINALYSIS

- Little diagnostic significance in most cases.
- Approximately 80% of cats with hyperadrenocorticism have concurrent diabetes mellitus (hyperglycemia, glucosuria).

OTHER LABORATORY TESTS

- ACTH-stimulation test—70% of cats with hyperadrenocorticism have an exaggerated response.
- LDDST—15–20% of normal cats may fail to decrease cortisol levels; typically unsuppressed with hyperadrenocorticism and non-adrenal illness.
- HDDST—normal cats show decreases in cortisol concentrations; typically decreased with non-adrenal illnesses; considered by many clinicians to be the best screening test for hyperadrenocorticism; unreliable for discriminating between adrenal tumors and pituitary-dependent causes of hyperadrenocorticism, because both conditions fail to show suppression.
- Endogenous ACTH levels—normal range for most labs is 20–100 pg/mL.

IMAGING

- Abdominal ultrasonography—adrenal masses are often small until end-stage disease.
- CT and MRI—small pituitary tumors may be difficult to visualize; MRI may be more successful.

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

Histopathology—suggestive, not diagnostic; epidermis and dermis are thin; attenuated collagen fibers are evident.



TREATMENT

- Underlying metabolic disease should be ruled-out.
- Many patients are debilitated and require supportive care.
- Surgical correction of the lacerations—difficult because the tissue cannot withstand pressure from sutures.
- Protect skin—clothing, reduce activities that can traumatize the skin, remove sharp edges from the environment, prevent damage from interaction with other animals.
- Discontinue exogenous corticosteroids if administered.
- Hyperadrenocorticism—adrenalectomy is the preferred treatment.
- Cobalt-60 radiation therapy—variable success in the treatment of pituitary tumors.



MEDICATIONS

DRUG(S)

- Medical management—may be useful for preparing patient for surgery and for minimizing postoperative complications (e.g., infections and poor wound healing).
- No known effective medical therapy for feline hyperadrenocorticism.
- o,p'-DDD (mitotane) 12.5–50 mg/kg PO q12h; response has been equivocal; side effects include anorexia, vomiting, and diarrhea.
- Ketoconazole (Nizoral) 10–15 mg/kg PO q12h; variable response; gastrointestinal disturbances, depression, fever, jaundice, and neurological signs commonly seen in cats.
- Metapyrone 65 mg/kg PO q12h; clinical improvement noted more often with this drug than the others.

CONTRAINdications/POSSIBLE INTERACTIONS

Hyperadrenocorticism—closely monitor diabetic cats; adjust insulin to prevent hypoglycemia when the cortisol levels fall.



FOLLOW-UP

Patients are often quite debilitated, making any form of treatment risky; close monitoring is required in all cases.



MISCELLANEOUS

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone
- CT = computed tomography
- HDDST = high-dose dexamethasone-suppression test
- LDDST = low-dose dexamethasone-suppression test
- MRI = magnetic resonance imaging
- o,p'-DDD = 1,1-(o,p'-dichlorodiphenyl)-2,2-dichloroethane

Suggested Reading

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Author Karen Helton Rhodes

Consulting Editor Alexander H. Werner

SMALL INTESTINAL DYSBIOSIS



BASICS

DEFINITION

• Small intestinal dysbiosis (SID) is a clinical syndrome caused by an alteration of the small intestinal microbiota. • Previously, a variety of different terms have been used to describe small intestinal dysbiosis: ◦ Small intestinal bacterial overgrowth (SIBO) has been defined as $> 10^4$ anaerobic and/or $> 10^5$ total bacterial colony-forming units (cfu)/mL in duodenal juice from dogs. However, these criteria are now controversial. ◦ Antibiotic-responsive diarrhea (ARD) has been used by several authors to describe patients that have diarrhea that responds to antibiotic therapy. Neither the type of bacteria nor the type of antibiotic that is effective has been defined for ARD. ◦ Tylosin responsive diarrhea (TRD) has been described by a group of clinicians in Finland. The term was coined based on the fact that several dogs with chronic diarrhea failed to respond to a variety of antibiotics or corticosteroids, but did respond to treatment with tylosin. • Currently, there is no consensus on the quantitative makeup of the gastrointestinal microbiota in healthy dogs or cats. • It should be emphasized that SID differs from colonization of the alimentary tract by known pathogenic bacteria (e.g., *Salmonella* spp., *Campylobacter jejuni*, enterotoxigenic *Clostridium perfringens*, enterotoxic *E. coli*, or others).

PATHOPHYSIOLOGY

• Bacteria are constantly ingested with food and/or saliva. • Host protective mechanisms prevent overgrowth of pathogenic or potentially pathogenic bacteria through gastric acid secretion, intestinal motility (peristalsis), secretion of antimicrobial substances in bile and pancreatic juice, and local enteric IgA production. • The ileocolic valve is a physiologic barrier between the large bowel, which is populated by large numbers of bacteria, and the less populated small bowel. • When these natural defense mechanisms fail and excessive numbers of certain bacterial species persist in the upper small intestine, they may cause pathology, even though they are not considered obligate pathogens. • Anaerobic bacteria (e.g., *Bacteroides* spp. and *Clostridium* spp.) have been considered to more likely cause pathology than many aerobic bacteria.

SYSTEMS AFFECTED

• Gastrointestinal—normal absorptive function is disrupted, resulting in loose stool and weight loss. • Hepatobiliary—the portal vein carries bacterial toxins and other substances to the liver, which may lead to hepatic changes.

GENETICS

- No genetic basis for SID has been identified. However, recent studies would suggest that histiocytic ulcerative colitis should be considered a type of dysbiosis of the large intestine. Since the majority of cases have been described in the boxer, genetic factors that predispose dogs of this breed to this type of dysbiosis are likely. • Certain canine breeds (e.g., German shepherd, Chinese Shar-Pei, and beagle dog) appear to be at an increased risk for SID.

INCIDENCE/PREVALENCE

Unknown

SIGNALMENT

Species

Dog and cat

Breed Predilections

Subjectively, German shepherd dog, Chinese Shar-Pei, and beagle appear to have an increased incidence.

Mean Age and Range

- Unknown. • Can be diagnosed in dogs and cats of any age (age range: < 1 year to > 8 years).

SIGNS

General Comments

Alterations in the gut microbiota can cause clinical signs of small intestinal disease, such as loose stool or diarrhea, weight loss, and/or others.

Historical Findings

- Chronic loose stools or diarrhea (small bowel or large bowel type diarrhea)—common. • Weight loss, despite a reasonable appetite—common. • Borborygmus and flatulence—common. • Vomiting—occasional/variable. • Clinical signs of the underlying disease process may be seen in cases of secondary SID. • Clinical signs may wax and wane or be continuous.

Physical Examination Findings

Unremarkable or evidence of weight loss and decreased body condition.

CAUSES

- Primary SID is probably uncommon, but a definitive cause of SID often remains undiagnosed and thus many dogs are diagnosed with idiopathic SID. • Secondary SID (more common): ◦ Altered small intestinal anatomy— inherited or acquired (e.g., congenital blind loop, partial obstructions, neoplasia, foreign body, intussusception, stricture, adhesion, or diverticulum). ◦ Altered intestinal motility—hypothyroidism, autonomic neuropathies. ◦ Exocrine pancreatic insufficiency (EPI)—approximately 70% of dogs with EPI have concurrent SID. ◦ Hypochlorhydria or achlorhydria—spontaneous or iatrogenic (e.g., proton-pump inhibitor treatment). ◦ Altered immune system-immunodeficiency,

decreased mucosal defense, and preexisting intestinal disease.

RISK FACTORS

Intestinal diseases that affect local defense mechanisms (e.g., inflammatory bowel disease [IBD], adverse food reactions, parasite infestation, others).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Secondary gastrointestinal disease (e.g., hepatic failure, renal failure, EPI, chronic pancreatitis, hypothyroidism, hypoadrenocorticism). • Primary gastrointestinal disease (i.e., infectious, inflammatory, neoplastic, mechanical, toxic, or other).

CBC/BIOCHEMISTRY/URINALYSIS

- Usually unremarkable.
- Hypoalbuminemia—an uncommon finding; when present, it suggests particularly severe intestinal disease and warrants an aggressive diagnostic and therapeutic approach.

IMAGING

Not useful for the diagnosis of primary SID. However, may reveal findings indicative of an underlying cause.

DIAGNOSTIC TESTS

Serum Cobalamin and Folate Concentrations

- Serum folate concentration may be increased—many bacterial species synthesize folate and an increased abundance of folate-producing bacterial species will lead to an overabundance of folic acid in the small intestine. • Serum cobalamin concentration may be decreased—many bacterial species compete with the host for dietary cobalamin. • The finding of an increased serum folate concentration and a decreased serum cobalamin concentration is suggestive, but not specific for SID in dogs. In addition, not all patients with SID show this pattern.
- Serum folate and cobalamin concentration is the only test for SID that is currently routinely available.

Qualitative and Quantitative Bacterial Culture of Small Intestinal Juice

- Aerobic and anaerobic quantitative culture of duodenal fluid has long been considered the “gold standard” for the diagnosis of SIBO in human patients. • Invasive—requires endoscopy or laparoscopy. Not practical and not routinely available. • Recent work would suggest the species of bacteria that comprise the small intestinal microbiota may be more important than bacterial numbers. • No standardized protocols have been established for sampling, handling, and culturing of duodenal juice, leading to high variability in bacterial counts.

SMALL INTESTINAL DYSBIOSIS

(CONTINUED)

Therapeutic Trial

- Treatment of patients with suspected SID with an antibiotic, a prebiotic, or a probiotic.
- Interpreting the results of a therapeutic trial may be difficult as more than one disease (e.g., IBD plus SID, dietary intolerance plus SID) may be present, and lack of a clinical response might lead to the incorrect conclusion that SID is absent; incorrect selection of the treatment that is trialed might also cause failure of a clinical response.

PATHOLOGIC FINDINGS

- No macroscopic findings upon exploratory laparotomy or endoscopy.
- Histopathology of small intestinal mucosal biopsies is typically unremarkable.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient medical management.
- SID can be managed with antibiotics, prebiotics, probiotics, or a combination thereof.
- Antibiotics: see below for medications
- Prebiotics: see below for diet.
- Probiotics: there has been a lot of interest in probiotic use for dogs and cats with chronic diarrhea, although little is known about the efficacy. Currently, because of quality issues with many products, only probiotics from major manufacturers can be recommended.
- Improvement may take a few days to several weeks.

NURSING CARE

- Usually none.
- Supportive care for emaciated or hypoalbuminemic patients

ACTIVITY

Unrestricted

DIET

- Highly digestible diet.
- A diet containing fructooligosaccharides has been shown to be beneficial in dogs with small intestinal dysbiosis.

S

CLIENT EDUCATION

- Some patients show clinical improvement within days.
- Some patients require weeks of therapy before demonstrating improvement—treat for 2–3 weeks before concluding that therapy is ineffective.
- Any concurrent or predisposing diseases (e.g., IBD, EPI, dietary intolerance/allergy, alimentary tract neoplasia, partial obstruction) must also be treated.
- Continuous or repeated treatment is often required.

SURGICAL CONSIDERATIONS

Only indicated for some underlying causes of SID (i.e., partial obstruction, diverticulum, or intestinal mass).



MEDICATIONS

DRUG(S) OF CHOICE

- Broad-spectrum, orally administered antibiotics effective against both aerobic and anaerobic bacteria are preferred.
- Tylosin (10–20 mg/kg PO q12h for 6 weeks) is the primary choice. Tylosin is usually used in a powder formulation that is marketed for use in poultry and pigs. Tylosin is administered in the food because of its bitter taste. It can be used long-term and is very safe and inexpensive. For small dogs and cats the drug should be reformulated into capsules. For larger dogs the dose can be approximated by using a teaspoon and administering the drug in food.
- Metronidazole (10–15 mg/kg PO q12h for 6 weeks) is used commonly in routine practice because of its activity against anaerobic bacteria. Metronidazole may also have immunomodulatory effects. However, metronidazole can have significant side effects.
- Dogs with SID may be cobalamin deficient, and parenteral supplementation of vitamin B₁₂ is indicated (250 µg (cats); 250–1,500 µg (dogs) SC); dose depending on body size; dose regimen is typically one dose weekly for 6 consecutive weeks and one dose a month later; serum cobalamin concentrations should be re-evaluated a month after the last dose to determine the need for continued supplementation).

PRECAUTIONS

- Metronidazole can be associated with gastrointestinal side effects and in rare cases with neurologic side effects.

ALTERNATIVE DRUG(S)

In dogs with EPI and SID, concurrent therapy for SID is only indicated if enzyme replacement alone does not resolve the diarrhea and/or lead to weight gain.



FOLLOW-UP

PATIENT MONITORING

- Body weight and, in hypoproteinemic patients, serum albumin concentrations are the most important parameters; improvement suggests effective therapy.
- Diarrhea should also resolve.
- If diarrhea persists despite improved body weight and/or increased serum albumin concentration, investigation for concurrent intestinal disease is indicated.

EXPECTED COURSE AND PROGNOSIS

Primary SID without complicating factors (e.g., IBD, lymphoma)—prognosis with appropriate therapy is usually good, although relapses can be seen following cessation of antibiotic therapy.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- SID has been suspected as a cause of IBD in some patients.
- Consider the possibility of concurrent EPI.

PREGNANCY/FERTILITY/BREEDING

Avoid oxytetracycline or metronidazole, especially during early pregnancy.

SYNOMYMS

SIBO, ARD, or TRD may be used synonymously by some authors.

SEE ALSO

- Diarrhea, Chronic—Cats
- Diarrhea, Chronic—Dogs
- Exocrine Pancreatic Insufficiency
- Inflammatory Bowel Disease
- Lymphoma—Cats
- Lymphoma—Dogs

ABBREVIATIONS

- ARD = antibiotic responsive diarrhea
- cfu = colony-forming units
- EPI = exocrine pancreatic insufficiency
- IBD = inflammatory bowel disease
- SIBO = small intestinal bacterial overgrowth
- SID = small intestinal dysbiosis
- TRD = tylosin responsive diarrhea

INTERNET RESOURCES

www.vetmed.tamu.edu/gilab

Suggested Reading

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Authors Jan S. Suchodolski and Jörg M. Steiner

Consulting Editor Stanley L. Marks



Client Education Handout
available online

SMOKE INHALATION



BASICS

OVERVIEW

- Injury occurs as a result of direct heat damage to the upper airway and nasal mucosa. Inhalation of other toxins directly irritates the airway, and particulate matter adheres to the airways and alveoli. Carbon monoxide decreases tissue oxygen delivery by preferentially binding to hemoglobin.
- Extent of damage depends on the degree and duration of exposure and the material that was burning.
- Can have serious lung injury with little cutaneous or oral evidence of burning.
- Lung reaction—initially bronchoconstriction, airway edema, mucus production and airway occlusion; then an inflammatory response, necrotizing tracheobronchitis, and pulmonary fluid accumulation owing to increased capillary permeability.
- Most show progression of lung dysfunction in the initial 2–3 days.
- Superimposed bacterial infections—common cause of morbidity late in the disease.

SIGNALMENT

Dog and cat

SIGNS

- Historical findings consistent with exposure.
- Smoky odor.
- Tachypnea and increased depth of respiration.
- Inspiratory effort suggests upper airway obstruction by edema.
- Postural adaptations to hypoxemia.
- Mucous membranes can be cherry red (from carbon monoxyhemoglobin), pale, or cyanotic.
- Auscultation of wheezes, harsh bronchovesicular sounds, or crackles.
- Cough
- Burned or shriveled whiskers, conjunctival edema, corneal ulcers.
- Neurologic signs can indicate carbon monoxide or cyanide toxicity.
- Cardiac arrhythmias and hypotension can be seen secondary to hypoxemia, smoke and carbon monoxide inhalation, and burn injuries.

CAUSES & RISK FACTORS

Exposure to smoke, usually from being trapped in a burning building.



DIAGNOSIS

CBC/BIOCHEMISTRY/URINALYSIS

- Neutropenia—poor prognostic sign; suggests neutrophil sequestration in the lungs.
- Thrombocytopenia—suggests platelet sequestration or consumption.
- Biochemistry profile—evidence of hypoxic damage to other organ systems can be present.

IMAGING

Thoracic radiographs—establish a baseline; findings vary from normal to a bronchointerstitial or alveolar pattern.

DIAGNOSTIC PROCEDURES

- Bronchoalveolar lavage or tracheal wash for cytology examination and culture—perform for suspected superimposed bacterial tracheobronchitis or pneumonia; results usually reveal an acute suppurative reaction with excessive mucus, neutrophils, and alveolar macrophages; intracellular bacteria indicate concurrent infection.
- Pulse oximetry or arterial blood gases can confirm hypoxemia; of less value with carbon monoxide exposure.
- Bronchoscopy—can demonstrate the severity of airway damage.



TREATMENT

- Initial management—stabilize respiratory function; establish patent airway; severe upper airway edema or obstruction can require intubation or temporary tracheostomy.
- Oxygen—administer immediately to displace carbon monoxide from hemoglobin; use the highest available concentration for 2–4 hours (or longer); after elimination of carbon monoxyhemoglobin, supplement as needed.
- Fluid administration—can be required but should be conservative to minimize pulmonary edema; use of synthetic colloids in animals with hypoproteinemia is controversial but is sometimes necessary for stabilization; cases with extensive dermal burns have high fluid requirements due to considerable loss of fluid and protein.
- Nebulization of saline with coupage—facilitates clearance of respiratory secretions.
- Mechanical ventilation needed in severe cases.
- Nutritional support—maintain body condition and immune status.



MEDICATIONS

DRUG(S)

- Suspected bacterial infection—broad-spectrum antibiotics after bacterial culture has been obtained.
- Bronchodilators—may improve respiratory function if severe bronchoconstriction occurs, especially in cats (e.g., terbutaline 0.01 mg/kg IV, IM, SC). Inhaled beta-agonists can also be beneficial in these patients.
- Single early, anti-inflammatory dose of corticosteroids or aerosolized corticosteroids may decrease airway edema though there is no conclusive evidence of efficacy.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Diuretics—decrease intravascular volume without a major beneficial effect.
- Corticosteroids—use only once and if absolutely necessary; can predispose the patient to bacterial infection.



FOLLOW-UP

PATIENT MONITORING

- Respiratory rate and effort, mucous membrane color, heart rate and pulse quality, lung auscultations, and PCV/TS for 24–72 hours.
- Repeat radiographs in 48 hours—ensure condition is resolving; monitor for bacterial pneumonia.
- Pulse oximetry and arterial blood gas analysis—to monitor hypoxemia and response to therapy.

POSSIBLE COMPLICATIONS

- Bacterial tracheobronchitis or pneumonia.
- Profound, generalized pulmonary inflammatory response or severe systemic inflammatory response syndrome—can develop ARDS. Bronchiectasis can develop secondary to airway injury and impaired mucociliary clearance.
- Severe cases can develop late (3–10 days after exposure) neurologic sequelae (seizures, cerebral edema) secondary to carbon monoxide toxicity.

EXPECTED COURSE AND PROGNOSIS

- Most patients deteriorate during the initial 24–48 hours after smoke exposure then gradually improve, unless bacterial pneumonia or ARDS develops.
- Severe burns or organ injury—poor prognosis.



MISCELLANEOUS

ABBREVIATIONS

- ARDS = acute respiratory distress syndrome
- PCV = packed cell volume

Suggested Reading

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SNAKE VENOM TOXICOSIS—CORAL SNAKES



BASICS

OVERVIEW

- Two clinically important species in North America—*Micruurus fulvius*, eastern coral snake (North Carolina to the north; southern Florida to the south; west of the Mississippi River) and *Micruurus tener*, Texas coral snake (west of Mississippi; in Arkansas, Louisiana, and Texas).
- Family Elapidae—fixed front fangs.
- Color pattern—bands fully encircling the body; red, yellow, and black; distinguished from the harmless tri-colored king snake (*Lampropeltis elapsoides*) by the arrangement of the bands: if yellow (caution) and red (danger) color bands touch, then stay clear; relatively small head; black snout; round pupils.

Bites

- Relatively uncommon due to snake's reclusive behavior and nocturnal habits.
- Often occur on the lip. Snakes remain attached due to chewing action.
- Distinct fang marks may not be obvious.
- Primary cause of death—respiratory collapse.
- Envenomations by *M. tener* seem to be less severe than *M. fulvius*.

SIGNALMENT

Dogs and cats

SIGNS

- Onset of clinical signs may be delayed several hours (up to 18 hours).
- Localized signs generally absent.
- Generalized weakness and ataxia.
- Bulbar paralysis—affecting cranial motor nerves, respiratory tract, and skeletal muscles; acute flaccid quadriplegia.
- Salivation—caused by dysphagia.
- Dyspnea.
- Dysphonias.
- Hyporeflexive spinal reflexes.
- Seizures.
- Urinary incontinence.

CAUSES & RISK FACTORS

- Size of the snake
- Size and duration of bite



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Myasthenia gravis
- Botulism
- Polyradiculoneuritis

- Tick bite paralysis
- Black widow spider bite (*Latrodectus* species)

CBC/BIOCHEMISTRY/URINALYSIS

- Hemolysis—dogs only
- RBC burring
- May note high creatine kinase
- Hemoglobinuria—dogs only

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- First aid—generally avoid; most effective measure is rapid transport to a veterinary facility for antivenin administration; Australian technique for Elapid bites is a pressure wrap of the bitten limb with ace-type bandage to decrease blood flow and venom uptake.
- CAUTION: do not wait for onset of clinical signs to initiate treatment.
- Inpatient—hospitalize for a minimum of 48 hours.
- Monitor CNS and respiratory function closely for 24 hours.
- Specific antivenin is extremely limited for *M. fulvius* envenomations in the USA and typically not accessible for veterinary use. However, protective cross-reactivity occurs with the following antivenins: Coralmyn [Fab₂ equine origin] (Instituto Bioclon, Mexico), Costa Rican coral snake antivenin (Instituto Clodomiro Picado, Costa Rica), and Australian tiger snake *Notechis scutatus* (CSL Limited, Parkville, Victoria, Australia). Expense may be a consideration.
- If antivenin unavailable—provide ventilatory support for several days in a critical care facility.



MEDICATIONS

DRUG(S)

- M. fulvius* reactive antivenin (see "Treatment")—indicated if the history includes recent coral snake interaction; evidence of puncture wounds; clinical signs consistent with coral

snake envenomation; administer 1–2 vials; additional vials may be necessary (technique same as for pit viper antivenin).

- Broad-spectrum antibiotics are not routinely recommended and should only be used if there is indication of infection.
- Neostigmine — may be useful to reverse NM blockade if antivenin not available. Has been used successfully to treat *M. frontalis* envenomation in Brazil.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Corticosteroids—not indicated.
- Observe precautions outlined for pit viper antivenin administration (see Snake Venom Toxicosis—Pit Vipers).



FOLLOW-UP

- Marked clinical signs may last 1–1.5 weeks.
- Full recovery may take months as receptors regenerate.



MISCELLANEOUS

SEE ALSO

Snake Venom Toxicosis—Pit Vipers

ABBREVIATION

- RBC = red blood cell
- CNS = central nervous system
- NM = neuromuscular

Suggested Reading

Pérez ML, Fox K, Schaer M. A retrospective evaluation of coral snake envenomation in dogs and cats: 20 cases (1996–2011). J Vet Emerg Crit Care 2012, 22(6):682–689.

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Consulting Editor Lynn R. Hovda

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SNAKE VENOM TOXICOSIS—PIT VIPERS



BASICS

OVERVIEW

- Pit vipers—*Crotalus* spp. (rattlesnakes), *Sistrurus* spp. (pigmy rattlesnakes and massasauga), and *Agiistrodon* spp. (copperheads and cottonmouth water moccasins); retractable fangs; heat-sensing pit between the nostril and eye; triangle-shaped head.
- Range—throughout the United States (not found in Alaska, Hawaii, Maine).
- Toxicity—considered hemotoxic; several species have subpopulations with lethal neurotoxic components (e.g., Mohave rattlesnake); general ranking of severity: (1) rattlesnakes, (2) moccasins, (3) copperheads.
- Venom—enzymes: hyaluronidase and phospholipase A (cause local tissue injury) and others that interfere with the coagulation cascade (cause major coagulation defects); non-enzymatic polypeptides: affect the cardiovascular and respiratory systems.
- Bite—85% of victims have altered laboratory values and clinically important swelling; severe hypotension from pooling of blood within the splanchnic (dogs) or pulmonary (cats) vessels; fluid loss from the vascular compartment secondary to severe peripheral edema.
- About 20–30% crotalid bites considered “dry bites” with little if any venom deposited and no associated toxicity.

SIGNALMENT

Dogs and cats

SIGNS

General Comments

May be delayed for 8 hours after envenomation.

Historical Findings

- Outdoors, rural setting, indigenous snake.
- Owner saw bite or heard snake.

Physical Examination Findings

- Puncture wounds on head and forelimbs in most animals
- Local tissue swelling and pain surrounding bite site
- Bruising, with possible necrosis and sloughing of bite site tissue
- Ecchymosis and petechiation of tissues and mucous membranes
- Hypotension and shock
- Tachycardia
- Shallow respiration
- Depression, lethargy, and muscle weakness
- Nausea and excessive salivation

CAUSES & RISK FACTORS

Snake-Associated

- Toxic peptide fraction:enzyme fraction ratio—higher in spring and lower in fall (not well documented); high in very young snakes.
- Amount of venom production since last bite.
- Size, fang length, aggressiveness, and motivation of snake.

Victim-Associated

- Bite site—bites to tongue and torso are of major concern.
- Size of victim.
- Elapsed time between bite and initiation of treatment.
- Activity level of victim after the bite—activity increases absorption of venom.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Angioedema secondary to insect envenomation (spider, scorpion, large centipede)
- Blunt trauma
- Penetrating wound
- Animal bite
- Penetration of foreign body
- Draining abscess

CBC/BIOCHEMISTRY/URINALYSIS

- Hemoconcentration
- Bursting of RBCs within first 24 hours
- Thrombocytopenia
- Hypokalemia
- Elevated CK
- Hematuria or myoglobinuria

OTHER LABORATORY TESTS

Clotting tests—reduced platelets and fibrinogen, may note prolonged ACT, PT, and PTT; may note elevated FDPs.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Clinical evaluation of bite for edema, ecchymosis, fang punctures, pain.
- ECG—may detect ventricular arrhythmia, especially in severely depressed patients.



TREATMENT

- Tissue reaction around the bite site—not a reliable indicator of systemic toxicity.
- Bite location—may affect uptake of venom; bites to tongue and torso are of major concern. Distal limb bites may result in significant tissue damage and compromise limb function.

- First aid measures—minimize activity, calm patient, provide analgesia if indicated; transport quickly to a veterinary facility.

- Antivenin is only proven specific treatment (see “Medications”). Expense may be an important factor.

- Intravenous fluids—correct hypotension.
- Repeat coagulation profile after administration of antivenin for comparison to earlier labs. Recurrence of clinical signs or coagulation abnormalities can occur with any antivenin. If initial coagulopathy resolved with antivenin administration, recurrence can occur within the next few days, although rarely as severe as initial. There are no documented cases of clinical bleeding with subsequent coagulopathy; however, the clinician should be aware of the possibility.



MEDICATIONS

DRUG(S)

- Analgesics to reduce pain and stress.
- Antivenin, (VenomVet™—Crotalidae polyvalent, equine origin, Fab2). Injectable solution, no need to reconstitute. Mix each vial of antivenin with 100–150 mL of a crystalloid fluid and administer IV slowly while taking into consideration the patient’s weight and overall fluid load. Infuse over 30 minutes–1 hour. For use in dogs only.
- Antivenin (Crotalidae polyvalent, equine origin, whole IgG)—1 vial mixed with 200 mL crystalloid fluids administered slowly IV with careful monitoring of the inner pinna for onset of hyperemia (indicator of possible allergic reaction), reactions much more common due to extraneous proteins.
- Antivenin (Crofab, polyvalent, ovine Fab₁) has completed clinical trials in dogs and successfully used in cats. Purified antibody fragments provide much less possibility for reactions. Has been submitted for USDA approval in animals. Only approved pit viper antivenin in United States for humans.
- Antivenin (Antivipmyn, polyvalent, equine Fab₂—Instituto Bioclón, Mexico) is in clinical trials for dogs. Purified antibody particles much less possibility for reactions.
- Always flush antivenin vial after initial removal of antivenin, second flush can increase antivenin collection by 30%.
- Allergic reaction—stop antivenin; give diphenhydramine; after 5 minutes, restart antivenin infusion at a slower rate.
- Antibiotics—Infection is rare and antibiotics not recommended unless there is evidence of infection.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- CAUTION: in animals receiving beta-blockers, the onset of anaphylaxis may be

SNAKE VENOM TOXICOSIS—PIT VIPERS

(CONTINUED)

masked; therefore, the condition may be more advanced once recognized and more difficult to treat effectively.

- Corticosteroids—of no value.
- DMSO—enhances uptake and spread of venom.
- Heparin—do not use.
- Rattlesnake vaccine for dogs is currently marketed. Its efficacy is unknown; only anecdotal evidence at this time. Not recommended until peer-reviewed efficacy data available.

**FOLLOW-UP**

- Repeated laboratory analysis—6 hours after admission to hospital.
- Clinical signs—may last 1–1.5 weeks.

**MISCELLANEOUS****ABBREVIATIONS**

- ACT = activated clotting time
- CK = creatine kinase
- DMSO = dimethyl sulfoxide
- ECG = electrocardiogram
- FDP = fibrin degradation products
- PT = prothrombin time
- PTT = partial thromboplastin time
- RBC = red blood cell

Suggested Reading

Julius TM, Kaelble MK, Leech EB, et al. Retrospective evaluation of neurotoxic

rattlesnake envenomation in dogs and cats: 34 cases (2005–2010). *J Vet Emerg Crit Care* 2012, 22(4):460–469.

Peterson ME, Matz M, Seibold K, et al. A randomized multicenter trial of Crotalidae polyvalent immune F_{ab} antivenom for the treatment of rattlesnake envenomation in dogs. *J Vet Emerg Crit Care* 2011, 21(4):335–345.

Pritchard JC, Birkenheuer AJ, Hanel RM, et al. Copperhead (*Agkistrodon contortrix*) envenomation of dogs: 52 cases (2004–2011). *J Am Anim Hosp Assoc* 2014, online 6131, doi 10.5326.

Author Michael E. Peterson

Consulting Editor Lynn R. Hovda

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SNEEZING, REVERSE SNEEZING, GAGGING



BASICS

DEFINITION

- Sneezing—a normal protective expiratory reflex that serves to expel air and material through the nasal cavity; commonly associated with nasal discharge.
- Reverse sneezing—a normal protective, repetitive inspiratory reflex that serves to remove irritants from the nasopharynx (also termed the aspiration reflex).
- Gagging (also called retching)—a normal protective reflex to clear secretions from the larynx, proximal trachea, pharynx, or esophagus; often misinterpreted as vomiting by owners.

PATHOPHYSIOLOGY

- Irritation of submucosal irritant receptors; various stimuli (infectious, parasitic, irritant, mechanical—especially accumulated secretions) will elicit these reflexes depending on where the irritation is applied.
- Sneezing—nasal mucosal irritation; frequency often diminishes with chronic disease.
- Reverse sneezing—caudodorsal nasopharyngeal mucosal irritation.
- Gagging—cervical tracheal (or laryngeal) mucosal irritation; oropharyngeal and esophageal mucosal irritation may also be involved. May follow a coughing episode as secretions are brought through the larynx or precede coughing due to aspiration into the trachea.

SYSTEMS AFFECTED

- Respiratory—frequently associated with infectious or inflammatory conditions involving the upper respiratory tract.
- Gastrointestinal—gagging may also be caused by swallowing, esophageal, or gastric disorders.

GENETICS

N/A

INCIDENCE/PREVALENCE

These are common, normal reflexes in both dogs and cats in response to mucosal irritation.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

- Any breed dog or cat may be affected.
- These reflexes per se are not associated with any specific age but rather with the conditions that cause them; examples include:
 - Young animals—infestation, cleft palate, primary ciliary dyskinesia.
 - Older animals—nasal tumors, dental disease.
- Acute sneezing in dogs is most often caused by a nasal foreign body, while in cats it is most often associated with acute viral rhinitis.

SIGNS

- Head and mouth position may help owners determine which of these reflexes are present.
- Sneezing typically results in sudden, explosive expiratory effort(s) with the mouth closed and head thrown downward; may result in the animal's nose hitting the ground.
- Reverse sneezing is a sudden, often paroxysmal, noisy, inspiratory effort with the head pulled back, mouth closed, and lips sucked in.
- Gagging is an expiratory effort; typically with the head and neck extended and mouth held open; usually ends with the animal swallowing (with little to nothing expelled).

CAUSES

- Any mucosal irritation or inflammation can elicit these reflexes. The same agent in the nasal cavity might elicit a sneeze, but when placed into the nasopharynx would result in a reverse sneeze. The reflex therefore localizes the site of irritation for further evaluation.
- Common nasal causes of sneezing and reverse sneezing include excess nasal secretions (see Nasal Discharge chapter), foreign body (especially if signs are acute and violent in onset), neoplasia, and parasites; dogs—*Pneumonyssoides*; dogs and cats—*Cuterebra*, *Eucoleus* (*Capillaria*), *Linguatula*.
- Extranasal diseases resulting in reverse sneezing, sneezing (and nasal discharge) as secretions may be forced up into the nasopharynx and the nasal cavities—pneumonia, megaesophagus, chronic vomiting, cricopharyngeal dysphagia, or achalasia.
- Reverse sneezing may be idiopathic, especially in small-breed dogs. In that case, there are no other associated clinical signs.
- Causes of gagging include:
 - Secretions being coughed up from the lower airways and into the larynx or cervical trachea.
 - Pharyngeal/laryngeal dysfunction resulting in airway aspiration due to loss of motor and/or sensory function that normally protects the airway.
 - Vomiting from esophageal and gastrointestinal disease.

RISK FACTORS

- Poorly vaccinated animals may develop nasal infection/inflammation and sneezing (kittens with upper respiratory infections, puppies with canine infectious respiratory disease complex).
- Productive coughing may produce excess secretions that can be propelled into the nasopharynx and lead to reverse sneezing.
- Chronic dental disease can cause rhinitis and either sneezing or reverse sneezing.
- Nasal mites may cause both reverse sneezing and sneezing in dogs (but not cats); in the United States, incidence is inversely proportional to heartworm preventive usage.

- Nasal foreign bodies elicit sneezing and/or reverse sneezing depending on their location; outdoor animals, especially hunting dogs, perhaps more at risk.
- Reverse sneezing is often associated with excitement.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Similar Signs

- Differentiate regular sneezing (occurs on expiration) from reverse sneezing (occurs on inspiration and localizes the site of irritation to the nasopharynx).
- Gagging is often misinterpreted as vomiting.

CBC/BIOCHEMISTRY/URINALYSIS

Results not specific of any particular cause of sneezing, reverse sneezing, or gagging.

OTHER LABORATORY TESTS

These reflexes are secondary to another process that has irritated and stimulated the mucosal surfaces in one or more areas. Diagnostic testing is designed to determine that specific cause.

IMAGING

- Sneezing and reverse sneezing—skull radiographs or CT.
- Gagging—chest radiographs and bronchoscopy may be required to look for excessive lower airway secretions and pneumonia.

DIAGNOSTIC PROCEDURES

- Sneezing and reverse sneezing—anterior and posterior rhinoscopy, periodontal probing.
- Gagging—determine presence or absence of gag reflex, laryngoscopy to determine intrinsic function (use doxapram to stimulate respiration).

PATHOLOGIC FINDINGS

Nonspecific inflammation can be found in the nasal cavity or nasopharynx.



TREATMENT

APPROPRIATE HEALTH CARE

Removal of the inciting mucosal irritation, where/when possible, will result in relief from these reflexes.

NURSING CARE

Outpatient therapy generally indicated, except perhaps following rhinoscopic biopsy.

ACTIVITY

Exercise and activity should be restricted after rhinoscopic biopsies to prevent excessive bleeding.

DIET

N/A

SNEEZING, REVERSE SNEEZING, GAGGING

(CONTINUED)

CLIENT EDUCATION

- Educate clients so they understand these are normal reflexes. Diagnostic testing is required to determine the underlying cause and to allow appropriate treatment.
- Close contact with other animals should be limited until treatment for the underlying cause (if infectious) is completed.
- Episodes of paroxysmal reverse sneezing may be lessened by inducing swallowing (rubbing the throat, giving water) or breath holding (cover nose and mouth).

SURGICAL CONSIDERATIONS

- Depending on the underlying cause, anesthesia for surgery or endoscopy may be needed to remove an abscessed tooth or a foreign body causing sneezing/reverse sneezing.
- Use surgery for laryngeal disease with caution when gagging is prominent due to an increased risk of aspiration pneumonia when concurrent esophageal dysfunction is present.



MEDICATIONS

DRUG(S) OF CHOICE

- There is no drug that specifically suppresses these reflexes; treatment is directed at the underlying irritant.
- Nasal bacterial infections (secondary to foreign body, dental disease, tumor, etc.) are best treated with antibiotics directed against gram-positive bacteria (most common).
- Nasal mites are treated with ivermectin (200–300 µg/kg PO or SC weekly for 3 weeks), selamectin (6–24 mg/kg applied topically every 2 weeks for 3 doses), or milbemycin (in collies and similar breeds at 0.5–1 mg/kg PO weekly for 3 weeks). All dogs in the household should be treated to prevent reinfection.
- When no underlying nasal condition is found to explain sneezing, treatment for nasal mites is recommended. If no improvement is observed, long-term, nonspecific treatment

with doxycycline and piroxicam (0.3 mg/kg PO daily) may be tried.

- Lower airway diseases with excess secretions are treated with antibiotics if bacterial infection is confirmed; gram-negative bacteria are most common.
- For nonspecific airway inflammation use an anti-inflammatory, prednisolone (1–2 mg/kg q12–24h) or piroxicam (0.3 mg/kg PO q24–48h) if no infection is confirmed.
- There is no treatment for gagging secondary to sensory loss in the larynx with recurring aspiration; elevation of food and water bowls is recommended. Altering the consistency of food offered may also be helpful.

CONTRAINdications

- Ivermectin in collies and similar breeds.
- Use of piroxicam concurrently with other NSAIDs or corticosteroids, as well as in patients with renal insufficiency.

PRECAUTIONS

The safety of most recommended drugs has not been established in pregnant animals.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Decongestants (ephedrine, topical vasoconstrictors) or antihistamines may reduce secretions and sneezing in some cases.



FOLLOW-UP

PATIENT MONITORING

Expect reduction in sneezing/reverse sneezing with appropriate therapy.

PREVENTION/AVOIDANCE

Limit access to foreign bodies, provide adequate dental care.

POSSIBLE COMPLICATIONS

If gagging is secondary to laryngeal sensory loss, serious aspiration pneumonia may develop.

EXPECTED COURSE AND PROGNOSIS

- Nasal mites should respond to treatment within 3 weeks.
- Sneezing and reverse sneezing secondary to foreign material resolve quickly after removal of the foreign body.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Nasal Discharge
- Rhinitis and Sinusitis

ABBREVIATIONS

- CT = computed tomography
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

Doust R, Sullivan M. Nasal discharge, sneezing and reverse sneezing. In: King LG, ed., *Textbook of Respiratory Disease in Dogs and Cats*. Philadelphia: Saunders, 2004, pp. 17–29.

McKiernan BC. Sneezing and nasal discharge. In: Ettinger SJ, Feldman EC, eds., *Textbook of Veterinary Internal Medicine*, 4th ed. Philadelphia: Saunders, 1994, pp. 79–85.

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Client Education Handout
available online

SOFT TISSUE SARCOMA



BASICS

DEFINITION

- A mesenchymal neoplasm arising in connective tissues.
- Soft tissue sarcomas are a heterogeneous group of different mesenchymal tumors demonstrating similar pathologic features and clinical behavior. Examples of tumors in this group include fibrosarcoma, leiomyosarcoma, peripheral nerve sheath tumor, and myxosarcoma.
- It is important to note that tumors of hematopoietic or lymphoid origin such as hemangiosarcoma are not included within the STS group.
- Benign and malignant histologic STS can arise; this chapter will focus on malignant STS.

PATOPHYSIOLOGY

- Tumors can arise in connective tissues in any anatomic location.
- Locally invasive behavior is typical with tumor extension beyond visible margins.
- Tumors often have low to moderate metastatic potential.

SYSTEMS AFFECTED

- Skin—STS most commonly arise from skin or subcutis.
- Musculoskeletal—STS may arise from muscle, fascial and fibrous tissues.
- Nervous—STS can originate from neurovascular structures.
- Respiratory—STS metastasize hematogenously and can metastasize to the lungs.
- Hemic/Lymph/Immune—lymph nodes are rare sites of metastasis.

GENETICS

There are no specific breed predilections that would suggest genetic predisposition.

INCIDENCE/PREVALENCE

- STS constitute 7% and 15% of skin and subcutaneous tumors in the cat and dog respectively.
- Incidence annually around 17 per 100,000 cats at risk; 35 per 100,000 dogs at risk.

SIGNALMENT

Species

Dog and cat

Breed Predilections

None identified but large-breed dogs have tended to be overrepresented.

Mean Age and Range

- Dogs—middle-aged, range 2–15 years. An exception is rhabdomyosarcoma of the bladder that often arises in younger dogs.
- Cats—middle-aged, range 1.4–18.8 years.

Predominant Sex

No predilection

SIGNS

Historical Findings

- Typically slow-growing, non-painful, fluctuant to firm mass (weeks to months).
- Rapid growth uncommon unless high grade.
- Signs depend on location and local structures affected by tumor presence or invasion.
- Tumors arising in the abdomen may elicit signs due to compression of the GI tract and could include vomiting and/or diarrhea, anorexia, and weight loss. Additionally signs of intestinal obstruction and occasionally perforation can occur with GI leiomyosarcoma.
- Urinary signs of hematuria and dysuria may be seen in young dogs with bladder rhabdomyosarcoma.
- Peripheral nerve sheath tumors affecting the brachial or lumbosacral plexus can cause signs of lameness and pain, muscle atrophy, limb weakness progressing to paralysis.
- Signs of hypoglycemia such as weakness, collapse, and seizures can occur with leiomyoma or leiomyosarcoma.

Physical Examination Findings

- Soft tissue mass that is soft, fluctuant, or firm on palpation.
- Often adhered to underlying tissue.
- Non-painful unless ulcerated or invading into muscles or nerves.

CAUSES

- *Dogs*—STS have been documented following radiation therapy, trauma, orthopedic implants, foreign bodies, and the parasite *Spirocerca lupi*.
- *Cats*—STS have arisen at sites of previous injections including vaccines.

RISK FACTORS

See above under "Causes"



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Abscess
- Cutaneous tumors such as adnexal tumors, basal cell tumors and mast cell tumors
- Fungal infection with granuloma formation

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal.
- Hypoglycemia can arise as a paraneoplastic syndrome in dogs with leiomyoma or leiomyosarcoma.

OTHER LABORATORY TESTS

N/A

IMAGING

- Three-view thoracic radiographs are recommended before treatment as the lungs are a common site of metastasis for STS.
- Imaging of the local extent of tumor may be indicated to plan surgery or radiation

treatment if the tumor is adherent to underlying structures. Contrast CT or MRI can be used to determine extent of disease and to optimize treatment planning.

- Abdominal ultrasound may be indicated for diagnosis of intra-abdominal STS and to allow assessment of liver, spleen, and abdominal lymph nodes.

DIAGNOSTIC PROCEDURES

- Fine-needle aspiration and cytology help to rule out other differential diagnoses and may provide tentative diagnosis but a non-diagnostic sample is possible as cells do not always exfoliate well.
- Incisional biopsy and histopathology is essential to confirm diagnosis, determine grade of the tumor, and plan surgical approach.
- Regional lymph node evaluation (cytology or histopathology) is indicated for assessment of enlarged regional lymph nodes and for high-grade tumors to confirm or deny presence of regional metastases.

PATHOLOGIC FINDINGS

Dogs

- Over 20 different histopathologic subtypes of STS exist; histologic distinction between tumor types is not necessary given the similarities in biologic behavior.
- Histologic grading based on differentiation, number of mitotic figures per 10 high power fields and percentage necrosis.
 - Grade I (low grade)
 - Grade II (intermediate grade)
 - Grade III (high grade) representing the most biologically aggressive grade.

Cats

- Some similarities between histopathologic subtypes compared to dogs. Peripheral nerve sheath tumors are rare in cats.
- Vaccine or injection site sarcomas have a more aggressive histologic appearance compared to other sarcomas.



TREATMENT

NURSING CARE

N/A

CLIENT EDUCATION

Early aggressive surgical management of STS is recommended for the best outcomes in both cats and dogs.

SURGICAL CONSIDERATIONS

- Early, aggressive, *en bloc* surgical excision is the treatment of choice. Conventional recommendations are 3 cm margins and 1 fascial plane deep (2 fascial planes deep for feline injection site sarcoma).
- Microscopically, cancer cells extend far beyond gross tumor borders.
- Pseudocapsule composed of compressed cancer cells is common.

SOFT TISSUE SARCOMA

(CONTINUED)

- The tumor should be excised *en bloc*; if it is peeled out, a healthy bed of cancer cells is left behind and can lead to tumor regrowth.
- Submit the entire sample to a pathologist for surgical margin evaluation; applying ink to surgical borders is advised to thoroughly evaluate margins.
- Toe or limb amputation may be necessary with large tumors that may be otherwise unresectable.
- Rib resection or abdominal wall resection may be required for tumors of the trunk.
- The first surgery usually provides the best opportunity for local tumor control.

RADIATION THERAPY

Dogs

Radiation therapy should be considered an option when complete surgical excision is not possible and can be applied on microscopic disease (postoperatively, fractionated) or on gross disease (hypofractionated).

Cats

Given the high rate of recurrence with feline injection site sarcoma following complete surgical resection, fractionated radiation therapy should be considered.



MEDICATIONS

DRUG(S) OF CHOICE

Dogs

- Doxorubicin-based chemotherapy is not consistently reported as beneficial but is often recommended after excision of a high-grade (grade III) tumor.
- Doxorubicin alone (1 mg/kg for small dogs or 30 mg/m² for medium and large dogs, IV, 5 doses q14–21 days).
- Low-dosage (or metronomic) cyclophosphamide chemotherapy (10 mg/m² PO q48h) in combination with piroxicam (0.3 mg/kg PO q24–48h) may help delay local recurrence when the tumor is incompletely resected.

Cats

- Role of postoperative chemotherapy in cats with STS is unclear. Chemotherapy treatment may improve local disease control but has minimal effect on survival in cats following wide surgical excision or RT.
- Doxorubicin alone (1 mg/kg IV q3 weeks for 5 doses).

CONTRAINDICATIONS AND PRECAUTIONS

- Doxorubicin—is cardiotoxic and should be avoided in dogs with underlying cardiac disease as cardiac failure can result. This drug is nephrotoxic in cats and should be avoided in cats with underlying renal disease. This drug is myelosuppressive in both dogs and cats and possesses vesicant properties. Severe local tissue necrosis can occur if extravasation occurs.
- Cyclophosphamide—can result in hemorrhagic cystitis. Monitor for signs of hematuria and pollakuria; discontinue medication if this occurs.

POSSIBLE INTERACTIONS

- Doxorubicin—none
- Cyclophosphamide—none

ALTERNATIVE DRUGS

Analgesic therapy should be administered as needed if pain or discomfort is present.



FOLLOW-UP

PATIENT MONITORING

Patient should be monitored for local regrowth and distant metastases with repeat physical examination and thoracic radiographs every 3 months for the first year, then every 6 months thereafter.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Surgical complications including infection or incisional dehiscence.
- Chemotherapy-related myelotoxicity, cardiotoxicity (dogs) or nephrotoxicity (cats).

EXPECTED COURSE AND PROGNOSIS

- Local recurrence, metastasis, and overall survival time is greatly affected by histologic grade as determined by an anatomic pathologist. Other factors that increase the risk of tumor recurrence are large tumor size at surgery (> 5 cm) and incomplete surgical margins.
- Cure from disease is possible with low and intermediate grade STS with treatment with wide surgical resection or surgery and adjuvant RT with median survival times of over 3 years.
- In many cases when STS are incompletely excised the tumor may recur within a year. Treatment options for dogs and cats following

incomplete tumor excision include staged scar resection to assess for residual tumor (to direct further treatment), wide surgical excision of scar or full-course fractionated RT.

- High-grade tumors carry a more guarded prognosis with a shorter median survival time of 1–2 years.



MISCELLANEOUS

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

While receiving chemotherapy drugs dogs should not be bred.

SYNONYM

Spindle cell tumor of canine soft tissue

ABBREVIATIONS

- CT = computed tomography
- MRI = magnetic resonance imaging
- RT = radiation therapy
- STS = soft tissue sarcoma

INTERNET RESOURCES

- http://www.merckmanuals.com/vet/integumentary_system/tumors_of_the_skin_and_soft_tissues/connective_tissue_tumors.html#v3281241
- http://www.cvm.ncsu.edu/vhc/tc/clinical_services/onco/dog_sts.html

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SPERMATOCELE/SPERM GRANULOMA



BASICS

OVERVIEW

- Spermatocele—a cystic distension of the efferent ductules or epididymis containing spermatozoa, usually associated with loss of patency of the duct.
- Sperm granuloma—the granulomatous chronic inflammatory reaction that develops when spermatozoa escape from the efferent ductules or epididymal duct into the surrounding tissue; clinically important when bilateral obstruction of the duct system leads to azoospermia.

SIGNALMENT

Dog and cat

SIGNS

- Suspected in azoospermic dog with normal-sized testes.
- Rarely associated with pain, or visible or palpable lesions.

CAUSES & RISK FACTORS

- Trauma causing a break in the epididymal duct—releases sperm antigens into the surrounding tissue.
- Adenomyosis—invasion of the epithelial lining cells of the epididymis into the muscular layers; may be a factor; associated with excess estrogenic stimulation.
- Epithelial hyperplasia of the epididymis—may be a precursor of adenomyosis; not often seen in dogs < 2.5 years old; noted to some degree in 75% of dogs > 7.75 years old; risk increases with age.
- Complication of vasectomy—especially when surgical technique was not meticulous.
- Congenital occlusion of epididymal duct.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Azoospermia (dogs)—testicular degeneration; hypoplasia; retrograde ejaculation; incomplete ejaculation.

- Scrotal signs (e.g., pain and palpable lesions, dogs)—epididymitis; orchitis; scrotal dermatitis.

CBC/BIOCHEMISTRY/URINALYSIS

- Urinalysis (cystocentesis) after ejaculation—rule out retrograde ejaculation.
- CBC and biochemistry profile—usually normal.

OTHER LABORATORY TESTS

- Assay for canine FSH—high concentration associated with degeneration and hypoplasia; normal concentration in azoospermic dogs with normal-sized testicles associated with bilateral blockage of the epididymis or retrograde ejaculation.
- Alkaline phosphatase concentration of seminal plasma—azoospermic samples with AP < 5,000 U/L consistent with bilateral epididymal blockage or incomplete ejaculation; see Infertility, Male—Dogs.

IMAGING

Ultrasonography—useful to differentiate from other conditions causing scrotal enlargement.

DIAGNOSTIC PROCEDURES

Surgical testicular biopsy and excisional biopsy of affected epididymal tissue—allows identification of epididymis; assessment of spermatogenesis; spermatoceles appear as yellow cysts within the epididymis.

PATHOLOGIC FINDINGS

Histologic examination of testicular specimen—complete spermatogenesis in an azoospermic dog indicates blockage.



TREATMENT

- Azoospermic dogs—rarely spontaneously recover.
- Bilateral blockage of the epididymis—probably not treatable except by microsurgical anastomosis of the ductus deferens to the cystic structure or patent segment of the epididymis; few attempts have been made to perform this procedure in dogs.



MEDICATIONS

DRUG(S)

None described in the literature to unblock the duct system



FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS

- Unilateral sperm granuloma—fair to guarded for fertility; breeding management will improve fertility; see Breeding, Timing.
- Bilateral sperm granuloma—poor prognosis for fertility.



MISCELLANEOUS

SEE ALSO

- Breeding, Timing
- Infertility, Male—Dogs

ABBREVIATION

- FSH = follicle-stimulating hormone

Suggested Reading

- Althouse GC, Evans LE, Hopkins SM. Episodic scrotal mutilation with concurrent bilateral sperm granuloma in a dog. J Am Vet Med Assoc 1993, 202:776–778.
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SPERMATOZOAL ABNORMALITIES



BASICS

OVERVIEW

- Teratozoospermia—presence of significant amounts ($\geq 40\%$) of spermatozoal abnormalities in the ejaculate.
- High percentage of spermatozoal abnormalities may cause infertility in dogs.
- Some fertile cats inherently have $\geq 40\%$ spermatozoal abnormalities.
- Spermatozoal abnormalities are sometimes classified into primary and secondary defects; primary defects occur during spermatogenesis, and secondary defects occur during transport and storage within the epididymis, or from inappropriate semen handling.

SIGNALMENT

- Dogs and cats of any age; older dogs and cats most likely to have other age-related conditions affecting sperm quality.
- No breed predilection for dogs or cats; Irish wolfhounds reported to have significantly lower semen quality than dogs of other breeds.

SIGNS

- Infertility after appropriately timed mating to several reproductively proven bitches.
- Spermatozoal abnormalities found during routine breeding soundness evaluation.

CAUSES & RISK FACTORS

Congenital

- Dogs with fucosidosis—lysosomal storage disease caused by a deficiency of the enzyme α -l-fucosidase; acrosomal defects and retention of proximal droplets are common; English springer spaniels—autosomal recessive inheritance pattern.
- Primary ciliary dyskinesia—ultrastructural abnormality of cilia causing absent or abnormal motility of ciliated cells; affected animals are infertile; probably autosomal recessive inheritance.
- Idiopathic—dogs, cats with inherent poor sperm morphology.
- Testicular hypoplasia—tortoiseshell or calico tomcat.
- Inbreeding in domestic cats produces significant reduction in percent morphologically normal cells within one generation.

Acquired

- Conditions disrupting normal testicular thermoregulation—trauma; hematocoele; hydrocele; orchitis; epididymitis; fever; obesity (increased scrotal fat); high environmental temperatures; exercise-induced heat exhaustion.
- Infections of the reproductive tract—prostatitis; brucellosis; orchitis; epididymitis.
- Drugs—anabolic steroids; androgens; estrogens; progestagens; corticosteroids; ketoconazole; amphotericin

B; cimetidine; phytoestrogen (coumestrol); GnRH antagonists (Acyline); intratesticular injections of zinc arginine • Testicular neoplasia • Prolonged sexual abstinence • Overuse • Testicular degeneration



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Excessive numbers of kinked or coiled tails may be iatrogenic artifacts caused by the eosin-nigrosin stain; reexamine the sample under phase contrast microscopy after dilution with formalin phosphate-buffered saline solution.

OTHER LABORATORY TESTS

- Hormonal profile—concentrations of gonadotropin (FSH) and steroid hormones should be determined to rule-out endocrinopathies.
- Azoospermic ejaculates should be examined for the presence of alkaline phosphatase to confirm azoospermia; complete ejaculates have $> 5,000$ U/L of alkaline phosphatase.
- Brucellosis—rapid slide agglutination test—used as a screening test (D-Tec[®] CB, Zoetis; (888)-963-8471); recommend recheck of dogs with positive slide test with agar gel immunodiffusion test (Cornell University Diagnostic Laboratory; (607)253-3900) or bacterial culture of whole blood or lymph node aspirate.

IMAGING

Ultrasonography—to diagnose testicular tumors, orchitis, hydrocele, hematocoele, spermatocele.

DIAGNOSTIC PROCEDURES

- Bright-field microscopic evaluation of dry-mount slide—eosin-nigrosin stain (Society for Theriogenology stain; Lane Manufacturing, Denver, CO) or modified Giemsa stain (Diff-Quik, Baxter Healthcare, Deerfield, IL) is used to stain spermatozoa; recommended to use pre-warmed stain and prepare slides on a heated slide warmer; faster drying decreases the incidence of artifacts such as kinked tails or coiled tails; a minimum of 100 (preferably 200) sperm cells are counted under 1,000X magnification.
- Acrosome staining—acrosomal damage can be evaluated by Coomassie Brilliant blue (Bio-Rad Laboratories, Hercules, CA) staining or Spermac stain (Conception Technologies, San Diego, CA), marketed for human sperm but works very well with dog sperm.
- Phase contrast or differential interference contrast light microscopic evaluation of wet-mount slide—samples diluted with formalin phosphate-buffered saline solution; verify

whether a high percentage of kinked or coiled tails seen on a stained slide is staining artifact.

PATHOLOGIC FINDINGS

- Biopsy—incisional biopsy or testicular fine-needle aspirate to determine status of spermatogenesis.
- Absence of spermatids or spermatocytes—impaired spermatogenesis.
- Neoplasia • Inflammation—peritubular lymphocytic accumulation • Degenerative changes • Hypoplasia



TREATMENT

- There is no specific treatment for spermatozoal abnormalities; if applicable, the underlying disease or condition should be treated accordingly.
- Antibiotics and anti-inflammatory agents for infectious diseases.
- Unilateral orchectomy for unilateral testicular tumors or severe orchitis.
- Sexual rest for edema or hematocoele associated with trauma.
- Frequent semen collection may temporarily improve sperm quality in dogs or cats with idiopathic teratozoospermia.
- Remove the dog or cat from environments that cause extreme heat stress.
- Alter exercise to reduce heat stress.



MEDICATIONS

CONTRAINDICATIONS

- Exogenous hormones—anabolic steroids; estrogens; testosterone; progestagens.
- Glucocorticoids.
- Chemotherapeutic agents.
- Ketoconazole; amphotericin B.
- Cimetidine.



FOLLOW-UP

PATIENT MONITORING

- If an underlying cause is identified and treated, a sperm evaluation should be performed at 30 and 70 days after the condition is resolved.
- In cases due to reversible causes, a complete improvement in sperm morphology does not occur before 70 days (approximate length of a complete spermatogenic cycle).

PREVENTION/AVOIDANCE

- Climate-controlled environment for animals not adapted to high environmental temperatures.
- Avoid heat exhaustion during exercise or grooming.

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SPIDER VENOM TOXICOSIS—BLACK WIDOW



BASICS

OVERVIEW

- Black widow spider—*Latrodectus* spp. (4 species indigenous to the United States (*L. mactans*, *L. geometricus*, *L. hesperus*, *L. variolus*); females toxic; 2–2.5 cm in length; shiny black; red or orange hourglass mark on the ventral abdomen; immature female brown with red to orange stripes that change into the hourglass shape as she darkens to black and ages.
- Bites—15% may be dry (no venom injected).
- Range—genus found in every state except Alaska; often found around buildings and human habitation.
- Venom—contains α -latrotoxin, a potent neurotoxin; opens cation-selective channels at the presynaptic nerve terminal; causes massive release of acetylcholine and norepinephrine, which causes sustained muscular spasms.

SIGNALMENT

Dogs and cats

SIGNS

Historical Findings

- Usually sudden onset.
- May be delayed several days with mild envenomation.

Physical Examination Findings

Dogs

- Progressive muscle fasciculations.
- Severe pain.
- Cramping of large muscle masses.
- Abdominal rigidity without tenderness.
- Marked restlessness, writhing, and contorted spasms.
- Hypertension and tachycardia anticipated.
- May note bronchorrhea, hypersalivation, hyperesthesia, lymph node tenderness, regional numbness, facial swelling and spasm (referred to as *Latrodectus facies*).
- Rhabdomyolysis possible.

Cats

- Early, marked paralysis.
- Severe pain—manifested by howling and loud vocalizations.
- Excessive salivation and restlessness.

- Vomiting—not unusual to vomit up the spider.
- Diarrhea.
- Muscle tremors and cramping.
- Ataxia and inability to stand—becomes adynamic and atonic.
- Respiratory collapse.
- Death without antivenin.

CAUSES & RISK FACTORS

- Very young or old age—increased risk
- Systemic hypertension—increased risk



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Intervertebral disc disease
- Acute abdomen

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis
- High creatine kinase—with severe muscle spasms
- Albuminuria

OTHER LABORATORY TESTS

Normal hemoccult test

IMAGING

Normal abdominal radiographs

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Inpatient—supportive care
- Monitor respiratory status



MEDICATIONS

DRUG(S)

- Antivenin (Lyovac [*Latrodectus*], equine origin)—1 vial mixed with 100 mL crystalloid solution IV given slowly with monitoring of the inner ear pinna for evidence of hyperemia (indicator of allergic response); dose usually sufficient for response within 30 minutes; with proper use, reactions

are rare. Variable availability. If allergic reaction occurs—stop antivenin; administer diphenhydramine; after 5–10 minutes, restart antivenin at a slower rate.

- New antivenin (Aracmyn—Instituto Bioclon, Mexico) has completed human phase III clinical trials but not yet approved for human use. It is an equine origin Fab₂ product and should be much less likely to trigger an allergic response.
- Studies suggest benzodiazepines are more effective than muscle relaxants for treatment of muscle pain related to black widow spider envenomation.
- Muscle spasms and severe pain are controlled by careful intravenous administration of narcotics or benzodiazepines at lowest effective dosage to avoid respiratory depression; methocarbamol relieves muscle spasms but has no effect on hypertension or respiratory depression.
- Intractable hypertension—sodium nitroprusside.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Intravenous fluids with hypertension



FOLLOW-UP

- Weekly monitoring of the wound site until healed
- Prognosis—uncertain for days; cats, usually fatal without antivenin
- Weakness, fatigue, and insomnia—may persist for months



MISCELLANEOUS

Suggested Reading

Peterson ME. Spider envenomation: Black widow. In: Peterson ME, Talcott PA, eds., Small Animal Toxicology, 3rd ed. St. Louis, MO: Saunders, 2013, pp. 817–821.

Author Michael E. Peterson

Consulting Editor Lynn R. Hovda

Acknowledgment Daniel Keyler for editorial assistance.

SPIDER VENOM TOXICOSIS—BROWN RECLUSE



BASICS

OVERVIEW

- Brown recluse family—*Loxosceles* spp. (11 species indigenous to USA); 8–15 mm in body size; legs 2–3 cm long; violin-shaped pattern on cephalothorax with the neck of the fiddle extending caudally; 6 eyes (3 paired diads) as opposed to other spider species with 8 eyes; active at night.
- Distribution—found throughout the Midwest from the Gulf Coast of the United States and up the Mississippi River valley to southern Iowa. Some species are found in eastern southern California, western Arizona, and southern New Mexico.
- Sixty percent of “brown recluse” spider bites in humans are misdiagnosed as they occur in areas with no endemic spider populations. See extensive “Differential Diagnosis” below.
- Bites—usually occur when spider becomes trapped in bedding; induce necrotic arachnidism, an indolent dermatonecrotic lesion mediated by the venom enzyme sphingomyelinase D, direct hemolysis of erythrocytes, platelet aggregation, renal failure, coagulopathy, and death.
- Currently no general consensus on treatment and multiple therapies have been used ranging from antihistamines, corticosteroids, dapsone, hyperbaric oxygen, and surgical excision to antivenom.
- Antivenom currently unavailable in USA (available only in Argentina, Brazil, and Mexico).

SIGNALMENT

Dogs and cats

SIGNS

- Clinical signs are not completely defined in canine and feline envenomations.
- In humans:
 - Local pain and stinging (may last 6–8 hours); followed by pruritus and soreness.
 - Classic target lesion—ischemic area with a dark central eschar on an uneven erythematous background; after 2–5 weeks, central eschar may slough, leaving a deep, non-healing ulcer that usually spares muscle tissue.
 - Less common—hemolytic anemia with hemoglobinuria in the first 24 hours; secondary renal complications.
 - Other possible systemic manifestations within the first 2–3 days after envenomation—fever; chills; rash; weakness; leukocytosis; nausea; arthralgia.
 - Envenomations to fatty areas develop more significant lesions.

CAUSES & RISK FACTORS

Brown recluse spider bite (genus *Loxosceles*)



DIAGNOSIS

- Brown recluse spider bite is frequently misdiagnosed in regions of the country that do not have endemic populations of the spider.
- Epidemiologic history of bite including site of lesion, progression timeline of signs, and visualization of small puncta assist with diagnosis.

DIFFERENTIAL DIAGNOSIS

- Bacterial or mycobacterial infection; MRSA by a large margin in humans
- Decubitus ulcer
- Third-degree burn
- Hemolytic anemia
- Jaundice
- Necrotizing vasculitis
- Thrombocytopenia
- Ehrlichiosis
- RBC parasitism
- Vascular occlusive/venous disease

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia
- Leukocytosis
- Thrombocytopenia
- Hemoglobinuria

OTHER LABORATORY TESTS

- BUN and creatinine.
- Coagulation profile—may reveal prolonged clotting times.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Routine wound care—may need aggressive supportive care.
- Supportive care—may include fluid therapy; presumptive treatment of bacterial superinfection; (rarely) blood transfusion.
- Mild, local envenomation—usually responds to cool compresses as sphingomyelinase D activity is temperature-dependent.
- Necrotic lesions—may need debridement after erythema has subsided.
- Severe envenomation—may require skin grafting after the lesion reaches full maturity.



MEDICATIONS

DRUG(S)

- Antibiotics—prevent secondary infection.
- Hyperbaric oxygen—some evidence indicates that hyperbaric oxygen treatment

may be beneficial for reducing size of the skin lesion.

- Dapsone—mixed results in various studies. 1 mg/kg q8h for 10 days; for dermatonecrotic lesions; leukocyte inhibitor; proposed to minimize inflammatory component of the envenomation; repeat if needed. Efficacy against brown recluse envenomation has not been studied in the dog and cat.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Do not use heat—exacerbates condition.
- Dapsone—may cause hypersensitivity and methemoglobinemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.
- Early surgical excision may cause larger defect than supportive care alone.
- Antihistamines, colchicine, anticoagulants, topical nitroglycerine, high doses of vitamin C, electric shock, and steroids have been proposed for treatments, but subsequently have been demonstrated to be ineffective.



FOLLOW-UP

Monitor wound site weekly until healed.



MISCELLANEOUS

ABBREVIATIONS

- BUN = blood urea nitrogen
- MRSA = methicillin resistant *Staphylococcus aureus*
- RBC = red blood cell

Suggested Reading

Gremski LD, Trevisan-Silva D, Ferrer VP, et al. Recent advances in the understanding of brown spider venoms: from biology of spiders to the molecular basis of toxins. *Toxicon* 2014; 80:91–120.

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Author Michael E. Peterson

Consulting Editor Lynn R. Hovda

Acknowledgment Daniel Keyler for editorial assistance.

SPINAL DYSRAPHISM



BASICS

OVERVIEW

- Abnormal spinal cord development along the median plane leading to a variety of structural anomalies—hydromyelia, duplicated or absent central canal, syringomyelia, and aberrations in the dorsal median septum and ventral medial fissure.
- Thoracic and lumbar spinal segments most commonly affected. • Dysraphism suggests an abnormality in closure of the neural tube; the term “myelodysplasia” may be preferable.

SIGNALMENT

Non-progressive

- Dog and cat. • Weimaraner—hereditary.
- Reported in English bulldog, Samoyed, Dalmatian, English setter, golden retriever, rottweiler, Manx cat. • No sex predilection.
- Signs apparent by 3–6 weeks of age—become more obvious as animal matures. In mild cases, may not be presented for examination until several months of age.

Progressive

- Adult Cavalier King Charles spaniels with syringomyelia resulting from occipital bone malformation (Chiari-like malformation; caudal occipital malformation syndrome [COMS]). • Adult Pomeranian with cervical syringomyelia and hydrocephalus. • Adult fox terrier with progressive paresis in the left pelvic limb.

SIGNS

Vary in severity.

Dogs

- Weimaraner—simultaneous flexion and extension of pelvic limbs (bunny hopping); proprioceptive deficits, base wide stance, and crouched pelvic limb posture. • Cavalier King Charles spaniel—neck or head pain; progressive forelimb weakness, paraparesis; imbalance; paroxysmal involuntary flank or neck scratching. • Less common signs include abnormal hair streams in the dorsal cervical area, kinking of the undocked tail, scoliosis, and koiosternia (depression of the sternum).

Cats

Manx cat—pelvic limb paresis or paralysis, urinary and fecal retention.

CAUSES & RISK FACTORS

- Genetic—Weimaraner; homozygous condition lethal; heterozygotes clinically affected. • *In utero* spinal cord damage caused by infection, trauma, and vascular compromise may cause syringomyelia (cavitation of the spinal cord). • Idiopathic in isolated patients. • Syringomyelia may be acquired as result of infection, trauma, or neoplasia. • Manx cat—breeding for absence of tail.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Intervertebral disc disease, myelitis, arachnoid cysts, and neoplasia must be differentiated from progressive causes of syringomyelia.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

N/A

IMAGING

- Survey radiographs and myelography—associated vertebral column anomalies and spinal cord compression in some patients.
- Without sophisticated imaging techniques, an antemortem diagnosis may be impossible except in Weimaraner and Manx cat.
- MRI—definitive imaging modality for syringomyelia, attenuation of fourth ventricle, overcrowding of brainstem in caudal fossa, and cerebellar vermal herniation (COMS, Chiari-like malformation); hydrocephalus if evident. • CT—reveal hydrocephalus, if evident, with COMS. • Skull radiographs—occipital bone defect may be demonstrated.



TREATMENT

- Mildly affected animals—may be acceptable pets. • Severely affected animals may benefit from a canine cart; consider euthanasia.
- Surgical considerations—foramen magnum remodeling (with occipital malformation) or ventriculoperitoneal shunt placement; laminectomy, ± syringo-subarachnoid shunting (may reduce pain or improve neurologic signs; sensory disturbances such as scratching infrequently resolve, and recurrence is possible).



MEDICATIONS

DRUG(S)

- Antibiotics—for urinary tract infection. Treat based on culture and sensitivity of urine.
- Corticosteroids—to improve signs in COMS by reducing CSF production and edema formation. Prednisone 0.25–0.5 mg/kg q12h or dexamethasone 0.025–0.05 mg/kg PO q12h; taper to alternate-day prednisone or twice-weekly dexamethasone.
- Carbonic anhydrase inhibitors—may alleviate signs in COMS by decreasing CSF production and allow for a reduction of steroid dosage. Acetazolamide 3.5–7.5 mg/kg q8–12h; methazolamide 5 mg/kg q8–12h or furosemide 5 mg/kg PO, IM, SC q12h.
- Omeprazole—decreases CSF production and may alleviate signs in COMS and allow

for a reduction of steroid dosage. Clinical data on use and effectiveness currently lacking; 0.5–1 mg/kg PO q24h. • Gabapentin—recommended for management of neuropathic pain; 10 mg/kg q8–12h.

- NSAIDs—may help manage neuropathic pain. Meloxicam (Metacam) 0.2 mg/kg once then 0.1 mg/kg q24h in dogs; carprofen (Rimadyl) 2.2 mg/kg PO q12h or 4.4 mg/kg PO q24h in dogs.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Avoid prolonged administration of NSAIDs, or combinations of NSAIDs and steroids because of risks of gastrointestinal ulceration and renal pathology. • Do not use NSAIDs in cats.



FOLLOW-UP

PATIENT MONITORING

- Secondary urinary tract infection—seen in severely affected animals; owing to disorders of micturition. • Avoid decubitus ulcers and urine and fecal scalds by properly caring for recumbent patients.

PREVENTION/AVOIDANCE

- Discourage breeding for absence of tail in Manx cats. • Do not breed Weimaraners that have produced affected puppies because of codominant inheritance.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Congenital vertebral arch (e.g., spina bifida) and vertebral body-disc malformation (e.g., hemivertebra and block vertebra)—alone often does not cause clinical signs.

ABBREVIATIONS

- COMS = caudal occipital malformation syndrome • CSF = cerebrospinal fluid
- CT = computed tomography • MRI = magnetic resonance imaging • NSAID = nonsteroidal anti-inflammatory drug

SEE ALSO

Syringomyelia and Chiari-like Malformation

Suggested Reading

Rusbridge C. Chiari-like malformation with syringomyelia in the Cavalier King Charles Spaniel: Long-term outcome after surgical management. Vet Surg 2007, 36(5):396–405.

Westworth DR, Sturges BK. Congenital spinal malformations in small animals. Vet Clin North Am Small Anim Pract 2010, 40(5): 951–981.

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SPLENIC TORSION



BASICS

OVERVIEW

- May occur as a separate entity or in association with gastric dilatation-volvulus syndrome.
- Acute or chronic.
- Pathophysiology—unknown.
- Systems affected—hemic/lymphatic/immune and cardiovascular.
- Isolated splenic torsion uncommon.

SIGNALMENT

- More common in large-breed, deep-chested dogs, such as German shepherd, standard poodle, and Great Dane.
- No sex predilection.

SIGNS

Historical Findings

- Acute—cardiovascular collapse and abdominal pain.
- Chronic—intermittent anorexia, vomiting, weight loss, and possibly hemoglobinuria.

Physical Examination Findings

- Pale mucous membranes, tachycardia, and other signs of hypoperfusion.
- Palpable abdominal mass (spleen).

CAUSES & RISK FACTORS

- Large-breed and deep-chested dogs.
- Prior stretching of gastrosplenic, phrenicosplenic, and splenocolic ligaments (e.g., prior gastric dilatation and volvulus).
- Historical gastric dilatation.
- Excessive exercise, rolling, and retching may contribute.
- Nervousness and anxiety have been associated with an increased risk of GDV but not of isolated splenic torsion.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other splenic disease (e.g., neoplasia and immune-mediated disease).

S

- Acute gastrointestinal disease with abdominal pain.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia
- Thrombocytopenia
- Leukocytosis
- High liver enzyme values
- Hemoglobinuria

OTHER LABORATORY TESTS

Coagulation test—DIC, with prolongation of clotting times and thrombocytopenia.

IMAGING

Abdominal Radiography

- Cranial or midabdominal mass may be seen.
- Spleen may be abnormally located.

Abdominal Ultrasonography

- Splenic congestion/lack of blood flow to spleen.
- Dilated splenic veins.
- Splenic infarction.

DIAGNOSTIC PROCEDURES

ECG—may show ventricular arrhythmias.

PATHOLOGIC FINDINGS

Splenic congestion and infarction.



TREATMENT

- Surgical emergency.
- After adequate cardiovascular stabilization, a splenectomy should be performed without untwisting the splenic pedicle.
- A permanent gastropexy should also be performed because of the association with gastric dilatation-volvulus syndrome.
- A splenic specimen should be submitted for histopathologic examination.
- Fluid support and cardiovascular monitoring indicated after splenectomy.



MEDICATIONS

DRUG(S)

- No specific drugs required.
- Postoperative pain relief advised.

- Heparin (unfractionated or low molecular weight) or plasma transfusion (rarely due to size of patient) may be considered if DIC and coagulopathy are documented.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

None



FOLLOW-UP

Surgical correction considered curative.



MISCELLANEOUS

ABBREVIATIONS

- DIC = disseminated intravascular coagulation
- ECG = electrocardiogram
- GDV = gastric dilation and volvulus

Suggested Reading

Neath PJ, Brookman DJ, Saunders HM. Retrospective analysis of 19 cases of isolated torsion of the splenic pedicle in dogs. J Small Anim Pract 1997, 38:337–392.

Stoneham A, Henderson A, O'Toole T. Resolution of severe thrombocytopenia in two standard poodles with surgical correction of splenic torsion. J Vet Emerg Crit Care 2006, 16:131–135.

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SPLENOMEGLY



BASICS

DEFINITION

Enlargement of the spleen; characterized as either diffuse or nodular.

PATHOPHYSIOLOGY

- Splenic functions—removal of senescent and abnormal erythrocytes; filtration and phagocytosis of antigenic particles such as microorganisms, degraded cellular material, macromolecules; production of lymphocytes and plasma cells; antibody production, reservoir for erythrocytes and platelets; iron metabolism and storage, hematopoiesis, as required. • Many disorders affect the function of the spleen.

Diffuse Splenomegaly

Four General Pathologic Mechanisms

- Inflammation (splenitis)—associated with infectious agents; classified according to cell type (e.g., suppurative, necrotizing, eosinophilic, lymphoplasmacytic, and granulomatous-pyogranulomatous).
- Lymphoreticular hyperplasia—hyperplasia of mononuclear phagocytes and lymphoid elements (in response to antigens); accelerated erythrocyte destruction. • Congestion—associated with impaired venous drainage.
- Infiltration—involves cellular invasion of the spleen or deposition of abnormal substances.

Nodular

Associated with neoplastic (tumor) or non-neoplastic disorders (infection, hyperplasia/regeneration, or inflammation).

SYSTEMS AFFECTED

Disorders of the spleen also may be associated with changes in the liver.

SIGNALMENT

- Dog and cat; certain conditions maybe more prevalent in specific breeds or sizes of dog.
- Splenic torsion—overrepresented in large, deep-chested breeds (e.g., German shepherd, Great Dane). • Hemangiosarcoma—middle-aged dogs; large breeds; predilection in German shepherd, golden retriever, and Labrador retriever. • Prominent spleen—may be normal in certain breeds (German shepherd, Scottish terrier).

SIGNS

General Comments

- Splenic enlargement—often nonspecific.
- Frequently reflects an underlying disorder rather than primary disease of the spleen.

Historical Findings

- Vomiting, diarrhea, anorexia—can be seen with infiltrative diseases such as lymphoma, mast cell tumor, FIP, lymphoplasmacytic enteritis (cats). • Lethargy, anorexia, vomiting, vague abdominal pain (in acute cases pain can be severe), mild to moderate

abdominal distention in deep-chested large-to giant-breed dogs (Great Dane, German shepherd overrepresented) — associated with splenic torsion (with or without concurrent gastric dilatation volvulus). • Weakness, lethargy, collapse (can be episodic), abdominal distention—can indicate a hemoabdomen secondary to hemangiosarcoma, bleeding/ruptured spleen from other neoplasia (rare) or benign conditions such as a hematoma.

Physical Examination Findings

- Prominent spleen on abdominal palpation or cranial/midabdominal mass; non-palpable spleen does not preclude splenomegaly.
- Dogs—smooth or irregular surface.
- Cats—usually diffuse, uniform enlargement. • Pallor, poor capillary refill time, poor peripheral pulses and tachycardia if splenic hemorrhage or splenic torsion.
- Abdominal distention if massive splenomegaly or splenic rupture (effusion).
- Petechia and ecchymosis if coagulopathy secondary to primary splenic disorder or underlying disease. • Concurrent hepatomegaly, thickened intestines, and/or mesenteric lymphadenopathy imply infiltrative or inflammatory disease.
- Peripheral lymphadenomegaly—suggests lymphoma leukemia. • Cardiac arrhythmias—may indicate clinically significant cardiac abnormality affecting the spleen (congestion) but ventricular arrhythmias also are associated with primary splenic disorders.

CAUSES

Dogs

Inflammation (Splenitis)

- Inflammatory cell type can help prioritize differentials. • Suppurative—penetrating abdominal wound; migrating foreign body; endocarditis; sepsis; infectious complication of splenic torsion. • Necrotizing—usually secondary to torsion or neoplasia; anaerobes; *Salmonella*; acute infectious canine hepatitis. • Eosinophilic—eosinophilic gastroenteritis. • Lymphoplasmacytic—subacute or chronic infectious disorders; infectious canine hepatitis; ehrlichiosis; pyometra; *Brucella*; *Leishmania*; coexistent inflammatory bowel disease. • Granulomatous—histoplasmosis; *Leishmania*. • Pyogranulomatous—blastomycosis; *Mycobacterium*; sporotrichosis.

Hyperplasia

- Infection—chronic bacteremia (bacterial endocarditis; discospondylitis; *Brucella*). • Immune-mediated disease—SLE; hemolytic anemia or thrombocytopenia.

Congestion

- Tranquillizers; barbiturates; portal hypertension; right-sided heart failure; splenic torsion.

Infiltration

- Neoplasia—lymphoma; acute and chronic leukemia; histiocytic sarcoma; multiple

myeloma; systemic mastocytosis; hemangiosarcoma, fibrohistiocytic nodule; metastatic neoplasia. • EMH—immune-mediated hemolytic anemia or thrombocytopenia; chronic anemia; infectious disease; malignancy; SLE. • Amyloidosis.

Cats

Inflammation

- Suppurative—penetrating wound or migrating foreign body; septicemia; salmonellosis. • Necrotizing—salmonellosis.
- Eosinophilic—hypereosinophilic syndrome.
- Lymphoplasmacytic—lymphoplasmacytic enteritis; hemotropic mycoplasmas; pyometra.
- Granulomatous—histoplasmosis; mycobacteriosis. • Pyogranulomatous—FIP, *Mycobacterium*.

Hyperplasia

- Infection—hemotropic mycoplasmosis.
- Immune-mediated—chronic hemolysis, SLE.

Congestion

Portal hypertension, congestive heart failure.

Infiltration

- Neoplasia—mast cell tumor (most common); lymphoma; lymphoproliferative disease; myeloproliferative disease; histiocytic sarcoma; multiple myeloma; hemangiosarcoma (rare). • Non-neoplastic—amyloidosis, EMH.

RISK FACTORS

- Cats—FeLV, FIP • Dogs—breed/age



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other cranial organomegaly or masses

CBC/BIOCHEMISTRY/URINALYSIS

Dogs

- Regenerative anemia secondary to splenic bleeding or hemolytic disease. • Nucleated RBC—may accompany EMH, indicates splenic dysfunction. • Spherocytes—hemolysis, microangiopathic shearing (schistocytes also). • Leukocytosis with a left shift—may indicate infectious or inflammatory conditions, marked regenerative response, or EMH.
- Thrombocytopenia—from increased consumption (DIC or bleeding) secondary to hemangiosarcoma or other neoplasia, increased destruction (immune-mediated), sequestration, or decreased production in the bone marrow. • Hypercalcemia may be associated with neoplasia, especially lymphoma. • Hyperglobulinemia may be associated with neoplasia or *Ehrlichia* infections. • Hemoglobinemia and hyperbilirubinemia—may occur with microangiopathic anemia, splenic torsion, hemangiosarcoma, and immune-mediated anemia with spleen as site of extravascular RBC removal.

SPLENOMEGLY

(CONTINUED)

Cats

- Direct RBC examination for hemoparasites.
- Regenerative anemia and splenomegaly—may indicate hemotropic mycoplasmosis.
- Macrocytosis and nonregenerative anemia—suggests retroviral infection or myeloproliferative disease.
- Eosinophilia—suggests hypereosinophilic syndrome, systemic mastocytosis, or lymphoma.
- Circulating blast cells—suggest myeloproliferative or lymphoproliferative disorder.
- Nucleated RBCs—may accompany EMH and splenic dysfunction.
- Thrombocytopenia—from increased consumption (DIC), increased destruction (immune-mediated), sequestration, or decreased production in the bone marrow.

OTHER LABORATORY TESTS

- FeLV and FIV testing.
- Buffy coat smears—circulating mast cells (may occur with inflammatory disease and neoplasia); blast cells.
- Coagulation panel—DIC commonly seen with hemangiosarcoma (includes prolonged clotting times, hypofibrinogenemia, and increased FDPs; d-dimers not specific for clinical application in differential diagnoses).

IMAGING

Abdominal Radiography

- Confirms or detects splenomegaly.
- Mass effect may appear in the left midcranial abdomen.
- May provide evidence of an underlying cause—concurrent hepatomegaly may indicate infiltrative disease or right-sided heart disease; splenic torsion may occur secondary to gastric dilation or volvulus.
- Effusion—may indicate hemorrhage from splenic rupture (hemangiosarcoma, hematoma) or portal hypertension influencing splenic perfusion. Visualization of the splenic tail along the ventral body wall on lateral radiographs of cats supports the diagnosis of splenomegaly.

Thoracic Radiography

- Three views (right and left lateral and dorsal-ventral views)—screen for metastasis and underlying disease in thoracic cavity and effusion.
- Evaluate sternal lymph nodes—these drain the abdominal cavity, reflecting disorders causing lymphadenomegaly.
- Evaluate for signs of congestive heart failure (size of the cardiac silhouette and pulmonary veins and evidence of pulmonary edema or pleural effusion).

Abdominal Ultrasonography

- Distinguishes between diffuse and nodular parenchymal patterns; nodular abnormalities easily identified.
- Diffuse enlargement with normal parenchyma—may occur with congestion or cellular infiltration.
- Hypoechoogenicity—may occur with splenic torsion, splenic vein thrombosis, lymphoma, or leukemia.
- Complex, mixed echogenic mass—hemangiosarcoma or hematoma.
- Hematomas—variable echogenicity; may

have internal septation and encapsulation and pass through a stage where they resemble target lesions suggesting neoplasia.

- Can identify concurrent abdominal diseases—liver, kidneys, intestines, and lymph nodes.
- Cannot differentiate between benign and malignant splenic disorders.
- Doppler color flow interrogation of splenic vasculature may detect splenic vein thrombi or splenic torsion.

Echocardiography

Evaluation of right atrium for mass lesions—when hemangiosarcoma suspected (based on ultrasonographic appearance and hematology) or to determine if there is cardiac disease causing splenic congestion.

DIAGNOSTIC PROCEDURES

Fine-Needle Aspiration

- Assess coagulation status before any aspiration.
- Procedure—patient in right lateral or dorsal recumbency; use a 23- or 25-gauge, 2.5–3.75 cm (1–1.5 in.) length needle; using ultrasound guidance.
- Non-aspiration method (when negative pressure is NOT applied to the syringe) results in higher yield of nucleated cells relative to the amount of blood than aspiration method.
- Specimens—evaluate cytologically for infectious agents (often found in macrophages); identify predominant inflammatory or infiltrative cell type.
- Neoplastic infiltrates—classified as epithelial, mesenchymal, or discrete (round cell).
- Aspiration of cavitated masses may cause rupture and is not recommended.

Bone Marrow Aspiration

- Indicated with cytopenias before splenectomy (spleen may be supporting hematopoiesis).
- May yield an infectious disorder (e.g., ehrlichiosis, mycosis, toxoplasmosis, leishmaniasis) or hematopoietic neoplasia.



TREATMENT

- Depends on underlying cause; supportive nursing care as needed.
- Important to determine if splenomegaly is appropriate for systemic conditions.
- Treatment and prognosis after splenectomy—based on histopathologic features: hemangiosarcoma may be missed in some tumors owing to regional necrosis with diagnosis rendered of hematoma.

SURGICAL CONSIDERATIONS

Splenectomy

- With anemia or leukopenia—rule out bone marrow aplasia/hypoplasia before surgery; spleen may be the source of hematopoiesis.
- Indicated for splenic torsion, splenic rupture, isolated splenic masses considered likely to be neoplastic, and mast cell infiltration (cats).
- Exploratory laparotomy—permits direct evaluation of all abdominal organs.



MEDICATIONS

DRUG(S)

Depend on underlying disease



FOLLOW-UP

PATIENT MONITORING

Ventricular arrhythmias (dogs)—associated with splenic mass lesions or torsion; may occur before, during, and up to 3 days post-splenectomy; evaluate (auscultation and electrocardiogram) surgical candidates before anesthesia; continuous cardiac monitoring during surgery and postoperatively.

POSSIBLE COMPLICATIONS

- Asplenic patient—increased risk of infection and red cell parasitism.
- Postoperative sepsis—uncommon complication.
- Antibiotics—indicated in asplenic patients receiving immunosuppressive therapy, if any sign of infection apparent.



MISCELLANEOUS

AGE-RELATED FACTORS

Neoplastic causes more likely in geriatric animals.

ZOONOTIC POTENTIAL

A variety of infectious diseases may involve the spleen.

SEE ALSO

See "Causes"

ABBREVIATIONS

- DIC = disseminated intravascular coagulation
- EMH = extramedullary hematopoiesis
- FDP = fibrin degradation product
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- RBC = red blood cell
- SLE = systemic lupus erythematosus

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Consulting Editor Sharon A. Center

SPONDYLOYSIS DEFORMANS



BASICS

OVERVIEW

- Degenerative, non-inflammatory condition of the vertebral column characterized by the production of osteophytes along the ventral, lateral, and dorsolateral aspects of the vertebral endplates.
- Most common location—dogs: thoracolumbar spine in the area of the antecervical vertebra and the upper lumbar vertebrae; cats: thoracic vertebrae.

SIGNALMENT

- Dog and cat.
- Dogs—commonly seen in large breeds, especially German shepherd; also boxer, Airedale terrier, and cocker spaniel.
- Occurrence increases with age; 50% of dogs by 6 years and 75% by 9 years; may be evident in young dogs with an inherited predisposition.
- Reported in 68% of asymptomatic domestic cats.
- Females > males.
- Boxers—positive correlation between spondylosis deformans and hip dysplasia; both heritable traits are detectable in predisposed animals by radiographic examination at 1 year.

SIGNS

General Comments

- Patients are typically asymptomatic; lesions of minor clinical importance.
- Pain may follow fracture of bony spurs or bridges.

Historical Findings

- Stiffness
- Restricted motion
- Pain

Physical Examination Findings

Neurologic deficits referable to the spinal cord or nerve root compression are unusual.

CAUSES & RISK FACTORS

- Repeated microtrauma
- Major trauma
- Inherited predisposition
- Acromegaly



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Discospondylitis—differentiated by radiographic evidence of endplate lysis.
- Spinal osteoarthritis—degeneration of articular facet joints.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

N/A

IMAGING

Spinal radiography—initially shows osteophytes as triangular projections several millimeters from the edge of the vertebral body; with progression, osteophytes appear to bridge the intervertebral space; true ankylosis is rare.

DIAGNOSTIC PROCEDURES

MRI, CT, or CT myelography—for unusual cases; demonstrate an atypical dorsal osteophyte compressing the spinal cord or nerve roots or encroaching on critical soft tissue structures.



TREATMENT

- Inform owner that the condition is usually an asymptomatic, incidental finding, and is probably not responsible for the clinical signs.
- Spondylosis—treat as outpatient with strict rest and analgesic, possibly acupuncture.
- Obesity—recommend weight-reduction program.
- Acupuncture—dry needle or electroacupuncture treatment at weekly or biweekly interval and tapered to as-needed basis can be very effective in relief of pain; useful in animals that do not tolerate medication or when clients prefer a natural alternative.



MEDICATIONS

DRUG(S)

Use only when the patient is exhibiting signs.

NSAIDs

- Preferred to steroids in dogs unless the patient has neurologic deficits, because of fewer side effects; administer after feeding.
- Carprofen (Rimadyl) 2.2 mg/kg PO q12h or 4.4 mg/kg PO q24h in dogs.
- Meloxicam (Metacam) 0.2 mg/kg once then 0.1 mg/kg q24h in dogs.
- Deracoxib (Deramaxx) 1–2 mg/kg once/day in dogs.
- Firocoxib (Previcox) 5 mg/kg PO q24h in dogs.
- If GI sensitivity, use in combination with an antacid (famotidine 0.5–1 mg/kg q24h or omeprazole 0.5–1 mg/kg q24h) or a gastrointestinal protector (misoprostol at 3–5 µg/kg PO q6–8h or sucralfate 0.5–1 g q8h) to reduce the possibility of gastrointestinal ulceration.

Non-NSAID Analgesics

- Use may enable reduction of dose or frequency of anti-inflammatory medications.
- Tramadol 2–5 mg/kg q8–12h PO in dogs or 1–4 mg/kg q12h in cats.
- Gabapentin 10 mg/kg q8–12h PO in dogs or cats.
- Buprenorphine 0.01–0.03 mg/kg PO q8h in cats.
- Acetaminophen 5 mg/kg q12h PO in dogs.

Corticosteroids

- Only use in patients with neurologic deficits.
- Prednisone 0.25–0.5 mg/kg PO q12h; or dexamethasone 0.025–0.05 mg/kg PO q12h; taper to alternate-day prednisone or twice-weekly dexamethasone.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Acetaminophen and NSAIDs—do not use in cats.
- Avoid prolonged administration of NSAIDs, or combinations of NSAIDs and either acetaminophen or steroids because of risks of gastrointestinal ulceration and renal pathology.



FOLLOW-UP

PATIENT MONITORING

- Gradually return the animal to normal activity after signs have subsided for several weeks.
- Relapse can occur with strenuous activity.
- With prolonged use of analgesic medications, periodic biochemistry testing is warranted.

PREVENTION/AVOIDANCE

Boxers—given genetic correlation between spondylosis deformans and hip dysplasia and possibility of early detection, selectively breed to decrease both traits.



MISCELLANEOUS

ABBREVIATIONS

- CT = computed tomography
- GI = gastrointestinal
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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Authors Richard J. Joseph and Anne E. Buglione

Consulting Editor Joane M. Parent

SPOROTRICHOSIS



BASICS

OVERVIEW

- Zoonotic fungal disease affecting the integument, lymphatics, or generalized.
- Caused by inoculation of the ubiquitous dimorphic fungus *Sporothrix schenckii* into subcutaneous tissue.

SIGNALMENT

Dog and cat

SIGNS

- Dogs—cutaneous form: numerous nodules that may drain or crust. • Cats—cutaneous form: lesions appear initially as wounds or abscesses mimicking wounds associated with fighting. • Cutaneolymphatic form—usually an extension of the cutaneous form through the lymphatics, resulting in the formation of new nodules and draining tracts or crusts; lymphadenopathy is common. • Disseminated form.

CAUSES & RISK FACTORS

- Dogs—hunting dogs from puncture wounds associated with thorns or splinters.
- Cats—intact male outdoor cats. • Animals exposed to soil rich in decaying organic debris.
- Exposure to infected animals or clinically healthy cats sharing a household with an affected cat. • Immunosuppressive disease.



DIAGNOSIS

Caution: this is a zoonotic disease and proper precautions should be taken to prevent exposure; the absence of a break in the skin does not protect against the disease.

DIFFERENTIAL DIAGNOSIS

- Infectious—bacterial (deep) and fungal diseases presenting with nodules and draining tracts (e.g., cryptococcosis, blastomycosis, feline leprosy, histoplasmosis) • Neoplasia
- Granulomas caused by infectious organisms and foreign bodies • Parasites—*Demodex*, *Pelodera*, *Leishmania*

CBC/BIOCHEMISTRY/URINALYSIS

None unless associated with generalized disease

OTHER LABORATORY TESTS

- Cultures of affected tissue is preferred; swabs culture may be adequate
- **Caution:** this is a zoonotic disease; laboratory personnel must be warned of the potential differential diagnosis; cultures should not be attempted until other differential diagnoses have been eliminated.
- Serologic testing and PCR assays are available.

DIAGNOSTIC PROCEDURES

- Cytology of exudates—cigar- to round-shaped yeast found intracellularly or free in the exudates, accompanied with pyogranulomatous inflammation.
- Biopsy—organisms usually numerous, especially in cats; fungal stains (PAS or GMS) may aid in the diagnosis; the absence of demonstrable organisms in tissues from dogs does not preclude diagnosis.



TREATMENT

- The zoonotic nature of sporotrichosis should be considered when treating an animal with this disease. • Outpatient therapy may be a consideration but increases the potential for human exposure.



MEDICATIONS

DRUG(S)

Supersaturated Solution of Potassium Iodide

Historical treatment—but seldom used due to the safety and efficacy of other therapies.

Ketoconazole and Itraconazole

- Dogs—ketoconazole: 5–15 mg/kg PO q12h until 1 month after clinical resolution or for a minimum of 2 months; resolution should occur within approximately 3 months; side effects are relatively mild with anorexia being the most common; itraconazole: capsular form 5–10 mg/kg q12–24h for a minimum of 2 months; fewer side effects are noted at the lower dose of 5 mg/kg q24h; often better tolerated than ketoconazole; acute hepatopathy and vasculitis have been reported (see Dermatophytosis); terbinafine: 30–40 mg/kg PO q24h for 30 days beyond clinical cure may also be effective.
- Disseminated disease—combination of amphotericin B and itraconazole is recommended; terbinafine may also be effective.
- Cats—itraconazole 15 mg/kg PO q24h or divided q12h for a minimum of 1 month beyond clinical cure; treatment of choice for cats (efficacy and fewer side effects); itraconazole oral suspension (containing cyclodextrin) 1.5–5.0 mg/kg q24h; compounded formulation of itraconazole is not recommended due to potentially inconsistent absorption; oral suspension is best administered on an empty stomach to improve absorption. Alternative: ketoconazole 5–10 mg/kg PO q12–24h for 1–2 months beyond clinical cure; gastrointestinal

disturbances more commonly seen in cats as are other side effects such as depression, fever, jaundice, and neurological signs.



FOLLOW-UP

PATIENT MONITORING

Reevaluation, including assessment of liver enzymes, recommended every 2–4 weeks.

PREVENTION/AVOIDANCE

Determine the source of the original infection, if possible, to prevent repeat infections.

EXPECTED COURSE AND PROGNOSIS

- Failure of response to therapy should not be unexpected. • Fluconazole and terbinafine remain relatively untested but may show promise for treatment.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- **Caution:** this is a zoonotic disease. • Client education is of paramount importance.
- Absence of a break in the skin does not protect against the disease. • Reports of zoonotic transmission from bites and scratches from rodents, parrots, cats, dogs, horses, and armadillos. • Clinically healthy cats sharing a household with an infected cat may be a source of infection.

ABBREVIATIONS

- GMS = Gomori's methamine silver (stain)
- PAS = periodic acid-Schiff (stain) • SSKI = supersaturated potassium iodide

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Consulting Editor Alexander H. Werner

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SQUAMOUS CELL CARCINOMA, DIGIT



BASICS

OVERVIEW

- Locally invasive malignant tumor usually arising from subungual epithelium.
- Cats—metastasis to one or multiple digits from primary pulmonary site reported.
- Dogs—most common digital tumor (~50%); up to 25% metastatic rate, up to 22% multiple digits affected (multicentric disease).
- Forelimb more commonly affected than hind limb.
- Organ systems: skin/endocrine, musculoskeletal.

SIGNALMENT

- Dog and rarely cat.
- Median age—dogs and cats 10 years; reported in dogs as young as 3 years old.
- No sex predilection in dogs; in a small study of cats, females were more common.
- Large breeds (> 75%) and black/dark-coated dogs (> 90%) predisposed; breeds include standard poodle, Labrador retriever, giant schnauzer, rottweiler, dachshund, flat-coated retriever, and possibly Beauceron, Briard, and miniature poodle.

SIGNS

- Swollen digit or digital mass which fails to heal.
- Lameness.
- Ulceration.
- Fractured or missing nail.
- Multiple digits affected in up to 22% of dogs; may present in one digit and develop additional tumors later—may be multicentric or metastatic disease.
- Multiple digits commonly seen in cats (30%); usually part of a metastatic process from a primary pulmonary carcinoma.
- Regional lymphadenomegaly of the sentinel draining lymph node (uncommon at time of diagnosis).
- Cough or respiratory signs consistent with either metastatic pulmonary disease (uncommon at diagnosis) or primary pulmonary neoplasia (cats).

CAUSES & RISK FACTORS

Risk factors—(dogs) hereditary; dark skin pigmentation



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Nailbed infection (paronychia)
- Trauma
- Other tumors—(dog) melanoma; soft tissue sarcomas; mast cell tumor; osteosarcoma
- Other tumors—(cat) fibrosarcoma, adenocarcinoma, osteosarcoma
- Benign lesions—epithelial inclusion cyst, keratoacanthoma

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

IMAGING

- Thoracic radiography—three views are important to rule out metastatic disease (develops in up to 25% of dogs) and rule out a primary pulmonary carcinoma (cats).
- Limb radiography—lysis of the third phalanx of the affected digit in 80% of patients with potential secondary extension proximally to phalanx 2 and 1.
- Abdominal ultrasonography—for hind limb lesions, evaluate intra-abdominal lymph nodes for presence of metastatic disease.

DIAGNOSTIC PROCEDURES

- Cytology—diagnostic utility limited if there is severe inflammation or secondary infection (common), or the tumor is well differentiated.
- Wedge biopsy of lesion—required to confirm diagnosis via histopathology.
- Cytology and/or biopsy of regional lymph nodes—indicated to assess metastatic disease.



TREATMENT

- Amputation of the affected digit at the level of the metacarpal or metatarsal phalangeal joint.
- In cats with a primary pulmonary tumor, amputation of a single affected digit may provide local palliative care; in cats with multiple affected digits due to metastases, surgical intervention might not be a durable option because digits from multiple limbs are generally affected.
- Palliative radiation could be considered for single digits if metastatic disease present or in the setting of multicentric/multiple digits affected in dogs or cats.
- Analgesics for pain control and antibiotics for secondary bacterial infections may be indicated.
- Benefit of chemotherapy has not been established; however in patients with advanced stage of disease chemotherapy useful for squamous cell carcinoma of other sites could be considered.



MEDICATIONS

DRUG(S)

Piroxicam (dogs) 0.3 mg/kg PO q24h for analgesia; (cats) no established dosages; however, 0.3 mg/kg PO q48h has been used anecdotally.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

None



FOLLOW-UP

PATIENT MONITORING

- Recheck with physical examination, thoracic radiographs, lymph node evaluation, ± abdominal ultrasound at 1–2 months, then every 3 months after treatment (complete surgical excision).

EXPECTED COURSE AND PROGNOSIS

- Complete surgical excision of the primary lesion and no evidence of metastasis—additional treatment may not be required.
- Survival time following complete surgical excision depends upon location of the tumor on the digit—SCC originating from subungual epithelium: 95% 1-year and 74% 2-year survival; SCC originating in other parts of the digit: 60% 1-year and 44% 2-year survival.
- In one study 1- and 2-year survival was 50% and 18%, respectively, while in two other studies, only 20–45% of dogs died of SCC (multicentric or metastatic) and the median survival time was not reached.
- Development of multicentric disease (multiple affected digits) in dogs appears more common than lymph node or pulmonary metastasis.
- Surgery to amputate affected digit, regardless of presence of metastases, provides positive impact on survival in the dog.
- Histologic grading does not appear predictive of development of multicentric or metastatic disease in dogs.
- Prognosis for cats is poor with median survival times of 2–3 months and metastatic rates of approximately 25%; survival times are similar in cats with primary and metastatic squamous cell carcinoma.



MISCELLANEOUS

ABBREVIATION

SCC = squamous cell carcinoma

SEE ALSO

- Melanocytic Tumors, Skin and Digit
- Squamous Cell Carcinoma, Skin

Suggested Reading

Bellucci S, Brisebard E, Watrelot D, Pillet E, Marchal T, Ponce F. Digital squamous cell carcinoma in dogs: epidemiological, histological, and immunohistochemical study. Vet Pathol 2013, 50(6):1078–1082.

Author Jackie M. Wypij

Consulting Editor Timothy M. Fan

SQUAMOUS CELL CARCINOMA, EAR



BASICS

OVERVIEW

- Malignant tumor of squamous epithelium occurring on the pinna, external ear, and/or middle ear (less common). • Pinna—most common location in cats; tumors of the pinna in dogs are rarely squamous cell carcinoma.
- Organ system: Skin/Endocrine.

SIGNALMENT

- Cat and dog. • Tumors of the pinna—common in cats with light pigmentation, average 12 years. • Ear canal tumors—seen in older dogs and cats. • No sex predilection.
- Cocker spaniels overrepresented for benign and malignant ear canal tumors in one study.

SIGNS

- Tumors of the pinna: ° Slowly developing lesions of the edge of the pinna
- Precancerous stage—crusty eczematous lesions (actinic dermatitis) ° Cancerous phase—proliferation and/or ulceration progresses ° Multiple cutaneous lesions (about 10–15% of cats) occur in haired skin, unrelated to sunlight exposure (multicentric squamous cell carcinoma *in situ* or MSCCIS).
- Tumors of the ear canal: ° Usually unilateral
- Usually arise from the external ear canal
- Mass lesion (raised, ulcerated, broad-based)
- Malodorous aural discharge ° Pruritis ° Pain
- Vestibular signs/Horner's syndrome (facial nerve paralysis, head tilt, circling) in ~10% of dogs; more common in cats with ear canal tumors ° Difficulty opening jaw ° Cervical lymphadenomegaly (retropharyngeal, mandibular).

CAUSES & RISK FACTORS

- Pinna—chronic sunlight (UVB) exposure in cats with white fur and light skin pigmentation. • Ear canal—chronic inflammation may be a risk factor.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pinna (cats)—lesions caused by trauma, vasculitis or cryoglobulinemia. • Pinna (dogs)—mast cell tumor, histiocytoma, trauma, sebaceous gland tumor. • Ear canal/middle ear (cat)—inflammatory/nasopharyngeal polyp (middle ear), most external ear tumors are malignant (ceruminous gland adenocarcinoma, other).
- Ear canal/middle ear (dog)—chronic otitis, 60% of external ear canal tumors are malignant (ceruminous gland adenoma or adenocarcinoma, papilloma), nasopharyngeal polyps rare.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

Thorough examination and cytology and/or biopsy of regional lymph nodes (mandibular, retropharyngeal) to evaluate for regional metastasis (rare for pinnal lesions).

IMAGING

- Thoracic radiography—three views needed to evaluate for pulmonary metastasis (rare with pinnal lesions). • Skull radiography—limited usefulness but may identify soft tissue structures and bony lysis of the bulla with ear canal/middle ear tumors.
- Computed tomography—ideal for evaluation of soft tissue and bone involvement prior to planning surgical resection of tumors involving the ear canal; 57–67% locally invasive into surrounding tissues.

DIAGNOSTIC PROCEDURES

- Cytology may confirm diagnosis; however, ulceration, inflammation, and secondary infection may limit diagnostic utility.
- Biopsy of pinna or aural mass to confirm diagnosis via histopathology; video otoscopy may aid in visualization of mass lesion and biopsy.

PATHOLOGIC FINDINGS

Distinguished microscopically by characteristic groups of epithelial cells and keratinizing cells forming keratin pearls.



TREATMENT

- Pinna: ° Appropriate surgical excision may require pinnectomy and possibly vertical ear canal ablation; must remove lesion with margin of normal tissue.
- Alternatives include photodynamic therapy (less predictable; multiple treatments may be required), cryosurgery (for small, superficial lesions), strontium plesiotherapy (superficial radiation therapy), electrochemotherapy with bleomycin, or curettage/diathermy.
- Ear canal/middle ear: ° Total ear canal ablation and bulla osteotomy (TECA-BO) is usually needed to achieve complete excision; lateral ear canal resection rarely achieves adequate control.
- Anecdotally radiation therapy may be used for palliation of nonresectable tumors or postoperatively for microscopic disease.



MEDICATIONS

DRUG(S)

- Pinna (cat): ° Imiquimod 5% cream—apply topically q24h ° Etretinate 0.75–1 mg/kg PO q24h; used successfully to prevent progression of precancerous lesions; may not be

commercially available ° Acitretin (1 mg/kg PO q24h) can be used in place of etretinate ° Vitamin E 400–600 IU PO q12h; may be beneficial to prevent or delay progression of precancerous lesions. • Ear canal tumors:

- Systemic chemotherapy—benefit not yet established; anecdotal benefit.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Women who are pregnant or planning to become pregnant should not handle acitretin.



FOLLOW-UP

PATIENT MONITORING

- Pinna—recheck with physical examination at 1 month, then every 3 months after treatment (complete surgical excision).
- Ear canal—recheck with physical examination, thoracic radiographs, lymph node evaluation, and possible computed tomography every 3 months after treatment.

PREVENTION/AVOIDANCE

- Limit sun exposure, especially between 10 a.m. and 3 p.m.
- Yearly tattoos on nonpigmented areas may be helpful.

EXPECTED COURSE AND PROGNOSIS

- Pinna—prognosis good with complete surgical excision; survival > 1.5 years with complete pinnectomy.
- Ear canal tumors locally invasive (57–67%) and recur locally despite surgery; prognosis is guarded.
- Dogs—median survival 5.3 months with bulla involvement compared to > 58 months without.
- Cats—median survival 3.8 months; worse prognosis with bulla involvement; median survival 1.5 months with neurologic signs.



MISCELLANEOUS

SEE ALSO

- Ceruminous Gland Adenocarcinoma, Ear
- Squamous Cell Carcinoma, Nasal Planum
- Squamous Cell Carcinoma, Skin

Suggested Reading

Sula MJ. Tumors and tumorlike lesions of dog and cat ears. Vet Clin North Am Small Anim Pract 2012, 42:1161–1178.

Author Jackie M. Wypij

Consulting Editor Timothy M. Fan

SQUAMOUS CELL CARCINOMA, GINGIVA



BASICS

OVERVIEW

- Malignant tumor of squamous epithelium.
- Rapid progression, locally invasive, highly bone-invasive (77%). • Most common oral malignancy in cats; one of most common oral malignancies in dogs. • Metastasis—approximately 10–20% metastasis in dogs and cats with potential involvement of draining lymph nodes (most common) and lung parenchyma.

SIGNALMENT

- Mean age (dogs and cats)—10.5 years (range, 3–15 years)
- More common in medium- and large-breed dogs

SIGNS

Historical Findings

- Mass
- Excessive salivation
- Dysphagia
- Halitosis
- Bloody oral discharge
- Weight loss
- Decreased appetite
- Poor grooming (cats)

Physical Examination Findings

- Erythematous, ulcerated, fleshy lesion
- Rostral mandible is most common site
- Loose teeth
- Facial swelling or deformity
- Exophthalmos
- Pain on opening jaw

CAUSES & RISK FACTORS

Potential risk factors in cats include flea collars, canned food, tuna, and tobacco smoke.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other oral malignancy—fibrosarcoma in cats; melanoma, fibrosarcoma, osteosarcoma in dogs
- Epulis
- Tooth root abscess
- Benign growth or polyp
- Gingival hyperplasia
- Eosinophilic granuloma complex

IMAGING

- Skull radiography—evaluate bone involvement deep to the mass; requires 40–50% bone destruction before evident radiographically.
- Dental radiography—more sensitive in evaluating local disease than skull radiography; best with mandibular masses.
- Computed tomography (CT scan)—ideal method to evaluate soft tissue extension, bone invasion, and assess regional lymph nodes prior to surgical planning.
- Thoracic radiography—three views to detect pulmonary metastasis (eventually develop in up to 36% of dogs, rare in cats).

DIAGNOSTIC PROCEDURES

- Cytologic evaluation of lesion—fine-needle aspirate samples often non-diagnostic; obtain impression smear from an incisional biopsy specimen (wedge); ulceration, inflammation, and secondary infection may limit diagnostic

utility.

- Large, deep tissue biopsy (down to bone)—required to differentiate from other oral malignancies via histopathology.

- Cytology and/or biopsy of regional lymph nodes (mandibular, retropharyngeal) to evaluate regionally metastatic disease (10–20% dogs and cats).



TREATMENT

DOGS

- Radical surgical excision required (e.g., hemimandibulectomy or partial maxillectomy); usually well tolerated; margins of at least 2 cm necessary.
- Radiation therapy—effective for long-term control; curative-intent treatment used alone or in combination with surgery or chemotherapy.
- Chemotherapy—alone or in combination with other treatment modalities, toceranib phosphate (Palladia) exerts single-agent activity in a substantial fraction (75%) of dogs treated.
- Piroxicam may have some antineoplastic effects.
- Cryosurgery—indicated for small lesions with no bone involvement.
- Photodynamic therapy—adjunct to surgery may be effective for local control of small tumors.
- Analgesics for pain control and antibiotics for secondary bacterial infections may be indicated.

CATS

- Surgery—most tumors are nonresectable; small rostral lesions may be excised with wide 2–3 cm margins (hemimandibulectomy); cats do not tolerate aggressive oral surgery as well as dogs.
- Palliative treatments include coarse-fraction radiation therapy (< 50% response).
- Metastasis less of a concern as most cats succumb to local disease progression.
- Bisphosphonates—used to palliate bone pain.
- Analgesics for pain control and antibiotics for secondary bacterial infections may be indicated.



MEDICATIONS

DRUG(S)

- Toceranib phosphate (Palladia) treatment of dogs at 2.75–3.25 mg/kg every other day.
- Cisplatin (dogs only) 60–70 mg/m² IV once every 3–4 weeks for four treatments; provides marked palliation of clinical signs; response depends on severity of the localized or metastatic lesion; must use saline diuresis (18.3 mL/kg/h IV over 6 hours; give cisplatin after 4 hours); pretreat with an antiemetic.
- Carboplatin—dogs, 250–300 mg/m² every 3 weeks IV; cats, 180–250 mg/m² every 3–4 weeks for 4–5 treatments.
- Mitoxantrone (cats) 5–6 mg/m² every 3 weeks IV for 4–5 treatments.
- Piroxicam (dogs) 0.3 mg/kg PO daily; may be useful to

induce partial remission in some patients; dosages in cats have not been well established; however, 0.3 mg/kg PO q48h has been used anecdotally.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Cisplatin—never use in cats.
- Do not administer cisplatin with NSAIDs due to nephrotoxicity.



FOLLOW-UP

PATIENT MONITORING

Recheck with thorough physical examination, lymph node evaluation, and three-view thoracic radiographs at 1–2 months, then every 3 months after treatment.

POSSIBLE COMPLICATIONS

Postoperative complications—tumor recurrence, ptalism, mandibular drift leading to malocclusion, difficulty prehending food, inability to groom.

EXPECTED COURSE AND PROGNOSIS

Dogs

- Negative prognostic factors—caudal or maxillary location, > 2 cm diameter, older age, incomplete excision.
- Surgical excision—median survival 15–16 months, 34 months combined with radiation therapy; mandibulectomy better outcome than maxillectomy.
- Photodynamic therapy—adjunct to surgery; median survival 17 months in 8 dogs that responded.
- Combination carboplatin and piroxicam with or without surgery—median survival time of > 18 months (7 dogs).
- Piroxicam—17% response rate with a median progression-free interval of 3.5–6 months.

Cats

- Surgical excision—median survival 1 year for resectable tumors (rare).
- Palliative radiation—median survival 2–5.8 months, up to 10 months with complete remission.
- In a small study of stereotactic radiation therapy, females had better outcome than males.

S



MISCELLANEOUS

SEE ALSO

- Fibrosarcoma, Gingiva
- Melanocytic tumors, Oral
- Squamous Cell Carcinoma, Tongue
- Squamous Cell Carcinoma, Tonsil

Suggested Reading

Sabhnlok A, Ayl R. Palliative radiation therapy outcomes for cats with oral squamous cell carcinoma (1999–2005). Vet Radiol Ultrasound 2014 Apr 25.

Author Jackie M. Wypij

Consulting Editor Timothy M. Fan

SQUAMOUS CELL CARCINOMA, LUNG



BASICS

OVERVIEW

- Rare primary tumor of bronchial epithelium with squamous metaplasia.
- High metastatic potential with involvement of regional lymph nodes, pleural surface (carcinomatosis), and pulmonary parenchyma and less commonly distant organs including digits in cats.
- Organ system: respiratory.

SIGNALMENT

- Dog and cat.
- Older animals, mean age—dogs, 11 years; cats, 12 years.
- Persian cats may be overrepresented for pulmonary carcinomas, but not necessarily of squamous histology.

SIGNS

Historical Findings

- Incidental finding
- Harsh, non-productive cough
- Dyspnea
- Lethargy or exercise intolerance
- Cachexia and weight loss
- Lameness and pain associated with digit metastasis or hypertrophic osteopathy

Physical Examination Findings

- Tachypnea
- Wheeze
- Abnormal lung sounds
- Hemoptysis
- Hypertrophic osteopathy
- Single or multiple digital lesions (metastasis) in cats
- Neuromyopathy (such as megaesophagus) and paraplegia (rare)

CAUSES & RISK FACTORS

- Urban environment and second-hand smoke suspected but have not shown definitive correlation in multiple studies.
- Dogs trained to smoke cigarettes may develop lung cancer.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other primary lung neoplasia (e.g., cats: adenocarcinoma, bronchoalveolar carcinoma, adenosquamous carcinoma; dogs: adenocarcinoma, bronchoalveolar carcinoma, histiocytic sarcoma, and anaplastic carcinoma). SCC is one of most rare histologic subtypes of carcinoma.
- Metastatic pulmonary neoplasia.
- Bronchogenic cyst.
- Bullae.
- Abscess.
- Fungal granuloma.
- Aspiration pneumonia.

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilic leukocytosis
- Hypercalcemia (rare)

IMAGING

- Thoracic radiography:
 - Three views; most often in caudal lung lobes
 - Most commonly identify a solitary mass with well-circumscribed margins
 - May identify tracheobronchial lymphadenomegaly or pulmonary metastatic lesions
 - May displace/compress trachea or mainstem

bronchi with airway obstruction and peripheral atelectasis

- May identify pleural effusion
- Computed tomography (CT scan):
- Ideal for evaluating surgical resectability
- Solitary, well-circumscribed, bronchocentric mass with internal air bronchograms
- More accurate than radiographs in detecting pulmonary and lymph node metastasis
- Mild to moderate heterogeneous contrast enhancement
- Limb radiography:
- Rarely, single or multiple digit metastases are identified in cats as bone lysis in the distal phalanx
- Rarely, hypertrophic osteopathy exemplified with periosteal bone proliferation

DIAGNOSTIC PROCEDURES

- Cytology via transthoracic fine-needle aspiration of peripheral lesions; ultrasound or CT guidance may aid in obtaining adequate samples.
- Cytology samples obtained via endoscopic bronchial brushing often non-diagnostic; may be useful for centrally located lesions.
- Cytologic analysis of pleural effusion or intrathoracic lymph node aspirates may be helpful if primary lesion is not amenable to aspiration.
- Tissue biopsy is necessary for definitive diagnosis and may be obtained via keyhole biopsy, thoracoscopy, or thoracotomy.
- Bronchoalveolar lavage and transtracheal wash are rarely diagnostic.
- Potential life-threatening complications of aspiration/biopsy procedures include pneumothorax, hemothorax, pleural effusion, infection, and rarely iatrogenic tumor seeding.



TREATMENT

- Surgery (thoracotomy and lung lobectomy)—wide and complete resection of affected lung lobe affords best opportunity for long-term control; biopsy lymph nodes even if they appear normal; lymph node extirpation is ideal but frequently difficult.
- In select cases, thorascopic surgery may be considered.
- Chemotherapy—potentially beneficial in adjuvant or palliative setting, intracavitary chemotherapy may be useful for carcinomatosis and pleural effusion.
- Palliative medications may include nonsteroidal anti-inflammatories/analgesics, cough suppressants, and antibiotic therapy for secondary bacterial infections.



MEDICATIONS

DRUG(S)

- Cisplatin—(dogs only) 60 mg/m² IV every 3 or 4 weeks for 4 treatments; nephrotoxic, so must use with saline diuresis (18.3 mL/kg/h); antiemetic also required.
- Doxorubicin—dogs > 10 kg, 30 mg/m² IV; dogs < 10 kg and cats, 1 mg/kg once every 2–3 weeks for 5 treatments; has provided marked palliation.

- Carboplatin—dogs, 250–300 mg/m² IV every 3 weeks; cats, 180–250 mg/m² IV every 3–4 weeks for four to five treatments.
- Mitoxantrone (pleural effusion)—dogs and cats, 5–6 mg/m² every 3 weeks; can give intracavitary and/or IV for four to five treatments.
- Vinorelbine—dogs, 15 mg/m² weekly for 4 weeks then every other week for four additional treatments; may be effective for pulmonary carcinomas.

CONTRAINdications/POSSIBLE INTERACTIONS

- Cisplatin—never use in cats.
- Do not administer cisplatin with NSAIDs; severe renal toxicity reported in dogs.



FOLLOW-UP

PATIENT MONITORING

After complete excision, consider chemotherapy options; recheck with three-view thoracic radiographs and/or CT scan in 1–2 months, then every 3 months.

EXPECTED COURSE AND PROGNOSIS

- Survival if untreated or with evidence of metastatic disease—usually < 3 months.
- Median survival with complete excision of primary tumor and no metastasis (dogs and cats)→ 300 days.
- Median survival with incomplete surgical excision of primary tumor or the presence of lung/lymph node metastasis (dogs and cats) < 75 days.
- Median long-term survival of cats with pulmonary carcinomas treated with surgery is 64–115 days.
- Negative prognostic factors (all lung tumors): large size, central location, metastasis, pleural effusion, high histologic grade, poorly differentiated, or respiratory signs at diagnosis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Paraneoplastic hypertrophic osteopathy

SEE ALSO

Adenocarcinoma, Lung

Suggested Reading

Maritato KC, Schertel ER, Kennedy SC, et al. Outcome and prognostic indicators in 20 cats with surgically treated primary lung tumors. J Feline Med Surg. 2014 Apr 7. Epub.

Author Jackie M. Wypij

Consulting Editor Timothy M. Fan

SQUAMOUS CELL CARCINOMA, NASAL AND PARANASAL SINUSES



BASICS

OVERVIEW

- Local invasion of neoplastic squamous epithelium from the nasal cavity and/or paranasal sinuses.
- Slowly progressive (months) and commonly bilateral.
- Low metastatic rate.
- Prevalence—15–17% of nasal neoplasia in cats and dogs.

SIGNALMENT

- More common in dog than in cat.
- Dogs—median age, 9–10 years (range, 3–16 years), male predilection; cats—median 10–2 years, male predilection.
- Dogs—predilection for sinonasal tumors in medium and large breeds.

SIGNS

Historical Findings

- Intermittent and progressive unilateral to bilateral epistaxis and/or mucopurulent nasal discharge
- Epiphora
- Sneezing
- Halitosis
- Anorexia
- Dyspnea
- Seizures secondary to cranial invasion (in up to 35% of dogs)

Physical Examination Findings

- Nasal discharge (epistaxis, mucopurulent, serosanguinous, and/or sanguinous)
- Facial deformity
- Stridor
- Ocular abnormalities: epiphora, decreased retropulsion, elevated third eyelid, exophthalmus
- Pain on nasal or paranasal sinus palpation
- Obstructed nasal airflow

CAUSES & RISK FACTORS

- Unknown.
- Doliccephalic breed, urban environment, and tobacco smoke exposure speculated to be risk factors.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other intranasal malignant neoplasia—adenocarcinoma, undifferentiated carcinoma, lymphoma (cats), sarcomas (dogs)
- Tooth root abscess
- Viral infection—cats
- Cryptococcosis—cats
- Aspergillosis; other fungal infection
- Foreign body
- Trauma
- Oronasal fistula
- Coagulopathy
- Hypertension
- Bacterial sinusitis—uncommon
- Lymphocytic-plasmacytic rhinitis
- Inflammatory polyps (cats)
- Parasites

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal; may have anemia if chronic and/or severe epistaxis.

OTHER LABORATORY TESTS

If epistaxis, evaluate coagulation profile and blood pressure to rule out hypertension and coagulopathy prior to intranasal biopsy.

IMAGING

- Skull radiography—asymmetrical osteolysis of caudal turbinates; superimposition of soft tissue mass; fluid density in the frontal sinuses; loss of teeth; displacement of midline structures; involvement of hard palate.
- Thoracic radiography—detect pulmonary metastasis (uncommon).
- Computed tomography (CT scan) or MRI (magnetic resonance imaging)—recommended imaging modalities for the identification of soft-tissue density mass, loss of turbinate detail, soft tissue/fluid opacity in sinus; best method for assessing tumor invasiveness, including bony invasion, invasion of cribriform plate or orbit.

DIAGNOSTIC PROCEDURES

- Rhinoscopy—mass effect, may be obscured by exudates.
- Diagnostic utility of cytology obtained by aspiration or squash preparation may be limited by inflammation or secondary infection.
- Deep tissue biopsy with histopathology—necessary for definitive diagnosis; methods include nasal hydropulsion, transnostril blind biopsy with forceps or bone curette, fiber-optic guided biopsy, percutaneous biopsy of facial deformities; biopsy via dental extraction site, rhinotomy.
- Precautions must be taken to minimize risk of penetrating the cribriform plate.
- Cytology and/or biopsy of regional lymph nodes—detect metastatic disease (up to 10% at diagnosis).



TREATMENT

- Surgery alone does not improve outcome in most studies; exenteration and radiation therapy may provide benefit.
- Definitive radiotherapy—with or without surgery; best clinical control in dogs and cats.
- Coarse-fraction radiation therapy also beneficial in dogs and cats for palliation.
- Adjunctive chemotherapy or single-agent toceranib phosphate (Palladia)—responses in dogs reported; recommended for nonresectable mass, palliation of clinical signs, metastasis, and as an adjuvant to radiation therapy.
- Analgesics for pain control.
- Anecdotally, nasal hydropulsion may be used for palliation of clinical signs.



MEDICATIONS

DRUG(S)

- Cisplatin (dogs only) 60–70 mg/m² IV once every 3 weeks for four treatments; nephrotoxic, use saline diuresis (18.3 mL/kg/h IV over 6 hours; give cisplatin after 4 hours); administer antiemetic prior to chemotherapy.
- Carboplatin—dogs, 250–300 mg/m² IV every 3 weeks; cats, 180–250 mg/m² IV every 3–4 weeks for 4 or

5 treatments.

- Mitoxantrone (dogs) 5–6 mg/m² IV every 3 weeks for 4 or 5 treatments.
- Toceranib phosphate (dogs) 2.75–3.25 mg/kg PO q48h long term.

CONTRAINdications/POSSIBLE INTERACTIONS

- Cisplatin—never use in cats.
- Do not administer cisplatin with NSAIDs due to nephrotoxicity.



FOLLOW-UP

PATIENT MONITORING

Recheck with physical examination, thoracic radiographs, lymph node evaluation, ± CT scan every 3 months after treatment or when signs recur.

POSSIBLE COMPLICATIONS

Acute or late side effects from radiation therapy (e.g., ocular cataracts or keratoconjunctivitis sicca, osteomyelitis/osteonecrosis, oronasal fistula).

EXPECTED COURSE AND PROGNOSIS

- Untreated carcinomas (all types)—median survival 3 months; epistaxis carries a worse prognosis.
- Definitive radiotherapy (all carcinomas)—median survival ~12–18 months (dogs and cats); 2-year survival 30–48% (dogs); 1-year survival 44% (cats).
- Coarse-fraction radiation therapy (all tumor types)—improved clinical signs in ~90% of dogs; median survival 4.8–10 months; median survival 10–12 months (cats).
- Surgical exenteration and radiation therapy (all tumor types)—survival ~4 years (dogs).
- SCC reported to have worse prognosis than other nasal tumors; median survival times of 6–9.4 months with radiation therapy; median survival time of 2 months in 8 dogs (with or without therapy); other studies do not demonstrate a difference with histologic subtype.
- Local recurrence with extension to the brain—common; brain involvement is a poor prognostic sign.
- Re-irradiation may be feasible.



MISCELLANEOUS

SEE ALSO

- Adenocarcinoma, Nasal
- Chondrosarcoma, Nasal and Paranasal Sinus
- Fibrosarcoma, Nasal and Paranasal Sinus

Suggested Reading

Fujiwara A, Kobayashi T, Kazato Y, Yayoshi N, Fujita M. Efficacy of hypofractionated radiotherapy for nasal tumours in 38 dogs (2005–2008). J Small Anim Pract 2013, 54(2):80–86.

Author Jackie M. Wypij

Consulting Editor Timothy M. Fan

SQUAMOUS CELL CARCINOMA, NASAL PLANUM



BASICS

OVERVIEW

- Malignant tumor of squamous epithelial cells of the nasal planum.
- Locally invasive and rarely metastasizes.
- Organ systems: skin/exocrine, respiratory.

SIGNALMENT

- Common in cat; rare in dog.
- Mean age—cats, 8.5–12.1 years; dogs, 9–10 years.
- More likely to develop in animals with a lightly pigmented nose (cats).
- No reported sex or breed predilection in cats.
- Dogs—overrepresentation of males and Labrador retrievers in one study.

SIGNS

- Cats—slowly progressive lesion; may begin as superficial crusting and scabbing, progress to carcinoma *in situ*, and develop into superficial and then invasive erosive carcinoma; other cutaneous sites may be affected (cats—multicentric squamous cell carcinoma *in situ*).
- Dogs—sneezing; epistaxis; swelling and ulceration of planum, proliferative lesion.
- Cervical lymphadenomegaly—occasionally in dogs, rare in cats.

CAUSES & RISK FACTORS

- Exposure to ultraviolet light (UVB)
- Absence of protective pigment (cats)



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infection/abscess
- Trauma
- Allergic dermatitis
- Other dermatitis
- Eosinophilic granuloma complex (cats)
- Immune-mediated disease
- Cutaneous lymphoma
- Mast cell tumor

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

S

OTHER LABORATORY TESTS

Cytologic examination and/or biopsy of regional lymph nodes should be performed to identify metastasis (rare in cats, occasionally in dogs).

IMAGING

- Thoracic radiography—three views to evaluate for metastasis (rare).
- Computerized tomography (CT scan)—evaluate soft tissue extension and bone invasion prior to surgical planning, essential for canine tumors in which extensive underlying structures are often involved.

DIAGNOSTIC PROCEDURES

- Cytologic examination—fine-needle aspirate of primary lesion may confirm diagnosis; however, ulceration, inflammation, and secondary infection may limit diagnostic utility.
- Biopsy and histopathology—a deep wedge or punch biopsy is often needed to definitively diagnose squamous cell carcinoma. Multiple samples recommended as lesion may have a spectrum of actinic changes ranging from squamous metaplasia to invasive carcinoma.

PATHOLOGIC FINDINGS

- Lesions—may vary in appearance depending on stage of disease in cats; typically ulcerative in cats; more likely proliferative in dogs.
- Histopathologic—characterized by irregular masses or cords of epidermal cells that proliferate downward into the dermis.
- Keratin formation, horn pearls, desmosomes, mitotic figures, and cellular atypia—frequent.



TREATMENT

- Superficial tumors—surgery, cryosurgery, irradiation (strontium-90 plesiotherapy), photodynamic therapy, electrochemotherapy with bleomycin, or curettage/diathermy.
- Invasive tumors—require radical surgical excision and adjunctive external beam radiotherapy (cats); dogs not as responsive to radiotherapy.
- Immediate postoperative nutritional support may be required, especially for cats.
- Analgesics for pain control and antibiotics for secondary bacterial infections may be indicated.



MEDICATIONS

DRUG(S)

- Etretinate 0.75–1 mg/kg PO q24h; synthetic retinoid; may be useful for early precancerous lesions; not commercially available in the United States or Canada.
- Acitretin (1 mg/kg PO q24h) can be used in place of etretinate.
- Imiquimod 5% cream for nasal planum lesions associated with MSCCIS—apply topically to affected lesions q24–48h; most cats respond but develop new lesions in other sites; these lesions often subsequently respond to topical therapy.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Women who are pregnant or planning to become pregnant should not handle acitretin.



FOLLOW-UP

PATIENT MONITORING

- Physical examination—at 1 month, then every 3 months after treatment.
- Biopsy—any new suspicious lesion.

PREVENTION/AVOIDANCE

- Limit sun exposure, especially between 10 a.m. and 3 p.m.
- Tattoos on nonpigmented areas may be helpful.

EXPECTED COURSE AND PROGNOSIS

- Prognosis—good for small, non-invasive tumors; guarded for invasive tumors.
- Survival with radiotherapy alone (cats)—mean, 17.7 months; 1 year, 61.5% with 81.8% recurrence.
- Surgery (cats, noseectomy)—median survival > 22 months.
- Strontium-90 plesiotherapy (cats, superficial)—98% response rate; median progression-free interval of 4.5 years; median survival > 8 years.
- Photodynamic therapy (cats, superficial)—96% response rate; often need multiple treatments; does not appear as effective as other therapies long term.
- Electrochemotherapy with bleomycin (pilot study)—81% complete remission, risk of recurrence, well tolerated.
- Curettage and diathermy (pilot study)—excellent response, risk of recurrence.
- Dogs (superficial tumors)—surgery alone may be curative.
- Dogs (invasive tumors)—in one study of 8 dogs, average survival time was 5.4 months; in another study of 17 dogs treated with surgery and/or radiation therapy, 70% of tumors recurred with a median survival time of 3–6 months.



MISCELLANEOUS

ABBREVIATION

MSCCIS = multicentric squamous cell carcinoma *in situ*

SEE ALSO

- Squamous Cell Carcinoma, Ear
- Squamous Cell Carcinoma, Skin

Suggested Reading

Jarrett RH, Norman EJ, Gibson IR, Jarrett P. Curettage and diathermy: a treatment for feline nasal planum actinic dysplasia and superficial squamous cell carcinoma. J Small Anim Pract 2013, 54:92–98.

Author Jackie M. Wypij

Consulting Editor Timothy M. Fan

SQUAMOUS CELL CARCINOMA, SKIN



BASICS

DEFINITION

- Malignant tumor of squamous epithelium.
- Multicentric squamous cell carcinoma *in situ* (MSSCIS)—also called Bowen's-like disease or Bowenoid carcinoma *in situ* (cats).

PATHOPHYSIOLOGY

- Local disease may progress from carcinoma *in situ* to invasive carcinoma.
- Metastasis is uncommon; most common sites are regional lymph nodes and lungs.
- ~10% MSSCIS, ~90% actinic (solar-induced).

SYSTEMS AFFECTED

Skin/Exocrine—skin and metastatic sites

GENETICS

Unknown

INCIDENCE/PREVALENCE

Represents 9–25% of all skin tumors in cats and 4–18% in dogs.

GEOGRAPHIC DISTRIBUTION

Solar-induced (actinic) SCC is more prevalent in sunny climates and high altitudes (increased ultraviolet UVB exposure).

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Cats—none reported; patients often have light or unpigmented skin; Siamese cats are underrepresented for solar-induced SCC likely due to their protective pigment.
- Dogs—Scottish terrier, Pekingese, boxer, poodle, Norwegian elkhound, Dalmatian, beagles, whippet, and white English bull terrier may be predisposed.

Mean Age and Range

- Dogs—8 years.
- Cats—9 years (2–16) for actinic form; 10 years (7–17) for MSSCIS.

Predominant Sex

None

SIGNS

Historical Findings

- Crusts, ulcer, or mass that may have been present for months and unresponsive to conservative treatment with topical antibiotic or anti-inflammatory therapies.
- MSSCIS (cats)—skin becomes pigmented; ulcer forms in the center; followed by a painful scabby lesion that may expand peripherally.
- Lips, nose, and pinna involvement—may start out as a shallow crusting lesion that progresses to a deep ulcer.
- Facial skin involvement (cats).

Physical Examination Findings

- Proliferative or erosive skin lesions; erosive lesions are most common in the cat.

- Cats—most common sites for solar-induced lesions are the nasal planum, eyelids, lips, and pinna.

- MSSCIS may occur in any site, unrelated to sun exposure or skin pigmentation; may note 2 to > 30 lesions on the head, digits, neck, thorax, shoulders, and ventral abdomen; hair in the lesion epilates easily; crusts cling to the epilated hair shaft.
- Dogs—most commonly affects toes, scrotum, nose, legs, and anus.

CAUSES

- Ultraviolet irradiation (UVB, actinic form).
- Recent studies show an association with papillomaviruses in feline SCC in approximately 50% of samples tested; dogs have also been shown to have papillomavirus-positive SCC.

RISK FACTORS

- Prolonged exposure to ultraviolet light (UVB).
- Light or nonpigmented skin.
- Previous thermal injury—burn scar.
- Risk factors for MSSCIS in cats are undetermined but may be associated with immunosuppression.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infection/abscess
- Dermatophytosis
- Trauma
- Allergic dermatitis
- Other dermatitis
- Eosinophilic granuloma complex
- Immune-mediated disease
- Cutaneous lymphoma
- Mast cell tumor

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal.

OTHER LABORATORY TESTS

- Cytologic examination—fine-needle aspirate of primary lesion may confirm diagnosis; however, ulceration, inflammation, and secondary infection may limit diagnostic utility.
- Cytologic examination of lymph nodes should be performed to identify presence of regional metastasis.

IMAGING

- Thoracic radiography—three views may detect lung metastasis (rare).
- Abdominal radiography or ultrasonography—evaluate and monitor sublumbar lymph nodes if skin disease involves the caudal half of the patient.

DIAGNOSTIC PROCEDURES

Biopsy and histopathology—a deep wedge or punch biopsy is often needed to definitively diagnose cutaneous SCC. Multiple samples

recommended as actinic form may encompass spectrum from actinic changes to carcinoma.

PATHOLOGIC FINDINGS

Gross

- Ulcerative tumors—most common; may appear shallow and crusted and progress to deep craters.
- Proliferative tumors—may have a cauliflower-like appearance; may ulcerate and bleed easily.
- MSSCIS—multiple painful ulcers that scab over and expand peripherally to reach more than 4 cm in diameter.

Histopathologic

- Cords or irregular masses of epidermal cells infiltrating into the dermis and subcutis.
- Large numbers of horn (keratin) pearls in well-differentiated tumors.
- Desmosomes and mitotic figures common.
- MSSCIS—dysplastic, highly ordered keratinocytes proliferate, replacing normal epidermis, but do not penetrate the basement membrane into the surrounding dermis.



TREATMENT

APPROPRIATE HEALTH CARE

- Superficial tumors suspected to be solar-induced—wide surgical excision may be locally curative; other treatment options include cryosurgery, photodynamic therapy, or irradiation (strontium plesiotherapy).
- Invasive tumors—require aggressive surgical excision; photodynamic therapy and strontium-90 plesiotherapy have little efficacy; external-beam radiation therapy has shown effectiveness postoperatively or alone for nonresectable tumors.
- MSSCIS may be treated with curative-intent surgery for local control; however, most cats develop new lesions in other sites; therefore treatment with immune-modulating drugs (imiquimod) may be most effective for multicentric disease.
- Topical synthetic retinoids—may be useful for early solar-induced superficial lesions.
- External beam radiotherapy—recommended for inoperable tumors or as adjunct to surgery.
- Adjunctive chemotherapy—recommended with incomplete surgical excision, non-resectable mass, and metastasis; cisplatin (dogs only), carboplatin, and mitoxantrone—reported to induce partial and complete remission.
- Electrochemotherapy (bleomycin) and curettage with diathermy show promise in pilot studies but not routinely available in clinical practice.

NURSING CARE

- Consider the use of analgesics as needed.
- Secondary skin infections may benefit from antibiotic therapy.

SQUAMOUS CELL CARCINOMA, SKIN

(CONTINUED)

- Interventional parenteral nutrition (feeding tube)—with nasal planum resection.

ACTIVITY

- Dictated by the location of the tumor and the type of treatment.
- Generally limit until sutures are removed, if surgery has been done.

DIET

Normal

CLIENT EDUCATION

- Inform client about the benefit of early diagnosis and treatment.
- Discuss risk factors associated with the development of the tumor (ultraviolet light exposure).
- Most cats (75%) with MSCCIS will develop new lesions in other sites.

SURGICAL CONSIDERATIONS

Wide surgical excision—treatment of choice for invasive and solar-induced tumors; skin flaps and body wall reconstruction sometimes required. Lower eyelid often easier to reconstruct than upper eyelid.



MEDICATIONS

DRUG(S) OF CHOICE

- Imiquimod 5% cream for MSCCIS—apply topically to affected lesions q24–48h; most cats respond but develop new lesions in other sites; these lesions often subsequently respond to topical therapy.
- Systemic chemotherapy anecdotally useful. Cisplatin—dogs only, 60 mg/m² IV every 3 or 4 weeks for four treatments; nephrotoxic, so must use with saline diuresis (18.3 mL/kg/h IV over 6 hours; give cisplatin after 4 hours); pretreat with an antiemetic.
- Carboplatin—dogs, 300 mg/m² IV every 3 weeks; cats, 200–250 mg/m² IV every 3–4 weeks for 4 or 5 treatments.
- Mitoxantrone—dogs and cats, 5–6 mg/m² IV every 3 weeks for 4 or 5 treatments.

CONTRAINDICATIONS

Cisplatin—do not use in cats, causes severe hydrothorax, pulmonary edema, and death; do not use in dogs with concurrent renal disease, potentially nephrotoxic; do not use in conjunction with NSAIDs.

PRECAUTIONS

- Chemotherapeutics—follow published guidelines and protocols for safe use; be familiar with potential side effects; may be toxic, seek advice from a medical oncologist before treatment if you are unfamiliar with cytotoxic drugs.
- Imiquimod—approximately 25% of cats develop local erythema; < 10% of cats develop elevated liver enzymes, neutropenia, or gastrointestinal upset; most cats develop new lesions which subsequently respond to imiquimod treatment.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

Topical synthetic retinoids (e.g., tretinoin)—may be useful for early solar-induced superficial lesions; may be irritating to skin.



FOLLOW-UP

PATIENT MONITORING

- Routine CBC and serum chemistry panel should be evaluated during medical therapy with chemotherapy or imiquimod cream.
- Physical examination at 1 month after resolution of tumor, then every 3 months after treatment or if the owner thinks the tumor is recurring.
- Thoracic radiography and lymph node evaluation at each 3-month recheck examination; abdominal radiography or ultrasound if the lesion is on the caudal portion of the patient.

PREVENTION/AVOIDANCE

- Limit sun exposure, especially between the hours of 10 a.m. and 3 p.m.
- Tattoos on nonpigmented areas may be helpful.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

Prognosis—good with superficial lesions that receive appropriate treatment; guarded with invasive lesions, advanced stage of disease, or recurrent lesions.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Squamous Cell Carcinoma, Ear
- Squamous Cell Carcinoma, Nasal Planum

SYNONYM

MSCCIS—also called Bowen's-like disease or Bowenoid carcinoma *in situ* (cats).

ABBREVIATIONS

- MSCCIS = multicentric squamous cell carcinoma *in situ*
- NSAID = nonsteroidal anti-inflammatory drug
- SCC = squamous cell carcinoma

Suggested Reading

Gill VL, Bergman PJ, Baer KE, Craft D, Leung C. Use of imiquimod 5% cream (Aldara) in cats with multicentric squamous cell carcinoma *in situ*: 12 cases (2002–2005). J Vet Comp Oncol 2008, 6(1):55–64.

Marks SL, Song MD, Stannard AA, et al. Clinical evaluation of etretinate for the treatment of canine solar-induced squamous cell carcinoma and preneoplastic lesions. J Am Acad Dermatol 1992, 27(1):11–16.

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Ruslander D, Kaser-Hotz B, Sardinas JC. Cutaneous squamous cell carcinoma in cats. Compend Contin Educ 1997, 19:1119–1129.

Vail DM, Withrow SJ. Tumors of the skin and subcutaneous tissues. In: Withrow SJ, Vail DM, eds., Small Animal Clinical Oncology, 4th ed. St. Louis, MO: Saunders Elsevier, 2007, pp. 375–401.

Author Jackie M. Wypij

Consulting Editor Timothy M. Fan



Client Education Handout
available online

SQUAMOUS CELL CARCINOMA, TONGUE



BASICS

OVERVIEW

- Malignant tumor of squamous epithelium.
- Rare tumor that occurs more commonly in cats than in dogs. • Usually grows rapidly.
- Cats—most common lingual neoplasia, usually located at the ventral base of the tongue at the frenulum; most often progresses locally prior to clinical evidence of metastasis.
- Dogs—one of most common malignant lingual neoplasia (25–32%); variably metastatic by way of lymphatic vessels to regional lymph nodes and lungs (0–43%).
- Organ system: gastrointestinal.

SIGNALMENT

- Cats—middle-aged or old (> 7 years).
- Dogs—average 10–11 years; females more commonly affected; large breeds more commonly affected especially poodle, Labrador retriever, Samoyed.

SIGNS

Historical Findings

- Excessive salivation • Halitosis • Dysphagia or difficulty prehending food • Oral bleeding
- Decreased appetite • Weight loss • Poor grooming (cats)

Physical Examination Findings

- Incidental finding • Tongue mass—variable appearance, often nodular and ulcerated
- Facial swelling or deformity
- Intramandibular swelling (cats) • Cervical lymphadenomegaly—occasionally

CAUSES & RISK FACTORS

Potential increased risk of feline oral squamous cell carcinoma associated with flea collars, canned food (particularly tuna), and possibly exposure to tobacco smoke.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other lingual malignancy (melanoma, sarcoma, mast cell tumor, granular cell tumor)
- Trauma • Ulcerative glossitis • Benign lesion (papilloma) • Infection/abscess

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

IMAGING

- Advanced imaging with computed tomography or magnetic resonance imaging provides greatest information regarding extent of disease. • Thoracic radiography—three views required to evaluate lungs for metastasis (usually nodular), more common in dogs.

DIAGNOSTIC PROCEDURES

- Cytology—aspire or impression smear from incisional biopsy specimen (wedge); may yield diagnosis; however, ulceration, inflammation, and secondary infection may limit diagnostic utility. • Deep wedge tissue biopsy—necessary for definitive diagnosis.
- Cytology and/or lymph node biopsy to evaluate for regional metastasis; more common in dogs.



TREATMENT

- Surgical—generally inoperable in cats; aggressive excision warranted in dogs; function of the tongue after recuperation is usually acceptable in dogs, but will require changes in husbandry practices. • Post-surgical care (e.g., esophagostomy) by owner often required. • Partial glossectomy—may be performed on the rostral half (mobile tongue) or longitudinal half of the tongue (40–60% removed); ~35–50% of patients have incomplete surgical margins. • Subtotal glossectomy may be considered in select cases.
- Other surgical methods (e.g., electrocautery and cryosurgery) do not offer any additional advantage to conventional excision.
- Response to radiotherapy—poor (< 7 weeks); may be used adjunctively on microscopic disease postoperatively.
- Systemic therapies—chemotherapy agents or toceranib phosphate effective in oral squamous cell carcinoma might exert anticancer activities for lingual squamous cell carcinoma. • Piroxicam may have antineoplastic activity in some patients.
- Supportive/palliative medications for analgesia and antibiotics for secondary bacterial infections should be considered.



MEDICATIONS

DRUG(S)

- Piroxicam (dog) 0.3 mg/kg PO q24h; dosages have not been established for cats; however, 0.3 mg/kg PO q48h has been used anecdotally.
- Carboplatin—dogs, 250–300 mg/m² IV every 3 weeks; cats, 180–250 mg/m² IV every 3–4 weeks for 4 or 5 treatments. Toceranib phosphate (Palladia) in dogs give 2.75–3.25 mg/kg q48h.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Chemotherapy may be toxic; seek advice from a medical oncologist before initiating treatment if you are unfamiliar with cytotoxic drugs.



FOLLOW-UP

PATIENT MONITORING

After complete surgical resection, recheck at 1–2 months and then every 3 months with physical examination and evaluation for metastasis.

POSSIBLE COMPLICATIONS

Possible complications postoperatively—long-term difficulty prehending food, local recurrence.

EXPECTED COURSE AND PROGNOSIS

- Prognosis—poor, owing to extensive local disease (cat) and local recurrence (28% for all lingual tumors) and moderate rate of metastasis (dog). • After surgical excision (subtotal glossectomy, dogs)—median survival 216 days, < 25% survive 1 year.
- Negative prognostic factors (dogs): caudal location, incomplete excision, recurrence, larger size (> 2 cm); histologic grade (grade I tumors median survival 16 months compared with grade II–III tumors, median survival 3–4 months), metastatic disease.
- Piroxicam—17% response rate in oral squamous cell carcinoma with a median progression-free interval of 3.5–6 months; one partial response in 3 dogs with lingual squamous cell carcinoma. • Prognosis in cats similar to other oral sites of squamous cell carcinoma; median survival ~3 months with palliative radiation/chemotherapy.



MISCELLANEOUS

SEE ALSO

- Melanocytic Tumors, Oral • Squamous Cell Carcinoma, Gingiva • Squamous Cell Carcinoma, Tonsil

Suggested Reading

Culp WT, Ehrhart N, Withrow SJ, et al. Results of surgical excision and evaluation of factors associated with survival time in dogs with lingual neoplasia: 97 cases (1995–2008). J Am Vet Med Assoc 2013, 242(10):1392–1397.

Author Jackie M. Wypij

Consulting Editor Timothy M. Fan

SQUAMOUS CELL CARCINOMA, TONSIL



BASICS

OVERVIEW

- Rapid and progressive local invasion of neoplastic squamous epithelium arising from the tonsillar fossa into tonsillar lymphoid tissue.
- More common in dogs than cats; comprises 9% of canine oral tumors.
- Highly invasive locally into soft tissues.
- Early metastasis; considered systemic at diagnosis as 70–90% eventually metastasize regardless of local control (lymph nodes, lungs, other distant organs).
- Commonly unilateral; may be bilateral.
- Organ system: gastrointestinal.

SIGNALMENT

- Median age 10–12 years (range, 2.5–17 years) dog and cat
- No known breed or sex predilection

SIGNS

Historical Findings

- Cough
- Excessive salivation
- Halitosis
- Dysphagia
- Oral bleeding
- Increased respiratory noise (stridor)
- Weight loss
- Decreased appetite
- Lethargy

Physical Examination Findings

- Abnormally large tonsil (oral mass)
- Cervical lymphadenomegaly possible
- Pain on opening jaw

CAUSES & RISK FACTORS

Exact cause unknown; however, ten times more common in animals living in an urban environment versus those in a rural environment.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Lymphoma (generally associated with lymphadenomegaly and bilateral disease)
- Abscess
- Metastatic neoplasm (oral melanoma, sarcoma)
- Tonsillitis
- Tonsillar crypt foreign body
- Salivary gland tumor
- Thyroid carcinoma
- Mast cell tumor

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

IMAGING

- Thoracic radiography—three-view to detect lung metastasis; 5–20% positive for metastasis at presentation; 60–85% metastasis at death.
- Computed tomography (CT scan)—evaluate local extension of primary tumor as well as mandibular and retropharyngeal lymph node involvement; recommended prior to surgical or radiation therapy planning.
- Abdominal ultrasonography—evaluate abdominal organs; in dogs 20% disseminated metastasis to multiple organs at death.

DIAGNOSTIC PROCEDURES

- Cytologic evaluation of lesion—fine-needle aspirate samples often non-diagnostic; obtain impression smear from an incisional biopsy specimen (wedge); ulceration, inflammation, and secondary infection may limit diagnostic utility.
- Large, deep tissue biopsy with histopathology—required to sufficiently differentiate from other oral malignancies.
- Cytology and/or biopsy of regional lymph nodes (mandibular, retropharyngeal) to evaluate for regional metastatic disease; in dogs 20–55% metastasis at diagnosis, 75% metastasis at death.



TREATMENT

- Surgery—most are inoperable; aggressive excision may be warranted in patients with airway obstruction; tonsillectomy, when done, should be bilateral.
- Postoperative care (e.g., esophagostomy or gastrostomy tube) by owner is often required.
- Other surgical methods (e.g., electrocautery and cryosurgery)—no advantage over conventional excision.
- Regional radiation therapy is effective for local control and palliation of clinical signs.
- Chemotherapy—anecdotal reports of cisplatin, carboplatin, doxorubicin being used with limited success.
- Piroxicam or toceranib phosphate (Palladia) may have antineoplastic effects in some dogs.
- Analgesics for pain control and antibiotics for secondary bacterial infections may be indicated.



MEDICATIONS

DRUG(S)

- Cisplatin (dogs) 60–70 mg/m² IV once every 3–4 weeks for 4 treatments; provides marked palliation of clinical signs; nephrotoxic—must use with saline diuresis (18.3 mL/kg/h IV over 6 hours; give cisplatin after 4 hours); pretreat with an antiemetic.
- Carboplatin—dogs, 250–300 mg/m² IV every 3 weeks; cats, 180–250 mg/m² IV every 3–4 weeks for 4 or 5 treatments.
- Piroxicam (dogs) 0.3 mg/kg PO q24h; toceranib phosphate (Palladia) 2.75–3.25 mg/kg q48h.
- Doxorubicin—dogs > 10 kg, 30 mg/m² IV; dogs < 10 kg and cats, 1 mg/kg once every 2–3 weeks for 5 treatments.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Cisplatin—never use in cats.
- Do not administer cisplatin with NSAIDs due to nephrotoxicity.



FOLLOW-UP

PATIENT MONITORING

Most patients euthanized within months for local progression or metastasis; patients with curative-intent therapies should be rechecked with physical examination and evaluation for metastasis at 1–2 months, then every 3 months. Local regrowth may be assessed by serial CT scans.

POSSIBLE COMPLICATIONS

Postoperative complications—tumor recurrence, may need feeding tubes postoperatively, especially cats (long term).

EXPECTED COURSE AND PROGNOSIS

- Prognosis—grave owing to extensive local disease and high rate of recurrence (tongue, pharynx, lymph nodes) and metastasis.
- Minimal information in cats; however, appear to carry a grave prognosis.
- Dogs: overall 11% 1-year survival.
- Untreated (dogs) median survival 2 months vs. treatment, median survival 7–8 months.
- Surgery has limited benefit—median survival 2–4 months (dogs).
- Surgery with radiation therapy or chemotherapy (dogs)—median survival 3–4 months.
- Palliative radiotherapy or chemotherapy (dogs)—75% response rate, 2–9 months median survival.
- Surgery, radiation therapy, and chemotherapy (dogs)—median survival 9–12 months.
- Piroxicam alone—17% response rate for all oral squamous cell carcinoma with a median progression-free interval of 3.5–6 months; 3 of 5 dogs with tonsillar SCC exhibiting a partial remission or stable disease.
- Negative prognostic factors in dogs include anorexia or lethargy at presentation.



MISCELLANEOUS

SEE ALSO

- Squamous Cell Carcinoma, Gingiva
- Squamous Cell Carcinoma, Tongue

Suggested Reading

Mas A, Blackwood L, Cripps P, et al. Canine tonsillar squamous cell carcinoma – a multi-centre retrospective review of 44 clinical cases. J Small Anim Pract 2011, 52(7):359–364.

Author Jackie M. Wypij

Consulting Editor Timothy M. Fan

STAPHYLOCOCCAL INFECTIONS



BASICS

OVERVIEW

- *Staphylococcus*—gram-positive, facultatively anaerobic, spherical bacteria (cocci); *staphyle* (Greek; “bunch of grapes”) from characteristic microscopic arrangement in clusters; produces a variety of infections characterized by pus formation involving all tissues of the body; can produce toxins (superantigens) that exert profound systemic signs (fever, hypotension, shock, multiorgan failure, death).
- Ubiquitous; live free in environment and as commensal parasites of skin and upper respiratory tract
- Pathogenic and non-pathogenic strains; wide spectrum of virulence, host range, and site specificities; not strictly host- or site-specific.
- Pathogenic strains—possess extracellular toxins and enzymes (e.g., coagulase, staphylokinase, hemolysin, epidermolyticus); staphylocoagulase in more pathogenic strains (e.g., *S. pseudintermedius*, *S. aureus*).

SIGNALMENT

- Dogs and cats.
- Very young—susceptible because of incomplete, developing immunity.
- Old, debilitated—susceptible because of impaired host defenses.
- Immunocompromised—more susceptible.

SIGNS

- Fever.
- Anorexia.
- Pain.
- Pruritus.
- Can affect every organ system.
- Abscesses and infections of the skin, eyes, ears, respiratory system, genitourinary tract, skeleton, and joints—common.
- Dogs—pyoderma; otitis externa; cystitis; prostatitis; pneumonia; abscesses; osteomyelitis; discospondylitis; arthritis; mastitis; bacteremia; endocarditis; wound infections; toxic shock syndrome.
- Cats—abscesses; oral infections; otitis externa; conjunctivitis; metritis; cholangiohepatitis; cystitis; bacteremia.

CAUSES & RISK FACTORS

- Opportunistic pathogens.
- Disease—from disturbance of the natural host-parasite equilibrium when local and general defense mechanisms are significantly lowered (e.g., chronic debilitating diseases).
- Secondary infection—allergies (atopy, food, fleas); endocrinopathies (hypothyroidism, hyperadrenocorticism); parasites (demodicosis); seborrhea.

- Burns or wounds—complications.
- Form biofilms (extracellular polysaccharide networks) of concern for infection of implants and invasive devices (e.g., IV catheters).
- Transmission—airborne organisms; carriers; and direct contact (droplet nuclei).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Dermatitis—allergies, seborrhea, parasites, immune-mediated
- Other infectious causes—viruses, bacteria, fungi, *Rickettsia*, protozoa
- Neoplasia
- Immune-mediated diseases

CBC/BIOCHEMISTRY/URINALYSIS

- Normal or high WBCs.
- Biochemistry—may suggest underlying cause (e.g., hypothyroidism, hyperadrenocorticism).
- Urinalysis—pyuria (with or without bacteruria) with cystitis.

OTHER LABORATORY TESTS

- Direct microscopy.
- Gram stain.
- Cytology—neutrophils and cocci singly or in pairs, short chains, or irregular clusters.
- Culture—avoid superficial contamination; collect samples by aspiration, wash, or biopsy; do not overinterpret a positive isolation; organisms can be isolated from normal animals.
- Organisms survive up to 48 hours in clinical specimens when kept cool (4°C; 40°F), particularly on swabs containing a holding medium.
- Antibiotic susceptibility testing.
- PFGE molecular typing.

IMAGING

Radiology—osteolytic and osteoproliferative lesions with osteomyelitis; interstitial or alveolar pulmonary pattern with pneumonia; radiodense uroliths (struvite).

DIAGNOSTIC PROCEDURES

CSF—if meningitis or discospondylitis suspected.

PATHOLOGIC FINDINGS

Characteristic abscess lesion—necrotic tissue, fibrin, and a large number of neutrophils.



TREATMENT

- Properly handle and dispose of contaminated objects.

- Organism resistant to many environmental insults and common disinfectants.
- Topical antibacterial cleaning of wounds and pyoderma—may be beneficial.
- Known or suspected MRS infected animals should be isolated.



MEDICATIONS

DRUG(S)

- Antibiotic resistance—great propensity owing to production of β -lactamase, which inactivates penicillins; may carry plasmids (segments of genetic material that may carry genes for antimicrobial resistance) that can be transferred to other strains of staphylococci or species of bacteria.
- History of previous antimicrobial therapy for staphylococcal infection—culture and antibiotic susceptibility testing indicated.
- Non-penicillinase-producing strains—penicillin G at 10,000–20,000 U/kg IM, SC q12–24h, or penicillin V at 8–30 mg/kg PO q8h.
- Penicillinase-producing strains—use penicillinase-resistant drugs.
- First-generation cephalosporins—rarely resistant; cephalexin at 22 mg/kg PO q8h; cefadroxil at 22 mg/kg PO q8–12h.
- β -lactamase-resistant synthetic penicillins—rarely resistant; oxacillin at 22–40 mg/kg PO q8h; dicloxacillin at 10–25 mg/kg PO q8h; and clavulanic acid-potentiated amoxicillin at 12.5–25 mg/kg PO q8–12h.
- Gentamicin—rarely resistant; 2–4 mg/kg IV, IM, SC q8h.
- Enrofloxacin—rarely resistant; 2.5–5 mg/kg PO, IM q12h.
- Trimethoprim-potentiated sulfonamides—infrequently resistant; 30 mg/kg IV, PO q12h.
- Chloramphenicol—infrequently resistant; 40–50 mg/kg IV, IM, SC, PO q8–12h.
- Penicillin allergy—try cephalosporin, clindamycin, or vancomycin (although strongly discouraged to reserve vancomycin for treatment of serious MRSA infections in humans).
- Methicillin-resistant (*express meC gene* which encodes an altered penicillin-binding protein [PBP-2a]) *Staphylococcus* increasingly isolated from dogs and cats is an emerging problem due to their multidrug resistance phenotype which limits treatment options and challenges infection control measures.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Avoid immunosuppressive drugs.

STAPHYLOCOCCAL INFECTIONS

(CONTINUED)

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

- Possible.
- Most people and pets carry their own pathogenic staphylococcal flora; disease not caused by mere exposure; however, transfer from dogs to humans possible.
- Bite infections contain a mix of aerobes and anaerobes from both the skin of the patient and the mouth of the animal including *Staphylococcus*.
- MRSA can be transmitted between animals and humans, thus pets pose risk of infection to owners and veterinary personnel (and

likewise human MRSA carrier can infect susceptible pet).

- Hand hygiene is an integral part of the prevention of the spread of MRSA between animals and between animals and humans.

ABBREVIATIONS

- CSF = cerebrospinal fluid
- MRS = methicillin-resistant *Staphylococcus pseudintermedius*
- MRSA = methicillin-resistant *Staphylococcus aureus*
- PFGE = pulsed field gel electrophoresis
- WBC = white blood cell

Suggested Reading

Cohn LA, Middleton JR. A veterinary perspective on methicillin-resistant

staphylococci. J Vet Emerg Crit Care 2010, 20:31–45.

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Weese JS. Staphylococcal infections. In: Greene CE, ed., Infectious Diseases of the Dog and Cat, 4th ed. St. Louis, MO: Saunders Elsevier, 2012, pp. 340–348.

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STEROID-RESPONSIVE MENINGITIS-ARTERITIS—DOGS



BASICS

OVERVIEW

- May be acute or protracted.
- Lesions—most impressive in CNS, affecting meninges and meningeal arteries; also vascular changes in the heart, liver, kidney, and gastrointestinal system.
- Genetic factors—may play a role; suspected in beagle colonies and in Nova Scotia duck tolling retrievers.
- Worldwide occurrence.

SIGNALMENT

- Dog. • Beagle, Bernese mountain dog, Nova Scotia duck tolling retriever, and Boxer predisposed; any breed can be affected.
- Mostly young adult dogs of both sexes; age range 5–18 months.

SIGNS

- Classical (acute)—hyperesthesia; cervical rigidity; stiff gait; fever up to 42°C (107.6°F).
- Protracted—neurologic deficits, usually reflecting a spinal cord or multifocal lesion.

CAUSES & RISK FACTORS

- Cause unknown.
- Pathologic findings, laboratory data, and marked response to steroids—suggest an immune-mediated disease related to a dysregulation of IgA production.
- Epidemiologic observations—altered immune response may be triggered by an environmental factor, possibly of infectious nature; genetic predisposition.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute—bacterial meningitis; meningeal tumors; discospondylitis.
- Protracted—bacterial meningitis; meningeal tumors (histiocytosis, meningioma, lymphosarcoma); viral encephalitides; granulomatous meningoencephalitis; protozoal infections; other CNS inflammatory lesions of unknown origin.

CBC/BIOCHEMISTRY/URINALYSIS

- Acute—leukocytosis with neutrophilia and left-shift.
- Protracted—CBC non-contributory.

OTHER LABORATORY TESTS

IgA levels (serum and CSF)—usually high; high serum C-reactive protein levels.

IMAGING

Radiographs to exclude discospondylitis, MRI to exclude differential diagnoses.

DIAGNOSTIC PROCEDURES

Cerebrospinal Fluid Analysis

- Acute—mild-to-moderate elevation of protein; moderate-to-marked pleocytosis,

predominantly polymorphonuclear cells.

- Protracted—normal, or mild elevation of protein; mild-to-moderate pleocytosis with mixed cell population, or with a predominance of mononuclear cells.

PATHOLOGIC FINDINGS

Acute

- Marked meningitis with macrophages, plasma cells, lymphocytes, and varying numbers of polymorphonuclear cells mostly in the cervical region.
- Lesions of the meningeal arteries—degenerative with perivascular inflammation.

Protracted

- Marked fibrous thickening and focal mineralization of the leptomeninges.
- Arterial walls—thickened and stenotic from cellular proliferation of the intima and fibrosis.



TREATMENT

- Inpatient—at onset, fluid therapy and ice packs useful for high body temperature.
- After initial treatment, managed as outpatient.
- Regular follow-ups—inform client about side effects of long-term steroid treatment.



MEDICATIONS

DRUG(S)

- Initial signs with mild CSF pleocytosis—NSAIDs; carefully monitor the patient.
- First relapse, or symptoms become worse with marked CSF pleocytosis—start long-term treatment (6 months) with prednisolone (4 mg/kg PO q24h for 1–2 days; then taper slowly); reexamine patient (including CSF collection and blood profile) every 4–6 weeks after initiation of therapy.
- Neurologic examination and CSF become normal, normal serum C-reactive protein levels—reduce steroid dose.
- Persistent pleocytosis—continue same steroid dosage.
- Treatment may be stopped after about 6 months.
- Immunosuppressive drugs if patient does not respond well to prednisolone alone; used in combination.
- Consider gastrointestinal protector to avoid ulcer.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Corticosteroids—high-dose treatment can lead to severe complications; non-life-threatening side effects (polyuria, polydipsia, polyphagia, and weight gain); not tolerated in about 5% of dogs.



FOLLOW-UP

PATIENT MONITORING

Control examinations—every 4–6 weeks; include blood examination and CSF collection; measurement of serum C-reactive protein levels until steroids discontinued.

PREVENTION/AVOIDANCE

Strictly control treatment schedule to prevent frequent relapses.

POSSIBLE COMPLICATIONS

- Subarachnoid bleed—may result in acute tetra- or paraplegia.
- Hypoxic lesions of spinal cord or brain.
- Side effects of immunosuppressive treatment.

EXPECTED COURSE AND PROGNOSIS

- Acute—prognosis relatively good in young dogs with early aggressive therapy.
- Protracted cases with frequent relapses—prognosis guarded; controlled studies note about 60% of dogs are cured after immunosuppressive treatment.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Polyarthritis

AGE-RELATED FACTORS

Old animals do not tolerate long-term steroid treatment well, but condition rare in dogs > 5 years of age.

SYNOMYS

- Aseptic meningitis
- Canine juvenile polyarteritis syndrome
- Corticosteroid-responsive meningomyelitis

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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Bathen-Noethen A, Carlson R, Menzel D, Mischke R, Tipold A. Concentrations of acute-phase proteins in dogs with steroid responsive meningitis-arteritis. *J Vet Intern Med* 2008, 22:1149–1156.

Tipold A, Schatzberg SJ. An update on steroid responsive meningitis-arteritis. *J Small Anim Pract* 2010, 51:150–154.

Author Andrea Tipold

Consulting Editor Joane M. Parent

STERTOR AND STRIDOR



BASICS

DEFINITION

- Abnormally loud sounds that result from air passing through a narrowed nasopharynx, pharynx, larynx, or trachea.
- Discontinuous sounds heard without a stethoscope.
- Stertor—low-pitched snoring sound that usually arises from the vibration of flaccid tissue or fluid; usually arises from nasal or pharyngeal airway obstruction.
- Stridor—higher-pitched sounds that result when relatively rigid tissues are vibrated by the passage of air; result of partial or complete obstruction of the larynx or cervical trachea.

PATOPHYSIOLOGY

- Airway obstruction causes turbulence as air travels through a narrowed passage; with worsening obstruction or increasing airflow velocity, the amplitude of the sound increases as the tissue, secretion, or foreign body composing the obstruction vibrates.
- Obstruction sufficient to increase the work of breathing augments respiratory muscle effort and exacerbates turbulence; inflammation and edema of tissues in the region of the obstruction may develop, further reducing the airway lumen and further increasing the work of breathing, creating a vicious cycle.
- Obesity further increases respiratory effort and exacerbates airway obstruction.

SYSTEMS AFFECTED

Respiratory

GENETICS

- Brachycephalic syndrome heritable in many breeds.
- Inherited laryngeal paralysis—identified in Bouvier des Flandres, Rottweilers, Siberian huskies, and Dalmatians.

INCIDENCE/PREVALENCE

Common

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Common in brachycephalic dogs or cats
- Acquired laryngeal paralysis—overrepresented in certain giant breeds (e.g., Saint Bernards and Newfoundlands) and large breeds (e.g., Irish setters, Labrador retrievers, and golden retrievers).

Mean Age and Range

- Affected brachycephalic animals and dogs or cats with inherited laryngeal paralysis are typically younger than 1 year of age when owners detect a problem.

- Acquired laryngeal paralysis typically occurs in older dogs and cats.
- Cats—diagnosed less commonly than are dogs; no obvious age pattern.

Predominant Sex

No sex predilection for any cause, although inherited laryngeal paralysis has a 3:1 male predominance.

SIGNS

- Change or loss of voice.
- Partial obstruction—produces an increase in airway sounds before producing an obvious change in respiratory pattern or gas exchange.
- Owners may indicate that the sound has existed for as long as several years.
- Breath sounds audible from a distance without a stethoscope—suspect narrowing of upper airway.
- Nature of the sound—ranges from abnormally loud to obvious fluttering to high-pitched squeaking, depending on the degree of airway narrowing.
- May note increased respiratory effort and paradoxical respiratory movements (chest wall collapses inward during inspiration and springs outward during expiration) when the effort is extreme; respiratory motions often accompanied by obvious postural changes (e.g., abducted forelimbs, extended head and neck, and open-mouth breathing).

CAUSES

- Brachycephalic airway syndrome (stenotic nares, elongated soft palate, everted laryngeal saccules, laryngeal collapse).
- Laryngeal paralysis—inherited or acquired.
- Laryngeal neoplasia—benign or malignant.
- Granulomatous/inflammatory laryngitis.
- Tracheal collapse, stenosis, obstruction, neoplasia, foreign body.
- Nasopharyngeal polyp, stenosis, foreign body.
- Acromegaly.
- Neuromuscular dysfunction or trauma.
- Anesthesia or sedation—only if predisposing anatomy exists.
- Cystic Rathke cleft.
- Cleft soft palate.
- Aplasia of soft palate.
- Redundant pharyngeal mucosal folds.
- Soft palate mass.
- Edema or inflammation of the palate, pharynx, and larynx (including everted mucosal lining of the laryngeal ventricles)—secondary to coughing, vomiting or regurgitation, turbulent airflow, upper respiratory infection, and hemorrhage.
- Secretions (e.g., pus, mucus, and blood) in the airway lumen—acutely after surgery; a normal conscious animal would cough out or swallow them.

RISK FACTORS

- High ambient temperature or humidity.
- Fever.

- High metabolic rate—as occurs with hyperthyroidism or sepsis.
- Exercise.
- Anxiety or excitement.
- Any respiratory or cardiovascular disease that increases ventilation.
- Turbulence caused by the increased airflow can lead to swelling and worsen the airway obstruction.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Systematically auscultate over the nose, pharynx, larynx, and trachea to identify the point of maximal intensity of any abnormal sound and to identify the phase of respiration when it is most obvious.
- Important to identify the anatomic location from which the abnormal sound arises and to seek exacerbating causes (see “Risk Factors”; e.g., a chronic airway obstruction may become manifest when the patient is exposed to extremely high ambient temperatures).
- Must differentiate sounds of pharyngeal, laryngeal, and tracheal narrowing from sounds arising elsewhere in the respiratory system.
- Nasal and tracheal narrowing and severe or extensive narrowing of the bronchi—can cause increased respiratory sounds.
- If the sound persists when the patient opens its mouth, a nasal cause can virtually be ruled out.
- If the owner describes a change in voice, the larynx is the likely abnormal site.

OTHER LABORATORY TESTS

Arterial blood gas occasionally indicated; hypoxia and hypoventilation occur with prolonged severe obstruction.

IMAGING

- Lateral radiographs of the head and neck—may help identify abnormal soft tissues of the airway (e.g., elongated soft palate or a nasal polyp); limited use for identifying laryngeal paralysis, although experienced radiographers can identify abnormally dilated or swollen laryngeal saccules; cartilaginous destruction is suggestive of neoplasia or granulomatous laryngitis; may detect external masses compressing the upper airway.
- Radiography and fluoroscopy—important for assessing the cardiorespiratory system; rule out other or additional causes of respiratory difficulty; such conditions may add to an underlying upper airway obstruction, causing a subclinical condition to become clinical.
- Digital radiology is preferred for best detail.
- Ultrasound can be used to assess laryngeal structure and function, can also be used to document cervical tracheal collapse but air is a poor acoustic window.
- Computed tomography can be used to provide additional anatomic detail.

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DIAGNOSTIC PROCEDURES**Pharyngoscopy and Laryngoscopy**

- Definitive diagnostic tests for direct visualization of pharyngeal or laryngeal changes
- Require heavy sedation that preserves laryngeal function
- Remember that the patient's ability to use muscles to open the airway is compromised by anesthesia; veterinarian and clients must determine if they are prepared to carry out surgical remedies if indicated.
- If correctable conditions are not identified and corrected—patient's recovery from anesthesia can be complicated by severe airway obstruction; must be prepared to perform a tracheotomy if airway is obstructed and a definitive surgical remedy cannot be pursued immediately.
- Assess timing and degree of movement of the vocal folds during light anesthesia—evaluate laryngeal paralysis. Use dopram (1 mg/kg IV) to stimulate respiration if needed.
- Normal palate—thin; just barely overlaps the tips of the epiglottis; easily displaced dorsally using the blade of the laryngoscope.
- Overlong soft palate—thick; usually inflamed; may lie 1 cm or more past the tip of the epiglottis.
- Patient should be as stable as possible before undergoing general anesthesia, but do not unduly delay procedure; appropriate surgical treatment is usually the only means of reducing the airway obstruction.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Inpatient management required for surgical treatment.
- Closely monitor effects of sedatives; sedatives can relax the upper airway muscles and worsen the obstruction; be prepared with emergency methods for securing the airway if complete obstruction occurs. Diazepam preferred.
- Extreme airway obstruction—attempt an emergency intubation; if obstruction prevents intubation, emergency tracheotomy or passage of a tracheal catheter to administer oxygen may be the only available means for sustaining life; a tracheal catheter can briefly sustain oxygenation while a more permanent solution is sought.

NURSING CARE

- Treatment requires removal of obstruction, supplemental oxygen is variably helpful.
- Intravenous fluids may be required, particularly if hyperthermia develops from increased work of breathing.

- Active cooling measures (ice packs in axilla and groin region, alcohol on foot pads, chilled IV fluids) helpful in alleviating hyperthermia but not indicated for fever.

ACTIVITY

Keep patient cool, quiet, and calm—anxiety, exertion, and pain lead to increased ventilation, potentially worsening the obstruction.

DIET

- NPO if anesthesia is planned.
- Avoid obesity that worsens respiratory effort.

CLIENT EDUCATION

Inform client that the patient can make the transition from being a noisy breather to having an obstructed airway in a few minutes or even seconds.

SURGICAL CONSIDERATIONS

- Laryngoscopy and bronchoscopy for foreign body retrieval and biopsy of laryngeal region and tracheal lumen. Use of small balloon catheters passed beyond the foreign body prior to expansion may be useful in removing some objects.
- Take particular care when inducing general anesthesia or when using sedatives in any patient with upper airway obstruction.
- Surgery—indicated to obtain a diagnosis through biopsy with histopathology, to manage obstruction while awaiting histopathology results or resolution of inflammation/infection (e.g., tracheotomy), or to resolve disease by excision, correction of obstructive lesion, and removal of foreign bodies.

**MEDICATIONS****DRUG(S)**

- Medical approaches—appropriate only if the underlying cause is infection, edema, inflammation, or hemorrhage; anatomic or neurologic causes are not amenable to medical treatment.
- Steroids—may be indicated if edema or inflammation is thought to be an important contributor; effect with intravenous administration should be apparent in approximately 1 hour. Single dose may be sufficient or a tapering dose might be required. Inflammatory laryngitis often requires higher doses administered over a longer dosing schedule with taper of the dose according to resolution of clinical signs.

PRECAUTIONS

Sedatives, analgesics, and anesthetics—avoid excessive suppression of laryngeal movement

and respiratory suppression to avoid aspiration in animals with laryngeal disease.

**FOLLOW-UP****PATIENT MONITORING**

Respiratory rate and effort need to be closely monitored. When owner chooses to take an apparently stable patient home, or if continual observation is not feasible, inform client that complete obstruction could occur.

PREVENTION/AVOIDANCE

Advise client to avoid exercise, high ambient temperatures, and extreme excitement.

POSSIBLE COMPLICATIONS

Serious complications may occur without therapy to relieve the obstruction; these include airway edema, pulmonary edema (may progress to life-threatening acute lung injury), and hypoxia; may require tracheotomy and/or artificial ventilation.

EXPECTED COURSE AND PROGNOSIS

- Varies with underlying cause.
- Even with surgical treatment, some degree of obstruction may remain for 7–10 days due to swelling.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Peripheral neuropathy often associated with laryngeal paralysis.

SYNONYMS

Snoring

SEE ALSO

- Acromegaly—Cats
- Brachycephalic Airway Syndrome
- Hypothyroidism
- Laryngeal Diseases
- Myasthenia Gravis
- Nasal and Nasopharyngeal Polyps
- Tracheal and Airway Collapse

Suggested Reading

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Author James C. Prueter

Consulting Editor Lynelle R. Johnson



Client Education Handout
available online

STOMATITIS



BASICS

DEFINITION

Inflammation of the mucous lining of any of the structures in the mouth; in clinical use the term should be reserved to describe widespread oral inflammation (beyond gingivitis and periodontitis) that may also extend into submucosal tissues (e.g., marked caudal stomatitis extending into submucosal tissues may be termed "caudal stomatitis").

PATHOPHYSIOLOGY

- Inflammation and other changes may develop in the normal oral mucosa because of the tremendous amount of vasculature in the area and its proximity to the external environment.
- Can also affect behavior due to discomfort and difficulties in eating; ophthalmic conditions due to proximity of some oral structures to ocular structures; and skin if inflammation extends to the peri-oral area.

SIGNALMENT

Species

Dogs and cats

Breed Predilections

- Ulcerative stomatitis in Maltese—higher incidence in males.
- Oral eosinophilic granuloma—most commonly in Siberian husky (may be hereditary).
- Gingival hyperplasia in large breeds (see Gingival Hyperplasia/Enlargement).
- Rapidly progressive periodontitis seen mostly in young adult animals, such as in the greyhound and the shih tzu.
- Localized juvenile periodontitis in the maxillary or mandibular incisor region—especially common in miniature schnauzer.

Mean Age and Range

- Juvenile-onset periodontitis in young cats.
- Periodontal disease associated with calculus is seen most often in old dogs and cats and in susceptible breeds.

Predominant Sex

None

SIGNS

General Comments

A definitive diagnosis of inflammation often cannot be made based on physical examination findings alone.

Physical Examination Findings

- Halitosis.
- Pain.
- Ulcerated lesions.
- Ptyalism.
- Edema.
- Periocular inflammation possible due to proximity to oral cavity.
- Extensive plaque and calculus. Look for lesions on oral buccal and labial surfaces that

are adjacent to teeth with large amounts of calculus.

CAUSES

Anatomic

- Periodontal disease due to overcrowding of teeth
- Lip frenulum attachment
- Tight-lip syndrome in shar-pei

Metabolic

- Uremia and high ammonia levels in saliva
- Vasculitis and xerostomia seen with diabetes mellitus
- Macroglossia and puffy lips as seen with hypoparathyroidism
- Lymphoma can be seen affecting the palate and/or tongue

Immune Mediated

- Pemphigus foliaceus
- Pemphigus vulgaris
- Bullous pemphigoid
- Systemic lupus erythematosus and discoid lupus erythematosus in the dog
- Acute hypersensitivity to drugs
- Caudal stomatitis in cats may have an immune-mediated component

Infectious

- Opportunistic oral flora secondary to oral lesions
- Mycotic stomatitis
- Systemic infections
- Leptospirosis: petechia
- Feline leprosy (mycobacterium): raised plaques
- Calicivirus or herpesvirus infections—cat
- Canine distemper
- Viral papillomatosis—dogs

Trauma

- Irritation from calculus and plaque
- Foreign objects—gum-chewers syndrome
- Electrical cord shock
- Chemical burns
- Lacerations
- Snake bite
- Blows
- Trauma of the palate from base-narrow mandibular canine teeth

Toxic

- Certain plants
- Chemotherapy
- Radiotherapy
- Chemical irritants

RISK FACTORS

- Poor oral health due to gingivitis, plaque, calculus, or periodontitis.
- Stress may be a factor in caudal stomatitis in cats.
- May be environmental factors in some cases.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Oral ulcers

- Chronic ulcerative paradental stomatitis (CUPS)
- Idiopathic osteomyelitis
- Lymphoma

CBC/BIOCHEMISTRY/URINALYSIS

Biochemical tests to detect other diseases

OTHER LABORATORY TESTS

- Immunologic testing
- Mycotic cultures
- Virus isolation
- Toxicologic studies
- Serum protein electrophoresis
- Endocrine tests

IMAGING

Radiography to identify osseous or dental abnormalities

DIAGNOSTIC PROCEDURES

Biopsy



TREATMENT

APPROPRIATE HEALTH CARE

- Correct nutritional or hydration deficiencies as needed, on an inpatient or outpatient basis.
- Dental disease or periodontal disease present should be treated.

NURSING CARE

Can place feeding tube if necessary.

ACTIVITY

N/A

DIET

Consider using a hypoallergenic diet to reduce the antigen load that accumulates on the tooth surfaces in plaque. Dietary adjustments may need to be made depending on the patient's ability to eat if painful.

CLIENT EDUCATION

Clients must be aware that this is a multifactorial, often chronic condition that will require constant management, with variable responses from patients.

SURGICAL CONSIDERATIONS

Sometimes most or all teeth must be extracted to resolve stomatitis, especially caudal stomatitis in cats.



MEDICATIONS

DRUG(S) OF CHOICE

- Antimicrobials—broad-spectrum antibiotics; amoxicillin-clavulanate; clindamycin; metronidazole (10 mg/kg PO q12h or 40–50 mg/kg as a loading dose on the first day, followed by 20–25 mg/kg q8h for 7 days or less); doxycycline (5 mg/kg PO loading dose, 2.5 mg/kg PO 12h later, and 2.5 mg/kg PO once daily thereafter); chlorhexidine solution or gel (CHX, VRx Products, Harbor City, CA)—plaque

(CONTINUED)

STOMATITIS

retardant; and Maxi/Guard (Addison Biological, Fayette, MO)—zinc-organic acid solutions and gels to promote tissue healing and retard plaque accumulation.

- Anti-inflammatory drugs—prednisolone or prednisone; for eosinophilic ulcer (2–4.4 mg/kg PO once a day; for chronic cases use 0.5–1 mg/kg PO every other day); for adjunctive therapy of feline plasma cell gingivitis–pharyngitis—may improve inflammation and appetite.
- Immunosuppressive drugs if secondary to autoimmune disease.
- Chemotherapy if secondary to lymphoma.
- Omega interferon (recombinant feline interferon)—submucosal infiltrations: 1–2 MU/buccal cavity, repeated 3 times at 2-week intervals if necessary, or 1 MU/kg SC q48h for 5 injections.

CONTRAINDICATIONS

Immunosuppressive therapy if secondary to infectious disease.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

Evaluate oral cavity periodically to monitor for resolution or recurrence of oral lesions.

PREVENTION/AVOIDANCE

- OraVet (Merial, Atlanta, GA) applied weekly to calculus-free teeth might be helpful

in preventing further inflammation to oral tissues.

- Oral rinses and brushing the teeth with oral medications may be helpful, especially with periodontal disease.

POSSIBLE COMPLICATIONS

Bacteremia from periodontal disease may cause renal, cardiac, hepatic, and pulmonary disease.

EXPECTED COURSE AND PROGNOSIS

Varies with underlying cause.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Periodontitis
- Oropharyngeal inflammation
- Gingivitis
- Alveolar mucositis
- Sublingual mucositis
- Labial/buccal mucositis
- Caudal mucositis
- Palatitis
- Glossitis
- Cheilitis
- Osteomyelitis
- Tonsillitis
- Pharyngitis

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

Dental prophylaxis procedures in pets have caused human infections from aerosolized

bacteria. Safety glasses and a mask are recommended when performing such procedures.

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- St. Vincent's stomatitis, an ulceromembranous stomatitis due to *Fusobacterium* spp. and spirochetes
- Trench mouth

SEE ALSO

- Gingival Hyperplasia/Enlargement
- Oral Ulceration
- Periodontal Diseases
- Stomatitis, Caudal—Cat

INTERNET RESOURCES

- <http://www.avdc.org/Nomenclature.html>
- <http://www.mypetsdentist.com/feline-stomatitis.pml>
- <http://www.thepetdentist.com/stomatitis-pets-animals.php>

Suggested Reading

Harvey CE, Emily PP. Oral lesions of soft tissues and bone: Differential diagnosis. In: Harvey CE, Emily PP, eds., Small Animal Dentistry. St. Louis, MO: Mosby, 1993, pp. 42–88.

Wiggs RB, Lobprise HB. Veterinary Dentistry: Principles and Practice. Philadelphia: Lippincott-Raven, 1997, pp. 104–139.

Author Larry Baker

Consulting Editor Heidi B. Lobprise



**Client Education Handout
available online**

STOMATITIS, CAUDAL—CAT



BASICS

OVERVIEW

- Inflammatory response affecting the oral cavity in cats.
- Oral and oropharyngeal inflammation is classified by location as:
 - Gingivitis—inflammation of gingiva.
 - Periodontitis—inflammation of non-gingival periodontal tissues (i.e., the periodontal ligament and alveolar bone).
 - Alveolar mucositis—inflammation of alveolar mucosa (i.e., mucosa overlying the alveolar process and extending from the mucogingival junction without obvious demarcation to the vestibular sulcus and to the floor of the mouth).
 - Sublingual mucositis—inflammation of mucosa on the floor of the mouth.
 - Labial/buccal mucositis—inflammation of lip and cheek mucosa.
 - Caudal mucositis—inflammation of mucosa of the caudal oral cavity, bordered medially by the palatoglossal folds and fauces, dorsally by the hard and soft palate, and rostrally by alveolar and buccal mucosa.
 - Palatitis—inflammation of mucosa or covering the hard and/or soft palate.
 - Glossitis—inflammation of mucosa of the dorsal and/or ventral surface of the tongue.
 - Cheilitis—inflammation of the lip (including the mucocutaneous junction area and skin of the lip).
 - Osteomyelitis—inflammation of jaw bone and bone marrow.
 - Stomatitis—inflammation of the mucous lining of any of the structures in the mouth; in clinical use the term should be reserved to describe widespread oral inflammation (beyond gingivitis and periodontitis) that may also extend into submucosal tissues.
 - Tonsillitis—inflammation of the palatine tonsil.
 - Pharyngitis—inflammation of the pharynx.

SIGNALMENT

- Cats
- Purebred breeds predisposed—Abyssinian, Persian, Himalayan, Burmese, Siamese, and Somali

SIGNS

- Ptyalism.
- Halitosis.
- Dysphagia.
- Anorexia—prefers soft food.
- Weight loss.
- Scruffy hair coat from lack of grooming.
- Erythematous, ulcerative, proliferative lesions affecting the gingiva, glossopalatine arches, tongue, lips, buccal mucosa, and/or hard palate.
- Gingival inflammation commonly completely surrounds the tooth, compared with gingivitis, which usually occurs on the buccal and labial surfaces.
- May extend to the glossopharyngeal arches as well as the palate.

CAUSES & RISK FACTORS

- Cause unknown; bacterial, viral, and immunologic etiologies suspected.

- Significant findings of feline calicivirus.
- Immunosuppression from FeLV or FIV can also lead to poorly responsive infections; most affected cats are negative for FeLV and FIV.

- Refractory cases with extensive proliferative lesion in the caudal oral cavity and pharynx warrant a more guarded prognosis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Periodontal disease
- Oral malignancy
- Eosinophilic granuloma complex

CBC/BIOCHEMISTRY/URINALYSIS

- Elevated globulin. Polyclonal gammopathy secondary to antibody production following bacterial invasion into periodontal tissues.
- Leukocytosis and eosinophilia may be present.

IMAGING

Intraoral radiographs to evaluate periodontal disease and tooth resorption.

DIAGNOSTIC PROCEDURES

Biopsy (especially unilateral lesions) to rule out neoplasia—primarily squamous cell carcinoma.



TREATMENT

- Initial therapy for early mucositis involves dental scaling above and below the gingiva and treatment (extraction) for teeth affected with grades 3 and 4 periodontal disease and/or tooth resorption.
- For cases of focal vestibular and alveolar mucositis, extraction of the locally affected teeth in proximity to the lesions usually results in resolution.
- For caudal stomatitis, extraction of the maxillary and mandibular teeth distal to the canines resulted in resolution of inflammation in 60% of cases without further need for medication, 20% of cases required control with medication, and 20% did not resolve in one published study.
- To aid the extractions: create a gingival flap in all quadrants for exposure. After completely elevating all of the roots, use a high-speed drill with water spray to create a trough of bone where the roots were, removing most of the keratinized gingiva, periodontal ligament, and periradicular alveolar bone. Before suturing, “smooth down” the alveolar margin to remove sharp edges with a round or football-shaped diamond bur.
- If patients do not respond to extraction of the teeth distal to the canines, consider a trial of prednisone 2 mg/kg every other day to control the inflammation or, remove all teeth; when extracting the teeth, pay meticulous attention to removing all dental hard tissue; take intraoral radiographs before and after surgery; postoperative application of fluocinonide 0.05% (Lidex Gel) to the gingival margin may help healing.



MEDICATIONS

DRUG(S)

- Medication and other therapies have been used with limited long-term success; lack of permanent response to conventional oral hygiene, antibiotics, anti-inflammatory drugs, and immunosuppressive drugs is typical.
- Medications should not be regarded as the primary method to control oropharyngeal inflammation.
- Antibiotics—clindamycin (5 mg/kg q12h), metronidazole, amoxicillin, ampicillin, enrofloxacin, tetracycline.
- Corticosteroids—prednisone (2 mg/kg initially daily, followed by every other day); methylprednisolone acetate (2 mg/kg q7–30 days) may also help control inflammation.
- Gold salts—Solganal (Schering) 1 mg/kg IM weekly until improvement (up to 4 months), then every 14–35 days.
- Chlorambucil 2 mg/m² orally every other day or 20 mg/m² every other week.
- Bovine lactoferrin (40 mg/kg) applied to the oral mucous membranes.
- Interferon—alpha or omega 30 IU/day 7 days on, 7 days off, indefinitely.
- CO₂ laser to decrease inflamed tissue.
- Cyclosporine—2 mg/kg BID.



MISCELLANEOUS

SYNOMYMS

- Lymphocytic plasmacytic stomatitis
- Stomatitis

ABBREVIATIONS

- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus

INTERNET RESOURCES

<http://www.avdc.org/Nomenclature.html>

Suggested Reading

Bellows, JE. Feline Dentistry. Oxford: Wiley Blackwell, 2010.

Wiggs RB, Lobrise HB. Veterinary Dentistry: Principles and Practice. Philadelphia: Lippincott-Raven, 1997.

Author Jan Bellows

Consulting Editor Heidi B. Lobprise



Client Education Handout
available online

STREPTOCOCCAL INFECTIONS



BASICS

OVERVIEW

- *Streptococcus*—gram-positive, non-motile, facultatively anaerobic spherical bacteria (cocci); grow in pairs or chains; commensal organisms; normal flora of the upper respiratory tract, oropharynx, lower genital tract, and skin; under appropriate conditions, capable of infecting all areas of body; primary infections involve respiratory, circulatory, integumentary, urogenital, or central nervous systems; frequent secondary invader of body tissues.
- Classified by ability to hemolyze RBCs and produce zone on blood agar plates around bacterial colony— α -hemolytic (green zone of partial hemolysis); β -hemolytic (clear zone of hemolysis); γ -hemolytic (no change; non-hemolytic); β -hemolytic usually more pathogenic than α -hemolytic, which is more pathogenic than non-hemolytic strains.
- Hemolytic strains further subdivided by antigenic differences in cell wall carbohydrates—Lancefield serogroups A–H and K–T (e.g., group G *S. canis*); some groups more likely to be associated with disease, depending on species (e.g., group G associated with cats and dogs; group A associated with humans).
- Produce exotoxins—streptolysins (hemolysins), streptokinases, deoxyribonucleases, and hyaluronidases.
- Produce adhesions to bind to extracellular matrix proteins.

SIGNALMENT

- Dogs and cats.
- Very young—more prone to infection because of incomplete, developing immunity; particularly kittens born to primiparous queen.

SIGNS

- Vary with site of infection and host immunocompetence.
- Weakness.
- Coughing.
- Dyspnea.
- Fever.
- Hematemesis.
- Hematuria.
- Lymphadenopathy.
- Pain.
- Dogs—abscesses; septicemia; endometritis; pyometra; vaginitis; mastitis; proctitis; otitis; arthritis; fading puppies; abortion; urinary tract infection; pyelonephritis; pneumonia; endocarditis; meningoencephalitis; necrotizing fasciitis and myositis; streptococcal toxic shock syndrome; wound infections; bitch sterility.
- Cats—abscesses; septicemia; peritonitis; cervical lymphadenitis; pharyngitis; tonsillitis; arthritis; pneumonia; fading kitten; necrotizing fasciitis.

OTHER LABORATORY TESTS

- Age, exposure, and immune response—important for determining disease.
- Virulence—depends on cellular products, surface components, and related substances.
- Opportunistic—wounds, trauma, surgical

procedures, viral infections, or immunosuppressive conditions.

- Co-infection with canine influenza virus (CIV) increases severity of disease.
- FeLV, FIP, immunodeficiency, respiratory viral infections, feline lower urinary tract disease—predisposing conditions.
- Maternal antibodies generally protect puppies and kittens against clinical disease.
- Carrier state occurs.
- Bacterial superantigens suspected as cause of multiple organ involvement in toxic shock syndrome and necrotizing fasciitis and myositis; association with enrofloxacin may be due to enrofloxacin-induced bacteriophages enhancing superantigen expression.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other infectious causes—viruses, bacteria, fungi, *Rickettsia*, protozoa.

CBC/BIOCHEMISTRY/URINALYSIS

- Normal or high WBCs with neutrophilic inflammatory response with a left shift or degenerative left shift.
- Cocci—may be found in circulating neutrophils in overwhelming sepsis.
- Biochemistry—may suggest predisposing conditions.
- Urinalysis—pyuria (with or without bacteruria) with cystitis.

OTHER LABORATORY TESTS

- Direct microscopy.
- Gram stain—of exudates; reveals chains of and single gram-positive cocci.
- Culture—affected tissues; exudate or needle aspirates; confirms diagnosis.
- Antibiotic susceptibility testing.
- PCR.

IMAGING

Radiographs—interstitial or alveolar pulmonary pattern with pneumonia; radiodense uroliths (struvite).

PATHOLOGIC FINDINGS

- Acute inflammation—gross or microscopic abscesses.
- Septicemia—post-mortem reveals omphalophlebitis, peritonitis, hepatitis, pneumonia, and myocarditis.



TREATMENT

- Good nursing care
- Rehydrate
- Drain and flush abscess
- Debride necrotic tissue



MEDICATIONS

DRUG(S)

- Penicillin—first choice; penicillin G at 10,000–20,000 U/kg IM, SC q12–24h, or penicillin V at 8–30 mg/kg PO q8h.

- Ampicillin 20–30 mg/kg IV, IM, SC, PO q8h; alone or in combination with gentamicin at 2–4 mg/kg IV, IM, SC q8h; for group B.
- Erythromycin 10–20 mg/kg IV, SC, PO q8h.
- Clindamycin 11 mg/kg PO q12–24h.
- Prophylactic treatment—all kittens born to primiparous queens indicated for neonatal infections.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Avoid immunosuppressive drugs.



FOLLOW-UP

PREVENTION/AVOIDANCE

- Avoid overcrowding and poor environmental sanitation.
- Prevention in newborns—dipping navel and umbilical cord in 2% tincture of iodine.
- Prevention in colonies—avoid overcrowding; maintain clean feeders; segregate infected animals.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Dogs and cats may show no clinical signs with group A streptococci but may serve as a reservoir for human infection.
- Streptococci isolated from people are usually of human, not animal, origin.
- *S. canis* infections in people reported from dog bites and ulcers or wounds in contact with dogs.

ABBREVIATIONS

- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- PCR = polymerase chain reaction
- RBC = red blood cell
- WBC = white blood cell

Suggested Reading

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STRONGYLOIDIASIS



BASICS

OVERVIEW

- Dogs—infection of small intestinal mucosa by *Strongyloides stercoralis*; only female nematodes are parasitic; can cause diarrhea and/or bronchopneumonia.
- Free-living males mate with females in the environment. In infected animals, female worms reproduce by parthenogenesis.
- Cats—natural *S. stercoralis* infection not reported in United States; *S. tumefaciens* uncommon—infection of large intestine causing grossly visible nodules.
- Multiple routes of transmission for infective larvae including skin penetration, ingestion, and transmammary; infective larvae can develop from eggs in GI tract and auto-infect host, resulting in persistent infection.
- Relatively host-specific; potential for transmission to humans.

SIGNALMENT

- Dogs and cats.
- Pups (possibly kittens) due to transmammary transmission of larvae from dam.

SIGNS

- S. stercoralis*—usually asymptomatic, can be severe, especially in young.
- Development of clinical signs follows larval migration pathway from skin penetration to lungs and then to small intestine.
- Debilitated pups or kittens.
- Dermatitis.
- Cough, bronchopneumonia.
- Diarrhea (especially in neonates); may contain blood or mucus; constipation.
- Cats (*S. tumefaciens*) usually asymptomatic; palpable firm colon.

CAUSES & RISK FACTORS

- Transmammary transmission if bitch is infected during late gestation or lactation; no dormant larvae occur in tissues of bitch.
- Infective larvae in environment contaminated with feces penetrate skin, especially under conditions of poor sanitation, high temperatures, and high humidity.
- Increased prevalence in kennels.
- Possible autoinfection due to rapid development of larvae to infective stage within host GI tract.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Multiple other parasite, viral, or bacterial enteric infections and non-infectious causes of diarrhea.

CBC/BIOCHEMISTRY/URINALYSIS

Eosinophilia can occur.

OTHER LABORATORY TESTS

N/A

IMAGING

Nodules of *S. tumefaciens* may be visible by colonoscopy.

DIAGNOSTIC PROCEDURES

- Egg with larva or just larvae may be detected in feces. Eggs are less than 50 μm , which is a good criterion for differentiating them from strongyle eggs which are larger. Detection of first stage larvae with rhabditiform (barbell-shaped) esophagus in fresh feces or third stage larvae with filariform (straight, cylindrical) esophagus and forked tail in incubated feces; repeated fecal examinations may be necessary because larvae are shed irregularly and in low numbers.
- Baermann method most sensitive, other methods include formalin-ethyl acetate.
- S. tumefaciens*—also examine nodules microscopically for adult females, eggs, and larvae.
- Necropsy—microscopic examination of small intestinal mucosal scrapings for adult females (2–2.5 mm \times 35 μm) with long cylindrical esophagus occupying one-third of body length and first-stage larvae (200–250 μm long) with rhabditiform esophagus.



TREATMENT

Usually anthelmintic treatment as outpatient unless intravenous fluid supplementation needed for dehydration.



MEDICATIONS

DRUG(S)

- Anthelmintic use is extra-label.

- Fenbendazole 50 mg/kg PO q24h for 5 days; may need to be repeated.
- Ivermectin 0.2 mg/kg SC or PO as single dose; repeat treatment may be needed; dose is extra-label.
- Adulicide/larvicide (fenbendazole) recommended for infection in neonates to eliminate larvae undergoing lung migration.

CONTRAINdications/POSSible INTERACTIONS

Do not give ivermectin at 0.2 mg/kg to heartworm-positive patients or to ivermectin-sensitive dog breeds, e.g., collies.



FOLLOW-UP

PATIENT MONITORING

Repeat fecal examinations monthly for 6 months after treatment to assure clearance of infection; larval shedding intermittent.

PREVENTION/AVOIDANCE

Kennels—implement thorough daily cleaning, disinfection with 1% bleach, and monthly anthelmintic treatment to eliminate or minimize number of infective larvae present in environment.



MISCELLANEOUS

ZOONOTIC POTENTIAL

S. stercoralis is probably underdiagnosed in humans. Humans can develop dermatologic lesions at the site of skin entry, severe abdominal discomfort, and diarrhea.

ABBREVIATION

- GI = gastrointestinal

INTERNET RESOURCES

<http://www.cdc.gov>

Suggested Reading

Bowman D.D. Georgis' Parasitology for Veterinarians, 9th ed. St. Louis, MO: Saunders, 2009, pp. 191–193.

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Acknowledgment The author and editors acknowledge the prior contribution of Julie Ann Jarvinen.



BASICS

OVERVIEW

- Stupor—unconscious but arousable with noxious stimuli.
- Coma—unconscious, not arousable with noxious stimuli.

PATHOPHYSIOLOGY

Ascending reticular activating system—network of neurons situated in the core of the brainstem; arousal system for the cerebral cortex; any severe pathologic change (anatomic or metabolic) that causes interruption can lead to depression, stupor, or coma.

SYSTEMS AFFECTED

- Nervous
- Cardiovascular
- Neuromuscular
- Ophthalmic
- Respiratory

SIGNALMENT

- Dog and cat
- No breed, age, or sex predilection

SIGNS

Historical Findings

- Possibility of trauma or unsupervised roaming.
- Past medical problems of significance—diabetes mellitus and insulin therapy; hypoglycemia; cardiovascular problems; hypoxic episodes; renal failure; liver failure; neoplasia.
- Patient's environment—possible heatstroke; hypothermia; drowning; exposure to drugs, including owner's medications narcotics, and toxins (e.g., ethylene glycol, lead, anticoagulants).
- Onset may be acute or slowly progressive, depending on underlying cause.

Physical Examination Findings

- Look for evidence of external or internal trauma.
- Severe hypothermia or hyperthermia.
- Evidence of hypoxia or cyanosis, ecchymosis or petechiation, or cardiac or respiratory insufficiency—warrants investigation for metabolic causes.
- Palpate for evidence of neoplasia.
- Retinal hemorrhages or distended vessels—hypertension.
- Papilledema—cerebral edema.
- Retinal detachment—infectious, neoplastic, or hypertensive causes.
- Chorioretinitis—infectious causes (distemper, FeLV-related diseases, toxoplasmosis, cryptococcosis, or coronavirus).
- Sustained bradycardia (with normal serum potassium)—midbrain, pontine, or medullary lesion.

Neurologic Examination Findings

- Differentiate cerebrum-diencephalon lesion from brainstem lesion (better vs. worse prognosis).
- Determine level of consciousness and if patient arousable.
- Pupillary light reflexes—small responsive pupils: cerebral or diencephalic lesion; dilated unresponsive pupils (unilateral or bilateral) or fixed in midposition: midbrain or severe

medullary lesions.

- Oculocephalic reflex (when cervical manipulation possible)—loss of physiologic vestibular nystagmus: brainstem involvement.
- Respiratory patterns—Cheyne-Stokes respiration: severe, diffuse cerebral or diencephalic lesion; hyperventilation: midbrain lesion; ataxic or apneustic breathing: pons or medulla lesion.
- Cranial nerves—no deficits with lesion of cerebrum-diencephalon; deficits of cranial nerve III: midbrain lesion; deficits of cranial nerves V–XII: pons and medulla lesions.
- Postural changes—decerebrate rigidity: midbrain lesion.

CAUSES

- Drugs—narcotics; anesthetics; depressants; ivermectin
- Anatomic—hydrocephalus.
- Metabolic—severe hypoglycemia; hyperglycemia; hyperosmolar syndromes; hypernatremia; hyponatremia; hepatic encephalopathy; hypoxemia; hypercarbia; hypothermia; hyperthermia; hypotension; coagulopathies; renal failure; lysosomal storage disease, severe hypothyroidism
- Nutritional—hypoglycemia; thiamin deficiency
- Neoplastic (primary)—meningioma; astrocytoma; gliomas; choroid plexus papilloma; pituitary adenoma; others
- Metastatic—hemangiosarcoma; lymphoma; mammary carcinoma; others
- Inflammatory non-infectious—granulomatous meningoencephalomyelitis
- Infectious—bacterial; viral (distemper, FCoV); parasitic (aberrant larva migrants); protozoal (neosporosis, toxoplasmosis); fungal (cryptococcosis, blastomycosis, histoplasmosis, coccidioidomycosis, actinomycosis); tick-borne diseases
- Idiopathic—epilepsy (post-status epilepticus)
- Immune-mediated—vasculitis and thrombocytopenia leading to hemorrhage
- Traumatic
- Toxins—ethylene glycol; lead; rodenticide anticoagulants; others
- Vascular—hemorrhage (bleeding disorders, hypertension); infarction (feline ischemic encephalopathy, microfilaria, or migrating adult heartworm)

RISK FACTORS

- Diabetes mellitus—insulin therapy
- Hepatic failure
- Insulinoma
- Severe heat or cold exposure without protection
- Free-roaming animals—trauma
- Young and unvaccinated animals
- Hypertension



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute onset—most commonly caused by toxins, drugs, trauma, or vascular accidents
- Slow progression of neurologic signs without systemic abnormalities—suggests primary neurologic disorders of inflammatory, neoplastic, or anatomic causes
- Bilateral

diffuse cortical signs—metabolic diseases, toxins, systemic infection, drugs, and nutritional causes

- Brainstem signs—trauma, inflammation, neoplasia, vascular accidents, or commonly from progression of cerebral disease causing tentorial herniation

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Lead toxicity—may show nucleated red blood cells or basophilic stippling
- Severe infection—inflammatory hemogram
- Severe anemia—suggests hypoxemia

Biochemistry

May see hypoglycemia, hyperglycemia, hypernatremia, azotemia, hyperosmolarity, and other metabolic derangements

Urinalysis

- Diabetes mellitus—glycosuria
- Renal failure—isosthenuria, granular casts
- Immune-mediated disease or severe infection—proteinuria
- Hepatic encephalopathy—ammonium biurate crystals
- Ethylene glycol toxicity—calcium oxalate or hippurate crystals

OTHER LABORATORY TESTS

- Serum ethylene glycol level and osmolar gap—acute onset.
- Serum ammonia concentrations and preprandial and postprandial bile acids—high levels indicate hepatic encephalopathy.
- Serum and CSF titers—suspected infectious disease.
- Arterial blood gases—evidence of hypoxemia; severe pH changes; hypo- and hyper-carbia.
- Coagulogram—including PT, PTT, fibrinogen, fibrin degradation product, d-dimer, platelet count, antithrombin, and buccal bleeding time; suspected intracranial bleeding or thrombosis.
- Serologic testing—FeLV, FIV, FCoV, protozoal and heartworm disease.
- Serum toxicity levels (e.g., lead, macrolide).
- Thyroid panel.

IMAGING

- Survey radiographs (chest and abdomen)—evidence of heavy metal, organ enlargement, infiltration, or neoplasia.
- Skull radiographs—fractures in trauma cases, masses.
- CT—excellent for detecting acute hemorrhage within calvaria; depressed fractures; penetrating foreign bodies.
- MRI with contrast—demonstrates cerebral edema, hemorrhage, mass, infiltrative diseases.

DIAGNOSTIC PROCEDURES

- CSF—cytology, protein and immunoglobulin concentrations, and titers for infectious diseases; perform only when no evidence of trauma, increased intracranial pressure, coagulopathies, or metabolic disease.
- Brainstem auditory-evoked response—determine brainstem function.
- ECG—determine cardiac dysfunction; abnormalities may contribute to stupor or coma or may be caused by brain disease.
- EEG—detect nonclinical seizure activity that can prolong stupor and coma.

STUPOR AND COMA

(CONTINUED)

PATHOLOGIC FINDINGS

Cerebral edema; hemorrhage; infarct; ischemia; inflammation; neoplasia; herniation; laceration; contusion; hematomas; skull fracture; necrosis and apoptosis.



TREATMENT

POOR PERFUSION

- Small volume fluid resuscitation technique; a combination of hydroxyethyl starch with balanced isotonic crystalloids. • Use peripheral veins, leaving the jugular vein blood flow unobstructed; shifting blood volume into the jugular veins is an important compensatory mechanism during high ICP.
- Maintain systolic BP > 90 mmHg; avoid hypertension. • Hydration—maintain with a balanced electrolyte crystalloid solution.
- The head and neck should be leveled with the body or elevated to a 20° angle. • Oxygen supplementation—avoid a cough or sneeze reflex during intubation or nasal cannula placement; administer lidocaine (dogs, 1–2 mg/kg IV) before intubation to blunt the gag and cough reflex. • PaO₂ must be > 50 mmHg to maintain cerebral blood flow auto-regulation in normal tissue.

VENTILATION

- PaCO₂—maintain between 35–45 mmHg.

REDUCE INCREASE IN ICP

- Prevent thrashing, seizures, or any other form of uncontrolled motor activity that can elevate ICP; diazepam infusion (0.5–1 mg/kg/h), midazolam (0.2–0.4 mg/kg), or propofol (3–6 mg/kg IV titrated to effect; then 0.1–0.6 mg/kg/min CRI); levetiracetam 20 mg/kg IV/IM/rectal q8h if seizure activity. • Ensure systolic BP > 90 mmHg. • 7% hypertonic saline (2–4 mL/kg IV); can reduce fluid volume needed to reach resuscitation endpoints; combine with colloid. • Furosemide 0.75 mg/kg IV; may decrease CSF production; used in patients with congestive heart failure, volume overload, hyperosmolar diseases, or anuric renal failure; use before mannitol. • Mannitol 0.1–0.5 g/kg IV bolus repeated at 2-hour intervals 3 or 4 times in dogs, and 2 or 3 times in cats; repeated doses must be given on time; improves brain blood flow and lowers ICP. • Hyperventilation (PaCO₂ 32–35 mmHg) for 48 hours using mechanical ventilation; requires intensive monitoring. • Ventriculostomy for drainage of CSF if critical elevation of ICP nonresponsive to medical treatment.

- Consider surgical decompression and exploration—if cerebral dysfunction is progressing to midbrain signs with a history of trauma or bleeding (tentorial herniation); high ICP not responsive to medical therapy (if monitoring instrumentation available);

depressed skull fracture fragments; penetrating foreign body; requires intensive monitoring.

NURSING CARE

- Prevent secondary complications of recumbency—eye lubrication; aseptic technique with catheters; turning. • Prevent urine/fecal scalding. • Careful nasogastric tube feeding for early trickle flow feeding; cisapride (0.5 mg/kg PO q8–12h) and metoclopramide (1–2 mg/kg/day) may promote GI motility.



MEDICATIONS

DRUG(S) OF CHOICE

Underlying Disease

- Glucocorticosteroids—inflammatory, immune-mediated and space-occupying intracranial abnormalities. • Lactulose enemas, flumazenil (0.02 mg/kg IV) and fluid support—hepatic encephalopathy. • Fluid diuresis, dialysis—renal failure. • Rehydration and insulin—diabetes mellitus with hyperosmolarity; lower glucose slowly.
- Glucose supplementation—hypoglycemia.
- Support intravascular volume; cool—hyperthermia. • Support intravascular volume; warm to ≥ 98°F—hypothermia.
- Gastric lavage and instillation of activated charcoal with a cathartic—toxin ingestion.
- Specific toxins may require specific therapeutics (e.g. ethylene glycol treated with ethanol and peritoneal/hemo dialysis).
- Antibiotics—use agents that cross the blood-brain barrier for suspected bacterial infections (e.g., trimethoprim-sulfa, clindamycin, doxycycline, and metronidazole). • Adjust crystalloid fluid selection to correct electrolyte disorders.
- Thiamin (cat, 5–50 mg; dog, 1–20 mg IV)—possible thiamin deficiency.

CONTRAINDICATIONS

N/A

PRECAUTIONS

- Avoid hypo- and hypertension, hypo- and hyperglycemia. • Avoid intravascular volume overload.



FOLLOW-UP

PATIENT MONITORING

- Serial neurologic examinations—detect deterioration that warrants aggressive therapeutic intervention. • BP—keep fluid therapy adequate for perfusion while avoiding hypertension. • Blood gases—assess need for oxygen supplementation or ventilation; monitor PCO₂ when hyperventilating.
- Blood glucose—ensure adequate level to

maintain brain functions while avoiding hyperosmolality. • ECG—detect arrhythmias that may affect perfusion, oxygenation, and cerebral blood flow. • ICP—detect marked elevations; track success of therapeutics.

- Electrolytes—detect hypernatremia and hypokalemia.

PREVENTION/AVOIDANCE

- Keep pets confined or leashed. • Prevent exposure to toxins or in-home medications.
- Routine healthcare program to minimize infectious and metabolic disease complications.

POSSIBLE COMPLICATIONS

- Residual neurologic deficits and seizures.
- Complications consistent with underlying disease.

EXPECTED COURSE AND PROGNOSIS

- Pathology of brainstem worse than pathology of cerebral cortex. • Glasgow Coma Score can provide prognostic information.



MISCELLANEOUS

ABBREVIATIONS

- BP = blood pressure • CSF = cerebrospinal fluid • CT = computed tomography
- ECG = electrocardiogram • EEG = electroencephalogram • FeLV = feline leukemia virus • FCoV = feline coronavirus
- FIV = feline immunodeficiency virus
- ICP = intracranial pressure • MRI = magnetic resonance imaging • PaCO₂ = partial pressure of carbon dioxide in arterial blood • PaO₂ = partial pressure of arterial oxygen • PT = prothrombin time • PTT = partial thromboplastin time

SEE ALSO

Brain Injury

INTERNET RESOURCES

- <http://www.accessmedicine.com>
- <http://www.cvmbs.colostate.edu/clinsci/wing/comascor.html>

Suggested Reading

Chrisman CL, Mariani C, Platt S. Dementia, stupor and coma. In: Neurology for the Small Animal Practitioner. Jackson, WY: Teton NewMedia, 2003, pp. 41–84.

Dewey CW. A Practical Guide to Canine and Feline Neurology, 2nd ed. Ames, IA: Wiley-Blackwell, 2008.

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Client Education Handout
available online

SUBARACHNOID CYSTS (ARACHNOID DIVERTICULUM)



BASICS

DEFINITION

Subarachnoid cysts refer to dilation of the subarachnoid space causing compression of the underlying spinal cord. The use of the term "cyst" is misleading, as most do not have a defined cyst wall with an epithelial lining and the term subarachnoid diverticulum is frequently used.

PATHOPHYSIOLOGY

- There are several proposed etiologies of subarachnoid cysts.
- Any disease process that causes arachnoiditis has the potential to cause adhesions that result in the formation of one-way valves through which CSF flows, but cannot return, thus producing a "cyst."

SYSTEMS AFFECTED

Nervous—spinal cord and brain (quadrigeminal cistern)

GENETICS

Certain breeds appear to be predisposed (e.g., pug, rottweiler for spinal cord, Pekingese, Shih Tzu for brain), but there is no data confirming heritability or a mode of inheritance.

INCIDENCE/PREVALENCE

No specific data

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Spinal: pug, rottweiler, French bulldog
- Brain: small brachycephalic breeds

Mean Age and Range

Dogs < 3 years, range 2.5 months–13 years

Predominant Sex

Male > female

SIGNS

Historical Findings

Spinal

- Owners report a slowly progressive ataxia and paresis involving all or just the pelvic limbs.
- Fecal incontinence—common early sign of thoracolumbar cysts, with urinary incontinence developing shortly after.
- Owners do not usually report that the pet is in pain. In a study of 122 cases, 19% of the dogs had pain.
- There may be prior history of traumatic spinal cord injury.

Brain

- Cerebellar signs
- Seizures

Physical Examination Findings

Usually normal, although possible secondary consequences of the myelopathy include abrasions of the dorsal aspect of the toes, wearing of the nails, and urinary tract infections.

Neurologic Examination Findings

Spinal

- Neurologic signs reflect lesion localization—hindlimb involvement for thoracolumbar cysts and all limbs for cervical cysts.
- Ataxia frequently characterized by hypermetria.
- Paresis.
- Proprioceptive placing deficits.
- Fecal and/or urinary incontinence; urine retention (due to defective voiding).
- Spinal reflexes may be reduced if the lesion is at the brachial or lumbosacral intumescence but otherwise are normal or increased.
- Spinal pain is rarely elicited.

Brain

- Quadrigeminal cysts are frequently an incidental finding. However, extremely large cysts can produce compression of the cerebellum and brainstem.
- Signs of cerebellar disease—hypermetria, intention tremor, wide based stance.
- Signs of brainstem compression—tetraparesis, head tilt.
- Seizures (the relationship between the cyst and the presence of seizures is unclear).

CAUSES

- Several proposed etiologies.
- Congenital malformation of the arachnoid mater (dilated septum posticum; in young dogs).
- Secondary to traumatic injury to the arachnoid, causing adhesions and development of one-way valves for CSF flow.
- Secondary to chronic microtrauma to the arachnoid, causing adhesions and development of one-way valves for CSF flow. This mechanism has been proposed for pugs with caudal thoracic subarachnoid cysts. Affected dogs have hypoplasia of their articular facets leading to chronic instability.

RISK FACTORS

- Traumatic spinal cord injury that damages the arachnoid mater.
- Hypoplastic articular facets associated with subarachnoid cysts in certain dog breeds (pugs).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Distinctive features—slowly progressive, nonpainful paresis and ataxia with a hypermetric gait, and presence of fecal and/or urinary incontinence in an animal that is still ambulatory.
- Any cause of focal myelopathy could cause the same neurologic presentation.
- Intervertebral disc herniation.
- Neoplasia.
- Trauma.
- Inflammatory or infectious myelitis.
- Congenital vertebral/spinal malformation.
- Intraspinal vascular malformation.

CBC/BIOCHEMISTRY/URINALYSIS

Urinalysis may show evidence of urinary tract infection (pyuria, hematuria, proteinuria, and bacteriuria).

OTHER LABORATORY TESTS

Aerobic urine culture if evidence of urinary tract infection.

IMAGING

- Thoracic radiography—in older patients to rule-out metastatic neoplasia.
- Spinal radiography—should be performed in all patients; typically unremarkable in patients with subarachnoid cysts. However, some patients may have evidence of spinal fractures, and occasionally there is evidence of a vertebral malformation (articular facet hypoplasia, spina bifida, hemivertebra, or block vertebra) co-localizing with the neurologic signs.
- Myelography—focal dilation of the subarachnoid space most commonly located dorsally but sometimes located ventrally; the dilation may be multilobed.
- CT myelography—further delineates the dilated subarachnoid space in transverse section; without intrathecal contrast, will not demonstrate the lesion.
- MRI—dilation of the subarachnoid space in sagittal and transverse section on T2-weighted images. T2-HASTE images provide even more definition of the CSF accumulation. The presence of active arachnoiditis can be detected on pre- and post-contrast T1-weighted images.

DIAGNOSTIC PROCEDURES

CSF—to rule out a primary inflammatory process; may show mild inflammation as secondary consequence of the subarachnoid cyst.

PATHOLOGIC FINDINGS

- At surgery, adhesions may be evident in the subarachnoid space. Occasionally a thin cyst wall is apparent (this is unusual).
- Histopathology of excised arachnoid—may show fibrosis or mild inflammation.
- Histopathology of the spinal cord shows chronic compressive injury—loss of gray and white matter, Wallerian degeneration, demyelination.



TREATMENT

APPROPRIATE HEALTH CARE

- Patients with mild signs can be managed medically; surgery recommended for young dogs with moderate, progressive signs.
- Non-ambulatory patients should be hospitalized for diagnostic workup and possible surgical decompression as soon as possible.

NURSING CARE

- Patients that have incomplete micturition should have their bladders manually expressed three to four times a day. If this is not possible, their bladders should be catheterized in a sterile fashion once to twice a day.

SUBARACHNOID CYSTS (ARACHNOID DIVERTICULUM)

(CONTINUED)

- Appropriate maintenance fluids should be administered in the immediate postoperative period.
- Postoperative pain should be assessed regularly (q6h) and treated as needed with opiates and nonsteroidal anti-inflammatory drugs.
- Surgical incisions should be ice packed for 5–10 minutes three times a day for 24 hours after surgery and then should be hot packed for a similar period for an additional 2–5 days.
- Rehabilitation is important; a patient-specific rehabilitation program should be developed to include gait training and improvement of strength.

ACTIVITY

- Paretic and ataxic patients need to be restricted to non-slip, flat surfaces to avoid falling.
- Exercise should be restricted to walking on a leash to avoid falling, but controlled exercise is important in maintaining muscle strength and joint integrity.
- Postoperatively, patients need to be restricted to a small, well-padded space (crate) to ensure that they do not fall while the laminectomy site is healing. Limited controlled exercise should be performed during this period.

CLIENT EDUCATION

- Clients need to be educated on the implications of a chronic compressive myelopathy; permanent damage to the spinal cord has already occurred and may not be reversible. The primary aim of treatment is to prevent further deterioration, with a hope of also producing a clinical improvement.
- There may be an initial deterioration immediately postoperatively; there is a small chance that this deterioration could be permanent.
- Incontinence, if present, is likely to be permanent.
- The disease may recur in spite of surgical therapy.

SURGICAL CONSIDERATIONS

- Surgical decompression of spinal subarachnoid cysts is recommended in young dogs and can be attempted in older animals.
- Marsupialization of the meninges may reduce the chance of a recurrence.
- Surgical treatment of quadrigeminal cysts is only recommended if there are clear signs of compression of adjacent cerebellum and cerebral cortex. Direct surgical exploration and decompression or shunt placement can be attempted.



MEDICATIONS

DRUG(S) OF CHOICE

- Anti-inflammatory doses of prednisone (0.5 mg/kg orally once to twice a day) may improve signs and reduce inflammation. If there is no improvement, prednisone should be tapered and discontinued.

- Omeprazole may reduce CSF production rate and improve signs. If there is no improvement it should be discontinued.
- Treatment with antiepileptic drugs should be initiated in dogs with more than 1 seizure a month or cluster seizures. Choice of antiepileptic drug depends on a number of patient and client factors. Phenobarbital (starting at 2 mg/kg q12h), zonisamide (starting at 5–10 mg/kg q12h) and levetiracetam (starting at 20 mg/kg q8h) are all appropriate choices for first-line therapy.

CONTRAINDICATIONS

N/A

PRECAUTIONS

Corticosteroids should be used with caution if the patient has urinary tract infection.

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- If response to prednisone is being assessed, the patient's gait and postural reactions should be reassessed in 1–2 weeks. The owner's assessment of continence is also important.
- If there is a positive response to medical management, the patient should be monitored every 8–12 weeks for maintenance of the improvement over the next 6 months and then every 6–12 months. The owner should be instructed to call if deterioration in clinical signs is detected.
- Surgical treatment—patient reassessed at 7–10 days for suture removal, evaluation of incision, and to ensure that there is no deterioration in gait, level of pain, continence; reassessment at 1–3 months and every 6–12 months subsequently. Telephone updates are acceptable if the patient is doing well.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Clients may encounter fecal and urinary incontinence.
- If incontinent, there is a predisposition to urinary tract infections.
- Signs may recur at any time.

EXPECTED COURSE AND PROGNOSIS

Spinal Cysts

- Surgical decompression produces a good long-term outcome (more than 1 year) in approximately 66% of dogs with spinal disease.
- Age at onset of signs and duration of signs are associated with outcome. Dogs less than 3 years of age and with a short duration of signs (less than 4 months) are more likely to have a good long-term outcome.
- There is

no data on the prognosis with medical management, but anecdotally the author can report a good long-term outcome in old dogs with mild signs when treated with prednisone and rehabilitation alone.

Quadrigeminal Cysts

Data on prognosis of quadrigeminal cysts managed medically or surgically is extremely limited but suggests that a positive outcome can be attained with both treatment strategies.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

Cervical cysts are more common in dogs < 3 years of age and thoracolumbar cysts are common in old pugs.

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

Arachnoid diverticula, arachnoid cyst, meningeal or leptomeningeal cyst

ABBREVIATIONS

- CSF = cerebrospinal fluid
- CT = computed tomography
- MRI = magnetic resonance imaging

SEE ALSO

Quadrigeminal Cyst

INTERNET RESOURCES

<http://www.ivis.org/advances/Vite/toc.asp>

Suggested Reading

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Author Natasha J. Olby

Consulting Editor Joane M. Parent

SUBINVOLUTION OF PLACENTAL SITES



BASICS

OVERVIEW

- Failure or delay of normal postpartum uterine involution (normally requires 12–15 weeks to complete).
- Failure of eosinophilic masses of collagen at placental sites to slough at 3–4 weeks postpartum.
- Failure of fetal trophoblastic cells to regress (normally occurs within 2 weeks); instead, they invade the maternal deep glandular endometrium and myometrium.
- Cause—unknown; hormonal or uterine basis not suspected based on coexistence of unaffected and subinvolved placental sites in the same uterus.

SIGNALMENT

- Dog only
- Bitch < 3 years most common
- Higher incidence in first litter
- No breed predilections

SIGNS

Historical Findings

- Patient presented > 12 weeks postpartum
- Serosanguineous vulvar discharge beyond 12 weeks postpartum
- Typically no systemic signs; rare occurrence of hypovolemic shock

Physical Examination Findings

- Serosanguineous vulvar discharge
- Firm, spherical structures within uterus on abdominal palpation

CAUSES & RISK FACTORS

- Unknown.
- Hormonal—unlikely, because only some of the placental sites may be involved.
- Uterine disease—unlikely, because of high first litter prevalence.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Metritis—differentiated by vaginal cytology and physical examination.
- Vaginitis—differentiated by vaginal cytology.
- Vaginal neoplasia—differentiated by vaginal cytology and vaginal endoscopy.
- Uterine neoplasia—differentiated by ultrasonography or exploratory laparotomy.
- Cystitis—differentiated by vaginal cytology and urinalysis obtained by cystocentesis.
- Coagulopathy—differentiated by clotting times.
- Trauma.
- Endogenous estrogen stimulation—bitch with an extremely shortened interestrous interval.

- Exogenous estrogen stimulation—oral medication or contact with topical hormone replacement product on human skin, bedding, or clothing.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

- Serology for *Brucella canis* negative
- Progesterone < 2 ng/mL

IMAGING

Uterine ultrasonography—focal uterine wall thickening; possible echogenic fluid in the lumen.

DIAGNOSTIC PROCEDURES

- Vaginal cytologic examination—key for diagnosis; reveals erythrocytes and parabasal epithelial cells; may note pathognomonic trophoblastic cells (polynucleated, heavily vacuolated).
- Guarded anterior vaginal or transcervical uterine culture—if vaginal cytologic examination or hemogram supports a diagnosis of secondary metritis.

PATHOLOGIC FINDINGS

- Gross—sites characterized by a thickened, hemorrhagic area that may be nodular.
- Histopathologic—definitive diagnosis; eosinophilic collagen masses with trophoblasts extending into the myometrium.



TREATMENT

- Usually outpatient.
- Spontaneous remission—occurs in most patients before or at next cycle; medical therapy is generally not warranted.
- Medical—for rare development of anemia, metritis, or peritonitis.
- Severely affected patients—may require blood transfusion (rare).
- Warn owner of the rare possibility of excessive hemorrhage; instruct owner to monitor mucous membrane color.
- Ovariohysterectomy—curative; treatment of choice if future breeding not desired.
- Surgical curettage of subinvolved sites—may also be performed; effectiveness unknown.



MEDICATIONS

DRUG(S)

- Oxytocin generally not successful.
- Ergonovine 0.2 mg/15 kg IM (10–30 µg/kg) once; do not use if uterus friable.
- Small study showed response to megestrol acetate 0.1 mg/kg q24h for 1 week, then 0.05 mg/kg q24h daily for 1 week; 5 of 6

treated bitches were successfully bred, with normal parturition and puerperal periods.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Ecbolics—may cause uterine rupture.
- Progestational drugs—increase the risk of metritis, which may mimic pyometra or induce cystic endometrial hyperplasia.



FOLLOW-UP

PATIENT MONITORING

- Mucous membrane color and amount of discharge.
- Packed cell volume—if anemia is a concern.
- Changes in discharge color or odor and vaginal cytologic examination and culture—diagnose secondary infection.

POSSIBLE COMPLICATIONS

Infection, blood-loss anemia, or uterine rupture—rare

EXPECTED COURSE AND PROGNOSIS

- Spontaneous resolution—the usual outcome in the majority of cases.
- Recurrence—not expected, occurs rarely.
- Prognosis for future reproduction—excellent with spontaneous resolution.



MISCELLANEOUS

Suggested Reading

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Author Joni L. Freshman

Consulting Editor Sara K. Lyle

SUBMISSIVE AND EXCITEMENT URINATION—DOGS



BASICS

OVERVIEW

- Excitement and submissive urination occur as distinct behavioral presentations but may overlap in some patients.
- Submissive urination is related to fearful responses—animal perceives potential threat or danger during interaction and displays submissive behavior, including urination, as appeasement gesture to abort potential escalation of aggressive interactions.
- Generally seen in interaction with people; however, submissive urination may occur during interactions with other animals, especially conspecifics.

SIGNALMENT

- Onset as puppy in dogs of either sex; generally < 1 year of age
- Anecdotally higher incidence in some small breeds, e.g. dachshund, cocker spaniel
- Not observed in cats

SIGNS

- Excitement: loss of urine control in situations of high arousal—greeting people, anticipation of activities such as walks or car rides; no actual urination posturing seen—urine is expelled while dog is engaged in activities such as jumping up or play; dog does not necessarily show submissive behaviour.
- Submissive/fear: expelling small amounts of urine during interactions with people or other animals or in frightening situations; partial or full squatting position; dog may lift one hind leg partially for inguinal presentation.
- Dogs may be excited and aroused yet submissive or fearful during greeting—when there are competing motivations this might therefore be described as conflict induced—the approach may be active with tail wagging and crouching/low body posture.

CAUSES & RISK FACTORS

See "Signs"



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Incontinence, ectopic ureter, patent urachus
- Cystitis

- Disorders of urethral competence (which may increase severity or frequency of urination during submissive or excitement urination)

- Disorders causing PU/PD may decrease pet's ability to maintain bladder control.

CBC/BIOCHEMISTRY/URINALYSIS

Indicated only to rule out medical disorders

IMAGING

Indicated only to rule out medical disorders

DIAGNOSTIC PROCEDURES

Indicated only to rule out medical disorders



TREATMENT

Excitement urination

- Avoid arousing situations.
- Do not greet dog when aroused/excited—greet dog away from front door and several minutes after arrival only after dog is calm.
- When entering home, toss treats away to redirect and distract pet; over time can gradually transition to tossing treats closer to person and eventually hand treats to pet when pet sits calmly on cue.
- Avoid high-pitch excited speech around pet; avoid eye contact if it arouses/excites the pet.
- Teach owner to reinforce calm behavior and teach behaviors incompatible with high arousal, e.g. sit or lie down for greetings and before walks.
- Owners should interact with pet in emotionally neutral, low-key manner.

Submissive/fear urination

- Avoid threatening or confrontational interactions; do not lean over pet, do not punish or raise voice with pet; avoid eye contact.
- Avoid deep, loud or high-pitch excited speech while around or interacting with the pet.
- Move slowly and consistently around pet to avoid potential startling or threatening actions.
- Squat down or greet/interact with pet while sitting in chair or on floor with the body turned partially away from the dog.
- Redirection or distraction with food treats or toys; toss treats away to redirect and distract pet; over time can gradually transition to tossing treats closer to person and eventually hand treats to pet when pet sits calmly on cue.

- Teach behaviors incompatible with submissive posturing using positive reinforcement (food treats): pet sitting upright with head and ears up and forward; eye contact.

- Owner should turn and walk away or back away if pet begins to show submissive posturing.



MEDICATIONS

- Medications generally not indicated but could consider: Phenylpropanolamine (12.5–50 mg PO up to q8h) temporarily to increase urethral sphincter tone while behavior modification is taking effect.
- Imipramine (2.2–4.4 mg/kg PO q12h) or clomipramine (1–3 mg/kg PO q12h): increase urinary retention through anticholinergic effects; serotonin and norepinephrine properties can help reduce excitement or fear that contribute to urinating.



FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS

Prognosis is good if owners can follow simple behavior modification steps; a number of pets will improve with maturity alone.



MISCELLANEOUS

SEE ALSO

Housesoiling—Dogs

ABBREVIATIONS

PU/PD = polyuria/polydipsia

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SUPERFICIAL NECROLYTIC DERMATITIS



BASICS

OVERVIEW

- Uncommon in dogs; rare in cats.
- Usually a cutaneous marker for advanced liver disease with or without concurrent diabetes mellitus.
- Lesion pathogenesis unclear; keratinocyte degeneration and necrosis possibly due to cutaneous nutritional deprivation; hyperglucagonemia, hypoaminoacidemia, zinc and essential fatty acid deficiencies believed to play a role.

SYSTEMS AFFECTED

- Skin/Exocrine
- Endocrine/Metabolic
- Hepatobiliary

SIGNALMENT

- No breed predilection
- Older dogs

SIGNS

- Skin—lesions often precede clinical evidence of internal disease by weeks or months; erythema, crusts, and erosions/ulcerations affecting the muzzle, mucocutaneous areas of the face, pinna, distal limbs (especially elbows and hocks), feet, perineum, perianal area, and external genitalia.
- Footpads—hyperkeratotic with fissures and ulcerations; pain when walking.
- Pruritus absent to severe.
- Secondary bacterial and/or yeast infection—mainly footpad lesions.
- Feline—alopecia and scaling of the limbs and trunk (two cases); erythema, ulceration, crusting, and alopecia of the limbs and trunk (one case); crusts and hyperkeratosis of paw pads (one case).

CAUSES & RISK FACTORS

- Specific cause unknown.
- Cutaneous nutritional deprivation—probably hypoaminoacidemia and/or deficiencies in essential fatty acids and zinc; due to metabolic abnormalities caused by hyperglucagonemia, liver dysfunction, or a combination.
- Usually associated with advanced liver disease with or without concurrent diabetes mellitus.
- Rarely associated with pancreatic or extrapancreatic glucagon-secreting tumor, ingestion of mycotoxins, or long-term phenobarbital and phenytoin therapies.
- Feline—one case each of pancreatic carcinoma, hepatic carcinoid, hepatopathy, and hepatopathy and intestinal lymphoma.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pemphigus foliaceus.
- Systemic lupus erythematosus.
- Zinc-responsive dermatosis.
- Toxic epidermal necrolysis.
- Drug eruption.
- Feline exfoliative skin diseases:

thymoma-associated exfoliative dermatitis and cutaneous epitheliotropic lymphoma. • Distal extremity erythema and footpad hyperkeratosis with fissures/ulcerations: suggestive of this condition in dogs.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia—occasional; normocytic, normochromic, nonregenerative.
- RBC abnormalities—polychromasia, anisocytosis, poikilocytosis, target cells.
- ALP, ALT, and AST—high activity with advanced liver disease.
- Total bilirubin—variably high.
- Albumin—frequently low.
- Biochemistry abnormalities other than hypoalbuminemia are unusual in dogs with glucagon-secreting tumors.
- Most patients eventually develop borderline or frank hyperglycemia.

OTHER LABORATORY TESTS

- Bile acid levels—variably high.
- Liver biopsy—vacuolar hepatopathy with parenchymal collapse and nodular hyperplasia.
- Elevated plasma glucagon levels—present with glucagon-secreting tumors; variable with chronic liver disease.
- Hypoaminoacidemia—common.
- High insulin levels may be noted.
- BSP retention—typically increased.

IMAGING

- Abdominal radiography and ultrasonography—“honeycomb” pattern on liver ultrasound in advanced hepatopathy.
- Usually unremarkable with pancreatic or rarely extrapancreatic glucagon-secreting tumor unless large enough to visualize.

DIAGNOSTIC PROCEDURES

Skin biopsy: sample early lesions; include crusts and avoid eroded/ulcerated lesions.

PATHOLOGIC FINDINGS

- Skin biopsy—diffuse parakeratotic hyperkeratosis with high-level intracellular and intercellular epidermal edema; irregular epidermal hyperplasia and mild-to-severe superficial perivascular dermatitis.
- Chronic lesions—marked parakeratotic hyperkeratosis and epidermal hyperplasia.



TREATMENT

- Usually as outpatients.
- Supportive care for systemic signs.
- Surgical excision of glucagon-secreting tumors—can be curative if no metastasis.
- Most cases caused by chronic irreversible liver disease.
- Oral nutritional support—high-quality protein diet or protein supplement for non-encephalopathic cases; three to six cooked whole eggs or yolks per day.
- Inform clients that this disorder indicates concurrent internal disease.
- Hydrotherapy and shampoos—remove crusts; lessen pruritus and pain.



MEDICATIONS

DRUG(S)

- Specific treatment—attempt to correct the underlying disease if possible.
- Nonspecific therapy—antibiotics and antifungal drugs for secondary skin infections.
- Amino acid hyperalimentation—intravenous administration of a 10% crystalline amino acid solution (e.g., Aminosyn) approx 25 mL/kg, administrated over 6–8 hours and repeated every 7–10 days or as needed for symptom relief. Oral amino acid therapy may be beneficial.
- Octreotide (somatostatin analogue) 2–3.2 µg/kg subcutaneously q6–12h as maintenance therapy for patients with nonresectable glucagon-secreting tumors.
- Glucocorticoids—can improve skin lesions; consider use carefully; encourages development of diabetes mellitus.
- Colchicine (0.03 mg/kg/day) may be beneficial in advanced liver disease.
- Zinc sulfate (10 mg/kg/day), zinc gluconate (5 mg/kg/day), or zinc methionine (2 mg/kg/day)—adjunctive therapy.
- Essential fatty acids—adjunctive therapy.



FOLLOW-UP

POSSIBLE COMPLICATIONS

- Liver failure
- Diabetes mellitus (indicates worse prognosis)
- Secondary bacterial and/or yeast skin infections

EXPECTED COURSE AND PROGNOSIS

- Prognosis poor; survival time reported as 5 months after development of skin lesions.
- Very rare incidence of recovery if hepatic/metabolic insult resolves.



MISCELLANEOUS

SEE ALSO

- Diabetic Hepatopathy
- Glucagonoma

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- BSP = sulfobromophthalein
- RBC = red blood cell

Suggested Reading

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Author Sheila M.F. Torres

Consulting Editor Alexander H. Werner

SUPRAVENTRICULAR TACHYCARDIA



BASICS

DEFINITION

Repetitive supraventricular premature depolarizations that originate from a site other than the sinus node, such as the atrial myocardium or atrioventricular nodal tissue.

ECG Features

- Heart rate—rapid, 150–350 bpm in dogs. The lower rate of supraventricular tachycardia depends on the size of the patient. Smaller dogs typically have higher sinus nodal rates than larger dogs.
- Rhythm usually very regular (R-R interval is constant) and may be sustained, but there can be frequent or infrequent short runs of supraventricular tachycardia, so-called paroxysmal SVT.
- Rarely, the rhythm during the tachycardia will be irregular, suggesting abnormal automaticity as the etiology.
- Usually the QRS complexes are typical of normal sinus complexes, narrow with a normal mean electrical axis. In some cases a coexisting bundle branch block or aberrant ventricular conduction makes it difficult, if not impossible, to differentiate an SVT from a ventricular tachycardia by examining the ECG.
- P waves can be normal or abnormal and typically differ in configuration from the sinus P waves. P waves may be buried in the previous T wave and therefore not visualized.
- Atrioventricular conduction is usually normal (1:1), but various levels of functional second-degree AV block may occur at higher atrial rates (2:1, 3:1, 4:1, etc.).

PATOPHYSIOLOGY

- SVT may be primary (idiopathic) or secondary to other cardiac disease, generally those creating atrial enlargement.
- May result from a reentrant mechanism or from abnormal automaticity in an ectopic focus. Reentrant SVT typically produces a very regular rhythm; SVT due to an automatic focus in atrial myocardium can produce an irregular rhythm.
- Most cases in dogs respond to drugs that specifically alter conduction and refractoriness in the AV nodal tissue, suggesting AV nodal reentry as the mechanism.
- Recent electrophysiologic studies revealed that some SVT in dogs is related to a congenital accessory pathway between the atria and ventricles that allows the electrical impulses to travel freely between the atria and ventricles without traversing the AV node and without conduction delay; in these patients, the SVT is caused by reentry through the accessory pathway and the AV node.

SYSTEMS AFFECTED

- Cardiovascular—CHF may develop secondary to progressive myocardial failure associated with a chronically high heart rate (so-called tachycardia-induced myocardial

failure).

- Neuromuscular—syncope or generalized episodic weakness due to reduced cardiac output and oxygen delivery.

SIGNALMENT

Species

Dog and rarely cat

SIGNS

General Comments

- Clinical signs may relate to the underlying cause.
- Dogs with slow SVT or infrequent paroxysmal SVT may exhibit no clinical signs.
- Dogs with fast SVT (heart rate usually > 300 bpm) generally exhibit episodic weakness or syncope.

Historical Findings

- Owners are generally unaware of the arrhythmia.
- Coughing or breathing abnormalities in dogs with CHF.
- Episodic weakness or syncope.

Physical Examination Findings

- Rapid, usually regular heart rhythm.
- However, in dogs with paroxysmal SVT the rhythm may be normal and regular during the physical exam.
- May have evidence of poor peripheral perfusion—pale mucous membranes, a prolonged capillary refill time, and weak pulses.
- May have no signs other than the rapid heart rate.
- Findings may reflect an underlying cardiac condition (e.g., heart murmur).

CAUSES

- Chronic valvular disease
- Cardiomyopathy
- Congenital heart disease
- Cardiac neoplasia
- Systemic disorders
- Ventricular preexcitation
- Electrolyte imbalances
- Digoxin toxicity
- Idiopathic

RISK FACTORS

Heart disease



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Sinus tachycardia.
- Atrial flutter.
- Atrial fibrillation.
- Ventricular tachycardia (SVT with right bundle branch block or aberrant conduction can look like ventricular tachycardia; resolution of arrhythmia after lidocaine administration usually confirms ventricular tachycardia).

IMAGING

- Echocardiography (including Doppler studies) may help characterize the type and severity of underlying cardiac disorders. Echocardiography is also important for assessing myocardial function in patients with idiopathic SVT.
- When viewed on an echocardiogram during bursts of SVT, the left ventricle has a normal end-systolic diameter and a small end-diastolic diameter, resulting in a decreased shortening fraction because of inadequate filling.
- Usually left or right atrial

enlargement in dogs with SVT secondary to other cardiac disorders.

DIAGNOSTIC PROCEDURES

- Long-term ambulatory (Holter) recording of the ECG may detect paroxysmal SVT in cases of unexplained syncope. This is generally only helpful if syncope is occurring regularly within a 24- to 48-hour period. Holter monitors may also help characterize the rate and frequency of sustained SVT and are useful in evaluating the efficacy of therapy.
- Event (loop) recorders may detect paroxysmal SVT in patients with infrequent episodes of syncope (< q24–48h).
- Sustained SVT must be distinguished from sinus tachycardia because the two arrhythmias have different implications and treatment. A precordial thump may help differentiate sinus tachycardia from SVT when the heart rate is in the 150–250 bpm range; it will usually stop an SVT for at least 1 or 2 beats, while a sinus tachycardia will not slow. A vagal maneuver (e.g., ocular pressure or carotid sinus massage) may break an SVT abruptly but only gradually slows sinus tachycardia.



TREATMENT

APPROPRIATE HEALTH CARE

- Asymptomatic patients can be managed on an outpatient basis; patients with a sustained SVT or signs of congestive heart failure should be hospitalized until stable.
- SVT is a medical emergency in dogs that exhibit weakness and collapse; non-pharmacologic interventions that may break an SVT include vagal maneuvers, precordial thump, and electrical cardioversion.
- Vagal maneuvers are often unsuccessful but may be used initially because of their ease of administration and non-invasive nature.
- Delivering a precordial thump can successfully (> 90% of the time) terminate an SVT in dogs, but this maneuver may break the rhythm for only a brief period. At other times the rhythm remains converted. To perform a precordial thump, the dog is placed on its right side and the left apex beat is located. This region is then “thumped” with a fist while recording the ECG.
- Emergency medical therapy is required in patients in which a precordial thump is unsuccessful (see below).

NURSING CARE

Treat CHF and correct any underlying electrolyte or acid-base disturbances.

ACTIVITY

Restrict until arrhythmia has been controlled.

DIET

Mild to moderate sodium restriction if in CHF.

(CONTINUED)

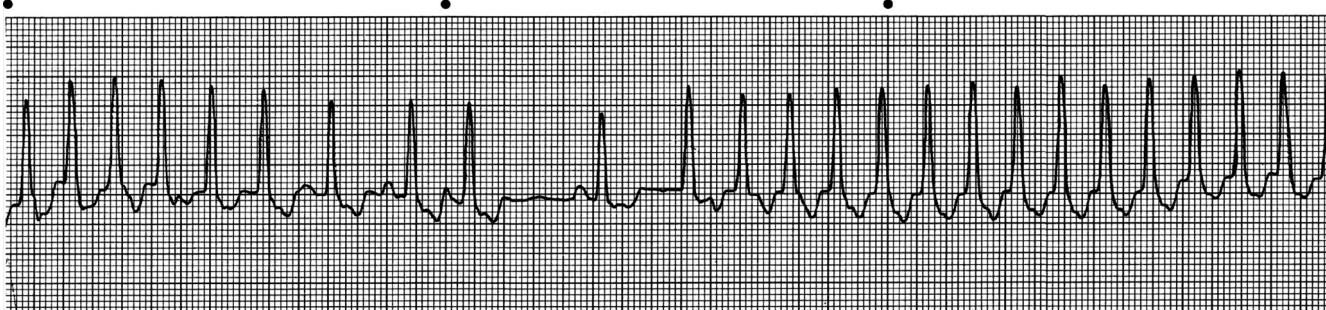
SUPRAVENTRICULAR TACHYCARDIA

Figure 1.

Sinus with an atrial premature complex and paroxysmal supraventricular tachycardia. Abrupt initiation and termination of the tachycardia help distinguish it from sinus tachycardia (lead II, 50 mm/second, 1 cm = 1 mV). (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

CLIENT EDUCATION

Owners should observe patients closely for signs of low cardiac output such as weakness and collapse.

SURGICAL CONSIDERATIONS

Consider transvenous catheter ablation for patients with accessory pathways.

**MEDICATIONS****DRUG(S) OF CHOICE*****Emergency Therapy***

- Administer one of the following drugs:
 - Calcium channel blockers—verapamil (0.05 mg/kg boluses IV over 3–5 minutes up to three times) or diltiazem (0.05–0.25 mg/kg IV over 5–15 minutes).
 - β -adrenergic blockers—esmolol (0.25–0.5 mg/kg slow IV bolus administration followed by a constant-rate infusion of 50–200 μ g/kg/min); moderate-to-severe myocardial failure is a relative contraindication to the administration of these drugs at these doses.
 - Electrical cardioversion or intracardiac electrophysiologic pacing methods may be considered in extreme cases.

Long-Term Therapy

- Digoxin—administer at either a maintenance oral dose or double the maintenance dose for the first day to produce a therapeutic serum concentration more rapidly; contraindicated in patients with accessory pathways.
- β -adrenergic blocker—atenolol (0.2–1 mg/kg PO q12–24h) can be administered as long as the patient does not have underlying moderate-to-severe myocardial failure.
- Diltiazem is the calcium channel blocker of choice for long-term control of SVT. The dosage required to control SVT has not been reported in the dog. Diltiazem is used more frequently to control the ventricular rate in patients with atrial fibrillation at a dosage of 0.5–1.5 mg/kg

PO q8h. In our clinic, we generally start in this dosage range but almost always need to increase the dose to 2–3 mg/kg PO q8h to effect control of SVT.

- Class I antiarrhythmic agents such as quinidine and procainamide can be tried when the aforementioned drugs are ineffective or when the SVT is thought to be due to an automatic, rather than a reentrant, rhythm. SVT caused by an automatic atrial focus may produce an irregular rhythm and may be refractory to conventional drug therapy. When the SVT is due to an accessory pathway, these drugs are more effective.

CONTRAINdications

Avoid use of calcium channel blockers in combination with beta-blockers; clinically significant bradyarrhythmias can develop.

PRECAUTIONS

Calcium channel blockers and β -adrenergic blockers have negative inotropic properties and should be used cautiously in dogs with documented myocardial failure.

ALTERNATIVE DRUG(S)

Emergency treatment—intravenous adenosine (1–12 mg IV rapidly). Adenosine is very expensive and short-lived; propranolol (0.02 mg/kg slow IV boluses up to a total dose of 0.1 mg/kg). Propranolol has a long half-life after IV administration and also has significant β_2 blocking effects and is generally not recommended unless no other alternative is available.

**FOLLOW-UP****PATIENT MONITORING**

Serial ECG or Holter monitoring

POSSIBLE COMPLICATIONS

Syncope and CHF

EXPECTED COURSE AND PROGNOSIS

Most is controlled effectively with medication

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Accessory pathways in some patients

AGE-RELATED FACTORS

In young dogs without evidence of structural heart disease, suspect a reentrant tachycardia involving an accessory pathway.

SYNONYMS

Atrial tachycardia, junctional tachycardia

SEE ALSO

Atrial Fibrillation and Atrial Flutter

ABBREVIATIONS

- AV = atrioventricular
- CHF = congestive heart failure
- ECG = electrocardiogram
- SVT = supraventricular tachycardia

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Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.



**Client Education Handout
available online**

SYNCOPE



BASICS

DEFINITION

Temporary loss of consciousness and vascular tone associated with loss of postural tone, with spontaneous recovery.

PATHOPHYSIOLOGY

Inadequate cerebral perfusion and delivery of oxygen and metabolic substrates leads to loss of consciousness and motor tone; impaired cerebral perfusion can result from changes in vasomotor tone, cerebral disease, and low cardiac output caused by structural heart disease or arrhythmias.

SYSTEMS AFFECTED

- Cardiovascular
- Nervous

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Sick sinus syndrome—cocker spaniel, miniature schnauzer, pug, dachshund
- Ventricular arrhythmias—boxer, German shepherd

Mean Age and Range

More common in old animals

CAUSES

Cardiac Causes

- Bradyarrhythmias—sinus bradycardia, sinus arrest, second-degree atrioventricular block, complete AV block, atrial standstill.
- Tachyarrhythmias—ventricular tachycardia, supraventricular tachycardia, atrial fibrillation.
- Low cardiac output (non-arrhythmic)—cardiomyopathy, AV valve endocardiosis, subaortic stenosis, pulmonic stenosis, pulmonary hypertension, heartworm disease, pulmonary embolism, cardiac tumor, cardiac tamponade.

Neurologic and Vasomotor Instability

- Vasovagal syncope—emotional stress and excitement may cause heightened sympathetic stimulation, leading to transient tachycardia and hypertension, which is followed by a compensatory rise in vagal tone, leading to excessive vasodilation without a compensatory rise in heart rate and cardiac output; bradycardia often occurs.
- Situational syncope refers to syncope associated with coughing, defecation, urination, and swallowing.
- Carotid sinus hyperactivity may cause hypotension and bradycardia—often the cause of syncope when one pulls on a dog's collar.

Miscellaneous Causes

- Drugs that affect blood pressure and regulation of autonomic tone.
- Hypoglycemia, hypocalcemia, and hyponatremia (rare).

- Hyperviscosity syndromes (e.g., polycythemia and paraproteinemia) cause sludging of blood and impaired cerebral perfusion (rare).

RISK FACTORS

- Heart disease.
- Sick sinus syndrome.
- Drug therapy—vasodilators (e.g., calcium channel blockers, ACE inhibitors, hydralazine, and nitrates), phenothiazines (e.g., acepromazine), antiarrhythmics, and diuretics.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differential Signs

- Must differentiate from other altered states of consciousness, including seizures and narcolepsy (a sleep disorder).
- Seizures are often associated with a prodromal and postictal period; syncope occurs without warning, and animal usually has rapid, spontaneous recovery. Unlike syncope, seizure activity is usually associated with tonic clonic muscle activity rather than flaccidity.
- Like syncope, narcolepsy occurs suddenly, results in muscle flaccidity, and resolves spontaneously. Unlike syncope, narcolepsy can last for minutes and can be terminated by loud noises or harsh external stimuli.
- Must differentiate from other causes of collapse such as musculoskeletal disease and neuromuscular disease (e.g., myasthenia gravis), which are not associated with loss of consciousness.

Differential Causes

- Syncope with excitement or stress suggests vasovagal syncope.
- Syncope with coughing, urination, or defecation suggests situational syncope.
- Syncope with exercise suggests low-output states associated with arrhythmias or structural heart disease.
- A murmur supports heart disease but does not confirm cardiac cause for syncope.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal
- Hypoglycemia or electrolyte disturbance in some animals

OTHER LABORATORY TESTS

- If animal is hypoglycemic, measure insulin concentration on same blood sample. Calculate an amended insulin:glucose ratio to rule out insulinoma.
- If animal is hyponatremic or hyperkalemic, consider an ACTH stimulation test.
- If low cardiac output is suspected, rule out occult heartworm disease.

IMAGING

Radiography may detect structural heart disease, evidence of pulmonary embolism or vascular changes supportive of heartworm disease.

Echocardiography

- May detect structural heart disease or pericardial disease that could lower cardiac output.
- Doppler echocardiography may aide in the diagnosis of pulmonary hypertension.
- Computed tomography pulmonary angiography may detect pulmonary embolism.
- Ventilation perfusion scintigraphy may detect pulmonary embolism.

DIAGNOSTIC PROCEDURES

- Have client monitor heart rate during any syncopal episode.
- Electroencephalogram, computed tomography of the head, cerebrospinal fluid tap if CNS origin suspected.

Electrocardiographic Findings

- Post-exercise ECG may reveal intermittent arrhythmia.
- Holter monitoring (24-hour ECG recording) or use of an ECG event (loop) recorder—useful for evaluating arrhythmic causes.
- Carotid sinus massage with ECG and blood pressure monitoring useful in evaluating carotid sensitivity.



TREATMENT

APPROPRIATE HEALTH CARE

- Avoid or discontinue medications likely to precipitate syncope.
- Treat as outpatient unless important heart disease is evident.

CLIENT EDUCATION

- Minimize stimuli that precipitate episodes.
- Low cardiac output—minimize activity.
- Vasovagal—minimize excitement and stress.
- Cough—remove collar.

SURGICAL CONSIDERATIONS

Pacemaker implantation for sick sinus syndrome and advanced AV block and persistent atrial standstill.



MEDICATIONS

DRUG(S) OF CHOICE

Bradyarrhythmias

- Correct metabolic causes.
- Anticholinergics (e.g., atropine, propantheline bromide, hyoscymine sulfate).
- Sympathomimetics (e.g., isoproterenol, bronchodilators).
- Pacemaker implantation in some patients.

(CONTINUED)

SYNCOPE

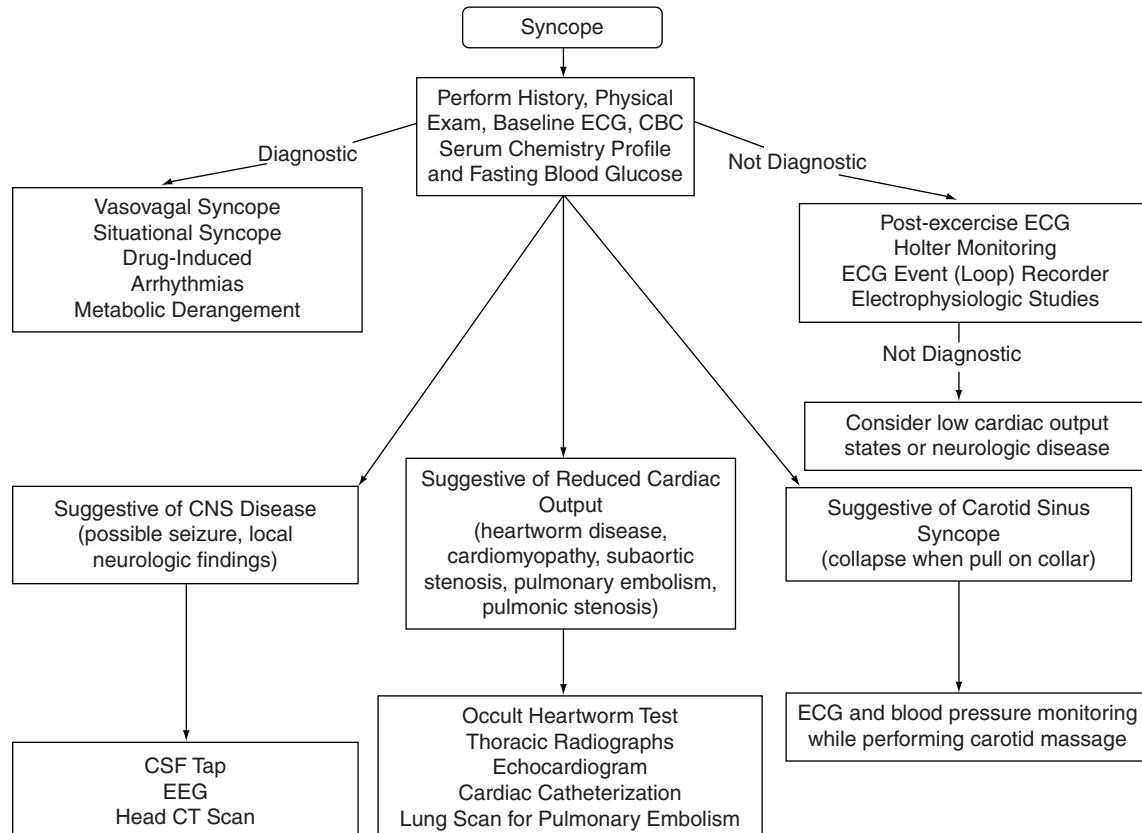


Figure 1.

Algorithm for syncope.

Tachyarrhythmias

- Atrial arrhythmias—administer digoxin, beta-blocker, or diltiazem.
- Ventricular arrhythmias—administer lidocaine, mexiletine, sotalol, or beta-blocker.

Low Cardiac Output

- Institute treatment to improve cardiac output, which varies according to specific cardiac disease.

Vasovagal

- Theophylline or aminophylline—sometimes helpful; mechanism of action in this setting is unclear.
- Beta-blockers (e.g., atenolol, propranolol, and metoprolol) may indirectly prevent vagal stimulation by blocking the initial sympathetic response.
- Anticholinergics may blunt the vagal response.

**FOLLOW-UP****PATIENT MONITORING**

ECG or Holter monitoring to assess efficacy of antiarrhythmic therapy

POSSIBLE COMPLICATIONS

- Death
- Trauma when collapse occurs

EXPECTED COURSE AND PROGNOSIS

Most noncardiac causes are not life-threatening; cardiac causes may be treated, but syncope in patients with cardiac disease may suggest higher mortality risk.

**MISCELLANEOUS****SEE ALSO**

- Myasthenia Gravis
- Narcolepsy and Cataplexy
- Seizures (Convulsions, Status Epilepticus)—Cats
- Seizures (Convulsions, Status Epilepticus)—Dogs

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- ACTH = adrenocorticotrophic hormone
- AV = atrioventricular
- CNS = central nervous system
- ECG = electrocardiogram

Suggested Reading

Davidow EB, Proulx J, Woodfield JA. Syncope: pathophysiology and differential diagnosis. Compend Contin Educ Pract Vet 2001, 2:609–618.

Rasmussen CE, Falk T, Domanjko Petrić A et al. Holter monitoring of small breed dogs with advanced myxomatous mitral valve disease with and without a history of syncope. J Vet Intern Med 2014, 28(2):363–370.

Author Francis W.K. Smith, Jr.

Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.



Client Education Handout available online

S

SYNOVIAL SARCOMA



BASICS

OVERVIEW

- Synovial sarcoma (or synovial cell sarcoma) is a malignant neoplasm arising from type B synoviocytes of the joint capsule or tendon sheath.
- Synovial sarcomas are locally aggressive and have moderate metastatic potential. At diagnosis up to 32% of dogs have metastases with the most common sites being the local lymph node and lungs.
- The disease is seen most commonly in the appendicular skeleton, specifically affecting the elbow, stifle, and shoulder joints. SS must be differentiated via immunohistochemistry from other types of joint tumors, namely histiocytic sarcoma, which has a more aggressive biologic behavior and a worse prognosis.

SIGNALMENT

- Dog—often large-breed dogs of either sex, predisposition of flat-coat and golden retrievers, mean age of 9 years
- Cat—rarely reported

SIGNS

- Slowly progressive lameness
- Palpable mass
- Weight loss
- Anorexia
- Clinical course may be protracted over months to years

CAUSES & RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other primary neoplasia (e.g., histiocytic sarcoma, chondrosarcoma, osteosarcoma).
- Metastatic neoplasia.
- Other bone or joint diseases (e.g., osteoarthritis, osteomyelitis).

S

CBC/BIOCHEMISTRY/URINALYSIS

No consistent abnormalities

OTHER LABORATORY TESTS

N/A

IMAGING

- Radiographs of the affected joint often demonstrate both bone and joint involvement with periarticular soft tissue swelling and periosteal reaction or multiple punctate osteolytic changes in adjacent bone.
- Thoracic radiographs should be obtained to screen for metastatic disease.
- Abdominal ultrasonography should be performed to evaluate intra-abdominal lymph nodes in animals with tumors on the pelvic limbs.

DIAGNOSTIC PROCEDURES

- Regional lymph nodes should be palpated and fine-needle aspirates performed.
- Biopsy and immunohistochemistry to differentiate from HS (HS is CD18+).



TREATMENT

Limb amputation; forequarter, coxofemoral disarticulation or hemipelvectomy to minimize risk of local recurrence.



MEDICATIONS

DRUG(S)

- The role of chemotherapy for SS is not known; however, doxorubicin is commonly utilized for the treatment of sarcoma histologies.
- Pain management with analgesic drugs as necessary.

CONTRAINDICATIONS/POSSIBLE

INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

Monitor for local recurrence and pulmonary metastatic disease every 2–3 months for the first year, every 6 months thereafter.

EXPECTED COURSE AND PROGNOSIS

- Localized disease at diagnosis—prognosis is excellent. Median survival time > 36 months. Lesser dose of surgery (i.e., marginal excision) is associated with poorer prognosis compared to limb amputation.
- Metastatic disease at diagnosis—poor prognosis with median survival time < 6 months. High-grade tumors (high mitotic rate, high percent tumor necrosis, high nuclear pleomorphism) also confer a worse prognosis.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Do not breed animals that are receiving chemotherapy.

ABBREVIATIONS

- HS = histiocytic sarcoma
- SS = synovial sarcoma

Suggested Reading

Craig LE, et al. Diagnosis and prognosis of synovial tumors in dogs: 35 cases. *Vet Pathol* 2002, 39:66–73.

Author Laura E. Selmic

Consulting Editor Timothy M. Fan

Acknowledgment The author and editors acknowledge the prior contribution of Ruthanne Chun.

SYRINGOMYELIA AND CHIARI-LIKE MALFORMATION



BASICS

DEFINITION

- CM is characterized by overcrowding of the CCJ and obstruction of CSF channels.
- A consequence is SM where fluid-filled cavities (syringes) develop within the spinal cord.
- The primary clinical sign is pain due to obstruction of the CSF pulse pressure and/or damage to spinal cord dorsal horn and/or axons conveying or modifying nociceptive sensory transmission to the brain.

PATHOPHYSIOLOGY

Chiari-like Malformation

Complex disorder involving skull base shortening and CCJ abnormalities including increased proximity of the atlas to the occiput. There may be increased parenchymal volume, for example CKCS have relatively increased cerebellar volume compared to other breeds. Overcrowding of the cerebellum in the caudal part of the caudal cranial fossa is correlated with the development of SM. Classical CM is characterized by herniation of the hindbrain into the foramen magnum.

Syringomyelia

The most accepted theory of SM pathogenesis is that obstruction to CSF flow in the subarachnoid space results in a mismatch in timing between the arterial and CSF pulse peak pressure. If peak CSF pressure is high when spinal arteriole and perivascular space pressures are low then the perivascular spaces act as a one-way valve drawing in CSF which collects in, then expands and disrupts, the spinal cord central canal and ultimately a syrinx develops.

SYSTEMS AFFECTED

- Nervous
- Ophthalmic

GENETICS

• SM associated CM has moderately high heritability ($H^2 = 0.37$). • Symptomatic SM-associated CM has high heritability ($H^2 = 0.81$). • Two novel genomic regions are strongly associated to CM in the Griffon Bruxellois. One region contains a single gene *Sall-1* which is involved in skull development.

INCIDENCE/PREVALENCE

- In some brachycephalic toy breeds, most notably the CKCS, prevalence of CM approaches 100%.
- SM prevalence increases with age with 25% CKCS affected at 1 y rising to 70% of CKCS > 6 y.
- Studies in the Griffon Bruxellois suggest 42–52% have SM, not always in association with classical CM.
- Prevalence of symptomatic CM and SM is difficult to determine because pain is subjective and difficult to measure directly.
- One study suggested 15.4% prevalence of symptomatic SM in 6 years old CKCS.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Brachycephalic toy-breed dogs and crosses.
- CKCS, King Charles spaniel, Griffon Bruxellois, Affenpinscher, Yorkshire terrier, Maltese, Chihuahua, Pomeranian, Boston terrier, Papillon.
- CM but not SM observed in the Persian cat.

Mean Age and Range

From 6 months old; however, dogs asymptomatic at 6 years old are less likely to ever develop clinical signs.

Predominant Sex

No sex predisposition

SIGNS

General Comments

CM and SM may be asymptomatic. CM alone may cause pain.

Historical Findings

- Pain behavior:
 - Vocalization—often posture-related, e.g., when dog stands, jumps or when picked up
 - Exercise intolerance or unwillingness to exercise
 - Withdrawn
 - Decreased interaction
 - Disrupted sleep
 - Sleeping with unusual head position, e.g., elevated or flexed
 - Allodynia, i.e., signs of discomfort from a non-noxious stimulus, such as touch or wearing a collar
 - Head scratching or rubbing
 - Partial eye closure
 - Signs exacerbated by excitement, exercise, weather conditions, time of day (morning)
- Phantom (reflex) scratching.
- Rhythmic scratch without making purposeful skin contact induced by touch, clothing, walking and excitement.
- Neurobehavioral disorders related to anxiety.

Physical Examination Findings

- Spinal pain.
- Non-contact scratching induced by touch of cervical dermatome corresponding to damaged cervical spinal cord.
- Cervicothoracic scoliosis/torticollis. Gait abnormalities—hypermetria; ataxia; weakness.
- Exotropia—ventrolateral strabismus when gazing to the ipsilateral side.

CAUSES

- SM can develop secondary to any obstruction to CSF channels.
- Degenerative—vertebral canal stenosis due to chronic and often multiple IVDD and facet disease.
- Anomalous—CM, arachnoid cyst/web.
- Neoplastic—mass causing obstruction of CSF channels and/or cerebellar herniation.
- Inflammatory/Infectious—feline infectious peritonitis, granulomatous meningoencephalomyelitis.
- Traumatic—sequel of spinal cord injury and arachnoid adhesions.

RISK FACTORS

Brachycephalism and miniaturization



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Spinal Pain/Weakness/Ataxia

- IVDD—acute onset, persistent localized pain in dogs > 2 y.
- Encephalitides—pain with rapidly progressive neurologic signs.
- Atlantoaxial subluxation—tetraparesis and pain especially on cervical flexion.
- Discospondylitis—fever and neutrophilia at onset; pain constant.

Scratching

Skin disease—in SM, there are no skin lesions.

Abnormal Head Position

Rule out vestibular dysfunction due to inner ear, cranial nerve VIII, or intracranial disease.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

IMAGING

Skull and Cervical Radiographs

Limited value; can suggest changes characteristic of CM (short basicranium, shallow caudal fossa). If wide SM, vertebral canal may be expanded especially at C2. Dynamic cervical images to assess for atlantoaxial subluxation.

Computed tomography

Can confirm cerebellar herniation and assess other bony abnormalities, e.g., atlanto-occipital overlapping. Limited value for assessment SM.

Magnetic Resonance Imaging

- To establish cause and extent of SM, i.e., CM or other causes of CSF obstruction.
- CCJ conformation varies between breeds.
- Classical CM—cerebellum and medulla displaced into the foramen magnum with little or no CSF around neural structures.
- Supraoccipital bone indents the cerebellum, which loses normal rounded shape.
- Cerebellar herniation minimal in some individuals.
- Flexed position increases size of cerebellar herniation.
- Medulla and cranial cervical spine kinked.
- Ventriculomegaly.
- SM—spinal cord fluid-containing cavities.
- Dogs with cervical SM often have more caudal SM; restricting MRI to the cervical region may underestimate severity.
- Maximum syrinx transverse width and asymmetry is strongest predictor of pain, reflex scratching and scoliosis.
- Narrow width symmetrical SM may be asymptomatic.

DIAGNOSTIC PROCEDURES

CSF—to rule out inflammatory diseases; protein may be elevated.

PATHOLOGIC FINDINGS

- Gross—Cerebellar herniation, ventriculomegaly, spinal cord cavitation.
- Histopathologic—in comparison to asymptomatic SM-affected dogs, dogs with history of behavioral signs of pain had asymmetrical syrinx with altered dorsal horn

SYRINGOMYELIA AND CHIARI-LIKE MALFORMATION

(CONTINUED)

structure and altered expression of pain-related neuropeptides, substance P, and calcitonin gene-related peptide.



TREATMENT

APPROPRIATE HEALTH CARE

Medical and surgical treatment options—main treatment objective is pain relief.

NURSING CARE

- Raise food bowls.
- Avoid neck collars and in some cases harnesses.
- Complementary therapy, e.g., acupuncture may be useful.

ACTIVITY

- Exercise to within own limits.
- Inability to exercise associated with higher neuropathic pain score.
- Grooming may not be tolerated and can exacerbate signs.

DIET

Obesity positively correlated with a reduced quality of life but not greater neuropathic pain.

CLIENT EDUCATION

Periodic exacerbations of pain common and dog may require "top-up" medication during this time.

SURGICAL CONSIDERATIONS

- CCD most common surgical procedure—establishing a CSF pathway via the removal of majority of supraoccipital bone and dorsal arch of C1; may be combined with a durotomy, with or without patching with a suitable graft material and with or without cranioplasty. Successful in reducing pain and improving neurologic deficits in ~ 80% cases; ~ 45% cases have satisfactory quality of life 2 y postoperatively. SM persists postoperatively.
- Clinical improvement probably attributable to improvement in CSF flow; most cases require additional medical management.
- Atlantoaxial stability should be assessed prior to CCD.



MEDICATIONS

DRUG(S) OF CHOICE

Non-neuropathic Pain

- NSAIDs—at data sheet dosage.
- Drugs that reduce CSF pressure—proton pump inhibitors (omeprazole 0.5–1.5 mg/kg q24h); or H₂ receptor antagonists (cimetidine 5–10 mg/kg q8h); or diuretics (furosemide 1–2 mg/kg q12h; acetazolamide 4–8 mg/kg q 9–12h).

Neuropathic Pain/MRI Evidence Spinal Dorsal Horn Damage

- First-line adjuvant analgesics—gabapentin 10–20 mg/kg q12h/q8h or pregabalin at 5 mg/kg q12h.
- Second-line (add-on) adjuvant analgesics—amitriptyline 0.25–2 mg/kg q12–24h (titrate up to effective

dose) or tramadol 2–5 mg/kg q8h or amantadine 3–5 mg/kg q24h.

Gait Abnormalities

- Drugs that reduce CSF pressure (as above).
- Corticosteroids—lowest possible dose that controls signs, starting with 0.5 mg/kg prednisolone or methylprednisolone daily; withdraw NSAIDs.

CONTRAINDICATIONS

Amitriptyline should not be combined with drugs metabolized by cytochrome P450 2D6, e.g., cimetidine.

PRECAUTIONS

- Furosemide may activate renin-angiotensin-aldosterone system which might be deleterious in dogs predisposed to MVD.
- Long-term acetazolamide or corticosteroids not recommended due to potential adverse effects.

POSSIBLE INTERACTIONS

CM/SM does not increase risk of anesthesia unless there is associated syringobulbia (syrinx in brainstem).



FOLLOW-UP

PATIENT MONITORING

- Periodic review of pain management and neurologic status.
- Serial MRI may be useful.
- Periodic CBC/biochemistry if receiving medication.

PREVENTION/AVOIDANCE

Purchase from a breeder that has health screening and can provide appropriate health certificates.

POSSIBLE COMPLICATIONS

Dogs with higher neuropathic pain scores are more likely to have anxiety-related behavior disorders which can have a negative impact on the owner-perceived quality of life of a dog.

EXPECTED COURSE AND PROGNOSIS

- Approximately three-quarters of CKCS with CM and/or SM-associated neuropathic pain deteriorate when managed medically. However, many dogs maintain an acceptable quality of life.
- 15–20% dogs are euthanized because of severe neuropathic pain.
- Early surgical intervention may improve prognosis; however, robust studies evaluating this hypothesis have not been performed.
- Surgery does not necessarily improve long-term prognosis as 25–47% of the operated dogs have recurrence or deterioration of the clinical signs within 0.2–3 y of surgery.



MISCELLANEOUS

ASSOCIATED CONDITIONS

CKCS with CM and SM have a high prevalence of MVD, pancreatic disorders including pancreatitis, biliary tree

calcification, epilepsy, myoclonus, fly-catching behavioral disorder, otitis media with effusion, deafness, macrothrombocytopenia, keratoconjunctivitis sicca, idiopathic facial nerve paresis, idiopathic vestibular disease.

AGE-RELATED FACTORS

Older brachycephalic toy breeds are more likely to have other comorbidities such as MVD.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

- Breeding stock of breeds predisposed to CM and/or SM should be MRI screened and official Health Schemes exist in many countries, for example the British Veterinary Association/Kennel Club CMSM Health Scheme.
- Breeding recommendations based on SM status and ages are available.

SYNOMYMS

- Caudal occipital malformation syndrome
- Occipital hypoplasia • Syringohydromyelia

SEE ALSO

N/A

ABBREVIATIONS

- CCD = craniocervical decompression
- CCJ = craniocervical junction • CKCS = Cavalier King Charles spaniel • CM = Chiari-like malformation • CSF = cerebrospinal fluid • IVDD = intervertebral disc disease • MRI = magnetic resonance imaging • MVD = myxomatous mitral valve disease • NSAID = nonsteroidal anti-inflammatory drug • SM = syringomyelia

INTERNET RESOURCES

- <http://www.veterinary-neurologist.co.uk>
- http://www.bva.co.uk/canine_health_schemes/ChiariMalformationSyringomyeliaSchemeCMSMScheme.aspx
- <http://ejcap.fecava.org/#/en/241046/109428/chiari-like-malformation-and-syringomyelia.html>
- <http://www.cavaliermatters.org/>

Suggested Reading

Bilston LE, Stoodley MA, Fletcher DF. The influence of the relative timing of arterial and subarachnoid space pulse waves on spinal perivascular cerebrospinal fluid flow as a possible factor in syrinx development. *J Neurosurg* 2010, 112 (4):808–813.

Lemay P, Knowler SP, Bouasker S, et al. Quantitative Trait Loci (QTL) study identifies novel genomic regions associated to Chiari-like malformation in Griffon Bruxellois dogs. *PLoS one* 2014, 9(4):e89816. doi:10.1371/journal.pone.0089816

Rusbridge C. Chiari-like malformation and syringomyelia. *Eur J Comp Anim Pract* 2013, 23:(3):70–89.

Author Clare Rusbridge

Consulting Editor Joane M. Parent

TAPEWORMS (CESTODIASIS)



BASICS

OVERVIEW

- Infection of dog and cat small intestine with adult tapeworms, including species of *Taenia* (especially *T. pisiformis* of dogs and *T. taeniaformis* of cats), *Dipylidium caninum*, *Echinococcus* spp., and *Mesocestoides*.
- Infection acquired by ingestion of intermediate host containing tapeworm larvae. *Taenia*, *Echinococcus*, and *Mesocestoides* acquired by predation on rabbits, rodents, birds, etc. *Dipylidium caninum* acquired by ingestion of adult fleas (or lice).
- Adult tapeworms cause no apparent harm to host other than perianal pruritus.
- PLC—occurs when dogs become accidental intermediate hosts caused by peritoneal infection with *Mesocestoides* larvae, is potentially fatal.
- Mesocestoides* adults and larvae can multiply asexually within host.

SIGNALMENT

Dog and cat

SIGNS

- Motile or dried, white to cream-colored, single proglottids or chains of proglottids of *Taenia* and *Dipylidium* visible on perineum or in feces; *Mesocestoides* proglottids smaller, more numerous, and resemble sesame seeds; *Echinococcus* proglottids too small to see.
- Dragging or rubbing anus on ground because of perianal pruritus.
- PLC—abdominal distension (ascites), anorexia, lethargy.

CAUSES & RISK FACTORS

- Taenia*, *Echinococcus*, *Mesocestoides*—eating viscera of intermediate hosts such as birds, reptiles, rabbits, rodents, sheep.
- Dipylidium* infections—eating fleas (or lice).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Adult tapeworms—anal sac impaction
- PLC—other causes of ascites

CBC/BIOCHEMISTRY/URINALYSIS

PLC—leukocytosis, hypoalbuminemia

OTHER LABORATORY TESTS

N/A

IMAGING

PLC—abdominal ultrasonography and radiography

DIAGNOSTIC PROCEDURES

- Fecal flotation to detect eggs; false negatives occur if eggs have not been released from proglottids.
- Crush minced segments between two glass slides to release eggs, add

drop of water, and examine microscopically for eggs.

- *Dipylidium*—press adhesive cellophane tape to perianal skin to collect egg packets, then apply tape to microscope slide; packets contain multiple eggs; individual eggs in packets are $\sim 50 \mu\text{m}$ in diameter, pale yellow, and contain a hexacanth embryo with three pairs of hooks.
- *Taenia*, *Echinococcus*—individual eggs (not in packets); spherical, brown, $\sim 30-35 \mu\text{m}$ in diameter; contain hexacanth embryo.
- *Mesocestoides*—individual eggs (not in packets) oval, thin-shelled; contain hexacanth embryo.
- PLC—abdominocentesis or laparotomy to obtain peritoneal fluid; detect larvae in peritoneal fluid by microscopy or PCR-RFLP.



TREATMENT

- Outpatient anthelmintic treatment for intestinal infection with adult tapeworms.
- Discuss need for flea (or louse) control to prevent recurrence of *Dipylidium*.
- PLC—in addition to anthelmintic treatment, may require peritoneal lavage or surgery to remove ascites fluid and larvae.



MEDICATIONS

DRUG(S)

Taenia

- Fenbendazole 50 mg/kg PO q24h for 3 days for adult *Taenia* in dogs.
- Praziquantel 2.5–7.5 mg/kg PO, SC, or IM.
- Praziquantel/pyrantel pamoate—label dose for cats.
- Praziquantel/pyrantel pamoate/febantel—label dose in dogs; for *Taenia*, *Echinococcus*, *Mesocestoides* (extra-label) and *Dipylidium*.
- Epsiprantel 5.5 mg/kg PO for dogs, 2.8 mg/kg PO cats, for *Taenia*, *Dipylidium*.
- Emodepside (3 mg/kg)/praziquantel (12 mg/kg), topically once in cats for *Taenia*, *Dipylidium*.
- Canine PLC—praziquantel, 5 mg/kg SC repeated in 2 weeks may be curative; fenbendazole, 50–100 mg/kg PO q24h for 4–8 weeks (extra-label); provides clinical remission but often not curative.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Do not use praziquantel or epsiprantel for puppies or kittens < 4 weeks old.



FOLLOW-UP

PATIENT MONITORING

- For infection with adult tapeworms, post-treatment examination for tapeworm

segments and/or eggs; incomplete removal of adult *Mesocestoides* can result in repopulation of intestine by asexual multiplication.

- For PLC—ultrasonography and/or abdominocentesis to detect recurrence; larvae difficult to eliminate and can repopulate peritoneal cavity by asexual multiplication.

PREVENTION/AVOIDANCE

- Implement flea (or louse) control to prevent recurrence of *Dipylidium* infection.
- Prevent hunting and scavenging to prevent ingestion of vertebrate intermediate hosts to prevent recurrence of infection (*Taenia*, *Echinococcus* or *Mesocestoides*).

EXPECTED COURSE AND PROGNOSIS

- Anthelmintic treatment will eliminate adult *Taenia*, *Echinococcus*, and *Dipylidium*, but reinfection often occurs.
- Incomplete removal of adult *Mesocestoides* by anthelmintic treatment can result in recurrence of infection in the absence of reinfection as a result of asexual multiplication by adults.
- Treatment of PLC provides clinical remission but often is not curative.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Children may be at risk for *Dipylidium* infection by ingestion of adult fleas; in children, tapeworm segments have been mistaken for pinworms (*Enterobius*).
- Ingestion of *Echinococcus* eggs can cause hydatid disease in humans.
- Taenia* and *Echinococcus* shed identical eggs. Strict sanitation should be practiced when taeniid eggs are observed due to the risk of hydatid disease.
- Human infection with adult *Mesocestoides* can occur; infection is not acquired from dogs or cats but by ingestion of vertebrate intermediate hosts.

ABBREVIATIONS

- PCR-RFLP = polymerase chain reaction restriction fragment length polymorphism
- PLC = peritoneal larval cestodiasis

INTERNET RESOURCES

- <http://www.cpcvet.org>
- <http://www.cdc.gov>

Suggested Reading

Bowman DD. Georgis' Parasitology for Veterinarians, 9th ed. St. Louis, MO: Saunders, 2009, pp. 131–147, 149–151.

Author Matt Brewer

Consulting Editor Stephen C. Barr

TAURINE DEFICIENCY



BASICS

OVERVIEW

• Taurine is an essential amino acid in cats; they must conjugate bile acids with taurine and cannot synthesize enough to cope with this obligatory loss, so deficient diets cause taurine deficiency in cats. All cat food manufacturers add taurine to their diets. Taurine is not essential in dogs and so most canine diets do not contain added taurine. However, some "cardiac" canine diets, especially those containing lamb and rice, have taurine added to them. • Taurine is found throughout the body, with highest concentrations in excitable tissues (e.g., myocardium, central nervous system, and retina), where its exact function is unknown. Taurine is actively concentrated in myocardial cells by a membrane pump that is influenced by catecholamines. • Taurine deficiency results in retinal degeneration and primary myocardial failure (i.e., dilated cardiomyopathy [DCM]), which has been identified in domestic cats, foxes, and some dogs. In each, the myocardial failure is usually fully or partially reversible with dietary taurine supplementation. • Mice devoid of the protein that transports taurine into cells develop DCM. Poor myocardial function is due to myocardial atrophy rather than abnormal cellular contractile function.

SIGNALMENT

• Cats—DCM due to taurine deficiency is currently rare because taurine is added to most cat foods. • Dogs—American cocker spaniels with DCM are almost uniformly taurine-deficient. Some giant-breed dogs (Newfoundlands) with DCM, especially those on a lamb and rice diet, have been taurine-deficient. Some mixed-breed dogs with DCM or breeds that uncommonly get DCM but with DCM have a low plasma taurine concentration.

SIGNS

See Cardiomyopathy, Dilated—Cats and Cardiomyopathy, Dilated—Dogs.

CAUSES & RISK FACTORS

• Cats fed home-cooked diets (e.g., vegetarian, boiled meat, or cooked chicken diets) are at risk; rarely, a commercial diet will cause taurine deficiency in cats. • Dogs—breed predisposition (American cocker spaniels, unusual breed with DCM, mixed breed), breed size (e.g., Newfoundlands), diet, and cystinuria are risk factors. Rarely, a common breed (e.g., Doberman pinscher) with DCM will be taurine deficient. Taurine deficiency might be a problem in certain lines of Portuguese water dogs fed certain diets.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Idiopathic dilated cardiomyopathy or myocardial failure due to another cause; see Cardiomyopathy, Dilated—Cats and Cardiomyopathy, Dilated—Dogs.

CBC/BIOCHEMISTRY/URINALYSIS

Cystinuria in some dogs

OTHER LABORATORY TESTS

- Place a heparinized blood sample on ice, and centrifuge within 30 minutes. Do not allow clotting because platelets are rich in taurine. Avoid hemolysis. A plasma taurine concentration < 40–60 nmol/mL is too low in dogs and cats. A whole-blood concentration < 200 nmol/mL is too low.
- Prolonged fasting in cats can produce a low plasma concentration; the whole blood concentration stays within the normal range longer.

IMAGING

DCM is usually diagnosed by identifying an increase in end-systolic diameter, along with a compensatory smaller increase in end-diastolic diameter and a consequent reduction in shortening fraction on an echocardiogram.

DIAGNOSTIC PROCEDURES

Examine any taurine-deficient patient for central retinal degeneration.



TREATMENT

• Use conventional heart failure therapy and pimobendan (0.25 mg/kg PO q12h) until supplementation has caused significant echocardiographic improvement; drug therapy can usually be discontinued after 3–6 months of taurine supplementation as long as there has been a substantial echocardiographic improvement in left ventricular function. • Most cats in heart failure do better if they are sent home. • There is no known benefit to taurine supplementation in a dog or cat with any other form of cardiac disease.



MEDICATIONS

DRUG(S)

• Supplement taurine (cats, 250 mg PO q12h; dogs, 250–1,000 mg PO q12h), usually for life. • Taurine supplements—obtain from a health food store. • Carnitine supplementation (1 g PO q12h) is also recommended for American cocker spaniels, especially if they do not respond to taurine supplementation alone.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

No adverse effects of taurine supplementation; excess taurine is eliminated in the urine.



FOLLOW-UP

Routine examinations for a heart failure patient; repeat echocardiogram in 3–6 months to document improvement. If there is substantial improvement, continue taurine supplementation but discontinue heart failure drugs.



MISCELLANEOUS

ABBREVIATION

• DCM = dilated cardiomyopathy

INTERNET RESOURCES

<http://www.vmth.ucdavis.edu/cardio/cases/case32/case32.htm>

Suggested Reading

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TEMPOROMANDIBULAR JOINT DISORDERS



BASICS

OVERVIEW

- Disorders of the TMJ lead to an alteration of the normal function of the masticatory system as the mobility and function of the joint are compromised.
- Genetic, traumatic, degenerative, or idiopathic causes may result in pain, occlusal dysfunction, joint laxity, chronic arthritis, or open-mouth locking.

SIGNALMENT

- Dog and cat. • No breed, sex, or age predisposition in most TMJ disorders.
- Open-mouth mandibular locking—basset hounds; Irish setters. • There may be a genetic predisposition in certain breeds (e.g., basset hounds) to develop TMJ disorders.

SIGNS

General Comments

- Difficulty opening mouth. • Difficulty closing mouth. • Laxity or excessive lateral movement of the mandible. • Pain and/or crepitus when masticating, yawning, and/or vocalizing.

Specific

- TMJ luxation/subluxation—history of trauma or mouth locked open; radiographic evidence of luxation. • Open-mouth mandibular locking—coronoid process of the mandible “slips” lateral to the ventral surface of the zygomatic arch and is locked in that position; large bulge palpated on affected side of face. • Traumatic injury—evidence of trauma; mouth dropped open; mobility of mandible (may have multiple fractures); radiographs indicate fracture. • Osteoarthritis/chronic post-traumatic changes—crepitus and pain when eating or if mandible is forced to move; radiographs may show osseous reaction indicative of arthritic changes.

CAUSES & RISK FACTORS

- Patients at a higher risk to experience injuries—young; free roaming. • Trauma may cause fractures or a luxation resulting in immediate problems, as well as future degenerative problems.
- Mandibular neuropraxia—carrying heavy objects by mouth. • MMM—adult; large breed (e.g., German shepherds).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Craniomandibular osteopathy. • Primary or secondary hyperparathyroidism. • Mandibular neuropraxia—stretching of the nerve branches (motor) of the masticatory muscles; usually caused by carrying heavy objects in the mouth; mandible hangs open but can be easily closed manually. • MMM—auto-immune disease of

type 2M myofibers of masticatory muscles supplied by trigeminal nerve with necrosis, phagocytosis, and fibrosis; trismus progresses to total inability to open jaws.

CBC/BIOCHEMISTRY/URINALYSIS

Findings are expected to be within normal limits.

OTHER LABORATORY TESTS

- Serum autoantibodies to type 2M myosin—to rule out MMM. • Cytology of fluid aspirated from TMJ—may be beneficial in diagnosis of a polyarthropathy in which the articular surfaces of the joint are inflamed.

IMAGING

- Skull radiography—essential to perform proper radiographic technique to visualize the TMJ. • MRI—gold standard for imaging the TMJ.

DIAGNOSTIC PROCEDURES

- Usually none. • Muscle biopsy—rule out MMM.



TREATMENT

- Definitive treatment is aimed at eliminating or altering the etiologic factor responsible for the disorder, as well as correcting the problem.
- TMJ luxation—traumatic: luxation often occurs in a rostral direction; in acute cases, place a “dowel” (pencil) across the mouth between the carnassial teeth; gently close the rostral portion of the mouth with a gentle “push” to reduce the luxation (push caudally for a rostral luxation); chronic luxation may not reduce and may require surgery.
- Open-mouth mandibular locking—immediate attention; sedate animal, open the mouth further and apply gentle pressure on the bulging coronoid process to allow it to slip back under the zygomatic arch; surgical management: excise ventral portion of the zygomatic arch and/or a dorsal portion of the coronoid process to relieve future locking.
- Injury or fracture at TMJ—depends on extent of damage; fixation is difficult; condylectomy sometimes necessary.
- Chronic osteoarthritis or ankylosis—if severe, condylectomy may be needed.
- “Dropped jaw” (trigeminal [mandibular] neuropraxia)—conservative treatment: rest, anti-inflammatory drugs. • MMM—immunosuppressant medications; possible forcible, gradual opening of mouth.



MEDICATIONS

DRUG(S) OF CHOICE

- Analgesics—for painful disorders.
- Anti-inflammatory drugs—for postoperative pain and chronic inflammation.

- Muscle relaxants—help prevent increased muscle activity due to chronic pain response.



FOLLOW-UP

PATIENT MONITORING

Each case should be carefully followed because of the progressive changes that may occur in the TMJ, especially after traumatic injury.

PREVENTION/AVOIDANCE

Avoid situations that allow for trauma (pets running loose).

POSSIBLE COMPLICATIONS

In many cases after surgical treatment involving TMJ disorders, arthritis may develop later.

EXPECTED COURSE AND PROGNOSIS

Depends on the disorder afflicting the TMJ and the degree to which it is affected.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Condition is typically unaffected by pregnancy. However, if medical treatment is considered, agents such as corticosteroids should not be used in pregnant patients.

SEE ALSO

Maxillary and Mandibular Fractures

ABBREVIATIONS

- MMM = masticatory muscle myositis
- MRI = magnetic resonance imaging
- TMJ = temporomandibular joint

INTERNET RESOURCES

<http://www.avdc.org/Nomenclature.html>.

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TESTICULAR DEGENERATION AND HYPOPLASIA



BASICS

OVERVIEW

- Degeneration—histologic changes in the testes after puberty; may be differentiated from hypoplasia by the increased thickness of the basement membrane in the degenerated testis.
- Hypoplasia—a variety of histologic lesions thought to be congenital (although often not obvious until after puberty) or heritable.

SIGNALMENT

- Dog and cat. • Dog—any age or breed; hypoplasia, generally young; degeneration, generally old. • Tortoiseshell cat—may be fertile; usually linked with sex chromosome abnormalities (see Sexual Development Disorders).

SIGNS

- Infertility. • Reduced testicular size and loss of normal turgidity. • Oligospermia (low numbers of spermatozoa in the ejaculate) or azoospermia (no spermatozoa in the ejaculate).
- Hypoplasia (dogs)—rarely any physical signs other than small testes. • Degeneration (dogs)—any previous scrotal or testicular lesion can be related.

CAUSES & RISK FACTORS

Degeneration

- Heat. • Irradiation. • Metals—lead salts; cadmium; organic mercurial compounds.
- Nitrogen-containing and halogenated compounds. • Other toxins. • Orchitis—*infectious* (such as brucellosis) or non-infectious (auto-immune). • Steroid hormones—estrogen: secreted by a Sertoli cell tumor or exogenous exposure. • Other hormonal abnormalities—hypothyroidism; hypocortisolism; hyperadrenocorticism.
- Increasing age—6.3% of beagles maintained to 7.75 years had incomplete spermatogenesis.
- Arterial sclerosis. • Some chemotherapeutic agents—cimetidine; ketoconazole; nitrofurans; flutamide. • Incisional testicular biopsies.
- Any previous scrotal or testicular lesion may be related. • Epididymal occlusion.

Hypoplasia

- Klinefelter (XXY) syndrome.
- Hypogonadotropic hypogonadism—may be acquired from traumatic or neoplastic lesion of the pituitary. • XX sex reversal—disorder of sexual development with the absence of SRY region (dogs).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Degeneration—old, azoospermic, or severely oligospermic previously fertile dogs with small testes. • Hypoplasia—young,

azoospermic, never-fertile dogs with small testes. • Spermatocoele. • Sperm granuloma. • Orchitis. • Neoplasia. • Ejaculatory failure—retrograde ejaculation; incomplete ejaculation.

OTHER LABORATORY TESTS

- Canine FSH assay—differentiate from blockage (spermatocoele); high concentration indicates incomplete spermatogenesis associated with hypoplasia or degeneration.
- Alkaline phosphatase concentration of seminal plasma—rule-out incomplete ejaculation; samples with AP < 5,000 U/L consistent with incomplete ejaculation or bilateral epididymal blockage.

IMAGING

Ultrasonography—testicular size; homogenous echogenicity of the parenchyma

DIAGNOSTIC PROCEDURES

- Semen evaluation—primary diagnostic procedure; dog: always obtained by use of an artificial vagina or collection cone; cat: obtained by electroejaculation, when available; collect two ejaculates on separate days or 1 hour apart; establish azoospermia or oligospermia. • Testicular biopsy (for azoospermia)—fine-needle: identify long spermatids and spermatozoa; Tru-Cut (tissue plug): most complete histopathologic diagnosis; fix tissue for sectioning in Bouin's or Zenker's fixative. • Karyotype—identify extra X chromosome or other numerical or structural chromosome anomaly.

PATHOLOGIC FINDINGS

- Normal spermatogenesis—indicates blockage in azoospermic dogs. • Basement membrane thickness—differentiates hypoplasia from degeneration.



TREATMENT

- Degeneration linked to adenohypophysis, adrenal gland, thyroid gland, or other metabolic disruption—goal is to correct the underlying cause. • No specific diagnosis—may try gonadotropin hormones; rare anecdotal reports of success.



MEDICATIONS

DRUG(S)

- Although no controlled studies validate an increase in spermatozoal output and fertility with the use of GnRH or gonadotropins, both drugs have been used in many species; most likely to cause improvement with cases of hypogonadotropic hypogonadism, which is rare in domestic animals. • hCG 500 IU SC two times/week. • GnRH 1 µg/kg SC with or with hCG (1,600 IU IM).



FOLLOW-UP

PATIENT MONITORING

Suspected testicular degeneration (dogs)—a repeat semen analysis performed at least 70 days after correcting any identified underlying cause is needed before reversibility can be assessed.

EXPECTED COURSE AND PROGNOSIS

- Hypoplasia (dogs)—prognosis for fertility poor. • Degeneration (dogs)—prognosis for fertility depends on the cause, site, and extent of injury; usually guarded to poor.



MISCELLANEOUS

SEE ALSO

- Brucellosis • Infertility, Male—Dogs
- Sexual Development Disorders
- Spermatocoele/Sperm Granuloma
- Spermatozoal Abnormalities

ABBREVIATIONS

- FSH = follicle-stimulating hormone
- GnRH = gonadotropin-releasing hormone
- hCG = human chorionic gonadotropin

INTERNET RESOURCES

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BASICS

OVERVIEW

- *Clostridium tetani*—an obligate anaerobic spore-forming Gram-positive rod found in soil and as part of the normal bacterial flora of the intestinal tract of mammals with a predilection for contaminated necrotic anaerobic wounds (puncture, surgery, lacerations, burns, frostbite, open fractures, abrasions).
- Germinating spores—in wounds, produce potent exotoxin tetanospasmin (tetanus toxin); resistant to disinfectants and to the effects of environmental exposure.

SIGNALMENT

- Dogs—occasionally (usually localized tetanus)
- Cats—rarely

SIGNS

Historical Findings

- Appear a few days to a few months after spores enter wound (fracture surgery and puncture).
- Wound—often necrotic; but may have healed over and may not be observed by owner.

Physical Examination Findings

The most common *initial* clinical signs in affected dogs are ocular and facial abnormalities.

Localized

- Mild rigidity of muscles or leg nearest the site of spore inoculation (wound).
- Stiffness of (hind) limbs; stilted gait; mild weakness and incoordination.
- Can resolve spontaneously—reflects partial immunity to tetanospasmin.
- Can be prodromal to generalized disease—when enough toxin gains access to CNS.

Progressive/Generalized

- Tail—stretches out; progressive tetany of muscles to point of sawhorse appearance.
- Convulsions (clonic)—limbs; whole body (opisthotonus); pain during contractions.
- Difficulty breathing—dyspnea.
- Difficulty opening jaws—lockjaw trismus.
- Difficulty eating—dysphagia.
- Eyes—lids retract (*visus sardonicus*); third eyelid prolapses when head is touched; eyeballs recede into orbit (*enophthalmos*).
- Wrinkled forehead.
- Erect ears.
- Grinning appearance—commissure of lips retracted.
- Salivation.
- Fever, painful urination (dysuria), and constipation—may be seen.
- Tetanic muscle spasms—from stimulation (sudden movement, sound, touch).

- Death—during spasm of laryngeal and respiratory muscles (fatal acute asphyxia).

CAUSES & RISK FACTORS

- Unattended wounds (e.g., punctures, surgical, compound bone fractures)—portal of entry for spores.
- Outdoor activities provide opportunities for trauma/exposure.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Intoxications mimicking tetanus—lead and strychnine poisoning.
- The dystonic reaction to neuroleptic drugs (atropine, acepromazine).
- Rabies.
- Meningitis-encephalitis.
- Immune-mediated polymyositis.
- Spinal trauma.
- Hypocalcemia.
- Look for: foot injury/trauma (footpad, nails, interdigital), foreign bodies in conjunction with puncture wounds.

CBC/BIOCHEMISTRY/URINALYSIS

- Initial leukopenia; switch to moderate leukocytosis; then gradual return to normal range.
- AST and CPK—some increase; result of muscle damage during later stages of disease.
- Urinalysis—essentially normal; high myoglobin from muscles damaged by constant excitation.

OTHER LABORATORY TESTS

- Serology—antitetanus antibody often undetectable in serum.
- Culture—wounds; usually unrewarding to culture for *C. tetani*; must use true anaerobic transport medium (do not refrigerate).
- Serum—to detect toxin (by mouse neutralization).
- CSF and blood cultures for bacterial pathogens of meningitis



TREATMENT

- Inpatient—good supportive and constant nursing care important; prolonged period (3–4 weeks).
- Feeding—patients often have difficulty in prehending food unless helped; pay particular attention to what consistency of food the patient easily ingests; placement of a gastrostomy tube may be necessary; force feeding or feeding with a stomach tube may exacerbate tetanic state, so not advised.
- Hydration—maintain with oral water; if inadequate give a balanced intravenous fluid.
- Keep patient in darkened quiet area; do not disturb.

- Keep patient on soft bedding; prevent decubital ulcers.

- Airway and ventilation—assess; may be necessary to perform endotracheal intubation; tracheostomy may be necessary later.



MEDICATIONS

DRUG(S)

Sedation

- To control reflex spasms and convulsions.
- Phenothiazines—drugs of choice; chlorpromazine; with or without barbiturates (e.g., phenobarbital).
- Heart rate—may drop when phenothiazines are used in combination; if < 60 beats/minute reverse the bradycardia with glycopyrrolate.
- Diazepam—alternative to Phenobarbital.

Tetanus Antitoxin

- First test for hypersensitivity reaction.
- Human tetanus immunoglobulin—administer 500–3,000 U IM at multiple sites, especially proximal to wound; or use equine tetanus antitoxin (10,000 U IV).
- Administer adsorbed tetanus toxoid intramuscularly.

Antibiotics

- Have no effect against toxin already bound to nerves.
- Metronidazole: dog, 15 mg/kg q12h, or 12 mg/kg q8h PO; cat, 10–25 mg/kg q24h PO.
- Penicillin—administer systemically and locally into the wound; 20,000 IU/kg q12h for 5 days; use crystalline penicillin on the first day and procaine penicillin thereafter.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Avoid glucocorticoids and atropine.
- Avoid narcotics—depress respiratory center.



FOLLOW-UP

PATIENT MONITORING

- Prevent decubital ulcers and peripheral nerve palsies—cautiously move stabilized patient.
- Monitor blood pressure and ECG.
- Bronchopneumonia possible.
- Constipation possible.

PREVENTION/AVOIDANCE

- Vaccinate—tetanus toxoid.
- Prevent skin wound trauma—clear runs and yards of wire, glass, etc.
- Wound management—early and thorough irrigation with hydrogen peroxide; debridement draining, especially in known tetanus-prone wounds.

TETANUS

(CONTINUED)

- Penicillin—administer for minimum of 3 days for all deep contaminated wounds.

EXPECTED COURSE AND PROGNOSIS

- Younger dogs with tetanus may be more likely to develop severe clinical signs.
- The prognosis for survival in dogs with tetanus is good if abnormalities in heart rate or blood pressure values do not develop.
- Prognosis—depends on number of factors; the more toxin bound to nerves, the poorer the prognosis; improve by removing source of additional toxin (debriding and cleaning wound); the closer the wound is to the head, the poorer the prognosis; the shorter the interval between injury and first tetanic spasm, the poorer the prognosis.

- Course of recovery—slow; requires rehabilitation to regain full use of limbs; most recover in 1 week; some have a course of 3–4 weeks; unattended disease can be fatal if the disease progresses to generalized disease (versus the typical localized tetanus that affects only a limb).

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

None, but tetanus spores ubiquitous in environment.

ABBREVIATIONS

- AST = aspartate aminotransferase
- CNS = central nervous system
- CPK = creatine phosphokinase
- CSF = cerebrospinal fluid
- ECG = electrocardiogram

INTERNET RESOURCES

<http://www.cdc.gov/vaccines/pubs/pinkbook/tetanus.html>

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Author Patrick L. McDonough

Consulting Editor Stephen C. Barr

TETRALOGY OF FALLOT



BASICS

OVERVIEW

- A congenital cardiac malformation that consists of a VSD, pulmonic stenosis, an overriding aorta, and right ventricular hypertrophy (Figure 1). The VSD is usually large, with an area that equals or exceeds that of the open aortic valve. The essential developmental abnormality is probably a cranial deviation of a component of the infundibular septum; the other defects are secondary.
- Hemodynamics are determined primarily by the size of the VSD and the severity of right ventricular outflow tract obstruction. A large VSD allows equilibration of left and right ventricular pressures, with shunt direction determined by the relationship between peripheral vascular resistance and the resistance to right ventricular ejection. Severe right ventricular outflow tract obstruction results in a right-to-left shunt with cyanosis and compensatory erythrocytosis as prominent clinical features.
- An uncommon congenital defect, but the most common congenital cardiac malformation that causes cyanosis in dogs and cats.

SIGNALMENT

- Dog and cat—uncommon in both
- English bulldog and Keeshond predisposed

SIGNS

Historical Findings

- Weakness • Syncope • Shortness of breath

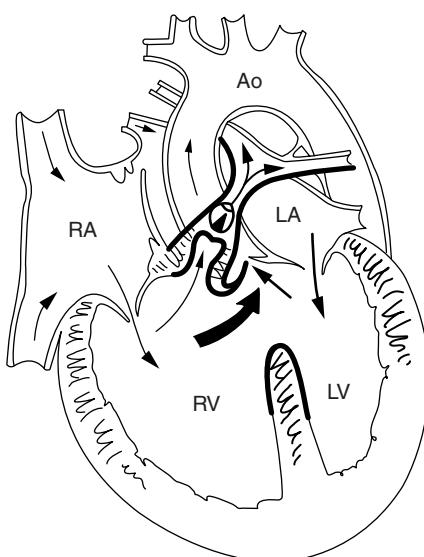


Figure 1.

Classic tetralogy of Fallot. RA = right atrium, LA = left atrium, RV = right ventricle, LV = left ventricle, AO = aorta. (From: Roberts W. Adult Congenital Heart Disease. Philadelphia: F.A. Davis Co., 1987, with permission.)

Physical Examination Findings

- A systolic ejection murmur at the left heart base, caused by right ventricular outflow tract obstruction in most patients; some with hyperviscosity and severe pulmonary stenosis do not have murmurs.
- Cyanosis—in most patients; degree of cyanosis depends on the direction and volume of shunt. If right ventricular outflow tract obstruction is mild, the direction of the shunt may be left to right; in this case, cyanosis is absent and the pathophysiology is that of an isolated VSD.
- Arterial pulses usually normal.
- Congestive heart failure occurs rarely, possibly because the right ventricle can unload into the left ventricle, preventing the development of suprasystemic right ventricular pressures.

CAUSES & RISK FACTORS

Congenital; a continuum of conotruncal defects that includes tetralogy of Fallot is inherited in Keeshonden; the mode of transmission is likely oligogenic. Genetic factors are probably etiologically important in the naturally occurring disorder.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pulmonic stenosis, aortic stenosis, ventricular septal defect, and atrial septal defect can all cause left basilar ejection murmurs.
- Patients with severe pulmonic stenosis and a right-to-left atrial-level shunt may have similar findings on physical examination.
- Other anatomic right-to-left shunts (PDA or VSD with high pulmonary vascular resistance) do not typically cause murmurs; differential cyanosis (cranial mucous membranes are pink; caudal mucous membranes are cyanotic) is observed if a PDA shunts right to left.

CBC/BIOCHEMISTRY/URINALYSIS

- Compensatory erythrocytosis if the shunt is right to left.

IMAGING

Thoracic Radiographic Findings

- Variable degree of right ventricular enlargement.
- Ascending aorta may be prominent.
- Pulmonary vessels are small.

Echocardiographic Findings

- Right ventricular hypertrophy.
- Large VSD visualized directly.
- Overriding of the VSD by the aorta.
- Narrow infundibulum and/or abnormal pulmonic valve.
- Doppler evidence of pulmonic stenosis.
- Contrast echocardiography typically delineates a right-to-left shunt.

Angiocardiography

- Reveals VSD, right ventricular hypertrophy, pulmonic stenosis, and direction of shunt.
- Non-selective angiography may confirm the diagnosis in patients that weigh less than approximately 10 kg.

DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

Right ventricular hypertrophy pattern in most dogs and cats.

Oximetry

Used to confirm peripheral desaturation of hemoglobin.



TREATMENT

- Most can be treated as outpatients.
- Exercise restriction recommended.
- Treat erythrocytosis by periodic phlebotomy to maintain a PCV of 62–68%.
- Palliative surgical procedures that enhance pulmonary blood flow have been performed.
- Definitive surgical correction requires cardiopulmonary bypass.



MEDICATIONS

DRUG(S)

Non-selective β -adrenergic antagonists such as propranolol may be palliative; they act as negative inotropes, thereby limiting dynamic right ventricular outflow tract obstruction, and also prevent the physiologic drop in peripheral vascular resistance that occurs during exercise. These hemodynamic effects serve to limit right-to-left shunting. Propranolol may also favorably affect the oxyhemoglobin dissociation curve.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Vasodilators contraindicated



FOLLOW-UP

- Monitor PCV every 1–3 months.
- Breeding affected animals is not advisable.
- Bacterial endocarditis, neurologic complications associated with erythrocytosis, arrhythmias, and sudden death are potential sequelae.
- Prognosis is poor; most patients with clinical signs live < 1 year, although survivals > 3 years have been documented.



MISCELLANEOUS

ABBREVIATIONS

- PDA = patent ductus arteriosus
- VSD = ventricular septal defect

Suggested Reading

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THIRD EYELID PROTRUSION



BASICS

DEFINITION

Abnormal protrusion (elevation) of the third eyelid.

PATOPHYSIOLOGY

- Dogs—movement of the third eyelid is passive.
- Cats—partial sympathetic nervous control of the third eyelid.
- Elevated third eyelid results from a space-occupying mass in the orbit pushing the third eyelid forward, enophthalmos, sympathetic denervation, or a painful eye.

SYSTEMS AFFECTED

- Nervous—autonomic nervous system
- Ophthalmic—third eyelid(s); orbit; globe

SIGNALMENT

See "Causes"

SIGNS

- May have none.
- May be associated with primary condition—exophthalmos; enophthalmos; blepharospasm; Horner's syndrome.
- Unilateral or bilateral—depending on cause.

CAUSES

Unilateral

Blepharospasm

- Painful ocular condition—corneal ulcer; glaucoma; uveitis; or ocular foreign body.
- May cause the globe to be retracted and secondary third eyelid elevation.

Space-Occupying Orbital Mass

- Often an abscess or neoplasm.
- May displace the third eyelid anteriorly.
- Usually causes exophthalmos.
- Abscess—generally seen in young patients; usually acute onset; painful on palpation.
- Neoplasm—usually seen in old patients; gradual onset; frequently not painful (see Orbital Diseases [Exophthalmos, Enophthalmos, Strabismus]).

Enophthalmos

- Globe—recedes into the orbit, causing third eyelid to appear elevated.
- Unilateral—may be caused by trauma, orbital fat atrophy, and inflammation; may be secondary to orbital neoplasia in cats (see Orbital Diseases).

Microphthalmus or Phthisis Bulbi

- Small globes—cause the third eyelid to appear elevated.
- Microphthalmus—congenital; may be idiopathic; inherited in specific breeds (collie eye anomaly); may result from toxin ingestion (griseofulvin in pregnant cats).
- Phthisis bulbi—occurs with severe damage to the globe (severe uveitis, glaucoma, or trauma); ciliary body fails to produce aqueous humor; diminished; small, fibrotic globe from chronic inflammation.

Other

- Horner's syndrome—clinical signs develop after sympathetic denervation; elevated third eyelid; enophthalmos; ptosis (drooping upper eyelid); miosis (see Horner's Syndrome).
- Neoplasia of the third eyelid—most common: adenocarcinoma of the gland of the third eyelid and squamous cell carcinoma of eyelid.
- Cherry eye—see Prolapsed Gland of the Third Eyelid (Cherry Eye).
- Everted or scrolled cartilage of the third eyelid—seen in Wiemaraners, Great Danes, German shorthaired pointers, and other breeds; the T-shaped cartilage of the third eyelid is rolled away from the surface of the eye instead of conforming to the corneal surface.
- Symblepharon—post-inflammatory adhesions between the third eyelid and cornea or conjunctiva. Common in cats who had ocular surface inflammation before the eyelids opened.

Bilateral

Exophthalmos

- Space-occupying lesions of both orbits.
- Usually caused by inflammatory lesions (e.g., eosinophilic myositis and extraocular muscle polymyositis).

Conformational

- Breed-specific—Doberman pinschers and pointers.
- Deep orbits and prominent third eyelids.
- Not pathologic.
- No treatment needed.

Plasmoma

- Immune-mediated thickening and hyperemia of the leading edge of the third eyelid.
- Seen almost exclusively in German shepherds.
- May be associated with chronic superficial keratitis (pannus).

Other

- Blepharospasm.
- Enophthalmos—caused by dehydration, bilateral orbital fat atrophy secondary to severe cachexia, and chronic masticatory muscle myositis.
- Haw syndrome (cats)—idiopathic bilateral elevation of the third eyelids; all other aspects of the ophthalmic examination are normal; usually resolves in 3–4 weeks without treatment.
- Dysautonomia (Key-Gaskell syndrome)—bilateral elevated third eyelids; dilated non-responsive pupils; KCS; dry mucosal surfaces; anorexia; lethargy; regurgitation; megaesophagus; bradycardia; megacolon; distended bladder (see Dysautonomia).
- Tranquilizers—many (e.g., acepromazine) cause bilateral third eyelid elevation.
- Fatigue—may cause transient third eyelid elevation, especially in dogs prone to ectropion.

RISK FACTORS

Depends on cause



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Most common causes of acute onset of unilateral condition—ocular pain (e.g., corneal ulcer and uveitis); orbital inflammation (e.g., orbital abscess and cellulitis).
- Middle-aged or older patient with unilateral, non-painful condition—third eyelid or orbital neoplasm likely.
- All patients—must rule out a small eye (microphthalmus or phthisis bulbi) and Horner's syndrome.
- Likely causes of bilateral condition—systemic illness (e.g., dehydration, cachexia, and dysautonomia); associated with conformational abnormalities.
- Prolapsed gland of the third eyelid—medial aspect of the third eyelid swollen; the third eyelid itself usually normal.

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis and a left shift—with orbital inflammatory processes.
- Blood work—generally unrewarding in differentiating causes.

OTHER LABORATORY TESTS

Dysautonomia—confirmed by measuring urine and plasma catecholamine concentrations and pharmacologic testing of the autonomic nervous system.

IMAGING

- Thoracic radiography—all patients with Horner's syndrome to rule out intrathoracic cause of sympathetic denervation; patients with suspected neoplasia to evaluate for metastatic disease.
- Orbital ultrasound—recommended to help localize suspected orbital mass and define its nature (e.g., solid or cystic).
- CT or MRI—further define suspected or known orbital mass.
- Skull radiographs—rarely show signs of orbital disease unless the lesion is very large and destructive.

DIAGNOSTIC PROCEDURES

- Thorough ophthalmic examination.
- Slit-lamp biomicroscope or some other source of magnification—recommended to localize any potential ocular abnormality.
- All patients with unilateral condition—examine both surfaces of the third eyelid and the conjunctival cul-de-sac carefully for a foreign body or symblepharon.
- Pharmacologic testing—localize lesion(s) with Horner's syndrome (see Horner's Syndrome).
- Exploratory surgery and biopsy—may be only means to make a definitive diagnosis for a suspected orbital or third eyelid mass.

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THIRD EYELID PROTRUSION**Cytology**

- For suspected mass lesions—orbital mass or mass of the third eyelid; fine-needle aspirate; may help make the diagnosis.
- Unguided fine-needle aspiration—attempt only if the mass is anterior to the equator of the eye.
- Ultrasonography-guided fine-needle aspiration—for masses posterior to the eye; help avoid delicate retrobulbar structures.
- Third eyelid scrapings (German shepherds with suspected plasmoma)—reveal plasma cells and lymphocytes.

**TREATMENT**

- Depends on cause.
- Painful condition—remove the cause of the irritation (e.g., foreign body); treat the primary ocular condition.
- Orbital cellulitis and abscess—generally respond well to drainage and systemically administered antibiotics.
- Orbital neoplasms—usually require wide surgical excision via an orbital exenteration; may require adjunct therapeutic modalities (e.g., radiotherapy or chemotherapy) if excision is incomplete.
- Microphtalmic eyes—usually none required; remove the globes if painful or subject to recurrent conjunctivitis.
- Blind traumatized eyes—enucleate to prevent formation of intraocular sarcomas (cats).
- Horner's syndrome—treat cause, if known (~50% of dogs and cats); otherwise will usually resolve without treatment in 4–12 weeks.
- Surgical removal of the entire third eyelid—indicated for third eyelid neoplasia; may require adjunct therapeutic modalities (e.g., radiotherapy or chemotherapy) if the surgical margins are not free of neoplasm.
- Radiotherapy around the eye—may result in severe keratitis, dry eye, and cataracts; discuss enucleation with the client before initiating treatment if eye will be in the field.
- Orbital exenteration—may be warranted if the mass extends into the orbit.

- Plasmomas—usually controlled with topically applied medications; not cured; inform client that some form of treatment will likely be needed for the life of the patient; topical corticosteroids (0.1% dexamethasone or 1% prednisolone acetate; q6h initially, reduced to q24h when the lesion appears resolved); topical 1% cyclosporine in oil (q12h) also effective.
- Haw syndrome—usually resolves in 3–4 weeks without treatment.
- See Dysautonomia.

**MEDICATIONS****DRUG(S) OF CHOICE**

See "Treatment"

CONTRAINDICATIONS

Topical corticosteroids—never use with a corneal ulcer.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

**FOLLOW-UP****PATIENT MONITORING**

Malignant neoplasm—take thoracic radiographs every 3–6 months to monitor for metastatic disease.

POSSIBLE COMPLICATIONS

- Neoplasm—extension to or infection of adjacent orbital structures (e.g., eye, orbit, orbital sinuses, and cranial cavity) possible; metastasis to distant sites (usually thorax or liver) possible (approximately 90% are malignant).
- Vision loss—from the lesion itself; from the elevation; from treatment (e.g., radiotherapy and exenteration).

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

- Middle-aged to older patients—at risk for neoplastic diseases of the third eyelid and orbit.
- Young patients—at risk for congenital abnormalities; affected by inflammatory conditions of the third eyelid more frequently than are old animals.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Elevated third eyelid
- Haw syndrome (cats)

SEE ALSO

- Ectropion
- Entropion
- Horner's Syndrome
- Orbital Diseases (Exophthalmos, Enophthalmos, Strabismus)
- Prolapsed Gland of the Third Eyelid (Cherry Eye)

ABBREVIATIONS

- CT = computed tomography
- KCS = keratoconjunctivitis sicca
- MRI = magnetic resonance imaging

Suggested Reading

Hendrix DVH. Diseases and Surgery of the Canine Conjunctiva and Nictitating Membrane. In: Gelatt KN, Gilger BC, Kern T, eds., Veterinary Ophthalmology, 5th ed. Ames, IA: Wiley-Blackwell, 2013, pp. 945–975.

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THROMBOCYTOPATHIES



BASICS

OVERVIEW

- Acquired or hereditary defects that can affect any of the main functions of platelets, including procoagulant activity. Defects are divided in 2 categories: intrinsic and extrinsic (e.g., vWD).
- Affected animals typically have normal platelet counts but have spontaneous or excessive bleeding; mucosal bleeding is the most common sign.
- Thrombocytopenic animals with concurrent thrombocytopathia will bleed more excessively than expected for the platelet count.

SIGNALMENT

- Acquired defects are the most common thrombocytopathias seen in companion animals. They occur in all breeds and at all ages.
- Hereditary platelet function defects may be diagnosed at all ages but may first appear in young animals when excessive bleeding occurs with loss of deciduous teeth.
- Hereditary defects are rare disorders that have been described in the following breeds/species:
 - Type I Glanzmann thrombasthenia—otter hound and Great Pyrenees
 - Storage pool disease—Chediak-Higashi syndrome—Persian cat; delta-granule—American cocker spaniel; cyclic hematopoiesis—grey collie
 - Thrombocytopathia (CalDAG-GEFI deficiency)—basset hound, spitz, and Landseer
 - Scott syndrome—German shepherd
 - P2Y12 (ADP) receptor mutation—Greater Swiss mountain dog

SIGNS

- Often mild spontaneous muco-cutaneous bleeding, such as epistaxis, petechiation, and gingival bleeding.
- Prolonged bleeding in some animals during or following diagnostic or surgical procedures.
- In Scott syndrome, postoperative hemorrhage is the most common sign.

CAUSES & RISK FACTORS

Acquired—Drugs

- NSAIDs (e.g., aspirin) inhibit platelet function by preventing the formation of thromboxane A₂. This effect is less pronounced to absent with more selective cyclooxygenase-2 antagonists (e.g., meloxicam, deracoxib).
- Potentiated sulfonamides and hydroxyethyl starch solutions suppress platelet function in dogs.

• Penicillins, tetracyclines, anesthetic/sedative agents, and antihistamines cause thrombocytopenia and/or platelet function defects in humans—however, effects have not been documented in dogs and cats.

Secondary to Systemic Disease

Disseminated intravascular coagulopathy, uremia, anemia, liver disease (cholestasis and acquired or inherited shunts), ehrlichiosis, leishmaniasis, immune-mediated thrombocytopenia, heart disease, and neoplastic disorders (both hematopoietic and non-hematopoietic neoplasms).

Hereditary

- von Willebrand disease—a deficiency (type I and III) or qualitative defect (type II) of von Willebrand factor.
- Basset hound, spitz, and Landseer hereditary thrombocytopathia—signal transduction defects due to CalDAG-GEFI mutations.
- Otter hound and Great Pyrenees with type I Glanzmann thrombasthenia—platelet defect caused by a mutation in glycoprotein IIb-IIIa (integrin $\alpha_{IIb}\beta_3$) receptor on the platelet surface.
- Storage pool disease: Chediak-Higashi syndrome and deficiency in delta-granule storage pool of ADP—aggregation defect caused by lack of adenine nucleotides.
- Scott syndrome in German shepherd—platelet procoagulant deficiency (failure to externalize phosphatidyl-serine on the platelet surface and inability of the platelets to support effective assembly of coagulation complexes).
- P2Y12 (ADP) receptor mutation in Greater Swiss mountain dog.



DIAGNOSIS

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia, if bleeding is severe; regenerative or nonregenerative.
- Platelet counts typically normal in dogs with inherited thrombocytopathies, but low counts with bizarre and giant platelets seen in some.
- Biochemical profile—no specific changes.

OTHER LABORATORY TESTS

- Platelet function analyzer-100 and vWF by immune assay—in animals suspected of vWD.
 - Platelet function testing—in specialized laboratories. The most common tests are platelet aggregation and flow cytometry.
 - Coagulation tests (thromboelastography, PT, and APTT)—to eliminate coagulopathy as a cause of hemorrhage; APTT may be prolonged in some animals with von Willebrand disease.
 - Genetic testing of carrier animals.

DIAGNOSTIC PROCEDURES

Mucosal bleeding time—to confirm platelet function defect; normal buccal mucosal bleeding time measured using a spring-loaded lancet that makes an incision 5 mm long by 1 mm deep (Triplett, Helena Laboratories, Beaumont, TX) is less than 4–5 minutes in dogs and less than 2–3 minutes in cats.



TREATMENT

- Transfusion—20 mL/kg (minimum 10 mL/kg) platelet-rich plasma or fresh frozen plasma (contains platelet particles) or 1 unit/10 kg (minimum 1 unit/30 kg) platelet concentrate or cryoprecipitate depending on condition.
- Whole blood or packed red cell transfusion to correct anemia (should be reserved for animals with hematocrit below 15% or clinical compromise due to anemia).
- In animals with acquired platelet function disorders, treat the underlying disease process or withdraw the offending agent.
- Elective surgical procedures should be avoided or accompanied by appropriate transfusion products.
- Avoid over-generous fluid therapy.
- Restrict activity during a bleeding episode.



MEDICATIONS

DRUG(S)

- Desmopressin acetate (DDAVP) (1 μ g/kg SC or IV diluted in 20 mL saline administered over 10 minutes) to dogs with von Willebrand disease during a bleeding episode (if effective, effect lasts 2–3 hours).
- Desmopressin (3 μ g/kg SC) improves bleeding time in dogs with thrombocytopathia due to aspirin and liver disease. It is beneficial in many thrombocytopathies in humans, so consider using in dogs with other thrombocytopathias.
- Give desmopressin to donor 30 minutes before collection of blood for transfusion to dogs with von Willebrand disease or thrombocytopathia.



FOLLOW-UP

- Take special precautions when performing surgical procedures on these animals.
- Make owner aware that animals with hereditary platelet function defects may have recurring bleeding episodes, but fatal episodes are uncommon.

(CONTINUED)

THROMBOCYTOPATHIES

- If a hereditary defect is identified, do not use the animal for breeding.

**MISCELLANEOUS****SEE ALSO**

- Thrombocytopenia
- Von Willebrand Disease

ABBREVIATIONS

- ADP = adenosine diphosphate
- APTT = activated partial thromboplastin time

- DDAVP = 1-desamino-8-d-arginine vasopressin
- NSAID = nonsteroidal anti-inflammatory drug
- PT = prothrombin time
- vWD = von Willebrand disease
- vWF = von Willebrand factor

Suggested Reading

- Boudreux MK. Inherited platelet disorders. *J Vet Emerg Crit Care* 2012; 22:30–41.
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THROMBOCYTOPENIA



BASICS

DEFINITION

Platelet count below the lower limit of reference interval, which varies with the method of platelet counting. Grade of thrombocytopenia—Grade 1: $100,000/\mu\text{L}$ to lower limit of reference range; Grade 2: $50,000$ – $99,000/\mu\text{L}$; Grade 3: $25,000$ – $49,000/\mu\text{L}$; Grade 4: $< 25,000/\mu\text{L}$.

PATHOPHYSIOLOGY

- Platelets are produced by bone marrow megakaryocytes and released into the blood, where they normally circulate 5–10 days.
- Thrombocytopenia is caused by one or more of decreased production; increased sequestration, utilization, destruction of platelets. • Thrombocytopenia may cause spontaneous or excessive hemorrhage.

SYSTEMS AFFECTED

- Hemorrhage may occur into any organ system. • Clinical hemorrhage—most commonly recognized in the skin/exocrine and gastrointestinal systems, followed by the renal/urologic and respiratory systems; less commonly recognized in the ophthalmic, nervous, and reproductive systems.

INCIDENCE/PREVALENCE

- Thrombocytopenia is a common hematologic abnormality. • Severe hemorrhage due to thrombocytopenia is uncommon (dogs) or rare (cats) in general practice.

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Hereditary asymptomatic thrombocytopenia with macroplatelets in Cavalier King Charles spaniel. • Hereditary asymptomatic mild thrombocytopenia in greyhound and Polish ogar dog.

SIGNS

General Comments

- Grade 1 thrombocytopenia—no increased risk of hemorrhage. • Grade 2—increased surgical hemorrhage may occur. • Grade 3—microscopic spontaneous hemorrhage may occur. • Grade 4—mild, moderate, and severe risk of spontaneous clinical hemorrhage at platelet counts of $< 25,000/\mu\text{L}$, $< 10,000/\mu\text{L}$, and $< 5,000/\mu\text{L}$, respectively.
- These figures are guidelines only because of variation in methods of platelet counting and imprecision of low platelet counts.
- Concurrent platelet function defect, von Willebrand disease, coagulopathy, vasculitis, or sepsis increases risk of hemorrhage. • Dogs with IMT have a lower risk of hemorrhage for a given platelet count. • Cats have a lower risk of hemorrhage than dogs.

Historical Findings

- Spontaneous or excessive mucous membrane, cutaneous, gastrointestinal, nasal, urinary and ocular bleeding. • Lethargy and collapse (hemorrhagic anemia). • Dyspnea and coughing (respiratory tract hemorrhage).
- Neurologic signs (CNS bleeding). • Clinical signs of the primary disease.

Physical Examination Findings

- Petechiae and ecchymoses • Persistent bleeding from wounds and venipuncture sites
- Melena, hematochezia, hematemesis
- Hematuria • Ocular hemorrhages
- Splenomegaly, hepatomegaly • Pale mucous membranes • Weakness • Dyspnea, hemoptysis • Heart murmur • Neurologic signs • Excessive bleeding in estrus • Clinical signs of the primary disease

CAUSES

- Decreased production—hereditary; bone marrow neoplasia; Sertoli cell tumor; infectious agents; immune-mediated; drugs; irradiation. Thrombocytopenia varies from mild to severe and may be an isolated hematologic abnormality or a feature of pancytopenia. • Increased sequestration—splenomegaly; severe thrombocytopenia is uncommon. • Increased utilization—DIC; local thrombosis (e.g., portal vein); vasculitis; severe thrombocytopenia is uncommon.
- Increased destruction—primary IMT or IMT secondary to neoplasia, infectious agents, aseptic inflammation, drugs. Most common cause of severe thrombocytopenia in dogs. • Increased loss—hemorrhage due to vitamin K antagonist poisoning may result in mild to moderate thrombocytopenia; hemorrhage due to major trauma may result in mild to severe thrombocytopenia after volume resuscitation.

RISK FACTORS

- Potentially any infection—most commonly associated with thrombocytopenia: FeLV; FIV; distemper; parvoviruses; *Ehrlichia* spp.; *Anaplasma* spp.; Rocky Mountain spotted fever; leptospirosis; *Borrelia burgdorferi*; bacterial sepsis; histoplasmosis; *Cytauxzoon felis*; *Babesia* spp.; *Rangelia* spp.; *Hepatozoon canis*, *Leishmania* spp.; *Theileria* spp. heartworm, *Angiostrongylus vasorum*, and aberrant larva migrans. • Potentially any non-infectious inflammation, e.g., vasculitis.
- Potentially any neoplasm—most commonly identified include hemangiosarcoma, thyroid carcinoma, lymphoma, histiocytic sarcoma and acute leukemias. • Large-field radiation therapy and cytotoxic drug therapy—predictable myelosuppression; lomustine causes a cumulative thrombocytopenia.
- Potentially any drug—drugs with known risk for unpredictable myelosuppression or IMT include estrogen, gold compounds, phenylbutazone, phenobarbital (dogs); chloramphenicol, griseofulvin, propylthiouracil, methimazole and carbimazole (cats); drugs with reported idiosyncratic reactions causing myelosuppression include cephalosporins and albendazole (dogs, cats), fenbendazole, sulfonamides, ACE inhibitors (dogs), and ribavirin. • Vaccination within 1 month—for IMT. • Toxins and venoms—zinc, autumn crocus (myelosuppression); mycotoxins, xylitol (acute hepatic injury—DIC); snake bite. • Hyperthermia—DIC.

carbamazole (cats); drugs with reported idiosyncratic reactions causing myelosuppression include cephalosporins and albendazole (dogs, cats), fenbendazole, sulfonamides, ACE inhibitors (dogs), and ribavirin. • Vaccination within 1 month—for IMT. • Toxins and venoms—zinc, autumn crocus (myelosuppression); mycotoxins, xylitol (acute hepatic injury—DIC); snake bite. • Hyperthermia—DIC.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Measurement error due to platelet clumping—most likely with traumatic venipuncture and in cats. EDTA-induced platelet clumping may occur in dogs (rare).
- Clerical error. • Local hemorrhage—rule out trauma, gastrointestinal ulceration, primary intranasal, urinary, and reproductive tract disorders. • von Willebrand disease—petechiae, ecchymoses, and ocular hemorrhages unusual. • Coagulopathy—petechiae, gastrointestinal hemorrhage, and epistaxis unusual; subcutaneous swellings, swollen joints, hemothorax, and hemoabdomen may be present.

CBC/BIOCHEMISTRY/URINALYSIS

- Confirm thrombocytopenia reported by a hematology analyzer by examination of a blood smear; examine feather edge for platelet clumps; estimate platelet count from red cell monolayer where about 50% of cells are touching; each platelet-per-oil immersion field represents $15,000$ – $25,000/\mu\text{L}$. • Mean platelet volume and platelet distribution width are inversely related to platelet count and usually do not assist in differentiating causes of thrombocytopenia. Platelet morphology changes are nonspecific.
- Plateletcrit (analogous to hematocrit)—best method to diagnose pathologic thrombocytopenia in a Cavalier King Charles spaniel. • Regenerative anemia—rule out hemorrhage or IMHA concurrent with IMT.
- Neutrophilia and left shift—rule out sepsis, non-septic inflammation, and nonspecific stimulation of granulopoiesis.
- Eosinophilia—rule out heartworm and other helminth infections. • Concurrent non-regenerative anemia and neutropenia—thrombocytopenia probably due to decreased production. • Schistocytes—DIC.
- Organisms in blood cells. • Abnormalities on a biochemistry profile and urinalysis reflect primary disease.

OTHER LABORATORY TESTS

- von Willebrand factor antigen. • PT, APTT, ACT—prolonged times increase likelihood of DIC; normal PT rules out vitamin K antagonism. • Fibrinogen degradation products and D-dimer—positive result increases likelihood of DIC or local

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thrombosis. • Cultures of abnormal organs, blood, and urine for bacterial or fungal sepsis. • Serologic and PCR tests for infectious organisms. • Fecal floatation and Baermann tests for parasitic larvae. • Antiplatelet/antimegakaryocyte antibody tests—negative results help rule out IMT. • Coombs' test—positive result increases likelihood of concurrent IMHA. • Antinuclear antibody test—positive result increases likelihood of SLE. • Flow cytometry for immature reticulated platelets (analogous to reticulocyte count).

IMAGING

Identify splenomegaly, hepatomegaly, neoplasms, infection, and internal bleeding.

DIAGNOSTIC PROCEDURES

Bone marrow biopsy—rule out reduced platelet production: neoplasia in bone marrow, histoplasmosis, maturation arrest, marrow aplasia, myelofibrosis, and marrow necrosis; no specific finding that rules in or out immune-mediated megakaryocytic hypoplasia; low diagnostic yield if the only hematologic abnormalities are thrombocytopenia causing bleeding and regenerative anemia (likely IMT). Not contraindicated in severe thrombocytopenia.

PATHOLOGIC FINDINGS

Internal bleeding; other findings reflect primary disease.



TREATMENT

APPROPRIATE HEALTH CARE

- Treatment of primary disorder. • Platelet transfusion—20 mL/kg (minimum 10 mL/kg) fresh whole blood, platelet-rich plasma, or fresh frozen plasma (contains platelet particles), or 1 unit/10 kg (minimum 1 unit/30 kg) platelet concentrate (fresh, room-temperature stored, cryopreserved, and lyophilized) or cryoprecipitate (where 1 canine unit refers to product derived from a 450 mL unit of whole blood); transfuse if critical hemorrhage is noted and consider prophylactic transfusion if platelet count < 5,000–10,000/ μ L; transfusions may be needed q1–3d if severe thrombocytopenia persists; most useful when thrombocytopenia is due to reduced production or loss and rapid resolution is anticipated; less useful in splenomegaly and DIC and least useful in IMT. • Whole blood or packed red cell transfusion to correct anemia—bleeding due to thrombocytopenia is worse in the presence of anemia. • Do not drain hematomas unless necessary (e.g., tracheal compression).

NURSING CARE

- Minimize IM and SC injections. Apply extended pressure after IV injection/catheterization and invasive procedures. Avoid

jugular venipuncture. • Avoid overexuberant fluid therapy.

ACTIVITY

Restrict activity with moderate-to-severe thrombocytopenia.

DIET

Avoid hard foods with severe thrombocytopenia (gingival bleeding).

SURGICAL CONSIDERATIONS

Extensive perioperative transfusion may be needed.



MEDICATIONS

DRUG(S) OF CHOICE

- See specific chapters for diseases causing thrombocytopenia. • Acepromazine has negligible effects on platelet function in dogs and cats and may be used to sedate animals to reduce risk of hemorrhage associated with excessive activity.

CONTRAINdications

NSAIDs that interfere with platelet function—opioids are preferred for analgesia; if NSAID use required, use selective cyclooxygenase-2 inhibitors (e.g., deracoxib).

PRECAUTIONS

- Heparin (used in DIC) may aggravate hemorrhage due to thrombocytopenia.
- Corticosteroid therapy may exacerbate infection and promote gastrointestinal ulceration.

POSSIBLE INTERACTIONS

Corticosteroids are prothrombotic.

ALTERNATIVE DRUG(S)

- Thrombopoietic stimulants: Oprelvekin—50 μ g/kg SC q24h for maximum of 2 weeks (to avoid risk of neutralizing antibody formation); most useful when thrombocytopenia caused by cytotoxic therapy; expensive. Romiplostim, eltrombopa, lithium carbonate—not recommended. • Plasmin inhibitors: aminocaproic acid, tranexamic acid; as for IMT; contraindicated in DIC; Melatonin and 5-methoxytryptamine—as for IMT.



FOLLOW-UP

PATIENT MONITORING

- Amount of bleeding—control of clinical hemorrhage is most important parameter to monitor to judge effectiveness of treatment.
- Serial platelet counts using same method
- Serial coagulation profiles—if DIC suspected.

PREVENTION/AVOIDANCE

Varies with cause.

THROMBOCYTOPENIA

POSSIBLE COMPLICATIONS

- Hemorrhagic shock • Uveitis
- Mild-to-severe neurologic signs (CNS bleeding)

EXPECTED COURSE AND PROGNOSIS

Varies with cause. If underlying cause of severe thrombocytopenia cannot be treated, prognosis poor because of limited ability to provide extensive platelet transfusions.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- If thrombocytopenia is from reduced production, may be concurrent anemia and neutropenia. • IMT may be solitary or associated with other immune-mediated disorders.

AGE-RELATED FACTORS

Varies with cause—e.g., FeLV in younger cats, IMT in middle-aged dogs, neoplasia in older dogs.

ZOONOTIC POTENTIAL

Thrombocytopenia may be due to a zoonotic infection (e.g., leptospirosis).

SEE ALSO

- Anemia, Immune-Mediated • Disseminated Intravascular Coagulation • Hyphema
- Pancytopenia • Petechia, Ecchymosis, Bruising • Splenic Torsion • Splenomegaly
- Thrombocytopathies • Thrombocytopenia, Primary Immune-Mediated • Vasculitis, Systemic • Specific chapters for various infectious diseases

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- ACT = activated clotting time • APTT = activated partial thromboplastin time
- DIC = disseminated intravascular coagulation • EDTA = ethylene diamine tetra-acetic acid • FeLV = feline leukemia virus • FIV = feline immunodeficiency virus
- IMHA = immune-mediated hemolytic anemia • IMT = immune-mediated thrombocytopenia • NSAID = nonsteroidal anti-inflammatory drug • PCR = polymerase chain reaction • PT = prothrombin time
- SLE = systemic lupus erythematosus

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INTERNET RESOURCES

<https://ahdc.vet.cornell.edu/sects/clinpath/modules/coags/acqbtpp.htm>

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- Author** Anthony C.G. Abrams-Ogg
Consulting Editor Alan H. Rebar

THROMBOCYTOPENIA, PRIMARY IMMUNE-MEDIATED



BASICS

DEFINITION

- Immune-mediated destruction of platelets with no identifiable cause.
- In secondary IMT, infectious diseases, neoplasia, vaccination, or drugs trigger the production of antibodies.

PATHOPHYSIOLOGY

- Antiplatelet auto-antibodies result in premature platelet destruction by macrophages mainly in the spleen by a Type II (antibody-dependent cytotoxicity) mechanism.
- In secondary IMT, platelet-bound antibodies can be antibodies bound to platelet antigens altered during course of disease or antibodies bound to foreign antigens or immune complexes.
- Auto-antibodies can be directed against megakaryocytes, thereby impeding marrow responsiveness.
- Antibody-mediated impairment of platelet function possible.
- Cause of immune dysregulation and auto-antibody production is unknown.

SYSTEMS AFFECTED

- CNS
- GI Tract
- Ophthalmic
- Respiratory
- Skin
- Urinary

GENETICS

Auto-immunity is frequently recognized in particular dog breeds and is often familial, suggesting a strong genetic influence.

PREVALENCE

Approximately 6% of canine and 3% of feline thrombocytopenia cases.

SIGNALMENT

Species

- Dog
- Rare (or rarely diagnosed) in cat

Breed and Familial Predilections

Cocker spaniel, poodle, Old English sheepdog, Irish setter; any breed can be affected.

Mean Age and Range

- Mostly middle-aged dogs
- Reported age range in dogs: 0.3–15 years (mean 5); in cats: 0.7–12 years (mean 6)

Predominant Sex

Female dogs, spayed or intact, are predisposed.

SIGNS

Historical Findings

- Dogs often presented due to acute onset (surface) hemorrhage.
- Chronic blood loss due to IMT is very rare.
- Sometimes lethargy, weakness, inappetence.
- Cats presented due to lethargy, inappetence, (surface) hemorrhage.
- Asymptomatic cases can be detected on (routine) health checks or presurgical screens.
- Specific questions: drug/travel history, vaccination history (vaccination within the last 4 weeks might indicate vaccine reaction).

Physical Examination Findings

- Mainly surface bleeding.
- Mucosal and cutaneous petechiae/ecchymoses.
- Gingival bleeding.
- Melena, hematemesis, hematochezia.
- Epistaxis.
- Ocular hemorrhage.
- Hematuria.
- Sometimes hematomas.
- Prolonged hemorrhage after trauma or venipuncture.
- Mucous membrane pallor due to blood loss anemia, hemorrhagic shock.
- Neurologic signs (rare) due to CNS bleeding.
- Fever, mild lymphadenomegaly unusual.
- Sometimes enlarged spleen palpable.



DIAGNOSIS

- Is based on
- Usually severe thrombocytopenia
- Positive platelet-bound antibody test (if available)
- Response to immunosuppressive therapy
- Careful exclusion of underlying diseases or potential triggers.

DIFFERENTIAL DIAGNOSIS

- Measurement error due to platelet clumping; especially in cats low platelet counts often incorrect (due to tendency to aggregate/large size).
- Decreased production:
 - Infectious diseases; vaccination within the last weeks; drugs/toxins; irradiation; primary bone marrow disorders; immune-mediated response against megakaryocytes; inherited macrothrombocytopenia of Cavalier King Charles spaniels.
 - Either isolated thrombocytopenia or pancytopenia.
- Thrombocytopenia can be severe dependent on underlying disease.
- Increased sequestration in an enlarged spleen:
 - E.g., inflammatory disorders, neoplasias; splenic torsion.
 - Thrombocytopenia mild to moderate unless other mechanisms contribute (e.g., secondary IMT, DIC).
 - Increased utilization or consumption:
 - DIC; local thrombosis; vasculitis/vascular damage with or without DIC.
 - Severe hemorrhage: may result in mild to moderate thrombocytopenia after volume resuscitation.
 - Increased destruction (most common cause of severe thrombocytopenia):
 - Primary IMT.
 - Secondary IMT due to infectious diseases (anaplasmosis, ehrlichiosis, Rocky Mountain spotted fever, bartonellosis, babesiosis, leishmaniasis, dirofilariosis, angiostrongylus infection, bacterial infections; FeLV, FIV, FIP, distemper, infectious hepatitis); sterile inflammation (in cats fat tissue necrosis, etc.); neoplastic diseases (lymphoma, leukemia, hemangiosarcoma, etc.); drugs/toxins (vaccines, sulfonamides, cephalosporins, phenobarbital, NSAID); blood transfusions; SLE.

CBC/BIOCHEMISTRY/URINALYSIS

- Thrombocytopenia often severe (< 30–40,000/ μ L), high risk of spontaneous bleeding; dogs and cats may be asymptomatic.

- Blood smear examination: to confirm low platelet count; to identify potential causes for secondary IMT; e.g., morulae, babesia, schistocytes, spherocytes, blast cells; anemia due to blood loss/concurrent IMHA possible.
- Leukogram can be normal; mild to moderate leukocytosis in one-third of the dogs (due to stress/inflammation), rarely leukopenia. Sometimes monocytosis, neutrophilia with/without left shift, lymphopenia, eosinophilia, eosinopenia.
- Concurrent neutropenia may indicate primary marrow disease or infectious disease.
- Coagulation testing generally normal; if abnormal consider secondary IMT, DIC and further tests.
- Chemistry results unspecific for IMT. Sometimes mildly increased liver enzymes, rarely hyperbilirubinemia due to hematoma resorption; hypoproteinemia/hypoalbuminemia due to blood loss. Hyperglobulinemia may indicate underlying disease (e.g., ehrlichiosis, leishmaniasis, FIP).
- Microscopic or macroscopic hematuria.

OTHER LABORATORY TESTS

- No gold standard immunodiagnostic test for IMT widely available. No test can distinguish between primary and secondary IMT; pIMT is a diagnosis of exclusion.
- Direct tests to detect platelet-bound antibodies have been evaluated. Flow cytometric assays performed in specialized laboratories appear to have a good sensitivity and specificity.
- Adjunct immunodiagnostic testing such as Coombs' test or antinuclear antibody titer if IMHA or SLE is suspected.
- Select other tests to exclude the above-listed differentials for thrombocytopenia (serology and/or PCR testing for infectious diseases; microbiology of urine and blood; etc.).

IMAGING

- Often diffuse splenomegaly, rarely hepatomegaly.
- Radiography and ultrasonography to exclude other causes of thrombocytopenia (e.g., splenic mass) or internal bleeding.

DIAGNOSTIC PROCEDURES

- Bone marrow evaluation not indicated if diagnosis seems straightforward and there is response to therapy within several days; indicated if concurrent neutropenia or nonregenerative anemia, atypical nucleated cells, or treatment failure.
- Number of megakaryocytes often increased, megakaryocytic hypoplasia is rare.
- Fine-needle aspiration of enlarged lymph nodes possible; no organs shall be aspirated due to high risk of severe bleeding. (Otherwise platelet products have to be available.)



TREATMENT

APPROPRIATE HEALTH CARE

- Uncomplicated cases with low bleeding risk and good owner compliance may be treated as

(CONTINUED)

THROMBOCYTOPENIA, PRIMARY IMMUNE-MEDIATED

outpatients. • Patients with severe thrombocytopenia have very high risk of bleeding and warrant strict refinement (e.g., cage rest). • Transfusion of platelet products: 10–20 mL/kg fresh whole blood, 1 unit of whole blood–derived platelet-rich plasma (ca. 8×10^{10} platelets) per 10 kg (minimum 1 unit/30 kg) in cases with critical hemorrhage. Platelets may be destroyed rapidly, but protect against catastrophic hemorrhage until specific therapy is beneficial. • Packed red blood cells or (preferably) fresh whole blood to correct blood loss anemia. • Management of hypovolemia with crystalloid solutions (colloids may impair platelet function).

NURSING CARE

- No IM and SC injections. Apply extended pressure after IV injections and invasive procedures (e.g., lymph node aspiration). Avoid cystocentesis and jugular venipuncture. Bone marrow aspiration is safe.
- Intensive nursing care in patients with moderate to severe hemorrhage, hypovolemia, CNS signs, etc.
- Avoid hard foods.

SURGICAL CONSIDERATIONS

- High risk of bleeding in dogs with severe thrombocytopenia.
- May need extensive peri- and intraoperative (platelet) transfusions.
- Splenectomy is a (controversial) option for refractory cases not responding to medical therapy.



MEDICATIONS

DRUG(S)

- Corticosteroids: methyl prednisolone 10 mg/kg IV once; prednisolone (dogs 1–1.5 mg/kg q12h, cats 1.5–2 mg/kg q12h initially); dexamethasone rarely used (0.1–0.5 mg/kg q24h). • Consider antibiotics (potential of underlying occult infection; predisposition to infection from immunoderegulation); doxycycline if tick-borne disease is not excluded.
- GI protectants (sucralfate and/or proton pump inhibitors) to prevent or treat GI ulceration.
- Other immunosuppressive agents when prednisolone fails, only controls the disease at persistently high doses, causes unacceptable side effects, and for the long-term control of refractory/relapsing cases. Most of these agents not effective in the acute management; few controlled studies available.
- Acute management—dogs: vincristine (0.02 mg/kg IV, once) or hIg (0.5 g/kg IV over 6–8h, once) in combination with prednisolone led to a more rapid increase in platelet counts compared to prednisolone alone; mycophenolate mofetil (7–10 mg/kg q12h)

(onset of action unknown; successful as first-line single agent in 5 dogs); cats: hIg. • Other immunosuppressive drugs for long-term control (initial dosages)—dogs, cyclosporine (5 mg/kg q12h), mycophenolate mofetil, azathioprine (initially 2 mg/kg q24h), leflunomide (3–4 mg/kg q24h), in combination with prednisolone; cats, chlorambucil (0.1–0.2 mg/kg q24h), mycophenolate mofetil. • Once the platelet count is in the normal range, the initial prednisolone dose will be tapered by approximately one-fourth to one-fifth every 2 weeks, finally switching to alternate-day therapy. Taper slowly over approximately 6 months if no relapse occurs.

PRECAUTIONS

- Discontinue any unnecessary medications (may have induced secondary IMT).
- Corticosteroids: GI ulceration; iatrogenic hyperadrenocorticism.
- Immunosuppression: predisposes to opportunistic infections.
- Cytotoxic medications: bone marrow suppression.
- Dose tapering too rapidly after remission may predispose to recurrence. Relapses are more difficult to control.



FOLLOW-UP

PATIENT MONITORING

- Hematocrit measurements 2–3 times daily in cases with severe hemorrhage (risk of life-threatening (GI) blood loss).
- Measure platelet count daily until $> 50,000/\mu\text{L}$; then every few days until platelet counts normalize. Then every 1–3 weeks during the period of drug dose tapering.
- CBC and biochemistry every 2–4 weeks.
- Microbiological urinalysis every 4–6 weeks due to risk of secondary infections (especially in females).

PREVENTION/AVOIDANCE

- Use vaccines judiciously. Role in recurrence is uncertain.
- Minimize stress that may initiate recurrence.

POSSIBLE COMPLICATIONS

- Excessive bleeding can be fatal; spontaneous death, e.g., due to CNS, pericardial bleeding.
- Side effects of medications (GI ulceration, Cushing habitus, opportunistic infections, bone marrow suppression).

EXPECTED COURSE AND PROGNOSIS

- Platelet counts will usually increase $> 50,000/\mu\text{L}$ a few days after starting treatment (after 1–15, median 5 days in 24 of 25 dogs).
- Vincristine or hIg in addition to prednisolone led to a more rapid increase to $50,000/\mu\text{L}$ (median 2.5–4 days).
- Few dogs never achieve normal platelet counts.

- Failure to respond to therapy should prompt reconsideration of the diagnosis.
- 5 of 19 dogs (26%) relapsed after 19–286, median 66 days; causes for relapse were dose reduction of prednisolone, lack of owner compliance.
- If relapses occur a second immunosuppressive drug should be added, a more gradual tapering is advised, leaving the animal on an alternating daily regimen possibly for the rest of its life.
- Survival to discharge in recent studies: 84–97%;
- prognosis is more favorable with intensive therapy including blood/platelet products if needed.
- Mortality rate in cats is 15% (2/13).



MISCELLANEOUS

ASSOCIATED CONDITIONS

Approximately one-third of dogs with primary IMT also have IMHA (Evans syndrome).

SYNOMYMS

- Auto-immune thrombocytopenia
- Idiopathic/auto-immune thrombocytopenic purpura

SEE ALSO

- Anemia, Immune-Mediated
- Disseminated Intravascular Coagulation
- Thrombocytopenia

ABBREVIATIONS

- CNS = central nervous system
- DIC = disseminated intravascular coagulation
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- GI = gastrointestinal
- hIg = human immunoglobulins
- IMHA = immune-mediated hemolytic anemia
- IMT = immune-mediated thrombocytopenia
- NSAID = nonsteroidal anti-inflammatory drug
- PCR = polymerase chain reaction
- pIMT = primary immune-mediated thrombocytopenia
- SLE = systemic lupus erythematosus

Suggested Reading

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Author Barbara Kohn

Consulting Editor Alan H. Rebar



Client Education Handout
available online

T

THUNDERSTORM AND NOISE PHOBIAS



BASICS

OVERVIEW

Thunderstorm phobia is a disorder in which there is persistent and exaggerated fear of storms or the stimuli associated with storms. Fears of noises other than thunder also occur, such as fireworks or gunshots. Pathophysiology involves physiologic, emotional, and behavioral components.

SYSTEMS AFFECTED

- Behavioral—avoidance or escape attempts.
- Cardiovascular—tachycardia.
- Endocrine/Metabolic—increased cortisol levels, stress-induced hyperglycemia.
- GI—inappetence, gastrointestinal upset.
- Musculoskeletal—self-induced trauma resulting.
- Nervous—adrenergic/noradrenergic overstimulation.
- Respiratory—tachypnea.
- Skin—displacement grooming.

SIGNALMENT

• Occurs in dogs and cats, but dogs more often presented for treatment. Cats with noise aversion might present with redirected aggression.

- No association with sex or neuter status.
- Any breed can be affected. In one study, thunderstorm phobias were most prevalent in herding breeds.
- Dogs may begin exhibiting signs as puppies but may not be presented until adulthood.

SIGNS

Historical Findings

• One or more of the following occurs during storms, or when the pet is exposed to the eliciting noise: panting, pacing, trembling, remaining near owner, hiding, salivating, destructiveness, vocalization, self-inflicted trauma, and inappropriate elimination.

• Stimuli that can elicit fear during storms include rain, lightning, thunder, wind, and possibly static electricity and changes in barometric pressure.

Physical Examination Findings

Unremarkable, except if self-inflicted or escape-related injuries.

CAUSES & RISK FACTORS

May include combinations of the following:

- Lack of exposure to storms or noises early in development.
- Unintentional reinforcement by owner.
- Highly aversive experience, such as exposure to a violent storm.
- Genetic predisposition for emotional reactivity.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Conditions causing similar behavioral responses include separation anxiety, barrier frustration, and other phobias.

- Underlying medical conditions including pain, GI, endocrine or dermatologic should be ruled out.

CBC/BIOCHEMISTRY/URINALYSIS

Results should be within normal ranges.

OTHER LABORATORY TESTS

Tests for thyroid or adrenal disease may be indicated.

IMAGING

Radiographs to help identify sources of pain.

DIAGNOSTIC PROCEDURES

Skin biopsies if a primary dermatologic condition is suspected.



TREATMENT

ENVIRONMENT

Avoid crate confinement if risk of injury.

BEHAVIOR MODIFICATION

- Neither punish nor attempt to comfort the animal during noise exposures or storms.
- Desensitization involves exposure to a recorded stimulus at a volume that does not elicit fear. The volume is gradually increased only if the animal remains relaxed.
- Counter-conditioning involves teaching a response (sit, relax) that is incompatible with the fear response. Food rewards are often used to facilitate learning.
- Audio recordings of noises or storms are commercially available.
- Improper use of these exercises can worsen the condition.
- Exercises will be ineffective if the animal does not react to recorded thunderstorm sounds.



MEDICATIONS

DRUG(S) OF CHOICE

- Use of medications is considered extra-label.
- Azapirones, TCAs, and SSRIs require 2–4 weeks for effect and must be given daily during storm season to control anxiety. They can be used in combination with fast-acting medications.

Medications for Acute, Short-Term Control of Anxiety or Adjunctive Use Benzodiazepines

- Alprazolam—dogs, 0.02–0.1 mg/kg PO q4–12h prn
- Clonazepam—dogs, 0.05–0.25 mg/kg q12h prn
- Diazepam—dogs, 0.5–1 mg/kg PO q4–12h prn
- Lorazepam—dogs, 0.02–0.2 mg/kg PO q8–24h prn

Alpha-2 Adrenergic Agonists

- Clonidine—dogs, 0.01–0.05 mg/kg PO q6–24h prn

Serotonin-2 Antagonists, Reuptake Inhibitors

- Trazodone—dogs, 2–10 mg/kg PO q12–24h

Azapirones

- Buspirone—dogs, 0.5–2.0 mg/kg PO q8–12h; cats, 2.5–7.5 mg/cat PO q12h

GABA Agonists

- Gabapentin—dogs, 10–20 mg/kg PO q12h; cats, 5–10 mg/kg PO q12h

Medications Used Daily Year Round or Throughout Thunderstorm Season

Selective Serotonin Reuptake Inhibitors

- Fluoxetine—dogs, 1–2 mg/kg PO q24h; cats, 0.5–1 mg/kg PO q24h
- Paroxetine—dogs, 1 mg/kg PO q24h; cats, 0.5–1 mg/kg PO q24h
- Side effects: inappetence and irritability

Tricyclic Antidepressants

- Clomipramine—dogs, 2 mg/kg PO q12h; cats, 2.5–5 mg/cat PO q24h
- Side effects: sedation, GI and anticholinergic effects, and cardiac conduction disturbances.

Phenothiazine Tranquilizers

- Acepromazine—dog 0.1–1 mg/kg PO q6–8h
- Poor anti-anxiety properties
- Use *only* if further sedation needed to prevent injury.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Use benzodiazepines with caution in cats and aggressive dogs—disinhibition of aggression possible.
- Avoid using TCAs and phenothiazines in breeding males, patients with seizure disorders, cardiac disease, diabetes mellitus, glaucoma, or thyroid disease.
- Decrease dose or avoid use of these medications in geriatric patients and patients with impaired hepatic or renal function.
- TCAs, SSRIs, SARIs, and phenothiazines should never be combined with monoamine oxidase inhibitors.



FOLLOW-UP

PATIENT MONITORING

With medication use, CBC and biochemistry profiles should be monitored periodically.

PREVENTION/AVOIDANCE

- Puppies and kittens should be exposed to a variety of stimuli under benign conditions.
- Ignore mild signs of anxiety during storms to avoid reinforcing these behaviors.

POSSIBLE COMPLICATIONS

Severe injuries and property damage

EXPECTED COURSE AND PROGNOSIS

Prognosis depends on severity, duration, and the ability to prevent injuries. The condition can progress if left untreated.



MISCELLANEOUS

ABBREVIATIONS

- GI = gastrointestinal
- SARI = serotonin-2 antagonist reuptake inhibitor
- SSRI = selective serotonin reuptake inhibitor
- TCA = tricyclic antidepressant

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THYMOMA



BASICS

OVERVIEW

- Originates from thymic epithelium, rarely metastasizes
- Infiltrated with mature lymphocytes
- May be associated with myasthenia gravis
- Classified as invasive or non-invasive

SIGNALMENT

- Rare in dog and cat
- Most common in medium- and large-breed dogs
- Dogs—mean age, 9 years
- Cats—mean age, 10 years

SIGNS

- From physical presence of tumor: coughing, tachypnea, dyspnea.
- Secondary to obstruction of cranial vena cava: swelling of the head, neck, or forelimbs.
- Paraneoplastic syndromes
- Muscle weakness and megaesophagus caused by myasthenia gravis (~ 20%), hypercalcemia ~ 30% (causing PU/PD), polymyositis, skin disease, hypergammaglobulinemia.

CAUSES AND RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Lymphoma (main rule out)
- Branchial cyst
- Ectopic thyroid carcinoma
- Chemodectoma
- Various subtypes of sarcoma
- Mesothelioma
- Non-neoplastic granuloma, abscess, or cyst

CBC/BIOCHEMISTRY/URINALYSIS

Lymphocytosis—occasionally

OTHER LABORATORY TESTS

- Antibody titers to acetylcholine receptors to confirm myasthenia gravis.
- Ultrasound-guided fine-needle aspiration and cytology of the mass: characterized by small lymphocytes, occasional mast cells, and possible epithelial population (versus a pure population of lymphoblasts with lymphoma). Thymomas can be cavitated/cystic, whereas lymphoma is homogenous.

- Biopsy may be needed to confirm diagnosis and immunohistochemical stains can be used.

IMAGING

- Thoracic radiography—typically reveals a cranial mediastinal mass with dorsal deviation of the trachea, and may show pleural effusion or megaesophagus.
- CT scan or MRI can be used prior to thoracotomy for surgical planning, though cannot predict ease of resection.

DIAGNOSTIC PROCEDURES

Tensilon test—evaluate for myasthenia gravis in patients with signs of muscle weakness, dysphagia, or regurgitation.



TREATMENT

- Inpatient.
- Surgical excision—treatment of choice, and possible in 70% of cases; thymoma tends to be highly invasive and difficult to resect in dogs and less invasive and easier to remove in cats; use an intercostal approach for small masses and a sternotomy for large masses. Recurrence ~ 17%, median survival time 635 days (compared to 76 days without surgery).
- Dogs with myasthenia gravis and aspiration pneumonia have a poorer prognosis with surgery.
- Radiotherapy—potentially beneficial by reducing the lymphoid component of the mass (> 75% of cases benefit); median survival time 248 days in dogs and 720 days in cats.



MEDICATIONS

DRUG(S)

- Chemotherapy—little information available.
- Prednisone (20 mg/m² PO q48h) and cyclophosphamide (50–100 mg/m² PO q48h)—used in a very limited number of patients, two of which had a partial remission likely associated with lymphodepleting effects.
- Myasthenia gravis—treat with prednisone and anticholinesterase drugs until the tumor can be removed.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Immunosuppressive drugs—do not use to treat myasthenia gravis with aspiration pneumonia.



FOLLOW-UP

- Thoracic radiography—every 3 months; monitor for recurrence.
- Cure—possible if tumor is surgically resectable; greater than 80% alive at 1 year if resectable and no associated megaesophagus; median survival > 1800 days for cats and almost 800 days for dogs. 10–20% recur and may respond favorably to a second surgery.
- Prognosis—poor with nonresectable tumor, though some dogs and cats have prolonged survival despite no therapy, likely a result of the indolent nature of the tumor.
- Patients with high lymphocyte proportion in tumor have a more favorable prognosis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Concurrent non-thymic tumors, polymyositis, and other autoimmune diseases—20–40% of patients.

SEE ALSO

Myasthenia Gravis

Suggested Reading

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TICK BITE PARALYSIS



BASICS

DEFINITION

Flaccid, lower motor neuron tetraparesis to tetraplegia caused by salivary neurotoxins from certain species of female tick.

PATHOPHYSIOLOGY

- Presynaptic disorder—tick injects salivary neurotoxin that interferes with the depolarization/acetylcholine release from the presynaptic nerve terminal of the neuromuscular junction; this effect is probably associated with an interruption of the calcium flux across axonal membranes.
- Australian *Ixodes holocyclus* tick—neurotoxin (holocyclotoxin) effects are more pronounced at higher temperatures; one adult tick is sufficient to cause neurologic signs, but infestation with *I. holocyclus* larvae or nymphs can also induce signs; holocyclotoxin also interferes with acetylcholine release at the autonomic nerve terminals.
- Signs—5–9 days after initial tick attachment.
- Not all infested animals develop tick paralysis; not all adult female ticks produce the toxin.

SYSTEMS AFFECTED

- Nervous—peripheral nervous system and neuromuscular junction most affected; cranial nerves can become involved, including the vagus and facial nerves with the North American ticks and, in addition, the trigeminal nerves and sympathetic nervous system with the Australian *Ixodes* tick.
- Respiratory—may see paralysis of the intercostal muscles and diaphragm; caudal brainstem respiratory center may be affected (rare with North American ticks; more common with Australian *Ixodes* ticks).

GENETICS

No genetic basis

INCIDENCE/PREVALENCE

- North America—somewhat seasonal (more prevalent in the summer months); in the warmer areas (southern United States) may become a year-round problem.
- Australia—distinctly seasonal, up to 75% of cases occur during southern hemisphere spring season (September–November).
- Overall incidence—low in the United States; higher in Australia.

GEOGRAPHIC DISTRIBUTION

- United States—*Dermacentor variabilis*: wide distribution over the eastern two-thirds of the country, California, and Oregon; *D. andersoni*: from the Cascades to the Rocky Mountains; *Amblyomma americanum*: from Texas and Missouri to the Atlantic Coast; *A. maculatum*: Atlantic and Gulf of Mexico seaboards.

• Australia—*Ixodes holocyclus*: coastal areas of the east; *I. cornuatus*, southern Australia (Tasmania).

- Other—cases with apparent tick paralysis have been described in South Africa (*Rhipicentor nuttalli*), southern Italy (*Rhipicephalus sanguineus*), and Iran (*Ornithodoros laborensis*).

SIGNALMENT

Species

- Australia—dogs and cats
- United States—dogs; cats appear to be resistant

Breed Predilections

None

Mean Age and Range

Any age

Predominant Sex

N/A

SIGNS

Historical Findings

- Patient exposed to ticks (wooded area) approximately 1 week before onset of signs.
- Onset—gradual; starts with weakness in the pelvic limbs, progresses to the thoracic limbs within 12–72 hours.

Neurologic Examination Findings

North American Ticks

- Neurologic signs—rapidly ascending, flaccid generalized lower motor neuron tetraparesis to tetraplegia.
- Patient becomes extremely weak to recumbent in 1–3 days, with hyporeflexia to areflexia and hypotonia to atonia.
- Pain sensation preserved, no hyperesthesia.
- Cranial nerve dysfunction—uncommon; may note facial weakness and reduced jaw tone; sometimes dysphonia and dysphagia early in the course; megaesophagus uncommon.
- Urination and defecation usually normal.
- No cardiovascular effects.
- Respiratory paralysis—uncommon in the United States; may occur if ticks are not removed; death may occur in 1–5 days.

Australian Ticks

- Neurologic signs—much more severe and rapidly progressive; ascending motor weakness can progress to tetraplegia within a few hours.
- Sialosis, depressed gag reflex, dysphonia, megaesophagus, vomiting/regurgitation.
- Sympathetic nervous system—mydriasis and poorly responsive pupils (common in cats); hypertension; tachyarrhythmias; pulmonary edema.
- Urinary bladder dysfunction may be present.
- Caudal medullary respiratory center involvement—progressive reduction in respiratory rate and increased respiratory effort.
- Respiratory muscle paralysis—much more prevalent; dogs and cats progress to dyspnea,

cyanosis, and respiratory paralysis within 1–2 days if not treated.

CAUSES

United States

- *D. variabilis*—common wood tick
- *D. andersoni*—Rocky Mountain wood tick
- *A. americanum*—lone star tick
- *A. maculatum*—Gulf Coast tick

Australia

- *I. holocyclus*—far more potent neurotoxin than that of the North American species.
- *I. cornuatus*—southern paralysis tick, occasionally causes paralysis in southern Australia.

RISK FACTORS

- Environments that harbor ticks.
- Australia—higher risk during spring, and in areas with higher rainfall, containing tree cover and areas of water; higher risk of death if dogs < 6 months old or if a toy-breed dog.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Botulism
- Acute polyneuropathy
- Acute polyradiculoneuritis (coonhound paralysis)
- Distal denervating disease
- Fulminant myasthenia gravis
- Generalized (diffuse) or multifocal myelopathy
- Intoxications (coral snake, black widow spider, lasalocid, blue and green algae)

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

Arterial blood gases—severely affected patients may show hypoventilation and respiratory acidosis (low PaO₂, high PaCO₂, low pH).

IMAGING

Thoracic radiography (*Ixodes* ticks)—megaesophagus, aspiration pneumonia, pulmonary edema

DIAGNOSTIC PROCEDURES

- History of exposure to ticks.
- Thoroughly search for a tick—head, neck, body and limbs, ear canals, mouth, rectum, vagina, prepuce, and in between the digits and footpads; clipping the entire fur may be needed; immediately remove tick.
- In some cases the offending tick may have dropped, a negative finding does not exclude tick paralysis.
- Electrodiagnostics—electromyogram; normal insertional activity without spontaneous myofiber activity; lack of motor unit action potentials; motor nerve stimulation shows a dramatic decrease in

(CONTINUED)

amplitude or a complete absence of compound muscle action potentials; decrease in motor nerve conduction velocities; normal sensory conduction and repetitive nerve stimulation.

PATHOLOGIC FINDINGS

- Pulmonary histopathologic findings in dead/euthanized dogs include diffuse bronchopneumonia, congestion, and alveolar edema.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—neurologic dysfunction suggesting tick paralysis; hospitalize until either a tick is found and removed or appropriate treatment to kill a hidden tick is performed.
- Remove tick with forceps, applying steady pressure, taking care to remove mouth parts.

NURSING CARE

- Inpatient supportive care—essential until patient begins to show signs of recovery.
- Oxygen cage—hypoventilation ($\text{PaCO}_2 < 45 \text{ mmHg}$) and hypoxia.
- Mechanical ventilation—respiratory failure ($\text{PaCO}_2 > 45 \text{ mmHg}$).
- Intravenous fluid therapy—if patient unable to eat/drink due to dysphagia, vomiting/regurgitation.
- Prevention of aspiration pneumonia—elevated feedings if megaesophagus present.

ACTIVITY

- Keep patient in a quiet environment.
- Ixodes* tick paralysis—keep patient in a cool, air-conditioned area (toxin is temperature-sensitive).

DIET

- Withhold food and water if patient has dysphagia or vomiting/regurgitation.

CLIENT EDUCATION

- Non-*Ixodes* tick—inform client that good nursing care is essential, although the patient's recovery is rapid (within 24–72 hours) after removal of ticks.
- Ixodes* tick—warn client that cranial nerve signs and weakness often continue to worsen for 24–48 hours even after tick removal; inform client that aggressive treatment to neutralize the toxin must be undertaken, and that patient death may ensue even if appropriate therapy is initiated.



MEDICATIONS

DRUG(S) OF CHOICE

- United States—if the tick cannot be found, topically apply a systemic insecticide such as fipronil or, alternatively, dip the patient in an insecticidal bath; often the only treatment needed.
- Australia—in addition to tick removal and use of topical acaricides, treatment often includes the use of commercially available tick antitoxin hyperimmune serum (TAS) to neutralize circulating toxin (0.5–1 mg/kg IV), depending on severity of clinical signs; adverse reactions to TAS administration can be reduced by premedication with atropine; if severe sympathetic signs, use of phenoxybenzamine, an α -adrenergic antagonist (1 mg/kg IV diluted in saline and given slowly over 20 minutes) can be beneficial.

CONTRAINdications

Drugs that interfere with neuromuscular transmission (e.g., tetracycline, aminoglycosides, procaine penicillin).

PRECAUTIONS

Ixodes tick—administer intravenous fluids at a slow rate to avoid further complications of pulmonary edema.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Non-*Ixodes* tick—reassess neurologic status daily after tick removal; should see rapid improvement in muscle strength.
- Ixodes* tick—monitor neurologic status, respiratory and cardiovascular functions intensively even after tick removal, because of the residual effect of neurotoxin.

PREVENTION/AVOIDANCE

- Vigilantly check for ticks up to 5–9 days after exposure.
- Frequent search for ticks in endemic areas during spring/summer months.
- Routine topical application of acaricidal solution/collar, or weekly insecticidal baths.
- Short-term acquired immunity develops after exposure to *Ixodes* neurotoxin.

POSSIBLE COMPLICATIONS

- No long-term complications if the patient survives the acute effects of the toxin.

TICK BITE PARALYSIS

EXPECTED COURSE AND PROGNOSIS

- Non-*Ixodes* tick—prognosis good to excellent if ticks are removed; recovery in 1–3 days.
- Ixodes* tick—prognosis often guarded; recovery prolonged; removal of tick does not always result in improvement; respiratory paralysis main cause of death; death in 1–2 days without treatment; 5% mortality rate reported in affected dogs, fatality rate in affected cats appears lower.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

Although humans can acquire the disease by being bitten by the same ticks (especially in Australia), tick paralysis is not transmitted to humans from affected pets.

PREGNANCY/FERTILITY/BREEDING

Unknown

SEE ALSO

- Botulism
- Coonhound Paralysis (Acute Idiopathic Polyradiculoneuritis)
- Myasthenia Gravis
- Polyneuropathies (Peripheral Neuropathies)

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Client Education Handout
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TICKS AND TICK CONTROL



BASICS

DEFINITION

- Dogs and cats are parasitized by ticks in the families *Ixodidae* and *Argasidae*.
- Arthropod ectoparasites feed only on the blood of their hosts; closely related to scorpions, spiders, and mites.
- Transmit pathogens—protozoa, bacteria, rickettsiae, and viruses.
- May cause toxicosis, hypersensitivity, paralysis, and blood-loss anemia.

PATOPHYSIOLOGY

- Blood-loss anemia—from heavy infestations.
- Damage to the integument—tick mouth parts cut through the host's skin; bites are generally painless; local irritation and infection may occur; tick adaptations exist to suppress the host response and allow ticks to feed for up to 1 week.
- Salivary secretions—neurotoxins may lead to systemic signs (tick paralysis); other pharmacologically active compounds cause impaired hemostasis and immune suppression at the tick-feeding site.
- Pathogens—acquired when ticks feed on infected reservoir hosts (often rodents and small feral mammals); transmitted while feeding on dogs and cats.

TICK BIOLOGY

- Hard ticks—four life stages: egg, larva, nymph, and adult; larvae and nymphs feed to repletion before detaching and molting; as adult female *Ixodid* ticks engorge, they may increase their weight by more than 100-fold; after detachment, females lay thousands of eggs and die; various tick stages may survive over winter, tolerate long starvation, low humidity, as well as water deprivation.
- In some species, organisms disseminate to the ticks' ovaries and transovarial transmission occurs: infected eggs hatch and produce infected larvae; in other species transstadial transmission occurs: immature ticks become infected while feeding on reservoir hosts and maintain infection through the molt from one life stage to the next.
 - Host infection occurs when infections acquired during a previous life stage are transmitted to new hosts when the next stage feeds.
 - Ticks generally acquire hosts by a passive ambush process; when a suitable host brushes against vegetation harboring questing ticks, they transfer to the host.
 - Amblyomma americanum* is unique in that it can be an active hunter and traverse distances of up to 60 feet to attack a suitable host.
 - In a unique symbiotic relationship *Ixodes scapularis* infected with *Anaplasma phagocytophylum* express an antifreeze

glycoprotein gene that enhances survival of the tick in cold weather.

SYSTEMS AFFECTED

- Skin/Exocrine
- Hemic/Lymphatic/Immune
- Musculoskeletal
- Nervous

GEOGRAPHIC DISTRIBUTION

- Strong geographic specificities exist for some tick species and their associated pathogens producing geographic prevalence of associated diseases.
- Ranges of ticks are expanding, therefore the geographic incidence of tick parasitism and infections vectored by them are expanding.
- Emergence of new tick-borne infections and co-infection has been noted and represents a strong trend.
- Expanding incidence of co-infections developing due to co-infected vector ticks or parasitism of hosts by ticks of more than one species.
- Ixodes scapularis* and *I. pacificus*—midwest, northeast, southeast, and south-central United States, and west coast, respectively.
- Rhipicephalus sanguineus*—throughout the continental United States; *R. sanguineus* is unique among hard ticks; it can survive and establish its life cycle inside dwellings and kennels at (low) household humidity (common name “kennel tick”).
- Dermacentor variabilis*—eastern seaboard and west coast.
- Amblyomma americanum*—found throughout the midwest, south-central, southeast, and parts of the northeast United States with strong range expansion.
- Amblyomma maculatum*—gulf coast states with range expansion.

SIGNALMENT

Species

- Dog and cat.
- Cats are efficient at removing ticks, but tick attachment and tick-vector diseases including Lyme disease, anaplasmosis, and cytauxzoonosis have been diagnosed in domestic felines.

SIGNS

- Attached ticks or tick-feeding cavities may be seen on the skin.
- Irritation secondary to bite.
- Petechiation secondary to infectious organisms (*Rickettsia rickettsii* invades vascular endothelium causing necrotizing vasculitis; *Anaplasma platys* causes thrombocytopenia).
- Blood-loss anemia (direct effect); thrombocytopenia, anemia, inclusion bodies in neutrophils, monocytes, RBCs secondary to infectious organisms transmitted.
- Limb/joint abnormalities secondary to infectious organisms (*Borrelia burgdorferi* and other organisms implicated in oligo- and polyarthritis).

- Cardiac—varying degrees of heart block secondary to infectious organisms (*B. burgdorferi*); rare.

- Renal—unique, generally fatal protein-losing nephropathy in dogs infected with *B. burgdorferi* linked to immune complexes associated with antigen and antibody from infection, but not related to vaccine antigen or vaccine-induced antibodies.

- Neurotoxin-induced paralysis, CNS signs develop secondary to infectious organisms (*R. rickettsii*).

- Pyogranulomatous myositis, periosteal reaction, neutrophilia, antigenic stimulation and amyloid deposition in viscera in *Hepatozoon americanum* infection in which the dog serves as the intermediate and reservoir host and the dog ingests the tick (*A. maculatum*) which is the definitive host.
- Weight loss, anemia, lethargy, fever, neutrophilia, hyperglobulinemia and hypoalbuminemia in *Hepatozoon canis* infection in which the dog serves as the intermediate and reservoir host and the dog ingests the tick (*A. americanum*) which is the definitive host.

CAUSES

Ticks—attracted to hosts by warmth, presence of carbon dioxide, physical contact, and host-associated odors.

RISK FACTORS

- Domestic animals—can be in close contact with ticks owing to encroachment of ticks into suburban environments and expansion of suburban environment into surrounding forests, prairies, and coastline areas.
- Travel—risk factor for exposure to ticks outside of a pet's normal environment.
- Risk is expanding as new cycles for maintenance of infectious organisms are emerging (and being discovered); expansion of *B. burgdorferi* in the midatlantic and southeast states may be associated with an emerging enzootic cycle involving *Ixodes affinis* ticks.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

N/A

OTHER LABORATORY TESTS

- Snappy 4Dx—in-office rapid assay for multiple vector-borne infections; detects antibodies (C₆ ELISA) induced by tick-borne infection with *B. burgdorferi*, *E. canis*, *E. ewingii*, *A. phagocytophylum* (formerly *E. equi*) and *A. platys*, as well as the insect-borne *Dirofilaria immitis*.
- Tests are sensitive and specific; *B. burgdorferi* test does not cross-react with vaccine-induced antibodies.

(CONTINUED)

- Abaxis VetScan Canine *Borrelia Burgdorferi* Antibody Test Kit—in-office visual and rapid test for qualitative detection of antibodies to *Borrelia burgdorferi* in canine whole blood, serum or plasma; uses peptides that bind antibodies elicited in response to certain *Borrelia* antigens in an amplified lateral flow sandwich assay; test is highly sensitive and specific, does not cross-react with vaccine-induced antibodies, and is very inexpensive.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient after removal of ticks.
- Removal—as soon as possible to limit time available for pathogen or neurotoxin transmission; grasp ticks close to the skin with fine-pointed tweezers and gently pull free.

NURSING CARE

Wash feeding cavity with soap and water; generally sufficient to prevent local inflammation or secondary infection.

CLIENT EDUCATION

Application of hot matches, petrolatum jelly, or other materials not only fails to cause tick detachment but allows for longer periods of attachment and feeding.



MEDICATIONS

DRUG(S) OF CHOICE

See “Prevention/Avoidance”



FOLLOW-UP

PREVENTION/AVOIDANCE

- Difficult to avoid environments that harbor ticks.
- Tick control does not always equal control of tick-borne diseases; often the goal is the perceived absence of ticks on the host animal (clinical repellence).
- Pets—there may be some period of attachment and tick feeding or live ticks may spend some time crawling on the animal after the ticks have been exposed to lethal levels of an acaricide; immature ticks of some species are very small.
- Tick-borne pathogens—may be transmitted very rapidly (viruses) or require several hours (*R. rickettsii*), less than 1 day (*A. phagocytophilum*), 1–2 days (*B. burgdorferi*), or 2–3 days (*Ehrlichia* species and *B. canis*).
- Ingestion of infected ticks makes tick control problematic for prevention of infection with *Hepatozoon* species.

Insecticides and Acaricides

- In the United States, the EPA licenses pesticides as safe and effective.
- Tick control required year-round in many areas.
- Acaricides meant only for dogs must not be applied to cats.
- Acaricidal collars—Preventic, Seresto, and Scalibor collars; contain rapid tick killers with clinical repellence: amitraz, deltamethrin, and flumethrin, respectively.
- Spot-on treatments (Frontline Top Spot, K9 Advantix, Ovitrol X-Tend spot-on, Activyl, and Vectra 3D)—gained wide use due to safety, ease of application, and owner compliance.
- Disease transmission interruption studies have been published for products containing fipronil, amitraz, and permethrin; rapid killing and clinical repellence are essential to prevent or interrupt tick feeding.
- At 4 weeks after application, efficacy in prevention of transmission of *B. burgdorferi* to dogs was 75–87.5% for fipronil (Frontline Top Spot) and 100% for permethrin (K9 Advantix and Vectra 3D); amitraz (Preventic Collar) was 100% effective at 7 days post-application.

POSSIBLE COMPLICATIONS

Tick-borne diseases or tick paralysis



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Canine babesiosis—vectored by *R. sanguineus*; *B. canis* infects canine RBCs, leading to sludging in capillaries and destruction in the spleen.
- Rocky Mountain spotted fever—vectored by *D. variabilis* and *R. sanguineus*.
- Canine monocytic ehrlichiosis—*E. canis* vectored by *R. sanguineus*; infects mononuclear cells and platelets; *E. chaffeensis* vectored by *A. americanum* infects mononuclear cells.
- Cyclic thrombocytopenia—caused by *A. platys*, the only intracellular pathogen of platelets.
- Granulocytic anaplasmosis—caused by *A. phagocytophilum* vectored by *I. scapularis* and *I. pacificus*; infects granulocytes; *E. ewingii* vectored by *A. americanum* also infects granulocytes and causes granulocytic ehrlichiosis.
- Lyme disease—vectored by *I. scapularis* and *I. pacificus*; caused by *B. burgdorferi*; associated with arthritis or syndromes leading to complete heart block, protein-losing nephropathy, and possibly neurologic abnormalities.
- American canine hepatosplenitis—caused by protozoal organism *H. americanum* after the dog ingests an infected *A. maculatum*.

- Canine hepatosplenitis—caused by protozoal organism *H. canis* after the dog ingests an infected *R. sanguineus*.
- Tick paralysis—caused by a neurotoxin; affects acetylcholine synthesis and/or liberation at the neuromuscular junction of the host animal; ascending flaccid paralysis initially affects the pelvic limbs 5–9 days after tick attachment.

VACCINES

- Currently for Lyme disease; two types for dogs: whole-cell, killed bacterin: LymeVax, Duramune Lyme, and Nobivac Lyme, and outer surface protein A (OspA): Recombitek Lyme.
- Safety and efficacy—both types have been demonstrated to be safe. Laboratory studies demonstrate high efficacy but fail to duplicate natural exposure; in an early study (1993) natural exposure study of whole-cell bacterin, incidence of disease was 1% in 1,969 immunized dogs and 4.7% in 4,498 unimmunized control dogs; in later studies (2002 and 2005) natural exposure studies the incidence of infection in dogs immunized with whole-cell bacterin and OspA subunit vaccine was determined to be 5% and 25%, respectively; bacterin had a preventable fraction of 92.2% and subunit OspA vaccine had a preventable fraction of 60.3%.
- Asymptomatic Lyme-positive dogs treated with doxycycline or amoxicillin concurrent with whole-cell bacterin immunization (author's Test, Treat and Vaccinate Protocol) and followed clinically for up to 4 years, no episodes of any forms of Lyme disease were observed (see “Further Reading for an extended list of references on vaccination studies”).

ZOONOTIC POTENTIAL

- Ticks may parasitize wildlife, domestic animals, or humans at different stages in their developmental cycles; infections acquired in early life stages may be transmitted when ticks feed again in the next stage.
- Humans, if parasitized, may be exposed to organisms in infected ticks. *B. burgdorferi*, *A. phagocytophilum*, *R. rickettsia*, and *E. chaffeensis* are also human pathogens.

SYNOMYMS

Acariasis

SEE ALSO

- Babesiosis
- Ehrlichiosis
- Hepatosplenitis
- Lyme Borreliosis
- Rocky Mountain Spotted Fever
- Tick Bite Paralysis

ABBREVIATIONS

- CNS = central nervous system
- ELISA = enzyme-linked immunosorbent assay
- RBC = red blood cell

TICKS AND TICK CONTROL

(CONTINUED)

INTERNET RESOURCES

<http://www.ct.gov/caes/search/search.asp?qu=tick+management&go.x=16&go.y=6>.

Suggested Reading

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Client Education Handout
available online

TOAD VENOM TOXICOSIS



BASICS

OVERVIEW

- Two species of primary concern—Colorado River toad (*Rhinella alvarius*) and marine or cane toad (*R. marina*); marine toad more toxic; both can be fatal.
- Toads—most active during periods of high humidity (the monsoon season of late summer in the desert Southwest for Colorado River toads); most encounters occur during the evening, night, or early morning.
- Toxin—produced from the parotid glands; defensive; rapidly absorbed across the victim's mucous membranes; contains several major components: indole alkyl amines (similar to the street drug LSD), cardiac glycosides, and noncardiac sterols.

SIGNALMENT

Primarily dogs; rarely, ferrets and cats

SIGNS

General Comments

Rapid onset

Historical Findings

- Crying and pawing at the mouth
- Frothing at mouth
- Ataxia or stiff gaited
- Seizures
- Animal found dead with toad in mouth

Physical Examination Findings

- Profuse hypersalivation
- Hyperexcitability with vocalization
- Brick red buccal mucous membranes
- Hyperthermia
- Collapse
- Marked cardiac ventricular arrhythmia—less common with Colorado River toad intoxication
- Cyanosis
- Dyspnea

CAUSES & RISK FACTORS

- Living in indigenous geographic region for toxic species and in close proximity to toads
- Moist, warm, outside environment
- Outdoor animal



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Caustics or other oral irritants

CBC/BIOCHEMISTRY/URINALYSIS

May note hyperkalemia

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Electrocardiogram—may reveal ventricular arrhythmias



TREATMENT

- Marine toad intoxication—medical emergency; death common.
- Decontamination—flush mouth with copious quantities of water for 5–10 minutes.
- Hyperthermia ($> 40.6^{\circ}\text{C}$; 105°F)—provide a cool bath; remove patient from bath once temperature reaches 39.4°C (103°F).
- Maintain airway.
- Rapid evaluation of cardiac function.



MEDICATIONS

DRUG(S)

- Atropine—0.04 mg/kg IM, SC; reduces the amount of salivation; helps prevent aspiration; use with bradycardia, heart block, or other sinoatrial node alterations as a result of the digitalis-like effect of the toxin; not recommended if severe tachycardia present.
- Esmolol or propranolol—esmolol is very short acting and may be used as a test dose. If arrhythmia responds to treatment, propranolol is used because the duration of action is much longer (hours; see “Contraindications/Possible Interactions”); rapid administration may be required to combat tachyarrhythmias; may be repeated in 20 minutes; may need continuous intravenous infusion for persistent arrhythmias.
 - Esmolol 0.05–0.1 mg/kg IV every 5 minutes for a maximum dosage of 0.5 mg/kg.
 - Propranolol 0.02 mg/kg IV slowly as needed up to a maximum dosage of 1 mg/kg.
- Anesthesia with pentobarbital (dogs)—increases tolerance to intoxication.

- Digoxin-specific Fab fragments (Digoxin Immune Fab) have been used successfully to treat toad venom induced cardiotoxic effects.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Cardiac disease or bronchial asthma—patient may not tolerate the use of beta-blockers such as esmolol and propranolol. Use a test dose of esmolol (very short duration of action) and monitor closely before using propranolol (much longer duration of action).
- Anesthetics (e.g., pentobarbital)—may depress function of an already compromised myocardium; use with caution.



FOLLOW-UP

- Continuous electrocardiographic monitoring—recommended until the patient is fully recovered.
- Colorado River toad intoxication—patients usually normal within 30 minutes of onset of treatment; death relatively uncommon if treated; do not underestimate the risk of secondary heatstroke.
- Marine toad intoxication—medical emergency; death common.



MISCELLANEOUS

Suggested Reading

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TOOTH FORMATION/STRUCTURE, ABNORMAL



BASICS

DEFINITION

Variation in Tooth Size

- Macrodontia—crown oversized, root normal
- Microdontia—crown normal shape, but small
- Peg tooth—small, cone-shaped tooth with a single cusp

Variation in Tooth Structure/Shape

- Fusion—two separate tooth buds joined to form an entire single tooth or joined at the roots by cementum and dentin.
- Gemination—developing tooth bud undergoes an incomplete split, resulting in two crowns with a common root canal.
- Dilacerated—distorted or malformed tooth (crown or root)—a general term that may be used for many different presentations.
- Dens-in-dente (tooth within a tooth)—external layers invaginate into internal structures with varying severity.
- Shell teeth—crown present, but little to no root development.
- Amelogenesis imperfecta—hereditary reduction in the amount of developed enamel matrix.

PATHOPHYSIOLOGY

- Stress or stimulus (trauma) at time of development can alter tooth formation.
- Infection, trauma to tooth buds, or traumatic extraction of deciduous teeth during permanent tooth formation can significantly alter the structure.
- Genetic or familial tendencies not known for most conditions.
- Dog/cat.

SIGNALMENT

Clinical Features

- See “Definition.”
- Fusion—fused crown will be larger than a single tooth. There will be a reduced number of teeth (two counted as one).
- Gemination tooth—actual number of teeth will be unaltered, but one tooth will be larger, with duplication of part of the crown (and possibly roots radiographically). “Siamese twin.”
- Dilacerated teeth.
 - Any variation in structure or form—extra root, curved root.

- Each tooth must be evaluated for integrity of the pulp system, as any disruption in the continuity of the crown and roots may result in exposure of the pulp to the external environment.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Trauma to tooth structures
- Developmental abnormalities

DIAGNOSTICS

- Complete oral examination.
- Intraoral radiographs.
- With any abnormal structure (dilaceration), pulpal integrity and the potential for crowding must be evaluated.
- Appropriate preoperative diagnostics when indicated prior to procedure.



TREATMENT

- Abnormal development of mandibular first molars in small-breed dogs.
- Dilaceration is more common, sometimes described as dens-in-dente.
- As one of the first permanent teeth to form, there may be a mechanical challenge (lack of space) in small dogs that impedes proper crown-root development.
- Invagination of the enamel and/or cementum at the neck of the tooth, often with some degree of gingival recession.

RADIOGRAPHIC SIGNS

- Discontinuity between crowns and roots
- Possible pulp exposure and pulp stones
- Roots are convergent with wide canals (non-vital pulp)
- Periapical/root abscession with extensive bone loss



MEDICATIONS

DRUGS

Procedures

- Appropriate antimicrobial and pain management therapy when indicated.

- Appropriate patient monitoring and support during anesthetic procedures.
- Fusion teeth—no treatment is necessary unless the groove between the two teeth and/or crowns extends to the gingival margin or below (nidus for periodontal disease).
- Gemination tooth—if tooth crowding results, extraction may be necessary.
- Dilacerated tooth—if there is pulpal exposure or compromise, extraction is generally necessary.
 - In some cases, endodontic and restorative therapy may allow preservation of the tooth.



FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS

- Good prognosis on teeth with moderate changes (peg teeth, fusion teeth, gemination tooth).
- Guarded prognosis on dilacerated teeth with pulpal compromise, though extraction typically successful.



MISCELLANEOUS

INTERNET RESOURCES

<http://www.avdc.org/Nomenclature.html>.

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Author Heidi B. Lobprise

Consulting Editor Heidi B. Lobprise



BASICS

DEFINITION

- Traumatic tooth injuries may involve fracture of enamel, dentin, and cement or damage to the periodontium.
- May involve the crown and root of the affected tooth.
- Classified as uncomplicated if they do not involve pulpal exposure and complicated if the pulp is exposed by the fracture line.

PATHOPHYSIOLOGY

- Untreated pulpal exposure invariably leads to pulpitis and eventually pulpal necrosis and periapical pathology.
- Pulpitis and pulpal necrosis may also occur with uncomplicated fractures, particularly if the fracture line is close to the pulp chamber, which exposes a large number of wide-diameter dentinal tubules and allows communication between the pulp and the external environment.

SYSTEMS AFFECTED

- Gastrointestinal—oral cavity.
- Infection in the oral cavity may cause systemic complications.

GENETICS

N/A

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dogs and cats

Breed Predilections

None

Mean Age and Range

Any age

Predominant Sex

None

SIGNS

Crown Fractures

- Clinical loss of tooth crown substance; may affect enamel only, or enamel and dentin; fracture line may be transverse or oblique.
- Uncomplicated fractures with the fracture line close to the pulp chamber—pale pink pulp is visible through the dentin; gentle exploring will not allow the explorer into the pulp cavity.
- In complicated crown fractures, the pulp chamber is open and readily accessed with an explorer.
- The fresh complicated fracture is associated with hemorrhage from the pulp.
- Older fractures may exhibit a necrotic pulp; clinically the pulp chamber is filled with dark necrotic material, and the tooth is often discolored.

Root Fractures

- May occur at any point along the root surface; often in combination with fracture of the crown, but may occur in isolation.
- Fracture line may be transverse or oblique; segments may remain aligned or be displaced.
- Clinical signs indicating a possible root fracture include pain on closure of the mouth or during open-mouth breathing.
- Abnormal horizontal or vertical mobility of a periodontally sound tooth may raise suspicion of a root fracture.

CAUSES

Generally the result of a traumatic incident (e.g., road traffic accident, blunt blow to the face, chewing on hard objects).

RISK FACTORS

Free-roaming behavior increases risk of trauma.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Crown fracture—attrition, abnormal tooth formation.
- Root fracture—luxation; definitive diagnosis of root fractures is by radiography.

CBC/BIOCHEMISTRY/URINALYSIS

Unaffected by tooth fracture.

OTHER LABORATORY TESTS

None

IMAGING

- Radiographs are mandatory.
- Intraoral radiographic technique and dental intraoral film are required.
- Radiographs reveal the full extent of the lesion and allow treatment planning.
- Radiographs are required for adequate performance of endodontic procedures and monitoring treatment outcome.

DIAGNOSTIC PROCEDURES

Transillumination to help determine tooth vitality: shine a bright light through the tooth (otoscope light); a vital tooth should transilluminate well.

PATHOLOGIC FINDINGS

Untreated pulpal exposure invariably leads to pulpitis and eventual pulpal necrosis and periapical pathology.



TREATMENT

APPROPRIATE HEALTH CARE

Depends on extent and severity of trauma to the patient.

NURSING CARE

Depends on extent and severity of trauma to the patient.

ACTIVITY

Restrict as indicated by nature of trauma.

DIET

In the immediate postoperative period (24–72 hours), moistening the patient's dry food may help decrease the chance of traumatizing the suture line. Continue to monitor the site.

CLIENT EDUCATION

A series of treatments may be necessary.

SURGICAL CONSIDERATIONS

Uncomplicated Crown Fractures

Remove sharp edges with a bur and seal the exposed dentin tubules with a suitable liner or restorative material.

Complicated Crown Fractures

All require endodontic therapy if the tooth is to be maintained; extraction is preferable to no treatment at all.

Mature Tooth

- Recent fracture in the mature tooth with the pulp still vital—two options exist, partial pulpectomy and direct pulp capping (vital pulpotomy) followed by restoration or conventional root canal therapy and restoration.
- For partial pulpectomy and direct pulp capping to succeed, the procedure should be carried out within hours of the injury.
- Tell the client at the beginning that the procedure may not be the final treatment—the tooth may require standard root canal treatment later if the pulp becomes necrotic.
- When the pulp is already chronically inflamed or necrotic, standard root canal therapy and restoration are the treatments of choice if the tooth is periodontally sound.

Immature Tooth

- A vital pulp is required for continued root development; as long as the pulp is vital the treatment of choice is partial pulpectomy and direct pulp capping, followed by restoration.
- If the pulp is necrotic, no further root development will occur; necrotic immature teeth need endodontic treatment to be maintained; remove the necrotic tissue and pack the root canal with calcium hydroxide paste; some apexogenesis (physiologic event, continued root development) and apification (closure of the apex, induced by treatment) can be stimulated if this procedure is performed; change the calcium hydroxide every 6 months until the apex is closed when a standard root canal is performed.
- Immature teeth may be present in the mature animal if trauma to the developing teeth caused pulp necrosis; treat such teeth as you would any immature teeth.

Root Fractures

- Treatment of crown and root fractures depends on how far below the gingival margin the fracture line extends.

TOOTH FRACTURE

(CONTINUED)

- If the fracture line does not involve the pulp and does not extend more than 4–5 mm below the gingival margin, restorative dentistry can be performed; if the fracture extends more than 5 mm below the gingival margin and involves the pulp, the tooth should usually be extracted.
- The fracture level determines the choice of treatment for horizontal root fractures; a fracture in the apical region carries a better prognosis than one close to the gingival margin.
- A horizontal fracture of the coronal part of the root usually mandates tooth extraction; the main exception is the lower canine, since jaw stability and strength depend on the canine roots. If the root is periodontally sound it must receive endodontic treatment after removal of the coronal portion.
- Horizontal midroot and apical fractures will heal if the tooth is immobilized; horizontal root fractures can heal by means of a dentino cemental callus, a fibrous union, or an osteofibrous union.
- If the pulp of the coronal fragment becomes necrotic the fracture will not heal; endodontic treatment of the coronal segment is indicated; the apical segment may be left in situ if there is no radiographic evidence of periapical pathology; if radiographic evidence of periapical pathology exists, remove the apical segment.



MEDICATIONS

DRUG(S) OF CHOICE

- A broad-spectrum bacteriocidal antibiotic drug for 5–7 days may be indicated, e.g., when long-standing infection is present.
- Appropriate analgesic regime – usually nonsteroidal anti-inflammatory drug for 3–5 days.

CONTRAINDICATIONS

None

PRECAUTIONS

None

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

- Check a partial pulpectomy and direct pulp-capping procedure with postoperative radiographs after 6 and 12 months, or at intervals determined by clinical signs, to detect pulp death and consequent periapical changes indicating the need for root canal treatment.
- Check the outcome of conventional root canal therapy radiographically 6–12 months postoperatively; evidence of periapical pathology at this time indicates the need for further endodontic therapy or extraction of the tooth; further endodontic therapy consists of redoing the root canal therapy, often in conjunction with surgical endodontics.
- Check root fractures radiographically 6–12 months postoperatively.
- Check uncomplicated fractures postoperatively with radiographs at 4–6 months to assess periapical status.

PREVENTION/AVOIDANCE

- Avoid situations in which teeth are likely to be damaged; keep animal from chewing on hard objects such as rocks.
- To avoid complications, institute treatment within hours of injury.

POSSIBLE COMPLICATIONS

- Untreated pulpal exposure invariably leads to pulpitis and eventual pulpal necrosis and periapical pathology.
- Arrested development of immature teeth.

EXPECTED COURSE AND PROGNOSIS

Varies with vitality of the pulp, location of the fracture, and whether the tooth is mature or immature; see "Treatment" section for detailed discussion.



MISCELLANEOUS

ASSOCIATED CONDITIONS

None

AGE-RELATED FACTORS

Treatment of mature and immature teeth differs; see "Treatment."

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

INTERNET RESOURCES

Dental fracture classification:
<http://avdc.org/Nameclature.pdf>

Suggested Reading

Gorrel C. Emergencies. In: Veterinary Dentistry for the General Practitioner, 2nd ed. Philadelphia: Saunder/Elsevier, 20132004, pp. 147–154.

Gorrel C. Pulp and Periapical Disease. In: Saunders Solutions in Veterinary Practice: Small Animal Dentistry. Philadelphia: Saunders/Elsevier, 2008, pp. 171–181.

Gorrel C, Robinson J. Endodontic therapy. In: Crossley DA, Penman S, eds., Manual of Small Animal Dentistry. Gloucestershire, UK: BSAVA, 1995, pp. 168–181.

Author Cecilia Gorrel

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Client Education Handout
available online

TOOTH LUXATION OR AVULSION



BASICS

OVERVIEW

- Luxation of a tooth can be either vertical (i.e., an intrusion or extrusion) or lateral.
- An intrusion occurs when the tooth is pushed apically into the alveolar bone. • An extrusion occurs when the tooth is dislocated vertically partially out of the alveolus.
- Lateral luxation—the affected tooth is tipped in either a labial or a palatal/lingual direction; can occur when trauma pushes the crown in one direction and the root in the opposite direction; always associated with a fracture of the lingual or labial alveolar bone plate that allows the tooth to luxate rather than fracture. • An avulsed tooth has been totally luxated from its alveolus.

SIGNALMENT

Dogs and cats

SIGNS

- Intrusion—tooth appears shorter than normal; no tooth mobility detected.
- Extrusion—tooth appears longer than normal and is mobile both vertically and horizontally. • Lateral luxation—tooth crown is displaced in either a labial or palatal/lingual direction. • Avulsion—intact tooth is totally displaced from its alveolus.

CAUSES & RISK FACTORS

- Luxation/avulsion—usually results from a traumatic incident (e.g., road traffic accident or dog fight). • The trauma causes injury to the periodontium, thus allowing abnormal tooth mobility and malpositioning. • The upper canine tooth is the most commonly luxated/avulsed tooth. • Advanced periodontitis will predispose.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Luxation—root fracture where the coronal segment is displaced • Avulsion—tooth lost due to severe periodontitis

CBC/BIOCHEMISTRY/URINALYSIS

Non-contributory

OTHER LABORATORY TESTS

N/A

IMAGING

General

- Radiographs are mandatory. • Intraoral radiographic technique and dental X-ray film are required.

Radiographic Findings

- Intrusion—narrowing of the periodontal ligament space in the apical region.
- Extrusion—widening of the periodontal ligament, especially in the apical section.
- Lateral luxation—widening and narrowing of the periodontal ligament space and fracture of the alveolar bone plate. • Avulsion—empty but intact alveolus.



TREATMENT

- Replace and fix the tooth in its normal position; bond with acrylic splints and fine ligature wire—an effective method of achieving stabilization and occlusal alignment. • Handle the avulsed tooth only by its crown and rinse gently with sterile saline solution; if severely contaminated, the tooth root can be gently cleaned with sterile gauze swabs moistened with saline. • Be gentle; tooth handling should be kept to a minimum; it is essential not to remove the periodontal ligament from the root; a viable periodontal ligament is necessary for healing.
- Replace the tooth in its bony socket; there is usually no need to remove the blood clot from the alveolus; the tooth is just firmly placed in its bony socket and fixed in that position.
- Contraindications for repositioning a luxated or avulsed tooth are deciduous teeth, severe periodontitis, caries, or resorptive lesion. • The two most important factors determining the result of treatment are the length of time the avulsed tooth has been out of its bony socket and the medium in which the tooth has been stored during this period.
- The sooner an avulsed tooth is reimplanted, the better the prognosis; optimal results are achieved if the tooth is reimplanted within 30 minutes of avulsion; do not let the avulsed tooth dry prior to reimplantation; the best medium for storing an avulsed tooth is saline; if not available, use milk. • Advise clients to place the tooth in either saline or milk and bring the affected animal in for treatment as quickly as possible.
- The appliance for fixation is usually left in place for 4–6 weeks; maintain oral hygiene during this period; a water pick or curved-tip syringe is used to flush debris from between the splint, teeth, and soft tissue; rinsing the oral cavity with chlorhexidine solution is also useful. • The appliances are removed with pliers or high-speed drill; at this stage the tooth should be stable or very slightly mobile; take radiographs; if the tooth is still loose, reimplantation has failed and it should be extracted.



MEDICATIONS

DRUG(S)

- Use of a broad-spectrum bacteriocidal antibiotic is recommended; if oral hygiene is maintained, only a short course is necessary.
- If no oral hygiene measures are possible, antibiotics may be indicated throughout the period of fixation. • Daily rinsing with 0.12% chlorhexidine gluconate solution will diminish the need for prolonged administration of antibiotics. • Appropriate analgesic regime—usually nonsteroidal anti-inflammatory drug for 3–5 days.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

None



FOLLOW-UP

- An avulsed tooth invariably develops pulpal necrosis; the tooth must receive endodontic therapy to prevent development of periapical pathology. • Best to perform endodontic therapy when the appliance is removed.
- External root resorption and ankylosis commonly follow reimplantation. • Luxated teeth often suffer pulp necrosis; check at regular intervals. • Signs of pulp pathology (e.g., tooth discoloration or radiographic evidence of periapical pathology) are indications for endodontic treatment.



MISCELLANEOUS

Suggested Reading

Gorrel C. Emergencies. In: Veterinary Dentistry for the General Practitioner, 2nd ed. Philadelphia: Saunders/Elsevier, 2013, pp. 154–157.

Gorrel C. Pulp and Periapical Disease. In: Saunders Solutions in Veterinary Practice: Small Animal Dentistry. Philadelphia: Saunders/Elsevier, 2008, pp. 171–173.

Gorrel C, Robinson J. Endodontic therapy. In: Crossley DA, Penman S, eds., Manual of Small Animal Dentistry. Gloucestershire, UK: BSAVA, 1995, pp. 168–181.

Author Cecilia Gorrel

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TOOTH—MISSING



BASICS

OVERVIEW

- Absence of tooth or teeth due to developmental conditions, not to trauma or extraction.
 - Total anodontia—absence of all teeth due to failure in development.
 - Partial anodontia—failure in development of part of the dentition (hypodontia, oligodontia—some teeth missing).
 - Edentulous—“without teeth”—but primarily due to tooth loss (e.g., end-stage periodontal disease).
- In dogs, premolars or distal molars are the most common missing teeth.
- If a deciduous tooth is missing, its permanent successor will probably not develop as well.
- If a permanent tooth is missing, and a deciduous tooth was not exfoliated and is still present, if root structure is still stable, that deciduous tooth might stay functional for a long time; lack of permanent tooth should be documented.

SIGNALMENT

- Any breed, size or gender, but smaller breeds predominate
- Some familial tendencies, breed prevalences

SIGNS

- Tooth not present (crown and root)
- Alveolar bone and gingival margin at site is regular, smooth, even slightly “scalloped” appearance
- No tooth structure present radiographically

CAUSES AND RISK FACTORS

- Dog/cat
- Total and partial anodontia—typically hereditary and may be associated with ectodermal dysplasia (rare).
- Bilateral patterns of missing teeth may be indicative of a genetic or familial tendency, as apposed to a single missing tooth.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Delayed eruption
- Unerupted teeth (see Dentigerous Cyst)
- Invulsed tooth
- Extracted or lost due to periodontal disease or trauma
- Fusion tooth—if two teeth have fused, there will be reduction in the tooth number (see Tooth Formation/Structure—Abnormal)

CBC/BIOCHEMISTRY/URINALYSIS

Typically not affected

OTHER LABORATORY TESTS

N/A

IMAGING

- Intraoral radiographs essential.
- Determine if teeth are truly missing, and/or if permanent teeth are present, if deciduous teeth are persistent/retained.
- Pre-purchase full mouth radiographs on 8–10-week-old puppies can identify if permanent tooth structures are present (though there is no guarantee they will erupt).

DIAGNOSTIC PROCEDURES

- Complete oral examination
- Appropriate preoperative diagnostics when indicated prior to procedure



TREATMENT

SURGICAL CONSIDERATIONS

- Appropriate antimicrobial and pain management therapy when indicated.
- Appropriate patient monitoring and support during anesthetic procedures.
- None indicated unless an unerupted or involved tooth is found radiographically.



MEDICATIONS

DRUGS

None indicated



FOLLOW-UP

None needed

EXPECTED COURSE AND PROGNOSIS



MISCELLANEOUS

- If multiple teeth are missing or they are missing bilaterally, there could be a familial tendency; consider removing from breeding stock.
- In some breeds (Doberman pinscher, rottweiler) or Schutzhund trained dogs, any missing teeth may be considered a serious fault, and pre-purchase radiographs on puppies may be helpful.

SEE ALSO

- Tooth Formation/Structure, Abnormal
- Dentigerous Cyst

Suggested Reading

Wiggs BW, Lobprise HB. Veterinary Dentistry: Principles and Practice. Philadelphia: Lippincott-Raven, 1997.

Author Heidi B. Lobprise

Consulting Editor Heidi B. Lobprise

TOOTH RESORPTION—CAT



BASICS

DEFINITION

Dental resorption of unknown etiology

PATHOPHYSIOLOGY

- The cause of feline tooth resorption is unknown; odontoclasts, found in the defects, cause resorption of dental hard tissue.
- Odontoclasts attach to the lacunar surface of intact dental tissue; resorption progresses and reparative bone-like or cementum-like tissue covers the excavated dentin; inflamed granulation tissue often occupies defects in the crown of the tooth.
- Most resorption occurs in the root; both external and internal resorption may take place over time, remodeling replaces dentinal tissue with bone-like or cementum-like tissues, radiographically appearing as ankylosis.

SYSTEMS AFFECTED

Gastrointestinal—oral cavity

INCIDENCE/PREVALENCE

- Nearly 50% of cats older than 5 years old will have at least one tooth affected by resorption.
- Prevalence increases with age.

SIGNALMENT

Species

Cats

Breed Predilections

Possibly Asian shorthaired, Siamese, Persian, and Abyssinian cats

SIGNS

Historical Findings

- Most affected cats do not show clinical signs; some show hypersalivation, or difficulty chewing; some cats pick up and drop food (especially hard food) when eating; others hiss while chewing.
- Some cats have behavior changes—reclusive or aggressive.

Physical Examination Findings

- A cotton-tipped applicator applied to the suspected tooth resorption (Stages 2–4) usually causes pain evidenced by jaw spasms.
- Tooth resorption can occur above or below the gingival margin; most are first noticed at the labial or buccal surface near the cementoenamel junction where the free gingiva meets the tooth surface, though root lesions usually precede these; calculus and hyperplastic gingival may obscure the lesion.
- Tooth resorption can be found on any tooth; the most common teeth affected are the mandibular third premolar and molar, followed by the maxillary third and fourth premolars.
- Under general anesthesia, the lesions are examined with a fine dental explorer which helps identify subgingival lesions at the cementoenamel junction; the furcation area is a frequent site, and the examiner must distinguish tooth resorption from disease limited to alveolar bone loss.

Classification of Tooth Resorption

- Stage 1 (TR 1): Mild dental hard tissue loss (cementum or cementum and enamel).
- Stage 2 (TR 2): Moderate dental hard tissue loss (cementum or cementum and enamel with loss of dentin that does not extend to the pulp cavity).
- Stage 3 (TR 3): Deep dental hard tissue loss (cementum or cementum and enamel with loss of dentin that extends to the pulp cavity); most of the tooth retains its integrity.
- Stage 4 (TR 4): Extensive dental hard tissue loss (cementum or cementum and enamel with loss of dentin that extends to the pulp cavity); most of the tooth has lost its integrity.
- (TR4a) crown and root are equally affected; (TR4b) crown is more severely affected than the root; (TR4c) root is more severely affected than the crown.
- Stage 5 (TR 5): Remnants of dental hard tissue are visible only as irregular radiopacities and gingival covering is complete.
- This classification is based on the assumption that tooth resorption is a progressive condition.
- See “Imaging” for additional classification scheme (Type 1–3).

CAUSES

- The etiology is unknown; likely multifactorial.
- Nutritional, inflammatory, and hereditary causes suspected.
- Hyperreactivity to inflammatory cells, dental plaque, and/or calculus; endotoxins; prostaglandins, cytokines, and proteinases are under investigation.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Oropharyngeal inflammation including caudal stomatitis

IMAGING

- Intraoral radiology is essential in making definitive diagnosis and planning treatment.
- Radiographic appearance varies from minute radiolucent defects of the tooth primarily at the cementoenamel junction to ankylosis with alveolar bone and root replacement resorption.
- Tooth resorption is also classified as Type 1–3 based on the radiographic appearance of the tooth and the periodontal ligament space.
- Type 1—a focal or multifocal radiolucency is present in the tooth with otherwise normal radiopacity and normal-appearing periodontal ligament space.
- Type 2—narrowing or disappearance of the periodontal ligament space in at least some areas and decreased radiopacity of part of the tooth.
- Type 3—features of both Type 1 and Type 2 are present in the same tooth. A tooth with this appearance has areas of normal and narrow or lost periodontal ligament space, and there is focal or multifocal radiolucency in the tooth and decreased radiopacity in other areas of the tooth.



TREATMENT

DIET

Add water to diet to soften.

CLIENT EDUCATION

Daily brushing and use of a cotton-tipped applicator applied to the gingival margin may help control plaque.

SURGICAL CONSIDERATIONS

- Stage 1 lesions—a shallow defect is noted; the lesion is minimally sensitive because it has not entered dentin; therapy includes thorough cleaning and polishing; gingivectomy and odontoplasty are adjunctive.
- Stage 2 lesions—penetrate the dentin; often require either extraction via flap exposure or crown reduction and gingival closure (see below).
- Stage 3 lesions—enters the endodontic system; require either extraction via flap exposure or crown reduction (see below).
- Stage 4 lesions—the crown is eroded or fractured with part of it remaining; gingiva grows over the root fragments, yielding a sensitive bleeding lesion upon probing; additional extraction may be needed (below).
- Stage 5 lesions—the crown is gone and scant root fragments remain; debride any inflamed areas. If the periodontal ligament is apparent (Types 1 and 3), the tooth should be surgically extracted via flap exposure.
- If the periodontal ligament is not apparent due to root replacement (Type 2), the crown can be reduced below the gingiva with a high-speed water-cooled drill followed by gingival closure over the root.



MEDICATIONS

None



MISCELLANEOUS

SYNOMYMS

- Cervical line erosion
- Chronic subgingival tooth erosion
- External odontoclastic resorptive lesions
- Feline odontoclastic resorption lesions
- FORL
- Idiopathic buccocervical erosion
- Neck lesions
- Subgingival resorative lesions

ABBREVIATIONS

TR = tooth resorption

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TOOTH ROOT ABSCESS (APICAL ABSCESS)



BASICS

OVERVIEW

- An abscess is a localized collection of pus in a cavity formed by the disintegration of tissues.
- Acute and chronic phases on the basis of severity of pain and presence or absence of systemic signs and symptoms.
- Accumulation of inflammatory cells at the apex of a non-vital tooth—periapical abscess.
- Phoenix abscess:** acute exacerbation of a chronic periapical abscess.
- An abscess spreads along the pathway of least resistance from the tooth apex, resulting in osteomyelitis and, if perforated through the cortex, a cellulitis that can burst through the skin to create a cutaneous sinus.
- Systemic spread of bacteria (bacteremia and pyemia) can affect other organ systems.
- Periodontal disease can extend to the apical region of the tooth, resulting in endodontic involvement (perio-endo lesion).
- Can involve any teeth; canines and carnassial teeth are most commonly affected.
- Can arise without the presence of bacteria (sterile abscess).

SIGNALMENT

- Dogs and cats.
- Any age can occur in deciduous and permanent dentition.
- Usually occurs in active animals that bite or chew a lot.

SIGNS

- Tooth is visibly broken with or having near pulpal exposure—90% of cases.
- Tooth may appear discolored.
- Tooth is not sensitive to percussion or cold or hot liquids or foods—note: acute tooth fracture with pulp exposure would be sensitive.
- Facial swelling: usually localized but can spread, resulting in a cellulitis.
- Cutaneous sinus exuding pus—suppurative apical periodontitis.
- Facial sensitivity may be slight but could be extensive if there is no draining.
- Animal does not want to chew, especially on the affected side (plaque and calculus may accumulate), or will bite, but release quickly instead of holding on.
- Tooth may be asymptomatic for a long time but will be affected eventually.
- Tooth may be clinically asymptomatic, yet bacteremia may be occurring.
- A deep periodontal pocket may extend to the apex of the affected tooth.
- Putrid odor.
- Tooth may be loose and painful on palpation.
- May have facial lymphadenitis.

T

- Sinusitis—maxillary sinus is most commonly affected.
- Sense of smell may be affected, especially with drug, bomb, or food-sniffing working dogs.

CAUSES & RISK FACTORS

- Any pulpal trauma: direct blow with fracture of crown; defense (fighting—canine teeth), chewing hard objects (carnassial teeth); malocclusive trauma; tug-of-war; bone plating that damaged roots.
- Bacteria—the pulp can be affected by bacteria from dental caries, exposed dentinal tubules, or extension into endodontic system.
- Thermal heat resulting in pulpal necrosis—electrical cord burns, iatrogenic caused by overpolishing during an oral hygiene procedure or use of rotary burs.
- A deep periodontal pocket, especially at the palatal root of a small dog, can involve the apex where bacteria can enter the pulp system.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Tooth resorption—radiographs show no apical lucency or abscessation.
- Squamous cell carcinoma and fibrosarcoma—rapidly growing and invasive; displace and increase mobility of the teeth.
- Cementomas—radiographically show enlarged apical roots with a thin radiolucent zone continuous with the periodontal ligament.
- Ameloblastoma—displaces and increases mobility to the teeth; slowly enlarges.
- Cysts—radiographs usually show a very large lytic area; can mimic apical abscesses, which can become cystic (radicular cysts, apical periodontal granulomas); conventional endodontic treatment is unsuccessful; primordial cyst occurs at the site of a congenitally missing tooth and radiographically has a round oval radiolucency with a thin radiopaque border.
- Dentigerous cyst—occurs from the follicular cyst of an impacted or embedded tooth (usually the first mandibular premolars in dogs); radiographs show a tooth within the cyst.
- Periapical scar—usually occurs on an endodontically treated tooth where there has been no further increase in the radiographic apical lucency after a 6-month post-treatment period.
- Normal anatomy—mental foramen can be mistaken for apical lucencies on radiographic interpretation (the middle mental foramen just apical to second mandibular premolar).

CBC/BIOCHEMISTRY/URINALYSIS

CBC may show a leukocytosis and/or a mild regenerative anemia.

IMAGING

- Key diagnostic aid—demonstrates thickening of the apical periodontal ligament; ill-defined radiolucency; shows bone loss at the apex as the lesion becomes chronic.
- As the lesion progresses, radiographic lesions consistent with osteomyelitis and cellulitis occur.
- If fistulization has occurred, can place a gutta percha cone into the sinus tract and take a radiograph to identify the affected tooth.

DIAGNOSTIC PROCEDURES

- Surgical removal of the abscess site (surgical endodontics) or extraction.
- Endodontic treatment evaluation in 6 months to a year.
- Transillumination with a strong fiber-optic light can help the clinician by distinguishing between a vital and necrotic pulp.

PATHOLOGIC FINDINGS

- Apical area has a central area of liquefaction necrosis containing disintegrating neutrophils and cellular debris, surrounded by macrophages, lymphocytes, and plasma cells; can see bacteria.
- Extension of the lesion into cancellous bone results in inflammation of the periapical bone and resorption.
- Chronic changes may develop tracts that can be lined with epithelium; osteomyelitis or cellulitis lesions may become fibrotic with a capsule (radicular cyst and/or a periapical periodontal granuloma).



TREATMENT

- Drainage and elimination of the focus of infection.
- Extraction of the tooth involved, with curettage of the apical infected area.
- Endodontic treatment of the involved tooth (surgical if lesion large).
- Chronic conditions require surgical removal of the granulation tissue and curettage of the tract.
- After treatment, cold packs on the area will help reduce inflammation.
- Complete rest for a few days.
- Give nothing hard to chew for a few days.



MEDICATIONS

DRUG(S)

- Antibiotics preoperatively to prevent systemic spread of infection.
- Broad-spectrum antibiotic postoperatively for 7–10 days.
- Analgesics preoperatively, intraoperatively, and postoperatively for 3–4 days.

(CONTINUED)

TOOTH ROOT ABSCESS (APICAL ABSCESS)

- If a surgical endodontic treatment or an extraction was performed, a protective collar may be required.

**FOLLOW-UP**

- Recheck 10 days postoperatively.
- General examination of the area; percussion to test for sensitivity, healing of the extraction

or surgical endodontic site, and integrity of the endodontic access fillings.

- Recheck in 6 months to a year; repeat radiographs to see if the lesion has resolved (in endodontic treatment).
- Avoid traumatic injuries (e.g., letting the dog chase cars, hard chew toys, stop fighting).
- Curtail bite work—avoid handler sleeves that have tears or hole in them and avoid torsion movements.

- Check the mouth regularly for any trauma to additional teeth.

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TOXOPLASMOSIS



BASICS

DEFINITION

Toxoplasma gondii—an obligate intracellular coccidian protozoan parasite that infects nearly all mammals; Felids are the definitive hosts; all other warm-blooded animals are intermediate hosts.

PATHOPHYSIOLOGY

- Severity and manifestation—depend on location and degree of tissue injury caused by tissue cysts.
- Infection—acquired by ingestion of tissue cysts in intermediate hosts or oocysts shed by felids; organisms spread to extra-intestinal organs via blood or lymph; results in focal necrosis to many organs (heart, eyes, CNS).
- Acute disseminated infection rarely fatal.
- Chronic disease—tissue cysts form; low-grade disease; usually not clinically apparent unless immunosuppression or concomitant illness allows organism to proliferate, causing an acute inflammatory response.
- Clinical disease—often associated with other infections that cause severe immunosuppression (e.g., canine distemper, FIP, and FeLV).

SYSTEMS AFFECTED

- Multisystemic—usually the same in cats and dogs.
- Ophthalmic—approximately 80% of affected cats have evidence of intraocular inflammation, most commonly uveitis.

INCIDENCE/PREVALENCE

- Approximately 30% of cats and up to 50% of people serologically positive for *T. gondii*.
- Most animals asymptomatic.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Cats more commonly symptomatic than dogs

Mean Age and Range

In one study, mean age 4 years; range 2 weeks–16 years

Predominant Sex

Male cats—more common

SIGNS

General Comments

- Determined mainly by site and extent of organ damage.
- Acute—at the time of initial infection.
- Chronic—reactivation of encysted infection; caused by immunosuppression.

Historical Findings

- Non-specific signs of lethargy, depression, and anorexia.
- Weight loss.
- Fever.
- Ocular discharge, photophobia, miotic pupils (cats).
- Respiratory distress.
- Neurologic—ataxia; seizures; tremors; paresis/paralysis; cranial nerve deficits.
- Digestive tract—vomiting; diarrhea; abdominal pain; jaundice.
- Stillborn kittens.

Physical Examination Findings

Cats

- Most severe in transplacentally infected kittens, which may be stillborn or die before weaning.
- Surviving kittens—anorexia; lethargy; high fever unresponsive to antibiotics; reflect necrosis/inflammation of lungs (dyspnea, increased respiratory noises), liver (icterus, abdominal enlargement from ascites), and CNS (encephalopathic).
- Respiratory and gastrointestinal (postnatal)—most common; anorexia; lethargy; high fever unresponsive to antibiotics; dyspnea; weight loss; icterus; vomiting; diarrhea; abdominal effusion.
- Neurologic (postnatal)—seen in < 10% of patients; blindness; stupor; incoordination; circling; torticollis; anisocoria; seizures.
- Ocular signs (postnatal)—common; uveitis (aqueous flare, hyphema, mydriasis); iritis; detached retina; iridocyclitis; keratic precipitates.
- Rapid course—acutely affected patients with CNS and/or respiratory involvement.
- Slow course—patients with reactivation of chronic infection.

Dogs

- Young—usually generalized infection; fever; weight loss; anorexia; tonsillitis; dyspnea; diarrhea; vomiting.
- Old—tend to localized infections; mainly associated with neural and muscular systems.
- Neurologic—quite variable; usually reflect diffuse neurologic inflammation; seizures; tremors; ataxia; paresis; paralysis; muscle weakness; tetraparesis.
- Ocular—rare; similar to those found in cats.
- Cardiac involvement—occurs; usually not clinically apparent.

CAUSE

T. gondii

RISK FACTORS

Immunosuppression—may predispose to infection or reactivation: FeLV, FIV, FIP, hemotropic mycoplasma, canine distemper, and glucocorticoid or antitumor chemotherapy or post-renal transplant.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Cats

- Intraocular disease (anterior uveitis)—FIP; FeLV; FIV; immune-mediated; trauma; lens-induced; corneal ulceration with reflex uveitis.
- Dyspnea (respiratory signs)—asthma; cardiogenic; pneumonia (bacterial, fungal, parasitic); neoplasia; heartworm disease; pleural disease (effusions); diaphragmatic hernia; chest wall injury.
- Neurologic (causes of meningoencephalitis)—viral (FIP, rabies, pseudorabies); fungal (cryptococcosis, blastomycosis, histoplasmosis); parasitic (cuterebriasis, coenurosis, aberrant heartworm

migration); bacterial; idiopathic disease (feline polioencephalomyelitis).

Dogs

- Often associated with other immunosuppressive diseases—e.g., signs of distemper may be seen.
- Differentiate from *Neospora* or *Sarcocystis* which are similar morphologically.
- Consider other conditions causing multifocal signs—infectious or inflammatory toxicity; metabolic disease.

CBC/BIOCHEMISTRY/URINALYSIS

CBC (Cats)

- Most show mild normocytic normochromic anemia.
- Leukopenia—approximately 50% of patients with severe disease; mainly owing to lymphopenia.
- Neutropenia—alone or in addition to lymphopenia and a degenerative left shift.
- Leukocytosis—may occur during recovery.

Biochemistry

- ALT and AST—marked increase in most patients.
- Hypoalbuminemia.
- Cats—icterus seen in approximately 25% of patients; mildly low serum calcium concentrations often seen with pancreatitis; amylase levels unreliable.

Urinalysis (Cats)

- Mild proteinuria—small proportion of patients.
- Bilirubinuria—especially with icterus.

OTHER LABORATORY TESTS

Serology

- IgM, IgG, and antigen serum titers—most definitive information from one sample; determine type of infection (active, recent, chronic) with a follow-up sample taken 3 weeks later.
- IgM—single serologic titer of choice for diagnosis of active infection; elevated 2 weeks post-infection (usually coincides with onset of clinical signs); persists for a maximum of 3 months; then falls; prolonged titer: reactivation or delay in antibody class shift to IgG (result of immunosuppression from FeLV or FIV infection or steroid therapy).
- IgG—titers rise 2–4 weeks post-infection; persist > 1 year; single high titer not diagnostic for active infection; four-fold increase over a 3-week period suggests active infection.

- Antigen—positive 1–4 weeks post-infection; because it remains positive during active or chronically persistent infections, does not add much to antibody titer results.
- A tentative antemortem diagnosis of clinical disease can be based on clinical and serologic parameters: (a) serologic evidence of recent or active infection—high IgM titers, four-fold change in IgG titers, (b) exclusion of other causes of the clinical syndrome, and (c) beneficial response to anti-*Toxoplasma* drugs.
- PCR—used to verify presence of *T. gondii* in biologic specimens; available from several laboratories.

(CONTINUED)

TOXOPLASMOSIS**IMAGING**

Radiographs—may see mixed pattern of patchy alveolar and interstitial pulmonary infiltrates, pleural and abdominal effusions, and hepatomegaly.

DIAGNOSTIC PROCEDURES

- PCR may be the most prudent choice in suspect cases since many protozoa are morphologically similar and are difficult to distinguish in tissues.
- CSF—high leukocyte count (both mononuclear cells and neutrophils) and protein in encephalopathic patients.
- Cytology—organism rarely detected in body fluids during acute infection (CSF, pleural or peritoneal effusions); bronchoalveolar lavage effective in identifying organisms in affected cats with signs of pulmonary involvement.
- Fecal—evaluation with Sheather's sugar solution may be diagnostic; fecal oocyst shedding rarely occurs during clinical disease; oocysts may be detected on routine examination in asymptomatic cats but are morphologically indistinguishable from *Hammondia* spp. and *Besnoitia*; distinguish organisms via mouse inoculation.

PATHOLOGIC FINDINGS

- Necrotic foci—up to 1 cm; most often in liver, pancreas, mesenteric lymph nodes, and lungs; necrosis of brain (1 cm areas of discoloration).
- Ulcers and granulomas—may be seen in stomach and small intestine.
- Potentially no gross lesions.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Usually outpatient.
- Inpatient—severe disease; patient cannot maintain adequate nutrition or hydration.
- Confine—patients with neurologic signs.

NURSING CARE

Dehydration—intravenous fluids

CLIENT EDUCATION

- Cats—prognosis guarded in patients needing therapy; response to therapy inconsistent.
- Neonates and severely immunocompromised animals—prognosis worse.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Clindamycin—25–50 mg/kg PO or IM daily, divided into two doses, for at least 2 weeks after clinical signs clear.
- 1% prednisone drops—every 8 hours for 2 weeks for uveitis; use concurrently.

PRECAUTIONS

Clindamycin—anorexia, vomiting, and diarrhea (dose-dependent).

ALTERNATIVE DRUG(S)

- Sulfadiazine (30 mg/kg PO q12h) in combination with pyrimethamine (0.5 mg/kg PO q12h) for 2 weeks; can cause depression, anemia, leukopenia, and thrombocytopenia, especially in cats.
- Folinic acid (5 mg/day) or brewer's yeast (100 mg/kg/day)—correct bone marrow suppression caused by sulfadiazine/pyrimethamine therapy.

**FOLLOW-UP****PATIENT MONITORING*****Clindamycin***

- Examine 2 days after initiation treatment—clinical signs (fever, hyperesthesia, anorexia, uveitis) should begin to resolve; uveitis should resolve completely within 1 week.
- Examine 2 weeks after initiation of treatment—assess neuromuscular deficits; should partially resolve (some deficits permanent owing to CNS or peripheral neuromuscular damage).
- Examine 2 weeks after owner-reported resolution of signs—assess discontinuing treatment; some neuromuscular deficits permanent.

PREVENTION/AVOIDANCE***Cats***

- Diet—prevent ingestion of raw meat, bones, viscera, or unpasteurized milk (especially goat's milk), or mechanical vectors (flies, cockroaches); feed only well-cooked meat.
- Behavior—prevent free-roaming to hunt prey (birds, rodents) or to enter buildings where food-producing animals are housed.

EXPECTED COURSE AND PROGNOSIS

- Prognosis—guarded; varied response to drug treatment.
- Acute—prompt and aggressive therapy often successful.
- Residual deficits (especially neurologic) cannot be predicted until after a course of therapy.
- Ocular disease—usually responds to appropriate therapy.
- Severe muscular or neurologic disease—usually chronic debility.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Young dogs—distemper.
- Cats—FeLV, FIP, and FIV; FIV infection does not affect clinical outcome or the ability of the animal to mount a protective immune response to subsequent reinfection; renal transplant.

AGE-RELATED FACTORS

Disease worse in neonates

ZOONOTIC POTENTIAL

- Biggest danger is infection of pregnant women or immunocompromised individuals.
- Young cats are most likely to be shedding oocysts.
- Important: oocysts need to be sporulated to be infectious. Unsporulated

oocysts are shed in the feces and need at least 24 hours to sporulate.

- Cats—healthy animals with a positive antibody titer pose little danger to humans; animal with no antibody titer at more risk of becoming infected, shedding oocysts in the feces, and constituting a risk to humans.
- Avoid contact with oocysts or tissue cysts—do not feed raw meat; wash hands and surfaces (cutting boards) after preparing raw meat; boil drinking water if source is unreliable; keep sandboxes covered to prevent cats from defecating in them; wear gloves when gardening; wash hands and vegetables before eating to avoid contact with oocyst soil contamination; empty cat litter boxes daily; disinfect litter boxes with boiling water; control stray cat population to avoid oocyst contamination of environment.
- Pregnant women—avoid all contact with a cat that is excreting oocysts in feces; avoid contact with soil and cat litter; do not handle or eat raw meat (to kill organism, cook to 66°C; 150°F).
- T. gondii* causes abortion in sheep; prevent cats from ingesting placenta or aborted fetuses and keep cats from defecating in sheep feed to break the life cycle and decrease the zoonotic potential.

PREGNANCY/FERTILITY/BREEDING

- Parasitemia during pregnancy—spread of organism to fetus; probably does not happen unless first-time infection of dam occurs during pregnancy (as with humans).
- Placental transmission rare.

ABBREVIATIONS

- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- CNS = central nervous system
- CSF = cerebrospinal fluid
- FeLV = feline leukemia virus
- FIP = feline infectious peritonitis
- FIV = feline immunodeficiency virus
- PCR = polymerase chain reaction

Suggested Reading

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Client Education Handout
available online

TRACHEAL AND AIRWAY COLLAPSE



BASICS

DEFINITION

- Static or dynamic reduction in the luminal diameter of the large conducting airway with respiration.
- Can involve the cervical trachea, the intrathoracic trachea, or both segments.
- Airway collapse (bronchomalacia) refers to collapse of lobar bronchi and smaller airways, which can be seen in conjunction with tracheal collapse (tracheobronchomalacia) or alone.
- Compression of the trachea or bronchi due to hilar lymphadenopathy or external mass lesions—not considered part of this condition.

PATOPHYSIOLOGY

- Hypocellular tracheal cartilage in the cervical region identified historically in some small-breed dogs.
- Lack of chondroitin sulfate and/or decreased glycoproteins within the cartilage matrix results in a reduction in bound water and loss of rigidity in the cartilage.
- Causes of bronchomalacia not established—cartilage abnormalities could include a mechanism similar to cervical tracheal collapse, defects in chondrogenesis, nutritional deficiencies, or degenerative changes caused by chronic airway disease.
- Collapse—weak tracheal cartilage allows flattening of the normal ring structure; trachea collapses in a dorsoventral direction when pressure fluctuates within the airway lumen. During inspiration, intrapleural pressure becomes more negative leading to a drop in intra-airway pressure. Atmospheric pressure exceeds airway pressure in the cervical region and lack of cartilage support results in cervical collapse. During forced expiration, intrapleural pressure becomes positive and exceeds intrathoracic intra-airway pressure. When cartilaginous airway walls are weakened by bronchomalacia, intrathoracic airway collapse occurs, on expiration.
- Increased tension on the trachealis dorsalis muscle or neurogenic atrophy of the muscle causes stretching of the dorsal tracheal membrane with protrusion into the airway lumen.
- Coughing—mechanical trauma to the tracheal mucosa from collapse of the dorsal tracheal membrane exacerbates airway edema and inflammation.
- Upper airway obstruction worsens clinical signs, and chronic increases in respiratory effort could lead to secondary abnormalities in laryngeal structure and function.
- Small airway disease augments the trans-airway pressure gradient and potentiates collapse in the intrathoracic region.

T

SYSTEMS AFFECTED

- Respiratory—chronic airway irritation.
- Cardiovascular—pulmonary hypertension.
- Nervous—can be involved when syncope

develops from hypoxia or a vasovagal reflex associated with cough.

GENETICS

Unknown, tracheal collapse common in small toy breed dogs.

INCIDENCE/PREVALENCE

Common clinical entity

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Primarily dog, rarely cat

Breed Predilections

Tracheal collapse—miniature poodles, Yorkshire terriers, Chihuahuas, Pomeranians, other small and toy breeds. Bronchomalacia—all breeds.

Mean Age and Range

- Middle-aged to elderly—onset of signs at 2–14 years of age
- Severely affected animals < 1 year of age.

SIGNS

Historical Findings

- Usually worsened by excitement, heat, humidity, exercise, or obesity.
- Dry honking cough.
- Often have a chronic history of intermittent coughing or difficulty breathing.
- Retching—often seen due to attempts to clear respiratory secretions from the larynx.
- Tachypnea, exercise intolerance, and/or respiratory distress—common.
- Cyanosis or syncope—seen in severely affected individuals.

Physical Examination Findings

- Increased tracheal sensitivity—virtually always seen.
- Respiratory distress—inspiratory with cervical collapse; expiratory with intrathoracic collapse.
- Stridor or musical sounds ausculted over narrowed cervical trachea.
- An end-expiratory snap—heard when a large intrathoracic airway collapses during forceful expiration then reopens.
- Crackles—due to small airway collapse or chronic bronchitis. Wheezes suggest concurrent bronchitis.
- Mitral insufficiency murmurs—often found concurrently in small-breed dogs.
- Normal to low heart rate and/or marked respiratory arrhythmia.
- Loud second heart sound—suggests pulmonary hypertension.
- Hepatomegaly—cause unknown.

CAUSES

- Unknown etiology—congenital, nutritional, or familial defects of chondrogenesis suspected.
- Chronic small airway inflammation suggested to contribute to bronchomalacia but relationship not clearly established.

RISK FACTORS

- Obesity
- Airway infection or inflammation
- Upper airway obstruction
- Endotracheal intubation



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infectious tracheobronchitis
- Tracheal or laryngeal obstruction or foreign body
- Chronic bronchitis
- Pneumonia—viral, bacterial, fungal, parasitic, eosinophilic
- Bronchiectasis

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—can show an inflammatory leukogram secondary to chronic stress or concurrent infection.
- Increased liver enzymes common.

OTHER LABORATORY TESTS

Elevated bile acids—mechanism unclear.

IMAGING

Thoracic Radiography

- Airway collapse evident on a lateral thoracic radiographic in a large percentage of dogs with airway collapse, however, the location of collapse on static radiographs agreed with the site determined by fluoroscopy in < 50% of cases.
- Inspiratory radiographs—show primarily cervical collapse and collapse at the thoracic inlet.
- Expiratory radiographs—show intrathoracic tracheal collapse; can also note collapse at the carina, ballooning of the cervical trachea, and cranial herniation of the lung lobe through the thoracic inlet.
- Right-sided heart enlargement—can be seen secondary to chronic pulmonary disease and cor pulmonale, or heart can be artificially enlarged due to obesity or breed conformation.

Fluoroscopy

Dynamic collapse of the cervical or intrathoracic trachea and/or dorsal tracheal membrane can be visible during tidal respirations—usually more easily identified after induction of cough. Cranial lung herniation through the thoracic inlet is common.

DIAGNOSTIC PROCEDURES

Caution is warranted in anesthetizing and intubating dogs with tracheal collapse because endotracheal tube irritation can worsen clinical signs. Loss of respiratory drive from anesthetic drugs or excess excitement on recovery can precipitate a crisis.

Tracheal Wash

Use oral intubation (rather than the transtracheal approach) with a small endotracheal tube and a sterile catheter when obtaining samples for cytologic examination and bacterial culture/susceptibility.

Bronchoscopy

- Grade the severity of collapse; Grade I—slight protrusion of the dorsal tracheal membrane into the airway lumen; diameter reduced by < 25%, Grade II—reduction of the tracheal lumen by 50%, Grade III—

(CONTINUED)

reduction of the tracheal lumen by 75%, Grade IV—tracheal rings flattened; < 10% of the tracheal lumen can be seen; in some cases (particularly Yorkies), a double lumen trachea is observed, where tracheal rings have bowed dorsally to contact the trachealis muscle.

- Identify small airway disease—collapse or inflammation. Submit airway samples for cytologic examination and bacterial/susceptibility; specific culture for *Mycoplasma* is recommended.

Cytology

- Unremarkable in uncomplicated tracheal or airway collapse.
- Neutrophilia without intracellular bacteria or marked bacterial growth—indicates airway inflammation.
- Sepsis and suppuration along with marked bacterial growth of a pathogen—suggests pulmonary infection.

PATHOLOGIC FINDINGS

- Dorsal trachealis muscle—elongated.
- Cartilage rings—flattened.
- Tracheal mucosal inflammation in some cases.
- Hypocellularity of the cartilage with low glycoproteins and chondroitin sulfate—can be noted via histopathologic examination or electron microscopy.
- Can also see changes associated with chronic inflammatory airway disease.

**TREATMENT****APPROPRIATE HEALTH CARE**

- Outpatient—stable patients.
- Inpatient—oxygen therapy and sedation for severe respiratory distress. Sedation and cough suppression—butorphanol ($50\text{ }\mu\text{g/kg}$ SC); addition of acepromazine ($25\text{ }\mu\text{g/kg}$ SC) can enhance sedative effects and further reduce the cough reflex.

NURSING CARE

Oxygen therapy and sedation with butorphanol and/or acepromazine for severely distressed patients.

ACTIVITY

- Severely limited until patient is stable.
- During management of disease—gentle exercise recommended to encourage weight loss.

DIET

- Many affected dogs improve after losing weight.
- Institute weight-loss program with restriction of caloric intake; use a gradual weight-loss program (1–2% weight loss per week).

CLIENT EDUCATION

- Warn client that weight gain, overexcitement, and humid conditions can precipitate a crisis.
- Advise client to use a harness instead of a collar.
- Advise owners that tracheal collapse is irreversible and that treatment strategies are designed to lessen

triggers of cough.

- For surgical candidates, advise owner of the likelihood of complications after surgery (e.g., persistent cough, respiratory distress, or laryngeal paralysis); some patients can require a permanent tracheostomy. For stent candidates, advise owners of need for extensive follow-up to avoid stent fracture, migration, or granulation tissue formation.

SURGICAL CONSIDERATIONS

- Treatment of upper airway obstructive disorders (elongated soft palate, everted laryngeal saccules)—can reduce tracheal signs.
- Placement of extraluminal C-shaped rings by a skilled surgeon in selected patients with cervical collapse will enhance quality of life and reduce clinical signs when adequate stabilization of the airway can be achieved and when bronchomalacia does not limit resolution of disease.
- Intraluminal stents are life-saving in selected cases with intrathoracic airway collapse that fail aggressive medical management.

DRUG(S) OF CHOICE

- Narcotic cough suppressants (butorphanol at $0.5\text{--}1\text{ mg/kg PO q4\text{--}8h}$ or hydrocodone at $0.22\text{ mg/kg PO q4\text{--}8h}$) used to break the cycle of cough; reduce dose rate to the least frequent administration that controls signs.
- Reduction of tracheal inflammation—prednisone (0.5 mg/kg PO q12h then 0.25 mg/kg q12h) for a total of 5–7 days may help. Inhaled steroids given via facemask and spacing chamber are preferred to avoid systemic effects of panting and weight gain.
- Sustained-release theophylline (10 mg/kg PO q12h)—thought to reduce the pressure gradient in small airways and decrease cough in dogs with intrathoracic airway collapse—bronchodilators have no effect on tracheal diameter.
- Bacterial infection uncommon but doxycycline ($3\text{--}5\text{ mg/kg PO q12h}$) is sometimes beneficial, perhaps through reduction in bacteria within the airway or reduction of inflammation.

RECAUTIONS

Avoid long-term steroid use because of the propensity for weight gain and diseases associated with immunosuppression.

POSSIBLE INTERACTIONS

Theophylline metabolism—increased by concurrent treatment with ketoconazole or phenobarbital, which results in inadequate plasma concentration; decreased by fluoroquinolones (e.g., enrofloxacin), erythromycin, cimetidine, steroids, β -blockers, mexiletine, and thiabendazole, which results in toxic plasma concentration and gastrointestinal upset, nervousness, or tachycardia; adjust dosages when concurrent use is necessary.

ALTERNATIVE DRUG(S)

Over-the-counter cough suppressants—rarely reduce cough.

TRACHEAL AND AIRWAY COLLAPSE**FOLLOW-UP****PATIENT MONITORING**

- Body weight
- Exercise tolerance
- Pattern of respiration
- Incidence of cough

PREVENTION/AVOIDANCE

- Avoid obesity in breeds commonly afflicted.
- Avoid heat and humidity.
- Use harness rather than leash.

POSSIBLE COMPLICATIONS

Intractable respiratory distress leading to respiratory failure or euthanasia.

EXPECTED COURSE AND PROGNOSIS

- Combinations of medications along with weight control can reduce clinical signs, but patient will likely cough throughout life and can suffer recurrent exacerbations of disease.
- Surgery—benefits many dogs with cervical collapse.
- Stent placement—benefits some dogs, primarily those with intrathoracic collapse. Medications usually required post-procedure.
- Prognosis—based on bronchoscopic evidence of airway obstruction and development of complications.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Chronic bronchitis.
- Laryngeal paralysis.
- Pulmonary hypertension.
- Breeds of dogs that develop tracheal collapse also commonly have mitral insufficiency.

SEE ALSO

- Bronchitis, Chronic
- Canine Infectious Respiratory Disease

Suggested Reading

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Client Education Handout available online

TRACHEAL PERFORATION



BASICS

OVERVIEW

Tracheal perforation is a loss of integrity of the tracheal wall, allowing leakage of air to create subcutaneous (SC) emphysema, pneumomediastinum, pneumopericardium, pneumothorax, and pneumoretroperitoneum. Caused by penetrating, intraluminal, or blunt cervical or thoracic trauma. Severity ranges from small perforation to complete avulsion. With complete avulsion, mediastinal tissues can form a pseudomembrane to maintain airway patency.

SYSTEMS AFFECTED

- Respiratory—compromise of airway, possible pneumomediastinum and pneumothorax.
- Cardiovascular—pneumothorax and tension pneumothorax can decrease venous return and cardiac output.
- Nervous, Musculoskeletal—depends on severity of hypoxia.
- Skin—SC emphysema, initially cervical but can affect entire body.

SIGNALMENT

Dog and cat—no breed, age, or sex predilection

SIGNS

- Onset: immediate or up to 1 week after injury.
- SC emphysema and respiratory distress are most common.
- Other signs: anorexia, lethargy, gagging, ptalism, vomiting, coughing, hemoptysis, inspiratory stridor, and shock.

CAUSES & RISK FACTORS

- Penetrating cervical wounds: bite wounds, gunshots, arrows.
- Iatrogenic perforation during transtracheal wash, jugular venipuncture, cervical surgery, radiation therapy, tracheal stent fracture, or failure to deflate cuff or to stabilize the tube while repositioning patient. Overinflation of endotracheal cuff can cause a linear tear in the trachealis muscle at thoracic inlet or intrathoracic trachea. Occurs most often with dental procedures.
- Blunt trauma can cause intrathoracic tracheal avulsion.

T



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Anesthesia—barotrauma resulting in alveolar rupture and pneumothorax.
- Penetrating wounds—perforation of esophagus or cervical bite.
- After blunt trauma—pulmonary contusions, pneumothorax, rib fractures.
- Other differentials include intrathoracic tracheal compression by mediastinal mass, spontaneous pneumothorax, pleural effusion, and bronchoesophageal fistula.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

Arterial blood gas analysis can show hypoxemia, hypercarbia, and respiratory acidosis.

IMAGING

- Lateral cervical and thoracic radiographs are essential. SC emphysema, pneumomediastinum, pneumopericardium, and pneumothorax can be seen.
- In cases of tracheal avulsion, site of disruption may be visible.
- Abdominal radiographs occasionally show pneumoretroperitoneum.
- Computed tomography can be useful to identify location and extent of tracheal damage.

DIAGNOSTIC PROCEDURES

- Tracheoscopy used to confirm tracheal perforation or avulsion and characterize severity; false-negatives can occur.



TREATMENT

- Hospitalization is indicated.
- Oxygen supplementation with 95% O₂ for 4 hours will decrease SC emphysema.
- Minimal handling to reduce stress, most cases of iatrogenic perforation will heal.
- If pneumothorax develops, thoracocentesis +/- thoracostomy tubes can be required.
- If patient decompensates, surgical exploration is indicated.
- Tracheal rupture secondary to blunt trauma or penetrating injury requires surgical repair.
- If tracheal avulsion is present, intubate only the proximal segment using an undersized endotracheal tube. Avoid positive-pressure ventilation to prevent disruption of pseudomembrane.
- Cervical tracheal perforation—approach via ventral midline, can require a partial median sternotomy. Damaged areas of trachea are often on the dorsolateral surface: debride and repair with 3-0 to 5-0 monofilament absorbable suture.
- Tracheal resection and anastomosis is indicated for severe tracheal damage or tracheal avulsion.
- Intrathoracic tracheal avulsion—approach via a right lateral 3rd or 4th intercostal thoracotomy. Open the pseudomembrane and intubate the caudal segment. Preplace sutures, guide an endotracheal tube from the cranial segment into the caudal segment, and complete repair.



MEDICATIONS

DRUG(S)

Broad-spectrum antibiotic therapy if caused by bite wounds.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Sedation—use with caution, can decrease respiratory drive.
- Corticosteroids are not indicated unless there is a large degree of upper airway swelling.



FOLLOW-UP

PATIENT MONITORING

- Monitor respiratory rate and effort, mucous membrane color, capillary refill time, pulse quality, and heart rate, and auscult frequently.
- Pulse oximetry and/or arterial blood gases.
- Thoracic radiographs to monitor pneumomediastinum, pneumothorax and help detect tracheal stenosis. Tracheoscopy required in some cases.

PREVENTION/AVOIDANCE

- Use of 3 mL syringe for cuff inflation for cats and small dogs to prevent overinflation of cuff.
- Disconnect endotracheal tube from anesthetic circuit when repositioning animal during anesthesia.

POSSIBLE COMPLICATIONS

- Tracheal stricture and stenosis at site of perforation or repair.
- Laryngeal paralysis from damage to recurrent laryngeal nerve.
- Dehiscence of tracheal anastomosis site.
- Sepsis (rare).
- Death, particularly at induction of anesthesia with complete tracheal avulsion.

EXPECTED COURSE AND PROGNOSIS

- Most cases respond well to appropriate therapy.
- Complete tracheal avulsion—guarded prognosis. Without surgery—extremely poor prognosis due to stricture formation.



MISCELLANEOUS

ASSOCIATED CONDITIONS

With tracheal perforation caused by blunt trauma, can have pulmonary contusions, pneumothorax, rib fractures, and hemothorax

PREGNANCY/FERTILITY/BREEDING

Hypoxia can result in fetal distress and death.

Further Reading

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TRANSITIONAL CELL CARCINOMA



BASICS

DEFINITION

Malignancy arising from the transitional epithelium within the kidney, ureters, urinary bladder, urethra, prostate, or vagina.

PATHOPHYSIOLOGY

The underlying etiology of TCC remains unclear. It is possible that an environmental carcinogen may initiate or promote the malignant transformation of the transitional epithelium.

SYSTEMS AFFECTED

- Renal/Urologic—the most common site affected is the trigone of the urinary bladder. Local invasion of the distal ureter is not uncommon and may lead to post-renal azotemia. The apex of the urinary bladder is more often affected in cats, although because of late detection the entire bladder is often involved by the time of diagnosis.
- Reproductive—the vagina is a possible site of primary TCC. The prostate may be involved through local invasion, or as the primary site of TCC.
- Other systems may be affected through metastases (e.g., most commonly regional lymph nodes and lungs; other sites include bone, brain, eye) or paraneoplastic syndromes (hypertrophic osteopathy has been reported secondary to TCC of the urinary bladder).

GENETICS

N/A

INCIDENCE/PREVALENCE

- < 1% of all reported malignancies in dogs
- Rare in cats

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Middle-aged to old, spayed female, small-breed dogs most commonly reported with the disease.

Species

Dog and cat

Breed Predilections

- Scottish terriers are at 18 times the risk compared to other breeds.
- West Highland white terriers, Shetland sheepdogs, Beagles, American Eskimo dogs, dachshunds.
- May occur in any breed.
- No breed predisposition in cats.

Mean Age and Range

Dogs—8 years, range 1 to 15+ years

Predominant Sex

Female

SIGNS

General Comments

- Signs are similar to those of bacterial urinary tract infection or urolithiasis.

- Consider TCC in animals showing temporary or no response to appropriate antibiotic therapy.

Historical Findings

- Complaints of recurrent stranguria, pollakiuria, hematuria, dysuria, urinary incontinence, or any combination of the above signs should initiate a search for TCC.
- Signs may temporarily respond to antibiotic therapy.

Physical Examination Findings

- Often normal.
- Occasionally, urethral thickening can be appreciated on digital rectal examination or a mass might be palpable in the caudal abdomen/urinary bladder region.
- Urethral/vaginal/prostatic TCC may be palpable on rectal examination.
- Enlarged intrapelvic or sublumbar lymph nodes can be palpable on rectal examination.

CAUSES

- Dogs—reported risk factors include obesity, environmental carcinogens, chronic exposure to organophosphates or carbamates, and (rarely) long-term or a large bolus dose of cyclophosphamide.
- Cats—unknown.

RISK FACTORS

Dogs—Scottish terrier breed, obesity, exposure to organophosphates or carbamates, cyclophosphamide therapy.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Non-neoplastic—bacterial urinary tract infection, urolithiasis, urethritis, vaginitis, prostatitis.
- Neoplastic—other primary neoplasia (e.g., squamous cell carcinoma, transmissible venereal tumor), or metastatic neoplasia (e.g., locally infiltrative prostatic carcinoma).

CBC/BIOCHEMISTRY/URINALYSIS

- CBC and biochemistry usually within normal limits.
- Biochemistry profile may show signs of renal and/or post-renal azotemia if urethral or urethral obstruction exists.
- Urinalysis may reveal epithelial cells with criteria of malignancy—caution should be exercised if the sample is inflammatory as epithelial cells may exhibit criteria of malignancy in the presence of inflammation.

OTHER LABORATORY TESTS

- Urine culture and sensitivity are indicated, as concurrent urinary tract infection is common; however, caution is advised when performing cystocentesis on patients suspected to have TCC as tumor seeding along the needle tract may occur.
- Biopsy (surgical, traumatic catheter, or cystoscopic) is gold standard for definitive

diagnosis. Even with a low yield of tissue samples of some traumatic catheterizations, typically enough cells are obtained to get a cytologic diagnosis.

IMAGING

Thoracic Radiography

- Metastatic patterns include multiple, well-defined interstitial nodules, increased interstitial pattern, and alveolar infiltrates.

Abdominal Radiography

- Unlikely to reveal specific urinary bladder disease unless the mass is mineralized (rare).
- May reveal sublumbar lymphadenomegaly or bony metastasis.

Double Contrast Cystography

- Dogs—space-occupying lesion, usually at trigone of the urinary bladder.
- Cats—space-occupying lesion, may be at the apex of the urinary bladder.
- Depending on the primary site, intravenous pyelography, voiding urethrogram, or vaginogram may be indicated.

Ultrasonography

- 2D ultrasonography is a highly sensitive imaging modality, helpful in identifying location and extent of disease; however, not a reliable method for monitoring response to therapy.
- 3D ultrasonography is a more accurate tool for monitoring tumor volume and response to therapy.

Computed Tomography

Computed tomographic imaging of TCC is the most accurate way to measure tumor volume.

OTHER DIAGNOSTIC PROCEDURES

Exploratory Laparotomy

- Used to obtain biopsies of the primary tumor and regional lymph nodes.
- Surgical cure very unlikely due to the infiltrative nature of the tumor.
- Because tumor seeding is recognized with TCC, change surgical gloves and instruments after handling the tumor.

Cystoscopy

A less invasive way to identify and biopsy TCC within the urinary bladder or urethra.

Traumatic Catheterization

Use a polypropylene catheter to traumatically obtain small tissue samples for histologic or cytologic diagnosis.

Ultrasound-Guided Biopsy

Not recommended, as seeding of the biopsy tract with viable tumor cells is a highly possible sequelae.

GROSS AND HISTOPATHOLOGIC FINDINGS

- Irregular to diffuse thickening of the urinary bladder mucosa.
- Metastasis to regional lymph nodes, lungs, and bones (i.e., vertebra, pelvis) possible.

TRANSITIONAL CELL CARCINOMA

(CONTINUED)



TREATMENT

Radiotherapy likely to become a more common option with intensity-modulated or TomoTherapy machine options.

INPATIENT VERSUS OUTPATIENT

- Initial workup and diagnosis takes 1–2 days.
- Stable patients need not be hospitalized.

ACTIVITY

Normal

DIET

Normal, unless concurrently in renal failure

CLIENT EDUCATION

- Long-term prognosis poor.
- Palliation often attainable.
- Disease not usually surgically resectable in dogs.

SURGICAL CONSIDERATIONS

- TCC is highly exfoliative and highly transplantable—multiple reports of surgically induced seeding of TCC exist.
- All surgical instruments and gloves should be replaced after contacting the tumor.
- Up to 50% of the urinary bladder can be resected with minimal loss of function.
- Tube cystostomy placement may greatly prolong survival times by bypassing urethral obstruction.
- Urethral stenting may also prolong survival by temporarily relieving obstruction.



MEDICATIONS

DRUG(S) OF CHOICE

- Piroxicam (0.3 mg/kg PO q24h with food) reported to have activity in approximately 15% of cases with a median survival of 180 days.
- Combination therapy of mitoxantrone (5 mg/m^2 IV q3 weeks) and piroxicam has a reported response rate of 35% with a median survival of 291 days.
- Metronomic (continuous, low-dose) chemotherapy with chlorambucil (4 mg/m^2 PO q24h) may play a role in the management of this disease.

CONTRAINDICATIONS

- Piroxicam—do not use in animals with known gastrointestinal erosions or ulcers, do not use in animals with renal insufficiency.

T

- Piroxicam—do not combine with cisplatin.
- Piroxicam therapy appears to be tolerated in cats, but at a reduced dosing frequency (q48h) in comparison to dogs.

PRECAUTIONS

- Animals with TCC may have renal damage either due to hydroureter, hydronephrosis, or pyelonephritis secondary to chronic urinary tract infection associated with the tumor.
- Dogs being treated with chemotherapy should be monitored for myelosuppression.
- Seek advice before initiating therapy if unfamiliar with cytotoxic drugs.

POSSIBLE INTERACTIONS

Cisplatin should not be used concurrent with other nephrotoxic drugs (e.g., aminoglycoside antibiotics).

ALTERNATIVE DRUG(S)

Antibiotics—antibiotic therapy should be administered as necessary.



FOLLOW-UP

PATIENT MONITORING

- Contrast cystography or ultrasonography every 6–8 weeks to determine disease status.
- Thoracic radiographs and abdominal ultrasound every 2–3 months to monitor for metastatic disease.

PREVENTION/AVOIDANCE

Advise client regarding frequent urination following cyclophosphamide therapy to minimize contact time with the urinary bladder mucosa.

POSSIBLE COMPLICATIONS

- Urethral or ureteral obstruction and renal failure.
- Metastatic disease to regional lymph nodes, lungs, or bone.
- Recurrent urinary tract infection.
- Urinary incontinence.
- Myelosuppression of gastrointestinal toxicity secondary to chemotherapy.
- Gastrointestinal ulceration secondary to piroxicam therapy.

EXPECTED COURSE AND PROGNOSIS

- Long-term prognosis is guarded.
- Progressive disease likely.
- Median survival: no therapy—4–6 months; with therapy—6–12 months.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Recurrent urinary tract infections
- Post-renal azotemia
- Paraneoplastic hypertrophic osteopathy

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYS

None

ABBREVIATION

- TCC = transitional cell carcinoma

Suggested Reading

Henry CJ, McCaw DL, Turnquist SE, et al. Clinical evaluation of mitoxantrone and piroxicam in a canine model of human invasive urinary bladder carcinoma. Clin Cancer Res 2003, 9:906–911.

Knapp DW, Richardson RC, Chan TCK, et al. Piroxicam therapy in 34 dogs with transitional cell carcinoma of the urinary bladder. J Vet Intern Med 1994, 8:273–278.

Naughton JF, Widmer WR, Constable PD, et al. Accuracy of three-dimensional and two-dimensional ultrasonography for measurement of tumor volume in dogs with transitional cell carcinoma of the urinary bladder. Am J Vet Res 2012, 73:1919–1924.

Schrempp DR, Childress MO, Stewart JC, et al. Metronomic administration of chlorambucil for treatment of dogs with urinary bladder transitional cell carcinoma. J Am Vet Med Assoc 2013, 242:1534–1538.

Weisse C, Berent A, Todd K, et al. Evaluation of palliative stenting for management of malignant urethral obstructions in dogs. J Am Vet Med Assoc 2006, 229:226–234.

Author Ruthanne Chun

Consulting Editor Timothy M. Fan



Client Education Handout
available online

TRANSMISSIBLE VENEREAL TUMOR



BASICS

OVERVIEW

- Sexually, or other direct contact, transmitted, naturally occurring tumor.
- Appears to be more common in temperate areas and large cities.

SIGNALMENT

Intact dogs of either sex

SIGNS

- Red, friable, lobulated mass on the mucosa of the vagina, penis or other mucous membranes.
- Oral mucosa may be affected.
- Owners may report blood dripping from the affected area or excessive licking of the genital area.
- Tumor protrusion may be noticed.

CAUSES & RISK FACTORS

- Direct transplantation of tumor cells onto abraded mucosa, either by coitus or oral transmission.
- Intact, free-roaming dogs are at greater than average risk.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other neoplasia (e.g., squamous cell carcinoma, cutaneous lymphoma).
- Vaginal hyperplasia.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually unremarkable.
- Urinalysis (free-catch) reveals hematuria and abnormal cells in some patients if the tumor is within the urogenital tract.

OTHER LABORATORY TESTS

N/A

IMAGING

- Thoracic radiographs, although this tumor type is rarely metastatic.

- Abdominal ultrasonography to evaluate mesenteric lymph nodes.

DIAGNOSTIC PROCEDURES

- Careful palpation of regional lymph nodes, and perform aspirates with cytology when clinically indicated.
- Examination of impression smears or aspirates of the tumor reveals homogenous sheets of round to oval cells with prominent nucleoli, scant cytoplasm, and multiple clear cytoplasmic vacuoles.
- Biopsy offers definitive diagnosis.



TREATMENT

- May spontaneously regress, treatment is recommended as spontaneous remissions are not reliable.
- Surgical excision of tumors is often followed by recurrence.
- Radiotherapy alone may be curative.
- Medical therapy is often curative.



MEDICATIONS

DRUG(S)

- Vincristine sulfate (0.5–0.7 mg/m² IV once weekly for 2 weeks beyond complete resolution of gross disease).
- If only partial or no remission, doxorubicin (30 mg/m² IV every 3 weeks) may be tried.

CONTRAINdicATIONS/POSSIBLE

INTERACTIONS

- Myelosuppression secondary to vincristine or doxorubicin administration.
- Doxorubicin may be cardiotoxic, use with caution once a cumulative dose of 150 mg/m² is reached.
- Tissue sloughing if either vincristine or doxorubicin is administered perivascularly.
- Seek advice before initiating therapy if unfamiliar with cytotoxic drugs.



FOLLOW-UP

PATIENT MONITORING

CBC and platelet count before each chemotherapy treatment.

PREVENTION/AVOIDANCE

- Neuter animals
- Prevent animals from roaming free

POSSIBLE COMPLICATIONS

- Tumor recurrence possible following incomplete surgical excision or re-exposure.
- Metastatic disease uncommon, but reported to occur in regional lymph nodes, eye, and spinal cord.

EXPECTED COURSE AND PROGNOSIS

Most cases of TTVT have an excellent response to therapy (primarily chemotherapy or radiotherapy) and an excellent prognosis.



MISCELLANEOUS

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

- Pregnant animals should not be treated with chemotherapy.
- Animals may be infected with TTVT during coitus.

ABBREVIATION

TTVT = transmissible venereal tumor

Suggested Reading

Ganguly B, Das U, Das AK. Canine transmissible venereal tumour: a review. Vet Comp Oncol 2013; doi:10.1111/vco.12060

Author Ruthanne Chun

Consulting Editor Timothy M. Fan

TRAUMATIC MYOCARDITIS



BASICS

OVERVIEW

- Traumatic myocarditis is the term applied to the syndrome of arrhythmias that sometimes complicates blunt trauma; it is a misnomer, because myocardial lesions (if present) are more likely to take the form of necrosis than inflammation.
- Direct cardiac injury may not be necessary for development of post-traumatic arrhythmia; extracardiac factors are likely to be etiologically important.
- The prevalence of serious arrhythmias after blunt trauma is relatively low but some patients develop clinically important rhythm disturbances; therefore, the cardiac rhythm of all victims of trauma should be carefully assessed.
- Ventricular tachyarrhythmias occur in most affected patients; supraventricular arrhythmias and bradycardias are uncommon. Ventricular rhythms that complicate blunt trauma are often relatively slow and detected only during pauses in the sinus rhythm; they are most appropriately referred to as AIVRs. The QRS complexes are wide and bizarre; the rate is > 100 bpm but generally < 160 bpm. Usually, these rhythms are electrically and hemodynamically benign.
- Dangerous ventricular tachycardias can also complicate blunt trauma and can also evolve from seemingly benign AIVRs, compromising perfusion and placing the patient at risk for sudden death.

SIGNALMENT

Dog; rarely cat

SIGNS

Historical Findings

- Trauma, most often from road accidents.
- Arrhythmias often noticed within 48 hours of trauma.

Physical Examination Findings

- Arrhythmias may be inapparent if the rate of an AIVR closely matches the sinus rate.
- Rapid, irregular rhythms in some patients.
- Signs of poor peripheral perfusion (e.g., weakness, pale mucous membranes, and weak femoral pulses) in patients with rapid, poorly tolerated ventricular rhythms.

CAUSES & RISK FACTORS

- Blunt trauma • Hypoxia • Autonomic imbalance • Electrolyte derangements
- Acid-base disturbances



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- AIVRs should be differentiated from ventricular tachycardia. • AIVRs—usually

initiated by late diastolic ventricular (escape) complexes or fusion complexes; heart rate is generally 100–160 bpm. • Ventricular tachycardia—usually initiated by a ventricular premature complex; heart rates exceed 160 bpm.

CBC/BIOCHEMISTRY/URINALYSIS

- Creatine kinase, liver enzymes, and lactic dehydrogenase often high because of organ trauma.
- High serum troponin concentrations suggest myocardial necrosis.
- Electrolyte derangements (particularly hypokalemia and hypomagnesemia) predispose to ventricular arrhythmia.

OTHER LABORATORY TESTS

N/A

IMAGING

Thoracic Radiographic Findings

Evidence of trauma, including pneumothorax, rib fractures, and pulmonary contusion in some patients.

DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

Ventricular arrhythmias, as previously discussed



TREATMENT

- Treat extracardiac conditions, including pain, electrolyte derangements, and hypoxia, which can predispose to ventricular arrhythmia.
- Thoracic radiographs for all patients with blunt trauma; identify and remedy disorders such as pneumothorax.
- The need for antiarrhythmic therapy is predicated on clinical signs and the electrocardiographic character of the arrhythmia; pharmacologic suppression of AIVR is usually unnecessary.
- Fluid therapy for shock.



MEDICATIONS

DRUG(S)

- First treat rapid ventricular rhythms or those associated with hemodynamic compromise with lidocaine (2 mg/kg boluses IV); a total of 6–8 mg/kg can be administered over 10–12 minutes. Start a lidocaine infusion (25–75 µg/kg/minute) if there is conversion to sinus rhythm, or clinically relevant slowing of rate after lidocaine boluses.
- If lidocaine administration fails to effect conversion to sinus rhythm, try procainamide, or, with caution, beta-blockers such as esmolol or propranolol, or even class III agents such as sotalol.
- Consider DC conversion while animal is under anesthesia or heavy sedation, to treat rapid, hemodynamically unstable ventricular rhythms that do not respond to drug therapy.

• Antiarrhythmic agents are not necessarily benign; they can worsen existing arrhythmias and provide a substrate for development of new arrhythmias (proarrhythmia); carefully weigh the relative risk or benefit of every contemplated intervention.

- CONTRAINdications/POSSible INTERACTIONS**
N/A



FOLLOW-UP

- ECG monitoring of animals with arrhythmias is recommended; generally, the arrhythmias that complicate blunt trauma are self-limiting and resolve within 48–72 hours.
- If antiarrhythmic therapy is deemed necessary, it can often be discontinued after 2–5 days.
- Although dangerous arrhythmias occasionally complicate blunt trauma, the prognosis usually depends on the severity of extracardiac injury.



MISCELLANEOUS

SEE ALSO

- Idioventricular Rhythm • Shock, Cardiogenic • Ventricular Tachycardia

ABBREVIATIONS

- AIVR = accelerated idioventricular rhythm
- ECG = electrocardiogram

Suggested Reading

Abbott JA. Traumatic myocarditis. In: Bonagura JD, ed., Kirk's Current Veterinary Therapy XII. Philadelphia: Saunders, 1995, pp. 846–850.

Author Jonathan A. Abbott

Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

TREMORS



BASICS

DEFINITION

Rhythmic, oscillatory, involuntary, abnormal, or normal movement of all or part of the body.

PATHOPHYSIOLOGY

Abnormal or normal movement caused by the alternate or synchronous contraction of reciprocally innervated, antagonistic muscles.

SYSTEMS AFFECTED

- Nervous
- Endocrine/Metabolic
- Musculoskeletal—muscle weakness or pain
- Behavioral—fear

GENETICS

The role of genetics in tremor syndromes is largely unknown with the exception of X-linked hypomyelination in male springer spaniels.

INCIDENCE/PREVALENCE

N/A

SIGNALMENT

- Dog and cat
- In general, any dog or cat may develop tremors. However, certain tremor syndromes have specific signalment.
- Corticosteroid-responsive tremor syndrome (generalized tremor syndrome, white shaker syndrome)—small to medium-size breed (< 15 kg), young adult dogs (< 5 years), regardless of coat color. A similar syndrome has recently been observed in 2 cats.
- Idiopathic head tremors (head bobbing)—Doberman pinschers, English bulldogs, French bulldogs, Boxers, and Labrador retrievers are overrepresented.
- Orthostatic tremors—young, adult, giant-breed dogs.
- Benign pelvic limb tremors in older dogs: terriers predisposed.
- Hypomyelination—puppies; chow chows, springer spaniels, Samoyeds, Weimaraners, and Dalmatians.

SIGNS

- Localized or generalized
- Localized—most often involves the head or the pelvic limbs

CAUSES

Tremors Primarily Affecting the Head

- Cerebellar lesions leading to intention tremors—degenerative; congenital; metabolic; infectious; immune-mediated; neoplastic; traumatic; toxic causes; vascular.
- Idiopathic head tremors (head bobbing)—unknown cause.

Tremors Primarily Affecting the Limbs

- Orthostatic tremors—unknown cause. Seen in the thoracic and pelvic limbs of young, adult, giant-breed dogs. Tremors are present

when standing and disappear in ambulating and recumbent animals.

- Compressive lesions of the spinal cord or nerve roots—lumbosacral stenosis; intervertebral disc disease; neoplasia; discospondylitis.
- Neuromuscular disease—peripheral neuropathy; neuromuscular junction abnormality; myopathy.
- Metabolic disorder causing weakness—hypoglycemia, hypoadrenocorticism, hypocalcemia, magnesium imbalance. Metabolic causes of tremors may also present as generalized tremors.
- Benign pelvic limb tremors in older dogs—unknown cause.

Generalized Tremors

- Corticosteroid-responsive tremor syndrome (generalized tremor syndrome, white shaker syndrome)—believed to be immune-mediated.
- Hypomyelination: specific defect in myelin formation unknown.
- Intoxications—metaldehyde (snail bait); mycotoxins (penitrem A and roquefortine); organophosphates; hexachlorophene; bromethalin; ivermectin; moxidectin; pyrethrins/pyrethroids; lead; 5-fluorouracil; macadamia nuts; theobromine; anatoxin-a; marijuana; zolpidem; clozapine, dysautonomia (although toxin is suspected, exact toxin is unknown); castor beans (*Ricinus communis*); carbon monoxide; many others.
- Degenerative neurologic disease—storage disease; Lafora disease; spongiform encephalopathy.
- Behavioral: fear.
- Hypothermia.

RISK FACTORS

- Presence of concurrent metabolic diseases that can cause tremors (hypoglycemia, hypoadrenocorticism, hypocalcemia, magnesium imbalance).
- Exposure to a known tremorgenic toxin.
- Exposure to fear-producing or hypothermia-inducing situations.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Differentiate tremor from constant repetitive myoclonus, seizures, and myokymia/neuromyotonia.
- Constant repetitive myoclonus—rhythmic contractions usually involving one or more pelvic limb muscles and/or muscles of mastication. Seen most often with distemper virus infection.
- Seizures—may be associated with autonomic disturbances (e.g., urination, defecation, and salivation) and alterations of consciousness.

- Myokymia/neuromyotonia—characteristic vermicular skin rippling caused by muscle contraction and often brought on by excitement or excessive stimulation.

Tremors Primarily Affecting the Head

- Assess for additional neurologic deficits suggesting cerebellar disease; intention tremors are a clinical sign of cerebellar disease; intention tremors worsen when the patient attempts to move the head in a goal-oriented manner; ataxia and dysmetria help determine the neuroanatomic diagnosis.
- Idiopathic head tremors (head bobbing)—patient usually young at onset; sporadic; up-and-down (yes) or side-to-side (no) direction; anatomic origin unknown; no other neurologic deficits present and mentation is not affected.

Tremors Primarily Affecting the Limbs

- Diseases of the lumbosacral spinal cord, cauda equina, and associated peripheral nerves; musculoskeletal diseases.
- Metabolic diseases (may also cause generalized tremors)—hypoglycemia, hypoadrenocorticism, hypocalcemia, magnesium imbalance.
- Neuromuscular disease—peripheral neuropathy; neuromuscular junction abnormality; myopathy.

Generalized Tremors

- Young dog (6–8 weeks)—congenital myelination abnormality; check breed incidences.
- Young adult dog—assess history for toxin exposure; consider corticosteroid-responsive tremor syndrome (generalized tremor syndrome, white shaker syndrome) in young, small-breed dogs.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal with associated primary brain disease.
- Assess for metabolic disease; may find hypoglycemia, hypocalcemia, magnesium imbalance, pattern consistent with hypoadrenocorticism.
- Some myopathies are characterized by high CK, AST, and ALT.

OTHER LABORATORY TESTS

If tremors are affecting the limbs and weakness is suspected, consider testing for hypoadrenocorticism (ACTH stimulation test) and myasthenia gravis (acetylcholine receptor antibody titer).

IMAGING

- Localized to the pelvic limbs—survey radiography, CT, and/or MRI of the vertebral column and spinal cord from L4 to S3.
- Generalized tremors—in hypomyelination, MRI may reveal lack of myelin; in corticosteroid-responsive tremor syndrome (generalized tremor syndrome, white shaker syndrome) MRI usually normal.
- Intention tremor—MRI of the brain, with special attention to the cerebellum.

TREMORS

(CONTINUED)

DIAGNOSTIC PROCEDURES

- CSF analysis—sensitive but nonspecific; in corticosteroid-responsive tremor syndrome (generalized tremor syndrome, white shaker syndrome) mild mononuclear pleocytosis, but CSF may also be normal; in other encephalitides involving the cerebellum, results vary with cause of disease and duration.
- Electromyography of hind limb muscles—may help diagnosing neuromuscular disease if pelvic limb tremor.

PATHOLOGIC FINDINGS

Dependent on underlying cause of tremor.



TREATMENT

- Treat the underlying primary disease.
- Outpatient, unless surgical treatment is indicated (lumbosacral disease that requires decompression and stabilization).
- Avoid excitement and exercise—may worsen many tremors.
- Degenerative neurologic diseases (e.g., storage disease, spongiform encephalopathy)—no treatment available.
- Hypomyelination—generally not treatable; some breeds improve with maturity (e.g., chow chows).
- Idiopathic head tremors (head bobbing)—no effective treatment available; benign tremor that occurs sporadically; has few health consequences.
- Suspected intoxication—remove patient from further exposure; consult with a poison control center for possible antidote.



MEDICATIONS

DRUG(S) OF CHOICE

- Usually do not respond to antiepileptic drugs (e.g. phenobarbital or diazepam).
- Tremors associated with some toxicities, especially metaldehyde (snail bait), may be treated with methocarbamol (dogs: 50–150 mg/kg IV, maximum dose 330 mg/kg in 24h) and appropriate decontamination.
- Corticosteroids—immunosuppressive dose to treat corticosteroid-responsive tremor

syndrome (generalized tremor syndrome, white shaker syndrome)

- Antibiotics—for discospondylitis; choose on the basis of culture and sensitivity of the lesion, blood, or urine.
- Cerebellar diseases—depends on the underlying etiology.
- Gabapentin—5–20 mg/kg up to q8h may be helpful in treatment of some tremors.

CONTRAINDICATIONS

Sympathomimetic drugs—may worsen condition.

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Monitor the primary disease
- Corticosteroid-responsive tremor syndrome (generalized tremor syndrome, white shaker syndrome)—monitor weekly initially to assess response to treatment.

PREVENTION/AVOIDANCE

Prevent re-exposure in the cases of toxicity.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

- Idiopathic head tremors (head bobbing)—excellent prognosis, no treatment needed.
- Orthostatic tremors—slowly progressive; disappear when patient ambulates or when patient is recumbent.
- Benign pelvic limb tremors in older dogs—can be slowly progressive; disappear when patient ambulates or when patient is recumbent.
- Hypomyelination—may stabilize and even improve as animal ages.
- Corticosteroid-responsive tremor syndrome (generalized tremor syndrome, white shaker syndrome)—most respond to corticosteroid therapy; some may need low-dose corticosteroid therapy indefinitely.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Shaking
- Shuddering

SEE ALSO

- Cerebellar Degeneration
- Hypomyelination
- Shaker/Tremor Syndrome (Corticosteroid Responsive)
- Head Bobbing
- See “Causes”

ABBREVIATIONS

- CNS = central nervous system
- CSF = cerebrospinal fluid
- CT = computed tomography
- MRI = magnetic resonance imaging

Suggested Reading

De Lahunta A, Glass E, Kent M.

Uncontrolled Involuntary Skeletal Muscle Contractions. In: Veterinary Neuroanatomy and Clinical Neurology, 4th ed. St. Louis, MO: Saunders Elsevier, 2015, pp. 509–524.

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Author Philip Schissler

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**Client Education Handout
available online**

TRICHINOSIS



BASICS

OVERVIEW

- The life cycle of the nematode *Trichinella* is unusual—the intermediate host and the definitive host are the same animal.
- Adults infect the small intestine of a wide range of carnivores (including dogs and people) and omnivores (pigs, rodents), causing mild GI disease.
- Larvae—burrow into the intestine, gain access to the bloodstream, and encyst in skeletal muscle throughout the body.
- Encysted larvae are infective for the next host.
- Of major zoonotic importance—humans obtain infection by eating poorly cooked meat containing sequestered larvae from a wide range of animals (pigs, bears, seals, horses).
- Causes severe myositis and sometimes death in humans.
- In China—eating dog meat is an important source of trichinosis in humans.
- Worldwide distribution.

SIGNALMENT

- Hunting dogs (including those that fox hunt)—high rate of infection.
- Puppies—more susceptible to infection than older dogs.

SIGNS

- Mild GI upset—vomiting, diarrhea.
- Myalgia, muscle stiffness—mild and rarely observed.
- Cardiac infection can result in syncope due to conduction disturbances.
- Non-healing ulcerative skin lesion in a cat—rare.

CAUSES & RISK FACTORS

- Trichinella spiralis*—dogs and cats become infected by eating L1 larvae sequestered in the muscle of other animals. *Trichinella nativa*—reported to cause a non-healing ulcerative skin lesion in a cat.
- Sources of infection—wild-caught rodents or the carcasses of carnivores; dogs: foxes, opossum, raccoons, and wild pigs.
- L1 larvae—molt to adults in the small intestine.
- Adult worms—produce large numbers of “pre larvae,” which are injected into the intestinal mucosa.
- Pre larvae—migrate via lymphatics initially, then the bloodstream to skeletal muscles

where they coil up and develop to L1 in cyst-like structures.

- L1 larvae—remain infective in the muscle for months to years.
- Ingestion of large numbers of larvae—results in same degree of muscle sequestration as very small infections because most infecting larvae in large infections pass right through the GI tract without developing to adults.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other causes of mild transient gastroenteritis—dietary indiscretion; early inflammatory bowel disease; drugs (antibiotics); parasites (giardiasis, trichomoniasis, whipworms); infectious agents; partial foreign body (hair balls in cats).

CBC/BIOCHEMISTRY/URINALYSIS

CBC—eosinophilia during acute stage of infection; may persist for several weeks in severe infections.

OTHER LABORATORY TESTS

- Identification of the small adults (female 3 mm, male 1.5 mm) in the feces—may require examination of feces collected over time.
- Adults and larvae in feces—distinguished from the larvae of *Crenosoma*, *Angiostrongylus*, and *Filaroides* by the stichosome esophagus (both adults and larvae), copulatory lobes (male), and presence of pre larvae within the uterus (female).
- May identify pre larvae in blood (100 µm as opposed to the ~300 µm of larvae of *Dirofilaria immitis* and *Dipetalonema reconditum*)—by modified Knot's technique.
- The meat industry has utilized squash preparations of tissue to search for encysted larvae.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Muscle biopsy—diagnostic method of choice; L1 larvae with characteristic stichosome esophagus in “cysts.”



TREATMENT

- No specific treatment required for GIT signs or myalgia.

- Albendazole—shown to significantly reduce muscle larval forms.
- Because of the efficacy of albendazole, fenbendazole is likely to be efficacious with no side effects.



MEDICATIONS

DRUG(S)

- Fenbendazole 50 mg/kg PO q24h for 10 days.
- Albendazole 50 mg/kg PO q12h for 7 days.

CONTRAINdications/POSSIBLE INTERACTIONS

Albendazole—has been shown to cause myelosuppression in cats and dogs at these doses.



FOLLOW-UP

If using albendazole—monitor CBC for signs of pancytopenia.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Trichinosis is common throughout the world. Human infection is associated with ingestion of undercooked pork, bear, and horse. Freezing of pork products for 20 days is typically adequate to kill *T. spiralis* in pork; however, this method may not be sufficient for species of *Trichinella* infecting bears and other wildlife.

ABBREVIATIONS

- GI = gastrointestinal
- GIT = gastrointestinal tract

Suggested Reading

- Saari S, Airas N, Nareaho A, et al. A nonhealing ulcerative skin lesion associated with *Trichinella nativa* infection in a cat. J Vet Diagn Invest 2008; 20:839–843.
Sleeper MM, Bissett S, Craig L. Canine trichinosis presenting with syncope and AV conduction disturbance. J Vet Intern Med 2006; 20:1228–1231.

Author Matt Brewer

Consulting Editor Stephen C. Barr

TRICHOMONIASIS



BASICS

OVERVIEW

- Enteric pear-shaped motile flagellated protozoa similar to *Giardia*—inhabits the large intestine of cats. Similar organisms live in the intestinal tract of a variety of mammals.
- One species, *Tritrichomonas blagburni*, causes diarrhea in cats.
- Co-infection with *Giardia*—common.

SIGNALMENT

Young cats—usually under 1 year (range: 3 months–13 years). Catteries have a particularly high prevalence.

SIGNS

Cats

- Intermittent large bowel diarrhea.
- Diarrhea occasionally contains blood and mucus.
- Anus—may become edematous, erythematous, and painful in kittens.
- Rectal prolapse—if anal irritation becomes severe.
- Diarrhea—improves with antibiotic treatment but reoccurs when treatment stops.
- Median length of time of diarrhea is about 9 months, with resolution in most cats by 2 years.
- Persistence of infection after the resolution of diarrhea is common.

CAUSES & RISK FACTORS

- Tritrichomonas blagburni*—causes diarrhea in cats.
- T. blagburni*—high prevalence in catteries and show cats, but very low in feral or indoor cats.
- Pathogenic factors leading to infected cats developing diarrhea—endogenous bacterial flora, adherence of parasite to host epithelium, and cytotoxin and enzyme elaboration.
- Parasites colonize the terminal ileum, cecum, and colon—leads to large bowel diarrhea.
- Pentatrichomonas* spp. (family: Trichomonads)—inhabit the large intestine of cats, dogs, and humans. Non-pathogenic in dogs and cats—except very rarely when it may become an opportunistic pathogen.
- T. foetus*—causes infertility and abortion in cattle.

T



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Cats

Dietary indiscretion; inflammatory bowel disease; neoplasia (especially GI lymphoma); drugs (antibiotics); toxins (lead); parasites (cryptosporidiosis, *Giardia*, hookworms, roundworms); bacterial agents (salmonellosis, GI bacterial overgrowth, clostridia); systemic organ dysfunction (renal, hepatic, pancreatic, cardiac); metabolic (hyperthyroidism).

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal—may reflect diarrhea

OTHER LABORATORY TESTS

- Direct fecal smear—low sensitivity.
- Method—dilute fresh feces 50:50 in saline, cover slip, examine at 40X objective with condenser lowered to increase contrast.
- Distinguish from *Giardia* (concave ventral disc, spiral forward motion)—*T. blagburni* has jerky forward motion, spindle-shaped, undulating membranes.
- T. blagburni* trophozoites—are not seen on fecal flotation.
- T. blagburni* trophozoites—will not survive refrigeration.
- Fecal protozoal culture—use commercial media in a 37°C incubator (In Pouch TF, Biomed Diagnostics, San Jose, CA).
- Method—inoculate with 0.05 g of fresh feces, examine for motile trophozoites daily for 12 days.
- Giardia* and *P. hominis*—do not grow after 24 hours in In Pouch culture system.
- PCR—more sensitive than fecal culture in cats and commercially available.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Essential to rule out coexisting disease (cryptosporidiosis, giardiasis, bacterial), especially if diarrhea persists after specific treatment.

- Treatment may decrease the severity of diarrhea but may also cause prolongation of time to resolution of diarrhea.



MEDICATIONS

DRUG(S)

- P. hominis*—metronidazole (20 mg/kg, PO q12h for 7 days).
- T. blagburni*—All attempted drug treatment protocols to date have failed.

CONTRAINdications/POSSIBLE INTERACTIONS

- Glucocorticoids may exacerbate clinical disease.
- High doses of metronidazole (usually > 30 mg/kg) for extended periods may cause neurologic signs.



FOLLOW-UP

- Most cats spontaneously resolve their diarrhea but may take years (range: 4 months–2 years).
- Relapses of diarrhea are common and often precipitated by dietary changes, stress of travel, and treatments of other conditions.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Possible zoonotic transmission should be discussed with owner.

ABBREVIATIONS

- FIP = feline infectious peritonitis
- GI = gastrointestinal
- PCR = polymerase chain reaction

Suggested Reading

Stockdale HD, Dillon AR, Newton JC, et al. Experimental infection of cats (*Felis catus*) with *Tritrichomonas foetus* isolated from cattle. Vet Parasitol 2008, 154:156–161.

Author Matt Brewer

Consulting Editor Stephen C. Barr

TRIGEMINAL NEURITIS, IDIOPATHIC



BASICS

OVERVIEW

Sudden bilateral paralysis of trigeminal mandibular branches resulting in inability to close the mouth. Lesions are characterized by extensive nonsuppurative trigeminal neuritis, demyelination, and rare axonal degeneration affecting all portions of the trigeminal nerve and ganglion without brainstem involvement.

SIGNALMENT

- Primarily adult dogs
- Rare in cats

SIGNS

- Acute onset of a dropped jaw.
- Inability to close the mouth.
- Drooling.
- Difficulty in prehending food, messy eating.
- Swallowing is intact when food and water are placed in the caudal portion of the mouth.
- Approximately one-third of affected dogs will exhibit decreased facial sensation.
- Few dogs have sympathetic involvement of the head (Horner's syndrome).
- Long-term muscle atrophy depending on degree of axonal involvement.

CAUSES & RISK FACTORS

Unknown; auto-immune disorder suspected



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Musculoskeletal disorders of the temporomandibular joints and jaw—differentiated by history of trauma, pain, and physical examination findings.
- Rabies—always initially consider until there is sufficient evidence to rule it out.
- Encephalitis involving the motor nuclei of bilateral trigeminal nerve.

- Neoplasia—involve both mandibular nerves with myelomonocytic leukemia, lymphoma, and neurofibrosarcoma reported; usually does not have an acute onset.
- Masticatory muscle myositis—presentation excludes this condition characterized by trismus and difficulty/inability to open the mouth (“locked jaw”).

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

N/A

IMAGING

MRI—diffuse enlargement of affected nerves that appear isointense to hyperintense on T2 weighted images if edema is present; contrast enhancement on post-contrast T1-weighted images.

DIAGNOSTIC PROCEDURES

- No specific test.
- Skull radiography, MRI, CSF, and muscle biopsy—to rule out differentials.



TREATMENT

- Recovery within 2–3 weeks of onset. Supportive treatment necessary during this period.
- Outpatient if owner is able to help the patient eat and drink.
- Patient cannot prehend or move food and water to the throat but can swallow if the bolus is placed in the caudal portion of the mouth and the jaw is manually held closed. Water and slurry food can also be placed, with a syringe, in the corner of mouth with the head slightly elevated.
- Fluids—subcutaneously if oral support insufficient.
- Esophagostomy or gastrostomy tubes—rarely necessary to maintain adequate food intake.



MEDICATIONS

DRUG(S)

Corticosteroids not indicated as there is no evidence that they improve recovery. Furthermore, side effects (polyuria and polydipsia) can make management difficult.



FOLLOW-UP

- Self-limiting disorder.
- Full recovery in 2–3 weeks.
- Bilateral symmetrical masticatory muscle atrophy but without trismus.



MISCELLANEOUS

SYNONYMS

- Dropped jaw
- Trigeminal neuropathy
- Mandibular paralysis

ABBREVIATIONS

- CSF = cerebrospinal fluid
- MRI = magnetic resonance imaging

Suggested Reading

Mayhew PD, Bush WW, Glass EN.

Trigeminal neuropathy in dogs: A retrospective study of 29 cases (1991–2000).
J Am Anim Hosp Assoc 2002, 38:262–270.

Author Mylène-Kim Leclerc

Consulting Editor Joane M. Parent

Acknowledgment The author and editors acknowledge the prior contribution of T. Mark Neer.

TULAREMIA



BASICS

OVERVIEW

- *Francisella tularensis*—small Gram-negative coccobacillus; type A, more virulent, found in rabbits and ticks; type B, waterborne, found in rodents and ticks; in North America principally found in wild lagomorphs (cottontail, jack, snowshoe) and rodents (moles, squirrels, muskrats, beavers); facultative intracellular parasite; survives and grows in liver-producing granulomas and/or abscesses.
- Peak occurrence—late spring; June—August; December.
- Northern hemisphere—absent from United Kingdom, Africa, South America, Australia; in United States most cases found in Missouri, Alaska, Oklahoma, South Dakota, Tennessee, Kansas, Colorado, Illinois, Utah, and Maine. Cases occurring in wildlife in Gateway National Recreation Area in New York City and New Jersey.
- Increasing number of tularemia outbreaks in regions of Europe outside the classic endemic areas in recent years has prompted renewed interest in this rare infectious disease.
- Infection—ingestion of tissue or body fluids of an infected mammal or contaminated water; bitten by blood-sucking arthropod (tick), flies, mites, midges, fleas, or mosquitoes; few bacteria needed to infect cats through skin, airways, or conjunctiva; larger number required to infect through the gastrointestinal tract.
- Skin contact—organism multiplies locally (papule) 3–5 days after contact; ulcerates 2–4 days later; spreads via lymphatics to regional LN and bloodstream; results in septicemia (lung, liver, spleen, LN, bone marrow).
- Ingestion—may involve lymphadenopathy of cervical and mesenteric LN followed by septicemic spread; distribution of lesions to face, oral cavity, tonsils, intestines, and LN.
- Acute disease—2–7 days after contact with organism.
- Tularemia has a high aerosol-related infection rate, low infectious dose, and the ability to induce fatal disease.
- *F. tularensis* is considered a potential biologic warfare agent; occurrence of a cluster of pneumonia cases in companion animals may indicate animals as sentinels and the potential risk for human disease.

T

SIGNALMENT

- Cat—occasionally
- Dog—rarely (dogs in oral contact with diseased wildlife or carcasses may act as “living fomites” to contaminate in-contact humans).

SIGNS

- Sudden onset of anorexia, lethargy, fever (40–41°C; 104–106°F).

- Enlarged palpable submandibular and cervical LN.
- Tender abdomen, palpable mesenteric LN, hepatomegaly—depending on stage of disease.
- Multifocal white patches or ulcers along glossopalatine arches and tongue.
- Icterus.

CAUSES & RISK FACTORS

- Organism—all *Francisella* biogroups may infect cats but may differ in virulence; some cats may have mild infection.
- Hunter or outdoor cats in endemic areas.
- Infected wildlife in the area of hunting activity.
- Exposure to infected blood-sucking parasites.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Any acute disease state manifested by acute lymphadenopathy, malaise, oral ulceration, and fatal outcome—consider tularemia.
- Pseudotuberculosis (*Yersinia pseudotuberculosis*)—usually vomiting and diarrhea.
- Babesiosis, Babesia, Theileria, in dogs and cats.
- Calicivirus in cats.
- Feline immunodeficiency virus.
- Toxoplasmosis, in cats

CBC/BIOCHEMISTRY/URINALYSIS

- Initially severe panleukopenia; then leukocytosis with left shift, toxic neutrophils, thrombocytopenia.
- Hyperbilirubinemia.
- Hyponatremia.
- Hypoglycemia.
- Alanine aminotransferase—elevated.
- Bilirubinuria.
- Hematuria.

OTHER LABORATORY TESTS

Serology with tube agglutination or ELISA—possible; difficult to perform except in reference laboratory; all animals do not necessarily respond serologically to infection.

DIAGNOSTIC PROCEDURES

- Direct smear—lesion or biopsy; difficult to see organism on Gram staining.
- Cultural isolation—by reference laboratory only; blood, pleural fluid, LN aspirate onto cysteine- or cystine-containing media; not recoverable on routine laboratory media; bacteria do not need CO₂ for growth.
- **Caution:** use extreme care when working with infected specimens or isolates due to low infectious dose.
- Direct fluorescent antibody testing—clinical materials or tissues; rapid assay of infection status.
- Molecular testing of tissues in laboratories having validated diagnostic protocols.

PATHOLOGIC FINDINGS

- Multifocal white patches or ulcers along glossopalatine arches and tongue.
- Oral, tonsillar ulceration.
- Lymphadenopathy of cervical, retropharyngeal, or submandibular LN with abscessation.
- Diffuse intestinal lesions.
- Mesenteric lymphadenopathy, hepatosplenomegaly, and icterus.



TREATMENT

- Inpatient with good nursing care; infection control protocols VERY important due to low infectious dose/zoonotic nature of disease.
- Early treatment important to prevent high mortality; treatment often unsuccessful.
- Treat for ectoparasites.



MEDICATIONS

DRUG(S)

Treat all cases empirically until laboratory confirmation obtained.

Cats

- Little information available on the efficacy of antimicrobials **because of high mortality if patient not treated early.**
- Early treatment with amoxicillin (20 mg/kg PO q8h for 5–7 days or 20 mg/kg IM or SC q12h for 5 days) in combination with gentamicin (4.4 mg/kg IM or SC q12h once and then q24h thereafter until a clinical response or until 7 days) has been successful.
- Fluoroquinolones are showing promise as a potential new treatment drug (ciprofloxacin).



FOLLOW-UP

PATIENT MONITORING

Monitor for DIC—may occur late in the infection

PREVENTION/AVOIDANCE

- Travel with pet—avoid endemic areas.
- Endemic areas—confine animals to control exposure to and ingestion of wildlife and their ectoparasites (ticks); ectoparasite control by periodic spraying or dusting of animal and pastures.
- Neuter cats—limit hunting behavior and wildlife exposure.
- Take precautions to limit contamination of food and water with carcasses of infected wildlife.

EXPECTED COURSE AND PROGNOSIS

Prognosis poor if not treated early; prognosis poor if mesenteric LN palpable.

(CONTINUED)

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

- Extremely high.
- All personnel in contact with patient or body fluids must use face mask, gloves, and gowns to avoid infection.
- Isolate patients.
- In emerging disease areas, cat ownership is a disease risk for humans.
- Bites and scratches pose a risk for humans.
- Do not mistake for bite abscess in cats or Plague.

SYNONYMS

- Rabbit fever
- Deerfly fever
- Market men's disease

ABBREVIATIONS

- DIC = disseminated intravascular coagulation
- ELISA = enzyme-linked immunosorbent assay
- LN = lymph node(s)

INTERNET RESOURCES

- <http://www.cfsph.iastate.edu/DiseaseInfo/disease.php?name=tularemia&clang=en>
- <http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/msds68e-eng.php>
- <http://www.cdc.gov/tularemia/>
- <http://www.bt.cdc.gov/agent/tularemia/>
- <http://www.bt.cdc.gov/agent/tularemia/tularemia-biological-weapon-abstract.asp#4>

Suggested Reading

Foley JE, Nieto NC. Tularemia. Vet Microbiology 2010, 140:332–338.

Gliatto JM, Rae JF, McDonough PL, Dasbach JJ. Feline tularemia on Nantucket Island, Massachusetts. J Vet Diagn Invest 1994, 6:102–105.

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Author Patrick L. McDonough

Consulting Editor Stephen C. Barr

TYZZER DISEASE



BASICS

OVERVIEW

- *Clostridium piliformis* (formerly *Bacillus piliformis*)—Gram-negative bacterium; 0.5 × 10–40 µm in size; an obligate intracellular pathogen.
- Infection—organism thought to initially proliferate in intestinal epithelial cells; spreads to the liver via the hepatic portal vein; hepatic colonization associated with multifocal periportal hepatic necrosis; occasional spread to other organs (focal myocarditis, enteric lymphadenitis).

SIGNALMENT

- Dogs and cats
- Any age; young at higher risk

SIGNS

- Rapid onset of lethargy, depression, anorexia, abdominal discomfort, hepatomegaly, and abdominal distention; followed by hypothermia. Death—within 24–48 hours.
- Fecal matter—diarrhea infrequent; small amounts of pasty feces more common.

CAUSES & RISK FACTORS

- *C. piliformis*.
- Contact with rodents—may be a risk factor.
- Neonates and immunocompromised animals (e.g., distemper, FeLV, feline panleukopenia, familial hyperlipoproteinemia)—seem to be at greatest risk.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Diagnosis usually made at necropsy—rapid and highly fatal disease diagnosis.

- Distinguished from other causes of sudden death and acute hepatitis.
- Other causes of acute enterocolitis in kittens.

CBC/BIOCHEMISTRY/URINALYSIS

ALT—marked elevations in blood samples taken shortly before death.

OTHER LABORATORY TESTS

- Serology—identify latent infections in rodent colonies; could be used to investigate illness in dogs and cats.
- Isolation of organism—requires inoculation of mice, embryonating eggs, or cell culture.
- Immunocytochemistry and PCR of affected tissues.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

Gross

- Multifocal whitish-gray to hemorrhagic foci throughout the liver; may also occur in other viscera.
- Focal myocarditis thickening and congestion of the intestine mesenteric lymphadenopathy—reported.
- Widely disseminated lesions, including severe myocarditis, hepatitis, enterocolitis, intestinal leiomyositis, and adrenal cortical adenitis, have been reported in a dog.

Histologic

- Multifocal hepatic necrosis.
- Necrotic ileitis or colitis.
- Intracellular filamentous organisms—usually numerous; difficult to visualize with H&E; require silver stains (e.g., modified Steiner or Warthin-Starry).



TREATMENT

None effective



MEDICATIONS

DRUG(S)

None

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

None



FOLLOW-UP

PREVENTION/AVOIDANCE

Avoid predisposing factors—may limit disease



MISCELLANEOUS

ABBREVIATIONS

- ALT = alanine aminotransferase
- FeLV = feline leukemia virus
- H&E = hematoxylin and eosin
- PCR = polymerase chain reaction

Suggested Reading

Barr SC, Bowman DD. Tyzzer's disease. In: Canine and Feline Infectious Diseases and Parasitology. Ames, IA: Blackwell, 2012, pp. 550–552.

Jones BR, Greene CE. Tyzzer's disease. In: Greene CE, ed., Infectious Diseases of the Dog and Cat, 4th ed. St. Louis: Saunders Elsevier, 2012, pp. 391–393.

Author Stephen C. Barr

Consulting Editor Stephen C. Barr

UNRULY BEHAVIORS: JUMPING, PULLING, CHASING, STEALING—DOGS



BASICS

DEFINITION

- Jumping—standing on rear legs with front legs on a person or object or leaping in the air with or without landing against the person.
- Pulling—to exert force on the leash to cause motion towards the source of the force (the dog).
- Chasing—pursuing a moving person, animal, or object.
- Stealing—the taking of an item not intended to be used by the dog.

PATOPHYSIOLOGY

- All are within the range of normal dog behaviors.
- Insufficient outlets for normal activities may contribute.
- Jumping up as part of excessive greeting can be associated with separation anxiety or social anxiety.
- Pulling can be associated with different motivational states including but not limited to fear, anxiety, excitement, and predatory behavior.
- Pathologic hyperactivity disorders may be a contributing factor in rare cases.

SYSTEMS AFFECTED

- Behavioral
- Gastrointestinal

SIGNALMENT

Species

Dogs

Breed Predilection

Herding and hunting breeds may be more likely to chase.

Mean Age and Range

More common in younger dogs but occurs at any age.

SIGNS

Historical Findings

- Jumping up on people occurs more commonly in association with arrivals or departures or greeting at other times; it is also associated with exploring the contents of countertops or tables.
- Pulling may be more likely in the beginning of a walk or when seeing, hearing or perhaps smelling a stimulus (e.g., person, other dog, or object of interest) but can occur at any point.
- Items displaced, chewed or ingested are common complaints in stealing.

Physical Examination Findings

- Usually unremarkable unless underlying medical problems.
- Nails worn down.

CAUSES

- Jumping up is normal greeting and play behavior. Excitement, encouragement of the behavior, or inadvertent rewarding of the behavior perpetuates it. Separation anxiety may result in excessive jumping on owners when returning home or leaving. Social anxiety may cause overly exuberant greeting of visitors, with jumping.
- Pulling can occur when a dog is not taught how to walk on leash

or in the presence of different motivational states. A dog may pull towards or away from something it is afraid of or excited/anxious about.

- Stealing is a normal acquisitive behavior. It can be an attention-seeking behavior or motivated by the appeal of the odor, texture or taste of an item with which to chew, eat or play. Stealing can occasionally be related to separation anxiety, in which the dog may steal an item when anxious as the owner is preparing to leave or when the dog is separated from the owner but the owner is still in the house.
- Chasing is a normal behavior, as part of herding, hunting, play, and defense.

RISK FACTORS

- Inadequate exercise.
- Under-stimulation.
- Stealing food—restricted or weight-reduction diets, phenobarbital, benzodiazepines, glucocorticoids, hyperadrenocorticism, and diabetes mellitus.
- Chasing—common in herding breeds.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Stealing

- Separation anxiety—escapes or attempts escape from confined areas in the owner's absence. Often occurs at entrances and in crates. Usually associated with other signs consistent with separation anxiety, including vocalization, urination, defecation, destruction, or salivation, in the owner's absence.
- Other anxiety or phobia (e.g., thunderstorm, fireworks).

CBC/BIOCHEMISTRY/URINALYSIS

- Usually unremarkable.
- May have abnormalities consistent with system affected.

OTHER LABORATORY TESTS

As indicated to rule out source of pain or endocrine or neurologic disease (LDDST, UC:Cr, bile acids, CSF analysis).

IMAGING

Radiographs, ultrasound, MRI, or CT scan if indicated by physical/neurologic exam findings.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient management

ACTIVITY

Increase the dog's daily exercise, opportunities for mental stimulation.

DIET

Review energy requirements in food-stealing cases.

CLIENT EDUCATION

Jumping

- During training, prevention of jumping-up behavior is essential.
- A head collar and leash facilitate training to gently guide the dog away from jumping.
- Train sit for all interactions (doggy please) so that a calm sit becomes the default behavior for anything of value.
- Greeting visitors outside might diminish jumping behavior. The dog's access to the situation can be restricted by confinement (e.g., other room, crate) until the visitor is seated. In some dogs this may also reduce the arousal associated with jumping up.
- Teach "Sit" and "Stay" as an alternative method to greet people, beginning with highly valued rewards (food treats, toys) in areas of the home where the dog is calm and tractable.
- Food rewards should be used consistently initially.
- Add the word "Stay" when the duration of sitting is a few seconds; take a step away, return to the dog, and give the food reward. Build up the time away from the dog to 3–5 minutes.
- Repeat exercises near the door and then with the addition of leaving and returning.
- Next ask the dog to sit for a food reward when returning from gradually longer absences.
- Familiar visitors can enter, ask the dog to sit, and give a food reward.
- Eventually the food rewards can be reduced to intermittent but frequent use.
- Dogs that like to retrieve and are too excited to sit may do better if a ball is tossed as a visitor enters. This may be particularly effective if the dog is taught to sit prior to an item being tossed.
- The owner should walk calmly to the door and speak in a quiet voice to avoid increasing the dog's excitement.
- People should avoid rewarding the jumping with any form of attention including pushing the dog off. Do not acknowledge or interact with the dog; hold arms against the body and turn body away from the dog. Some dogs will stop jumping and ignore the person, at which point they can say sit and reward if successful.
- Stepping on the dog's toes, squeezing the paws, and other punishment are usually ineffective and can lead to fear and aggression, therefore should be avoided.

Pulling

- A dog's natural walking speed may be faster than their owner's.
- A no-pull harness or head collar can be helpful and may be all that is needed.
- A brief play session in a fenced in yard before a walk, may decrease initial energy and decrease pulling (although some dogs get more aroused immediately after exercise).
- Pulling related to fear, anxiety, or excitement requires desensitization (gradual exposure) and counter-conditioning (teaching a different response) to the stimulus as discussed under chasing below.
- With proper application of positive reinforcement pulling can be resolved.
- One method is to use a

UNRULY BEHAVIORS: JUMPING, PULLING, CHASING, STEALING—DOGS

food lure to reward the dog for walking next to a person. Have highly desirable small treats in the hand on the same side as the dog; initially give every few seconds. If the dog pulls ahead, stop, call the dog's name and/or ask it to "Look" (see chasing), reward the behavior and resume walking. Over time decrease the frequency of giving the treat until it is every minute or two. Many dogs learn to come to the owner for a treat when they learn the "Look" command. • A second method is to stop walking as soon as the dog starts to pull. When the dog stops moving call the dog's name and/or ask it to "Look" and reward the behavior and continue walking when the leash is slack. If the dog pulls again repeat the process. • Other methods involve leash corrections which are a form of punishment with the intent of reducing undesirable behaviors rather than training what is desirable. Sharp jerking on the leash or turning suddenly may cause fear, pain, discomfort, and injury to the neck and trachea.

Chasing

• A no-pull harness or head collar can be helpful in controlling the dog and reorienting it toward the owners, in the presence of the chase stimulus. Herding breeds exhibit a phenotypic behavior that may respond better to control and management than to treatment. • Dogs that chase need to be desensitized and counter-conditioned to the stimulus. • The owner should practice the same sit-and-stay exercises as described above, with the addition of a "Look" command using a treat brought up to the owner's eye. This will help get the dog's attention and focus it on the owner when it sees the moving stimulus. • Initially work with the dog inside without distractions, to train, sit, stay, and look. • Next work in a quiet yard with the dog on a leash, have the dog sit, stay, step away, return, look, and give the food reward. When the dog is successful, the process can be repeated in different parts of the yard with gradually more intense distractions. • Training should begin without the chase stimulus present. If the owner is able to keep the dog's attention, the owner should then stage the chase stimulus (such as a bike or person jogging) to pass by at a sufficient distance and slow enough speed while training and rewarding sit, stay and look. Over future sessions, the intensity of the stimulus can be gradually increased. • When the dog is able to ignore the chase stimulus in the yard, the owner can incorporate the same exercises in a park or on a walk while maintaining sufficient distance from the stimuli. When the owner sees the chase stimulus, he or she should ask the dog to sit, stay, and look, and then reward the dog.

Stealing

- The dog's investigative behavior and attempts to initiate play and chase may result in stealing. If the result is enjoyable the behavior is rewarded. • Adequate attention, exercise, and toys before times of inattention (e.g., making dinner, working, watching TV) will help to decrease the motivation for stealing. • If the dog steals, the owners should ignore the dog, walk away, get a treat, and call the dog. As the dog drops the item, the owner can say "Drop," "Good dog," and give the dog the treat or click and treat if the dog is clicker trained. The dog is being rewarded for relinquishing the item. • The owner might also need to use a stay and give a second treat or a chew toy to be able to retrieve the dropped item. Another option is to scatter a number of treats for the dog to pick up while the item is removed. • If the dog retreats under furniture, the owner should not pursue. If the dog feels threatened or cornered, it may defend itself aggressively. If it is imperative that the item be retrieved, the client may need to lure the dog out of hiding with even higher-value treats or offer a walk or favored game. The owner should keep a log of when and what the dog steals, where they were at the time, and what they were doing to determine when and why the dog is stealing and whether it might be due to separation anxiety. In addition, the owners should video record the dog to see its response during their absence. See separation anxiety for more details. • For food stealing, food needs to be kept out of the dog's reach, since acquiring food is highly rewarding. Confinement training or gating the dog out of food preparation and dining areas may be necessary. • Products that deter with mild aversion such as motion-activated alarms or sprays can help correct the stealing behavior. If the dog steals food because it is on a diet, a protein source such as plain cooked chicken or other meat or low-calorie foods such as raw or cooked vegetables can be added to help increase the feeling of fullness.



MEDICATIONS

DRUG(S) OF CHOICE

None



FOLLOW-UP

PATIENT MONITORING

Every 2–3 weeks initially.

PREVENTION/AVOIDANCE

Close supervision, exercise, and exposure to varied stimuli as a young puppy and attending puppy classes and ongoing training can help to prevent and manage unruly behaviors.

POSSIBLE COMPLICATIONS

Injury as a result of escaping a fence, chasing a stimulus, or ingesting an inappropriate item.

EXPECTED COURSE AND PROGNOSIS

Generally good response to treatment for jumping, pulling, and stealing if the owner is consistent. Guidance and support of a force-free reward-based trainer may help to improve success. Chasing behaviors may be more difficult and resistant.



MISCELLANEOUS

AGE-RELATED FACTORS

Younger dogs need more activity than many owners anticipate.

SEE ALSO

- Compulsive Disorders—Dogs • Fears, Phobias, and Anxieties—Dogs • Separation Distress Syndrome • Pediatric Behavior Problems—Dogs

ABBREVIATIONS

- CSF = cerebrospinal fluid • CT = computed tomography • LDDST = low dose dexamethasone suppression test • MRI = magnetic resonance imaging • OCD = obsessive-compulsive disorder • UC:Cr = urine cortisol:creatinine ratio

Suggested Reading

Landsberg G, Hunthausen W, Ackerman, L. Unruly behaviors. In: Behavior Problems of the Dog and Cat, 3rd ed. Philadelphia: Elsevier Saunders, 2013, pp. 237–248.

Lindell E. Control problems in dogs. In: Horwitz D, Mills D, Heath S, eds., BSAVA Manual of Canine and Feline Behavioural Medicine. Gloucestershire, UK: BSAVA, 2002.

Author Marsha R. Reich

Consulting Editor Gary M. Landsberg



**Client Education Handout
available online**



BASICS

OVERVIEW

Occurrence of a urolith (calculus) within the lumen of a ureter (ureterolith); most ureteroliths originate in the renal pelvis and so commonly occur in association with nephroliths. If the uroliths pass through the ureters into the lower urinary tract, a dog or cat may be asymptomatic or may have silent hematuria. If both ureters become totally obstructed in an otherwise healthy untreated dog or cat, death will occur in approximately 4 or 5 days.

SIGNALMENT

- Dog and cat.
- Breed, age, and sex predispositions vary with type of nephrolith.

SIGNS

- May be initially asymptomatic.
- Pain (ureteral colic) during passage of ureteroliths or following acute ureteral obstruction.
- Renomegaly if ureteral obstruction leads to hydronephrosis.
- “Big kidney, little kidney syndrome” is being recognized with increasing frequency in cats in which obstruction of one ureter has previously occurred, resulting in a shrunken end-stage kidney; signs of renal failure and hydronephrosis occur due to obstruction of the remaining functional kidney.
- Unilateral ureteral obstruction results in azotemia and uremic clinical signs only when the function of the contralateral kidney is compromised.
- Signs referable to a lower urinary tract infection or septicemia may be present concurrently with ureterolithiasis.
- Ureteral rupture may occur, resulting in urine accumulation in the retroperitoneal space.
- Cats with distal ureteral obstruction may have signs of dysuria and pollakiuria.

CAUSES & RISK FACTORS

- For a list of causes, see chapters on each urolith type.
- Most ureteroliths in dogs and cats are composed of calcium oxalate. Dogs may form struvite nephroliths and subsequent ureteroliths from infection with urease-producing bacteria. Cats may have ureteroliths composed of dried solidified blood clots.
- Circumcaval ureters (more commonly in right ureter) appear to predispose cats to obstruction of the ureter by ureteroliths and secondary ureteral stricture formation.
- Prior treatment of nephroliths by extracorporeal shock wave lithotripsy, medical dissolution, or surgery to remove nephroliths may be additional risk factors.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Consider in all cases of renal failure unilateral or bilateral renomegaly, abdominal pain, or fluid accumulation in the retroperitoneal space. Obstruction to urine outflow to both kidneys will not produce the same magnitude of renomegaly as unilateral obstruction because the patient will perish as a result of bilateral disease before the changes in the kidneys occur.
- Radiopacities detected by survey abdominal radiography that may be confused with ureteroliths include particulate fecal material in the colon, mammary gland nipples, peritoneoliths, calcified lymph nodes, and mineralization of the renal pelvis.
- Radiolucent ureteroliths may be difficult to differentiate from ureteral blood clots. Other causes of ureteral obstruction include intraluminal tumors, ureteroceles, ureteral strictures (secondary to ureteroliths, circumcaval ureter, prior surgery or trauma), and extraluminal compression. Hydroureter and hydronephrosis may occur because of ureteral ectopia, pyelonephritis, and obstruction of the ureteral opening at the trigone (most commonly due to transitional cell carcinoma of the bladder).

CBC/BIOCHEMISTRY/URINALYSIS

These tests evaluate renal function and screen for concurrent disease before the ionized treatment of ureterolithiasis. Urinalysis, serum calcium concentration, and fractional excretion of electrolytes may permit estimation of urolith composition pending results of definitive analysis.

OTHER LABORATORY TESTS

- Submit all retrieved ureteroliths for quantitative analysis to determine appropriate preventive strategies.
- Patients (other than Dalmatians and bulldogs) with urate stones should be evaluated for portosystemic shunts.
- Blood pressure should be monitored since hypertension is common with CKD secondary to ureteral obstruction.

IMAGING

- Radiography—radiopaque ureteroliths may be visualized. If obstruction and hydronephrosis have occurred, renomegaly may be apparent. If ureteral rupture occurs, contrast in the retroperitoneal space may be lost. Small uroliths may not be visualized on radiographs even if they are radiopaque.
- Contrast radiography—when ureteroliths are suspected, but cannot be documented, an intravenous urogram may help to identify the site of obstruction and will also distinguish ureteral rupture from retroperitoneal hemorrhage. In many instances the damaged tubules do not concentrate contrast media

URETEROLITHIASIS

adequately, resulting in poor delineation of the ureter. Intraoperative nephropelvocentesis is performed during surgical placement of SUB or ureteral stents in cats, allowing for confirmation as part of the surgical correction.

- Ultrasonography—valuable for detecting hydronephrosis or hydroureter. Changes suggesting pyelonephritis may also be detected by ultrasound. The dilated proximal ureter may be traced to the ureterolith and thus allow ultrasonographic confirmation. Ureteroliths are not observed ultrasonographically in approximately 25% of cats with ureteroliths.

- Computed tomography before and after IV contrast can be used to confirm obstructive ureteroliths if they are suspected but not confirmed by other imaging modalities.

DIAGNOSTIC PROCEDURES

- Nuclear scintigraphy alone should not be used to determine whether or not to preserve or surgically remove a kidney.
- Voiding urohydropropulsion may be performed to retrieve ureteroliths that have spontaneously passed into the bladder.

PATHOLOGIC FINDINGS

Gross changes in the kidney—progressive dilation of the pelvis and calyces; in advanced cases, the kidney may be transformed into a thin-walled sac with only a thin shell of atrophic cortical parenchyma; ureteral dilation proximal to the site of obstruction is typical.



TREATMENT

- Remove or bypass ureteroliths that are causing obstruction (i.e., causing hydronephrosis or hydroureter) or that have not moved on sequential radiographs.
- Ureteroliths in dogs have been successfully treated with ESWL. Calcium oxalate uroliths from cats are intrinsically resistant to fragmentation via shockwave lithotripsy and this mode of therapy has been less successful in this species.
- Surgical techniques recommended for removal of ureteroliths vary, depending on the site of obstruction, the presence or absence of infection, and the degree of function of the associated kidney. SUB is effective for relief of ureteral obstruction in cats and is often the preferred surgical procedure for cats.
- Ureteroneocystotomy may be performed for ureteroliths in the middle and distal ureter: the ureter proximal to the obstruction is excised and reimplanted into the bladder. Ureteroliths in the proximal ureter may be removed by ureterotomy. Performance of a ureterotomy or ureteroneocystotomy in cats requires experience in microsurgical techniques. When the contralateral kidney functions normally and severe end-stage hydronephrosis is present in the affected

URETEROLITHIASIS

(CONTINUED)

kidney, ureteronephrectomy may be appropriate.

- Ureteral stent placement to bypass obstructive ureteroliths relieves the obstruction and causes passive ureteral dilation. Ureteral stents may be placed surgically in dogs and cats or through cystoscopy in female dogs.



MEDICATIONS

DRUG(S)

- Medical dissolution is largely ineffective for ureteroliths.
- Therapy aimed at prevention of recurrent disease is imperative following relief of obstruction.
- For ureteroliths that are not causing severe obstruction or severe renal functional problems, allowing time for the ureterolith to spontaneously pass down the ureter to the bladder may eliminate the need for ureteral surgery.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Attempts to prevent one type of urolith may promote formation of a second type.



FOLLOW-UP

PATIENT MONITORING

- Following SUB placement, sampling the SUB for urinalysis and culture along with flushing the SUB under ultrasonographic monitoring is recommended every 3 months.
- Following successful removal of ureteroliths, recheck every 3–6 months for recurrence of uroliths and to ensure owner compliance with preventive measures; urinalysis, radiographs (or ultrasound), and a urine culture are usually appropriate.

PREVENTION/AVOIDANCE

- Elimination of factors predisposing to the development of urolithiasis.
- Specific therapy depends on the mineral composition of the urolith.

POSSIBLE COMPLICATIONS

Hydronephrosis, CKD, recurrent urinary tract infection, pyelonephritis, sepsis, ureteral rupture, ureteral stricture, hypertension.

EXPECTED COURSE AND PROGNOSIS

Highly variable; if unilateral disease is present, the opposite kidney retains adequate

function, and recurrence is prevented, the prognosis is good. Prognosis is good for cats with SUB or ureteral stent placement that recover renal function to stage 1–2 CKD.



MISCELLANEOUS

ABBREVIATIONS

- CKD = chronic kidney disease
- ESWL = extracorporeal shock wave lithotripsy
- SUB = subcutaneous ureteral bypass

Suggested Reading

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Kyles AE, Hardie EM, Wooden BG, et al. Management and outcome of cats with ureteral obstruction: 153 cases (1984–2002). *J Am Vet Med Assoc* 2005; 226:937–944.

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BASICS

OVERVIEW

- Occurs when the mucosal lining of the distal portion of the urethra prolapses through the external urethral orifice.
- Systems affected include urinary, reproductive (bleeding may only occur during penile erection), and hemic/lymph/immune (blood loss can be severe enough to cause anemia, especially in smaller breeds of dogs).
- Prolapsed urethras often appear as a congested, pea-shaped mass protruding from the distal end of the penis. They often are associated with varying degrees of hemorrhage. Excessive licking may result in further traumatic damage to the exposed urethral mucosa.

SIGNALMENT

- Dog, cat (rare).
- Most common in English bulldog, Boston terrier, and Yorkshire terrier.
- Mean age, 18 months; range, 4 months–5 years.
- Reported in male dogs and extremely rare in male cats.

SIGNS

- Intermittent or persistent bleeding from the urethra independent of urination.
- Intermittent or persistent licking of the penis.
- Dysuria and pollakiuria caused by concomitant disorders may also be present.

Physical Examination Findings

- Red to purple, pea-sized, doughnut-shaped mass protruding from the distal end of the penis.
- Pale mucous membranes if bleeding is severe.
- Necrosis of the prolapsed urethra may occur secondary to drying or self-induced trauma from licking.
- Uroliths may be palpable in the urinary bladder or urethra.

CAUSES & RISK FACTORS

- May result from sexual excitement and/or unrelated disorders (e.g., infections, uroliths, neoplasia) of the lower urinary tract.
- Increased intra-abdominal pressure secondary to dysuria associated with urocystoliths may be a predisposing factor.
- Other proposed causes include abnormal development of the urethra with superimposed increased intra-abdominal pressure as a consequence of brachycephalic airway syndrome, dysuria, or sexual activity. This increased intra-abdominal pressure could impair venous return of blood through the pudendal veins, predisposing susceptible dogs to engorgement of the corpus spongiosum surrounding the distal urethra.
- Breed predisposition (bulldogs and Boston terriers).

• Abnormal urethral anatomy associated with increased intra-abdominal pressure secondary to upper airway obstructive syndrome, any cause of persistent dysuria, and/or sexual excitement may be risk factors. Increased intra-abdominal pressure could impair venous return of blood through the pudendal veins, predisposing susceptible dogs to engorgement of the corpus spongiosum surrounding the distal urethra.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Prostatic disease
- Persistent penile frenulum
- Fractures of the os penis
- Balanoposthitis
- Urethritis
- Testicular disease
- Urethroliths
- Coagulopathy
- Urethral neoplasia

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—may reveal regenerative anemia.
- Serum biochemistries—usually normal.
- May not detect significant hematuria in urine collected by cystocentesis, but a voided urine sample may reveal hematuria.
- Urine culture and sensitivity.

OTHER LABORATORY TESTS

Coagulation profile may rule out coagulopathy.

IMAGING

- Survey abdominal radiographs—useful to rule out radiodense uroliths and to evaluate the prostate gland.
- Double-contrast cystography and positive-contrast urethrography—useful to rule out radiolucent uroliths, other urethral disorders, and prostatic disease.
- Abdominal ultrasonography—useful to further evaluate the prostate and urinary bladder.

DIAGNOSTIC PROCEDURES

- Ejaculation—useful to evaluate urethra during penile erection; some urethral prolapses are present only during penile erection.
- Evaluation of ejaculates may also facilitate evaluation of prostatic fluid for evidence of prostatic disease.



TREATMENT

- May not be required if prolapsed urethra is asymptomatic or only associated with episodic bleeding.
- If prolapsed urethra is present only during penile erection, consider castration prior to attempting surgical removal of prolapsed

URETHRAL PROLAPSE

tissue; diethylstilbestrol given for 3–6 weeks after surgery may reduce frequency of erections. If cause is unknown, a recent retrospective study found castration status did not affect prolapse development or outcome.

- Consider surgery for patients with excessive bleeding, pain, or extensive ulceration and/or necrosis of the prolapsed tissue. Also consider surgery if troublesome relapses are associated with medical management.

• Satisfactory results have been obtained by manual reduction of the prolapse followed by urethropexy using a grooved director instrument that reduces the prolapsed urethra at the same time as guiding suture placements. Grooved director instruments are often included in standard spay instrument packs or can be purchased from most medical supply companies.

- If surgery is necessary, Elizabethan collars or similar restraint devices may be needed to prevent licking-induced trauma to the surgical site.

• CO₂ laser surgical technique may improve hemostasis, visualization and accuracy of the surgeon. In addition, it may decrease postoperative swelling. Prior to performing procedure, insert an appropriate catheter into the urethral lumen to avoid accidental transection of the urethra with the laser. When performing the procedure, do not use superpulse settings because they may interfere with hemostasis. Choosing a larger tip size (0.8 mm) for the laser may improve hemostasis.

- A recent study revealed that postoperative hemorrhage and prolapse recurrence may be reduced with use of a simple continuous suture pattern for urethral anastomosis and by administration of postoperative sedation.

• Regardless of treatment chosen, advise the client that recurrence is possible (57% in a recent study), particularly if an underlying cause for the urethral prolapse cannot be found and corrected.

- Because brachycephalic breeds are at risk for this problem, use caution in choosing an anesthetic regimen; monitor brachycephalic breeds carefully during anesthesia to ensure maintenance of adequate oxygenation.



MEDICATIONS

DRUG(S)

- Bacterial urethritis warrants use of appropriate antibiotics.
- May need to consider using diethylstilbestrol for 3–6 weeks after surgery to reduce frequency of erections.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Because of the possibility of bone marrow suppression, consider risk:benefit ratios before

URETHRAL PROLAPSE

(CONTINUED)

giving estrogens, especially if patients are already anemic.



FOLLOW-UP

PATIENT MONITORING

Re-evaluate the patient at least 7–10 days following surgery, for evidence of severe hemorrhage or recurrence of urethral prolapse.

PREVENTION/AVOIDANCE

If urethral prolapse is associated with penile erection, advise owners to prevent contact with female dogs or situations likely to cause penile erection.

POSSIBLE COMPLICATIONS

- Most common postoperative complication was hemorrhage (39%) which was less common when a simple continuous pattern was used for resection and anastomosis.

- Prolapse recurred 57% of time but was less common in dogs that were given postoperative butorphanol or acepromazine.
- Advise owners that recurrence of the prolapse may occur, especially if an underlying cause has been detected and eliminated or controlled.

EXPECTED COURSE AND PROGNOSIS

- Urethral prolapse may persist without significant sequelae. Therefore, some dogs may not require therapy.
- Other dogs may not have problems after castration and/or surgical correction of a prolapsed urethra.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Concurrent urethritis is common
- Concurrent urolithiasis may be a predisposing cause

Suggested Reading

Fossum TW. Urethral prolapse. In: Small Animal Surgery, 3rd ed. St. Louis, MO: Mosby Elsevier, 2007, pp. 687–689.

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URINARY RETENTION, FUNCTIONAL



BASICS

DEFINITION

Incomplete voiding unassociated with urinary obstruction

PATHOPHYSIOLOGY

Micturition voiding phase disorder.

Incomplete voiding due to neurogenic or myogenic failure, or both; associated with hypocontractility of the urinary bladder, or excessive outlet resistance, or both.

SYSTEMS AFFECTED

- Renal/Urologic • Endocrine/Metabolic
- Neuromuscular

GEOGRAPHIC DISTRIBUTION

• Worldwide. • Dysautonomia: Europe (Great Britain, Scandinavia), USA (Midwest), sporadic cases in Dubai, New Zealand, and Venezuela.

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Chondrodystrophic breeds with IVDD.
- Manx cats with congenital sacral spinal lesions.
- Large-breed dogs (German shepherd dogs) with acquired cauda equina syndrome.
- Labrador retrievers, German shorthaired pointers, German shepherd dogs with dysautonomia.

Mean Age and Range

Young adult dogs with functional urinary obstruction

Predominant Sex

More common in males than females

SIGNS

General Comments

Signs include primary and secondary abnormalities of voiding dysfunction.

Historical Findings

- Frequent attempts to urinate, straining to urinate, or not voiding.
- Attenuated, interrupted, or prolonged urine stream.
- Urinary leakage occurs when pressure in bladder exceeds urethral outlet closure pressure (overflow or paradoxical incontinence).
- Vomiting, lethargy, painful abdomen with rupture or inflammation of the urinary tract.

Physical Examination Findings

- Palpably distended urinary bladder and/or inappropriate residual urine (normal 0.2–0.4 mL/kg) after attempts of voiding.
- Possibly, abnormal neurologic examination (see "Differential Diagnosis").
- Rarely, abdominal distension, abdominal pain, or signs of post-renal azotemia.
- Overflow urinary incontinence.

CAUSES

Hypocontractility of the Urinary Bladder (Detrusor Muscle), (Detrusor Atony)

- Usually caused by bladder overdistension.
- Can have neurologic dysfunction or previous urinary obstruction.
- Neurogenic causes include lesions of the pelvic nerves, sacral spinal cord, and suprasacral spinal cord.
- Sacral spinal cord lesions (e.g., congenital malformations, cauda equina compression, lumbosacral disc disease, and vertebral fractures/dislocations) can result in a flaccid, overdistended bladder with weak outlet resistance (lower motor neuron bladder).
- Suprasacral spinal cord lesions (e.g., intervertebral disc protrusion, spinal fractures, and compressive neoplasms) can result in a distended, firm bladder that is difficult to express (upper motor neuron bladder).
- Dysautonomia could lead to detrusor atony with urine retention.
- Electrolyte disturbances or metabolic disorders associated with generalized muscle weakness can affect detrusor muscle contractility.
- Canine hyperadrenocorticism can cause polyuria, bladder distention, and mild urine retention.
- Drugs causing varying degrees of myogenic failure include tricyclic antidepressants, calcium channel blockers, anticholinergic agents, and opioids.

Functional Urinary Obstruction

- Excessive or inappropriate outlet resistance prevents complete voiding during bladder contraction.
- In patients with suprasacral spinal lesions (typically T3–L3) or midbrain disorders, urethral outlet resistance becomes uninhibited and remains excessive or is not coordinated with voiding contractions (detrusor-urethral dyssynergia).
- Associated with sacral lesions and local neuropathy.
- Idiopathic.
- Excessive urethral resistance (often called urethrospasm) may be seen after urethral obstruction or in association with urethral or pelvic surgery, urethral inflammation, or prostate disease.

RISK FACTORS

- Urethral obstruction
- Pelvic or urethral surgery
- Anticholinergic medications
- Epidural analgesia



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- When no voiding is observed, differentiate from oliguria, anuria, and urinary tract rupture.
- Differentiate from physical and mechanical obstruction. Clinical signs associated with urinary obstruction include pollakiuria, stranguria, and hematuria; patients with mechanical obstruction may void a few drops of urine after long periods of straining.
- Neurologic findings in dogs with supraspinal lesions affecting micturition include paralysis or paresis of pelvic and

sometimes thoracic limbs, hyperreflexia of affected limbs, and cervical, thoracolumbar, and lumbar pain. The bladder is usually distended, firm, and difficult to express. In patients with chronic or partial lesions, reflexive voiding may return, characterized by incomplete, involuntary detrusor contractions with outlet spasticity.

• Neurologic findings in dogs with sacral lesions affecting micturition include pelvic limb paresis with hyporeflexia, depressed anal and tail tone, perineal sensory loss, and depressed bulbospongiosus reflexes. Lumbosacral pain can be the only sign. The bladder is typically distended, flaccid, and easy to express.

• A urine stream that can be initiated but is abruptly halted is typical of idiopathic detrusor-urethral dyssynergia. Manual palpation may confirm detrusor contractions, which persist after flow terminates, and may suggest a high residual urine volume.

• In patients recovering from urinary obstruction, inability to void may result from re-obstruction, excessive (functional) urethral resistance, or detrusor atony caused by overdistension. If the urinary bladder can be expressed via gentle palpation applied through the abdomen, detrusor atony is likely. If resistance to manual expression is encountered and urethral obstruction can be ruled-out by examination or transurethral catheterization, functional obstruction is likely.

• Clinical signs accompanying urine retention in patients with dysautonomia may include mydriasis, prolapsed third eyelids, xerostomia, regurgitation or vomiting, megaesophagus, reduced or absent anal tone, diarrhea or constipation, and bradycardia.

CBC/BIOCHEMISTRY/URINALYSIS

- Test results rule-out metabolic causes of neuromuscular disease; also used to evaluate post-renal azotemia.
- Urinalysis may reveal UTI, trauma, or inflammation.

IMAGING

- Use survey radiographs and ultrasound to rule-out obstructing uroliths, pelvic trauma, lumbosacral disease, caudal abdominal masses.
- Use contrast cystourethrography or vaginourethrography, or occasionally, cystourethroscopy, to rule-out obstructive lesions.
- Use myelography, epidurography, CT, MRI to localize neurologic lesions.

DIAGNOSTIC PROCEDURES

- Neurologic exam—assessment of caudal spinal and peripheral nerve function through examination of anal tone, tail tone, perineal sensation, and bulbospongiosus reflexes.
- Transurethral catheterization may be required to rule-out urethral obstruction; catheters should pass easily in animals with no mechanical obstruction and in those with extramural urethral compression (e.g., caused by a smooth bladder neck mass, a large prostate gland, or a caudal abdominal mass).
- Diagnosis of dysautonomia is based on systematic pharmacologic testing of

URINARY RETENTION, FUNCTIONAL

(CONTINUED)

autonomic responses. • Use urodynamic procedures to confirm detrusor atony or functional urethral obstruction, or to document detrusor-urethral dyssynergia; detrusor areflexia may be documented by cystometrographic studies; inappropriate urethral resistance or urethral spasm occasionally is documented by resting urethral pressure profilometry; combined cystometry and urethral pressure measurements or uroflow studies are necessary to document dyssynergia.

PATHOLOGIC FINDINGS

Detrusor Atony

- Previously overdistended bladder may not be discernable on gross pathology.
- Caudal vertebral hypoplasia or aplasia and various sacral spinal cord lesions (abnormal cover, meningomyeloceles, intradural lipomas) in some Manx cats.
- Light microscopy in chronic cases may show widespread degeneration of smooth muscle cells, cholinergic axons, and intrinsic nerves.

Functional Urethral Obstruction

- Various suprasacral neurologic diseases (e.g., IVDD, FCE)
- Urethritis
- Prostatitis



TREATMENT

APPROPRIATE HEALTH CARE

Usually managed as inpatients until adequate voiding function returns.

NURSING CARE

- Manage azotemia, electrolyte imbalances, and acid-base disturbances associated with acute urine retention (rare).
- Identify UTI and treat appropriately.
- Keep the urinary bladder small by intermittent or indwelling transurethral catheterization or frequent manual compression.

CLIENT EDUCATION

Advise clients that complete voiding function may not return. Monitor for signs of complete obstruction, uremia, and UTI.

SURGICAL CONSIDERATIONS

Consider surgical options for salvaging urethral patency in some patients; perineal urethrostomy indicated in male cats with unmanageable distal urethral resistance.

U



MEDICATIONS

DRUG(S) OF CHOICE

Detrusor Atony

- Bethanechol (5–25 mg/dog PO q8–12h; 1.25–7.5 mg/cat q8–12h)—a cholinergic agent; may increase detrusor contractile input in partially denervated or acutely overdistended bladders.
- Metoclopramide (dog and cat, 0.2–0.5 mg/kg PO q8h)—a

dopamine antagonist; may stimulate detrusor contraction.

- Cisapride (dog, 0.5 mg/kg PO q8h; 1.25–5 mg/cat q8–12h)—a smooth muscle prokinetic agent; may promote bladder emptying.

Functional Urethral Obstruction

- Prazosin (dog, 1 mg/15 kg PO q8–24h; cat, 0.25–0.5 mg/cat PO q12–24h or 0.03 mg/kg IV) or phenoxybenzamine (dog, 0.25–0.5 mg/kg PO q12–24h; cat, 1.25–7.5 mg/cat PO q12–24h)— α -adrenergic antagonists reduce smooth muscle contraction in the urethra.
- Diazepam (dog, 2–10 mg/dog PO q8h; cat, 1–2.5 mg/cat PO q8h or 0.5 mg/kg IV)—relaxes striated muscle of the external urethral sphincter.
- Acepromazine (dog, 0.5–2 mg/kg PO q6–8h; cat, 1–2 mg/kg PO q6–8h)—a phenothiazine tranquilizer and general muscle relaxant with α -adrenergic blocking effects on urethral tone; may be effective in cats with excessive urethral resistance.
- Dantrolene (dog, 1–5 mg/kg PO q8–12h; cat, 0.5–2 mg/kg PO q8h or 1 mg/kg IV) striated muscle relaxant; appears to be effective in reducing distal urethral resistance in cats.
- Baclofen (dog, 1–2 mg/kg PO q8h)—a spinal reflex inhibitor; acts as a skeletal muscle relaxant; limited clinical evaluation in dogs and cats.

CONTRAINDICATIONS

- Baclofen in cats.
- Acepromazine, phenoxybenzamine, and prazosin have vasodilatory effects—use with caution in volume-depleted or azotemic patients and those with cardiac disease.
- Acepromazine and diazepam—can cause sedation; use with caution in lethargic patients.

PRECAUTIONS

- Confirm adequate outlet for urine flow before administering bethanechol since it can increase muscular contraction of the urinary bladder neck and proximal urethra. Pretreat with α -agonists (e.g., phenoxybenzamine, prazosin).
- Prazosin may cause potent “first-dose” hypotension; to minimize risk, initial dosage should be one-half of total dosage.
- Acute hepatopathy is an uncommon complication of oral diazepam in cats.

POSSIBLE INTERACTIONS

Cisapride can enhance the sedative effect of diazepam.



FOLLOW-UP

PATIENT MONITORING

- Reassess residual urine volume by urinary bladder palpation or by periodic transurethral catheterization.
- Slowly withdraw medications after primary causes are corrected and adequate voiding function has occurred for several days.
- Perform serial urinalysis and

urine culture to detect UTI in patients with chronic urine retention.

POSSIBLE COMPLICATIONS

- UTI
- Permanent detrusor muscle injury and atony; bladder or urethral rupture
- Post-renal azotemia

EXPECTED COURSE AND PROGNOSIS

- Good for acute detrusor atony caused by overdistension, acute reversible neurologic lesions, acute functional obstruction associated with irritative urethral disorders or resolving obstruction—recovery often occurs within 1 week.
- Fair to poor for chronic detrusor atony or chronic functional obstruction—urinary function usually recovers as motor function of the limbs recovers. If functional obstruction responds to α -agonists, prolonged administration may be required.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- UTI
- Azotemia

PREGNANCY/FERTILITY/BREEDING

Bethanechol is contraindicated

SYNOMYMS

- Dysfunctional voiding
- Neuropathic bladder
- Reflex dyssynergia, detrusor-urethral dyssynergia
- Urethospasm

SEE ALSO

- Azotemia and Uremia
- Dysuria and Pollakiuria
- Feline Idiopathic Lower Urinary Tract Disease
- Intervertebral Disc Disease, Thoracolumbar
- Lumbosacral Stenosis and Cauda Equina Syndrome
- Prostatitis and Prostatic Abscess
- Urinary Tract Obstruction

ABBREVIATIONS

- CNS = central nervous system
- UTI = urinary tract infection

INTERNET RESOURCES

- <http://www.vin.com>
- <http://www.dvm360.com>

Suggested Reading

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Client Education Handout
available online

URINARY TRACT OBSTRUCTION



BASICS

DEFINITION

Restricted flow of urine from the kidneys through any point of the urinary tract to the external urethral orifice.

PATHOPHYSIOLOGY

- Physical or functional obstruction of the urinary tract resulting in partial or complete cessation in renal excretory function. As luminal pressure builds it is transmitted to the level of the kidney and its functional units (nephrons). As tubular pressure exceeds filtration pressure, GFR ceases. Ensuing pathophysiologic consequences depend on site, degree, and duration of obstruction. Complete obstruction produces a pathophysiologic state characterized by uremia, acidemia and hyperkalemia.
- Perforation of the excretory pathway with extravasation of urine (urethral tear or bladder rupture) is a functional equivalent.

SYSTEMS AFFECTED

- Renal/Urologic.
- Cardiovascular, gastrointestinal, nervous, and respiratory systems also affected relative to duration of obstruction and severity of metabolic derangement.

SIGNALMENT

- Dog and cat
- More common in males than females

SIGNS

Historical Findings

- Pollakiuria (common)
- Stranguria
- Diminished to absent urine stream
- Vocalizing, frequent trips to the litter box (cats)
- Gross hematuria
- Signs of uremia that develop when urinary tract obstruction is complete (or nearly complete): lethargy, reduced appetite, and vomiting

Physical Examination Findings

- Excessive (i.e., overly large or turgid) or inappropriate (i.e., remains after voiding efforts), palpable distension of the urinary bladder, especially in conjunction with lower urinary tract signs.
- Abdominal distention/discomfort.
- Uroliths are often palpable in the urethras of obstructed male dogs.
- Signs of severe uremia: dehydration, weakness, hypothermia, and/or bradycardia with moderate hyperkalemia, altered mentation, or sinus tachycardia from pain/stress.

CAUSES

Intraluminal Causes

- Urolithiasis—most common in male dogs.
- Urethral plugs—most common in male cats.
- Idiopathic—no overt intraluminal physical obstruction; may involve functional obstruction (see below).
- Additional causes include blood clots, sloughed tissue.

Intramural Causes

- Neoplasia of the bladder neck or urethra—more common in dogs.
- Prostatic disorders (neoplasia, prostatitis, etc.) in male dogs.
- Edema, hemorrhage, or spasm of muscular components at sites of intraluminal obstruction and/or associated with lower urinary tract inflammation. Can contribute to persistent or recurrent obstruction to urinary flow after removal of the intraluminal material and/or following catheterization attempts.
- Stricture at a site of prior injury or inflammation, may impede urine flow or may predispose to intraluminal obstruction.
- Ruptures, lacerations, and punctures—usually caused by traumatic incidents.

Miscellaneous Causes

- Displacement of the urinary bladder into a perineal hernia
- Neurogenic (see Urinary Retention, Functional)

RISK FACTORS

- Urolithiasis, particularly in males
- Feline lower urinary tract disease, particularly in males
- Prostatic disease in male dogs



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Owners may have difficulty distinguishing urinary obstruction from constipation.
- Signs of feline idiopathic cystitis can also be difficult to distinguish from obstruction, especially if there are no signs of systemic illness. Determination of bladder size (large/firm with obstruction, small with cystitis) can help distinguish.
- Animals whose urinations are not routinely observed by owners can present for signs referable to systemic illness (uremia) rather than concern for obstruction.
- Evaluation of any azotemic patient, in conjunction with history and physical exam, should include consideration of possible post-renal causes (e.g., urinary obstruction).
- Once recognized, diagnostic efforts focus on assessing the degree of systemic impact and metabolic derangement, as well as identifying the location and cause of obstruction.

CBC/BIOCHEMISTRY/URINALYSIS

- Results of a hemogram are usually normal, but a stress leukogram may be seen.
- Biochemical analysis reveals azotemia, hyperphosphatemia, metabolic acidosis, hyperkalemia, and decreased ionized calcium proportional to the duration of complete obstruction. Cats may also have stress hyperglycemia.
- Hematuria and proteinuria are common. Crystalluria may be associated with urolithiasis, though can be present in the absence of stones. Atypical epithelial cells may be seen in patients with neoplasia.

OTHER LABORATORY TESTS

- Given the potential for concurrent urinary tract infection in obstructed dogs (especially secondary to uroliths), urine culture may be beneficial. However, cats with obstruction are unlikely to have bacterial cystitis, and presenting urine culture is not recommended.
- Uroliths passed or retrieved should be sent for crystallographic analysis to determine their mineral composition.

IMAGING

Abdominal Radiography

- Uroliths—often demonstrated by survey radiography; some are difficult or impossible to see because of their size, composition, or location.
- Positive-contrast urethrography is beneficial for detecting intraluminal and intramural lesions of the urethra; double-contrast cystography is the most sensitive method of detecting lesions of the bladder lumen and wall.

Abdominal Ultrasonography

Ultrasonography is highly sensitive in detecting lesions of the bladder and proximal urethra (including the prostate gland in male dogs) and upper urinary tract (i.e., ureter or renal pelvis) obstruction.

ADDITIONAL DIAGNOSTIC PROCEDURES

- Electrocardiography may detect abnormalities secondary to hyperkalemia, including tall T waves, prolonged PR interval, widened QRS complexes, loss of P waves, bradycardia, and atrial standstill.
- Transurethral catheterization has diagnostic and therapeutic value. With attempted passage of the urinary catheter, the location and nature of obstructing material may be determined. Some or all of the obstructing material (e.g., small uroliths and feline urethral plugs) may dislodge and pass antegrade out of the urethra or retrograde into the bladder. Animals that cannot urinate despite being readily catheterized likely either have intramural lesions or functional urinary retention.
- Cytologic evaluation of specimens obtained with the assistance of catheters may be diagnostic, particularly carcinomas of the urethra or bladder and some prosthetic diseases.
- Cystoscopy can be helpful, particularly in female dogs with intramural lesions of the bladder neck or urethra.



TREATMENT

EMERGENCY MANAGEMENT

- Complete obstruction is a medical emergency that can be life-threatening; treatment should be started immediately.
- Initial goals are combating metabolic derangements of post-renal uremia, especially significant hyperkalemia, and establishing urinary patency.
- Intravenous fluids

URINARY TRACT OBSTRUCTION

(CONTINUED)

administration of isotonic crystalloid based on degree of cardiovascular compromise, dehydration, and potential for post-obstructive diuresis. • For severe hyperkalemia ($K^+ > 8 \text{ mmol/L}$, significant bradycardia/ECG changes); administer calcium gluconate (1 mL/kg over 3–5 minutes, titrated based on resolution of ECG changes), regular insulin (0.1–0.2 U/kg IV once) and dextrose bolus (1 mL/kg IV, diluted, over 5 minutes). May need 50% dextrose to continue on dextrose infusion (2.5–5%) for 4–6 hours to avoid hypoglycemia. For more severe hyperkalemia or acidemia ($K^+ > 10 \text{ mmol/L}$, pH < 7.1) consider sodium bicarbonate (1 mL/kg IV over 5–10 minutes). • Decompressive cystocentesis may allow more immediate relief of intravesicular pressure, resumption of GFR, and decreased back-pressure for catheterization efforts. • Urethral catheterization under heavy sedation or general anesthesia (see below) to relieve physical obstruction and establish urethral patency. • Flushing urinary bladder until clear effluent, attach to sterile collection system.

NURSING CARE

- Post-obstructive management geared toward maintaining fluid balance, continued correction of metabolic derangements, and sedation/analgesia (see below). • Rate of fluid administration should be determined based on maintenance, dehydration and ongoing losses. Some patients can experience a post-obstructive diuresis, with significant urinary losses. It is important to keep up with these losses to avoid dehydration.
- Hyperkalemia should resolve within hours after de-obstruction and may eventually need to be supplemented. Azotemia should also significantly decrease within 12–24 hours.
- Patients with urolithiasis will often require cystotomy for stone removal with associated postoperative care.



MEDICATIONS

DRUG(S)

- Sedation/analgesia/anesthesia for urethral catheter placement should be selected based on patient stability, and potential concern for decreased renal clearance. Acepromazine plus an opioid (e.g., methadone, buprenorphine) if stable, opioid plus benzodiazepine if unstable. Ketamine and a benzodiazepine is a commonly used injectable combination. General anesthesia, after premedication and induction, may be indicated as it provides the most urethral relaxation, especially for obstructed dogs.
- In the post-obstructive period, continued sedation and analgesia is beneficial.

- Urethral relaxants, such as acepromazine and/or prazosin, may be beneficial for post-obstructive cats or patients with neurogenic urine retention.
- Antibiotics may be indicated with infection (e.g., UTI or prostatitis), ideally only when strongly suspected or with documented evidence (such as cytology or positive culture). Antibiotics should not be administered to prevent UTI while a urinary catheter is in place as this is not effective and can promote bacterial resistance.

CONTRAINdications

- Corticosteroids are contraindicated while a urinary catheter is in place. This can predispose to the development of urinary tract infection. • Given their potential impact on renal blood flow, nonsteroidal anti-inflammatory medications should be initially avoided in more metabolically compromised patients.

PRECAUTIONS

- Avoid drugs that reduce blood pressure (e.g., acepromazine) or induce cardiac dysrhythmia (e.g., ketamine) until dehydration and hyperkalemia are resolved.



FOLLOW-UP

PATIENT MONITORING

- If the initial electrocardiogram indicates life-threatening changes, continuous monitoring to guide treatment and evaluate response is warranted. • Assess urine production and hydration status frequently, and adjust fluid administration rate accordingly (as described above). • Monitor renal values and electrolytes. Sicker patients may require more frequent monitoring (q6–12), whereas once daily may be sufficient for more stable patients. • The urinary catheter can be removed once metabolic derangements and post-obstructive diuresis has resolved, and/or the urine appears to be clear of gross debris, clots, etc. • After urinary catheter removal, close monitoring to verify the ability to urinate adequately for at least 12–24 hours. • Cats may benefit from continued pain medication and urethral relaxation for 5–7 days at home, as well as recommendations for increased water intake and environmental enrichment to help decrease risk of re-obstruction.

POSSIBLE COMPLICATIONS

- Death. • Injury to the excretory pathway (e.g., urethral tear) while trying to relieve obstruction. • Urine leakage or bladder rupture if decompressive cystocentesis performed. • Hypokalemia during

post-obstructive diuresis. • Recurrence of obstruction.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Bradycardia secondary to hyperkalemia
- Azotemia, hyperphosphatemia, and metabolic acidosis

AGE-RELATED FACTORS

In older dogs, the underlying cause of obstruction (e.g., neoplasia and prostate disease) often is difficult to treat.

SYNOMYS

Urethral obstruction

SEE ALSO

- Azotemia and Uremia • Feline Idiopathic Lower Urinary Tract Disease • Hyperkalemia
- Urinary Retention, Functional

Suggested Reading

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Client Education Handout
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UROLITHIASIS, CALCIUM OXALATE



BASICS

DEFINITION

Formation of calcium oxalate (CaOx) uroliths within the urinary tract and associated clinical conditions (e.g., urinary obstruction, idiopathic hypercalcemia, chronic kidney disease).

PATOPHYSIOLOGY

Presence of hypercalciuria, hyperoxaluria, hypocitraturia, and defective crystal growth inhibitors.

Hypercalciuria

In dogs, normocalcemic hypercalciuria is thought to result from either intestinal hyperabsorption of calcium (so-called absorptive hypercalciuria: type 1—dietary independent, type 2—dietary dependent, and type 3—phosphaturic induced hypervitaminosis D) or reduced renal tubular reabsorption of calcium (so-called renal-leak hypercalciuria). Hypercalcemic hypercalciuria results from excessive glomerular filtration of mobilized calcium, which overwhelms normal renal tubular reabsorptive mechanisms (called resorptive hypercalciuria, since bone resorption is associated with high serum calcium concentrations).

Hyperoxaluria

In humans, hyperoxaluria is associated with inherited abnormalities of excessive oxalate synthesis (i.e., primary hyperoxaluria types I, II, and III), excess consumption of foods containing high quantities of oxalate or oxalate precursors, pyridoxine deficiency, and disorders associated with fat malabsorption (i.e., fat complexes with intestinal calcium augmenting intestinal absorption of oxalate). Lack of oxalate degrading bacteria in the intestine can increase the quantity of oxalate absorbed from the diet and the quantity excreted in urine.

Hypocitraturia

Urine citrate inhibits calcium oxalate urolith formation. By complexing with calcium ions to form the relatively soluble salt calcium citrate, citrate reduces the quantity of calcium available to bind with oxalate. In normal dogs, acidosis is associated with low urinary citrate excretion, whereas alkalosis promotes urinary citrate excretion.

Defective Crystal Growth Inhibitors

In addition to urinary concentrations of calculogenic minerals, large molecular weight proteins in urine, such as Tamm-Horsfall mucoprotein, nephrocalcin and osteopontin, have a profound ability to enhance solubility of calcium oxalate. Preliminary studies of urine obtained from dogs with calcium oxalate uroliths revealed that nephrocalcin had fewer carboxyglutamic acid residues than nephrocalcin isolated from normal dog urine.

Feeding Diets Promoting Urine Acidification

Epidemiologic studies have revealed that feeding diets designed to promote aciduria is a common risk factor in cats and dogs. In several species, acidic urine is associated with hypercalciuria (bone mobilization of calcium, increased glomerular filtration of calcium, and decreased renal tubular reabsorption of calcium) and hypocitraturia (increased renal tubular reabsorption).

SYSTEMS AFFECTED

Renal/Urologic

INCIDENCE/PREVALENCE

In dogs, calcium oxalate accounts for approximately 42% of the uroliths removed from the lower urinary tract and 45% of those removed from the upper urinary tract. In cats, calcium oxalate accounts for approximately 42% of the uroliths removed from the lower urinary tract and 90% of those retrieved from the upper urinary tract.

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Dogs—reported in many breeds. Six breeds represent 60% of cases: miniature schnauzer, Lhasa apso, Yorkshire terrier, bichon frise, shih tzu, and miniature poodle.
- Cats—Himalayan, Scottish fold, Persian, ragdoll, and Burmese are at greater risk.

Mean Age and Range

- Dogs— 8.5 ± 3 years; 60%, 6–11 years
- Cats—97% > 2 years; 53%, 7–15 years

Predominant Sex

Mostly male dogs (73%) and male cats (55%)

SIGNS

General Comments

- Asymptomatic in some animals.
- Depend on location, size, and number of uroliths.
- Animals with nephroliths are typically asymptomatic but may have persistent hematuria.
- Ureteral obstruction associated with contralateral microrenale, ipsilateral hydronephrosis, and acute onset of uremia occurs frequently in cats with chronic kidney disease.

Historical Findings

- Typical signs of urocystoliths or urethroliths include pollakiuria, dysuria, and hematuria. Some may present for urethral obstruction.
- Nephroureteroliths common in cats with chronic kidney disease.

Physical Examination Findings

- Detection of urocystoliths are by abdominal or urethral palpation; failure to palpate uroliths does not exclude them from consideration.

- Large urinary bladder if patient has complete urethral obstruction (more common in cats).

- Urocystoliths with irregular contours rarely cause complete urethral obstruction.

CAUSES

See “Pathophysiology”

RISK FACTORS

- Oral calcium supplements given independent of meals.
- Feeding acidifying foods that promote formation of acidic urine (less than a pH of 6.6 in dogs and 6.25 in cats) was associated with CaOx urolithiasis. In normal cats alkaline urine was associated with the lowest saturation for CaOx.
- Excessive dietary protein, sodium (greater than 1.2% DMB or 350 mg/100 kcal) and vitamin D promote hypercalciuria.
- Additional dietary oxalate (e.g., chocolate and peanuts) and ascorbic acid promote hyperoxaluria.
- Exogenous or endogenous exposure to a high concentration of glucocorticoids and furosemide promote hypercalciuria
- Pyridoxine (vitamin B₆)-deficient diets (e.g., homemade) promote hyperoxaluria.
- Consumption of dry diets is associated with a higher risk for calcium oxalate urolith formation than consumption of high-moisture canned diets.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other common causes of hematuria, dysuria, and pollakiuria, with or without urethral obstruction, include urinary tract infection, urinary tract neoplasia, and idiopathic feline lower urinary tract disease.
- Other common radiodense uroliths include those composed of magnesium ammonium phosphate, calcium phosphate, cystine, and silica.

CBC/BIOCHEMISTRY/URINALYSIS

- Urinary tract mineralization may resemble uroliths.
- Results usually unremarkable.
- Urinary sediment evaluation may reveal calcium oxalate crystals, but absence of crystalluria does not exclude uroliths as a possibility.
- Hypercalcemia (rare in dogs, more common in cats) should be further evaluated to determine its cause and contribution to urolith formation.

OTHER LABORATORY TESTS

Quantitative mineral analysis of uroliths

IMAGING

- Calcium oxalate uroliths ≥ 2 mm in diameter are radio-opaque and easily detected by survey radiography.

UROLITHIASIS, CALCIUM OXALATE

(CONTINUED)

- Intravenous urography, contrast pyelography, or ultrasonography is required to verify ureteral obstruction.



TREATMENT

APPROPRIATE HEALTH CARE

- CaOx uroliths are not amenable to medical dissolution.
- Small stones that can pass through the urethra (< 3 mm in most dogs > 5 kg) should be removed by voiding urohydropropulsion or basket retrieval. Percutaneous cystolithotomy or routine cystotomy can be used to remove stones in smaller dogs and male cats.
- Consider laser lithotripsy, percutaneous cystolithotomy, or routine cystotomy to remove larger stones from the urinary bladder.
- Urethral surgery is discouraged. Retrograde urohydropropulsion is an effective procedure to flush urethral stones back into the urinary bladder prior to their removal.
- Persistently obstructed ureters require urgent intervention to minimize progressive kidney damage. If fluid therapy, α -adrenergic blocking agents, and diuretics do not relieve the obstruction in 1-3 days, consider ureteral stents in dogs and subcutaneous ureteral access devices in cats to preserve kidney function. When performed by trained surgeons, ureterotomy may be considered for dilated ureters containing very few stones.
- Removal of unobstructing nephroliths is usually not necessary.

ACTIVITY

Reduce during the period of tissue repair after surgery.

DIET

- No reports of dissolution of CaOx uroliths with therapeutic foods. Epidemiologic studies support feeding high moisture foods that promote formation of less acidic urine ($pH > 6.3-6.6$) to minimize formation of calcium oxalate.
- Hypercalcemia in cats without evidence of hyperparathyroidism or malignancy is sometimes minimized by feeding Hill's Prescription Diet Feline w/d. Management of idiopathic hypercalcemia with bisphosphonates and other drugs that inhibit osteoclast function are controversial; their use should be determined on a case-by-case basis weighing their risks and advantages.

CLIENT EDUCATION

- Urolith removal does not alter the factors responsible for urolith formation; eliminating or minimizing risk factors is necessary to minimize recurrence.
- Approximately 50% of dogs reform uroliths within 2 years; a third of cats reform uroliths in 2 years.
- Patients with hypercalcemia typically reform uroliths at a faster rate.

SURGICAL CONSIDERATIONS

- Consider surgical removal of lower tract uroliths that cannot be removed by minimally invasive procedures (e.g., voiding urohydropropulsion, basket retrieval, intracorporeal laser lithotripsy, percutaneous cystolithotomy).
- Avoid performing disfiguring urethrostomies and urethrotomies by using retrograde urohydropropulsion to flush urethroliths into the bladder or using lithotripsy to fragment urethroliths.
- Shock wave lithotripsy is an alternative to surgery for removal of nephroliths and ureteroliths in dogs.
- To minimize urolith reformation over suture nidus, minimize surgical procedures to remove uroliths and use absorbable suture and suture patterns that minimize suture exposure in the lumen of the urinary bladder.
- Only surgeons trained in ureteral surgery should attempt ureterolith removal. However, in lieu of surgery consider ureteral stents in dogs and subcutaneous ureteral access devices in cats.
- Consider parathyroidectomy for patients with primary hyperparathyroidism and hypercalcemia.



MEDICATIONS

DRUG(S) OF CHOICE

No available drugs effectively dissolve calcium oxalate uroliths.

PRECAUTIONS

Steroids and furosemide promote calciuria.



FOLLOW-UP

PATIENT MONITORING

- Post-surgical radiographs are essential to verify complete urolith removal.
- To prevent the need for repeated surgery, evaluate abdominal radiography every 3-5 months to detect urolith recurrence early. Small uroliths are easily removed by voiding urohydropropulsion or stone basket retrieval.

PREVENTION/AVOIDANCE

- Even with appropriate contemporary therapy, CaOx urolith recurrence is common (up to 50% in dogs and 33% in cats in 2 years). Therefore, regular monitoring and compliance check-ins are essential to adjust therapy to extend the interval between recurrences.
- Only recommend high moisture foods (e.g., can, loaf, gravies). Feeding dry foods, combining dry and wet foods, or adding water to dry food is usually ineffective in maintaining consistent low urinary concentrations (specific gravity < 1.020 in

dogs and < 1.030 in cats) of calculogenic minerals.

- Feeding high-sodium foods ($\geq 350 \text{ mg}/100 \text{ kcal}$) should not be recommended as a substitute for feeding high-moisture foods. Their efficacy to promote low urine specific gravity appears to be short-lived (3-6 months) and their use is contraindicated in dogs and cats with kidney disease.
- Avoid feeding diets that promote urine acidification. Diets that promote formation of acidic urine in dogs ($\text{pH} < 6.6$) and cats ($\text{pH} < 6.25$) were associated with CaOx uroliths. A linear increase in urine pH was associated with a linear decrease in urine CaOx saturation in normal cats.
- Commercially manufactured diets have been designed to prevent CaOx recurrence, but they may not be an ideal for all patients.
- Hills Prescription diet u/d for dogs has been shown to decrease calcium and oxalate excretion in dogs with calcium oxalate urolithiasis. This food has lower levels of sodium and protein, and promotes a neutral to alkaline urine. Although it has passed AFCO feeding trials, some consider that the protein quantity is too low. If this is the case consider feeding $\frac{1}{2}$ u/d and $\frac{1}{2}$ of a canned moderate protein senior food that does not acidify the urine (e.g., Prescription diet g/d). Because u/d is higher in fat, dogs with hereditary hyperlipidemia (e.g., some miniature schnauzers) may benefit from a similar feeding mixture.
- Hills Prescription diet w/d has been recommended for dogs with CaOx urolithiasis and fat/lipid intolerance or fat/lipid responsive diseases (e.g., dogs with a history of pancreatitis). Because this diet promotes formation of acidic urine, administer potassium citrate to promote a more favorable urine pH (> 6.5).
- Royal Canin SO has been shown to decrease CaOx relative supersaturation in dogs with calcium oxalate uroliths, but the urine samples were collected by owners in this study, raising the suspicion of incomplete sample collection. Because this diet promotes acidic urine, concomitant administration of potassium citrate is necessary to achieve a more favorable urine pH (> 6.5). We do not recommend dry foods to prevent CaOx uroliths.
- Avoid supplements with vitamins C and D.
- Reevaluate patients in 2-4 weeks after initiation of diet therapy to verify appropriate reduction in specific gravity (< 1.020 for dogs and < 1.030 for cats), appropriate urine pH (≥ 6.5), and amelioration of crystalluria. Do not use inappropriately collected or stored urine samples (e.g., urine collected by owners, refrigerated, or contaminated with debris) to monitor therapeutic efficacy. To promote less-concentrated urine strongly recommend canned or gravy formulations of food or add additional water to all types of food. If urine

(CONTINUED)

is acidic, consider administration of potassium citrate (75 mg/kg PO q12h); adjust dosage to achieve a pH between 6.5 and 7.5. Potassium citrate medications formulated with cranberry are not recommended because cranberry is a source of vitamin C; vitamin C supplementation should be discouraged because of its ability to increase urine oxalate.

- Vitamin B₆ (2–4 mg/kg PO q24–48h) may help minimize oxalate excretion, especially for animals fed homemade or pyridoxine-deficient diets.

- If dietary changes are inadequate at slowing the rate of recurrence, consider hydrochlorothiazide diuretics (dog, 2 mg/kg and cat, 1 mg/kg, q12–24h).
- If the patient is hypercalcemic, correct underlying cause if possible. Consider either Prescription Diet w/d or c/d multicare for cats with idiopathic hypercalciuria; bisphosphonates should be used cautiously.
- *Oxalobacter formigenes* is an intestinal bacterium that ingests oxalate as its sole nutrient. By metabolizing dietary oxalate in the intestine, less oxalic acid is available for absorption and less is excreted in urine. To preserve healthy populations of intestinal *Oxalobacter*, avoid indiscriminate or prolonged use of antimicrobics.

POSSIBLE COMPLICATIONS

- Urocystoliths can pass into and obstruct the urethra in male dogs and cats, especially if the patient is dysuric.
- Dogs that do not consume their daily requirement of some urolith prevention foods may develop various degrees of protein calorie malnutrition.

- Diet-associated hyperlipidemia develops in some patients consuming foods with higher fat content. Miniature schnauzers with hereditary hyperlipidemia are predisposed to pancreatitis when consuming some prevention foods; Hill's Prescription Diet Canine w/d can be used as an alternative. This diet should be supplemented with potassium citrate as needed to maintain a urine pH between 6.5 and 7.5.

EXPECTED COURSE AND PROGNOSIS

- Approximately 50% of dogs and 33% of cats reform uroliths in 2 years. Treatment to minimize recurrence is helpful.
- Patients with persistent hypercalcemia typically reform uroliths at a faster rate.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Conditions predisposing to hypercalciuria (e.g., hyperadrenocorticism, acidemia, hypervitaminosis D, and hyperparathyroidism) or hyperoxaluria (e.g., vitamin B₆ deficiency, hereditary hyperoxaluria, and ingestion of chocolate and peanuts).

AGE-RELATED FACTORS

Rare in young (< 1 year old) animals

PREGNANCY/FERTILITY/BREEDING

Diets used to prevent calcium oxalate uroliths are not appropriate.

SYNONYMS

Oxalate urolithiasis

SEE ALSO

Crystalluria

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Client Education Handout
available online

UROLITHIASIS, CALCIUM PHOSPHATE



BASICS

OVERVIEW

- Calcium phosphate (CP) uroliths within the urinary tract and associated clinical conditions.
- Forms of CP identified in dogs and cats include: calcium phosphate apatite (CAP), calcium phosphate carbonate (CPC), calcium hydrogen phosphate dihydrate (Brushite), and uncommon minerals—tricalcium phosphate (whitlockite) and octacalcium phosphate.
- CP uroliths represent a small fraction (dogs < 1.0%, cats < 0.5%) of all uroliths submitted to the MUC from 1981 to 2013 (Table 1).
- A greater percentage of CP uroliths are found in the upper tract (kidney and ureter) (2.5% cats, 3.5% dogs), than in the lower tract (bladder and urethra). • CP uroliths (excluding brushite) do not have a characteristic shape. Brushite uroliths are typically round and smooth. • Color of CP uroliths are usually cream or tan. Blood clots mineralized with CP are typically black.

SIGNALMENT

- Dog and cat. • Rarely detected in animals < 1 years old. • CPC uroliths occur primarily in female dogs (72%).

SIGNS

- Depend on location, size, and number of uroliths. • Pollakiuria, dysuria, hematuria, and urethral obstruction.
- Nephroureteroliths—typically asymptomatic but may have persistent hematuria or signs referable to concomitant renal failure (primarily cats).

CAUSES & RISK FACTORS

- CPC—commonly a minor component of struvite and calcium oxalate uroliths. • Pure CP uroliths—usually associated with metabolic disorders, e.g., primary hyperparathyroidism, renal tubular acidosis, and excessive dietary calcium and phosphorus.
- Urinary tract infections—Increased calcium excretion in combination with urinary tract infection with urease producing bacteria may be risk factors favoring CPC. • Nephroliths, urocystoliths, and urethroliths composed of blood clots mineralized with CP suggest dystrophic mineralization of tissue, in contrast to metastatic mineralization reflecting abnormal calcium and phosphorus metabolism. • Other risk factors—see Urolithiasis Calcium Oxalate.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other common causes of hematuria, dysuria, and pollakiuria, with or without urethral obstruction, include urinary tract infection and urinary tract neoplasia.
- Other radiodense uroliths—magnesium ammonium phosphate, calcium oxalate, and silica.
- Metastatic or dystrophic mineralization of urinary tract parenchyma may resemble uroliths.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually unremarkable.
- Hypercalcemia or azotemia rarely detected; post-renal azotemia in some animals with complete urinary outflow obstruction.
- Urinary sediment analysis—amorphous crystals in some patients; brushite (calcium hydrogen phosphate dihydrate) forms are elongated, rectangular, lath-shaped crystals.

OTHER LABORATORY TESTS

- Quantitative analysis of retrieved uroliths is necessary to confirm their mineral composition.
- Serum concentrations of parathyroid hormone, parathyroid hormone-related peptide, and hydroxycholecalciferol may help establish underlying causes.

IMAGING

- CP uroliths are radiodense (as dense as bone) and are often detected by survey radiography.
- CP uroliths may be detected by ultrasonography.

OTHER DIAGNOSTIC PROCEDURES

CP uroliths in the urethra and bladder may be detected by cystoscopy.



TREATMENT

- Medical dissolution of CP uroliths remains a goal for the future.
- Consider surgical removal of lower tract uroliths that cannot be removed by minimally invasive procedures (e.g., voiding urohydropropulsion, basket retrieval, intracorporeal lithotripsy, laparoscopic cystotomy).
- Avoid performing disfiguring urethrostomies by using basket retrieval to remove urethroliths, retrograde urohydropropulsion to flush urethroliths into the bladder or using lithotripsy to fragment urethroliths.
- Shock wave lithotripsy is an alternative to surgery for removal of

nephroliths, ureteroliths, and urocystoliths in dogs. • Correction of hyperparathyroidism or other causes of hypercalcemia should minimize further urolith formation.



MEDICATION

DRUG(S)

No effective medications available for dissolving CP uroliths.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Vitamin D supplements, other mineral supplements, glucocorticoids



FOLLOW-UP

PATIENT MONITORING

- Radiography after surgery to verify complete urolith removal is a standard of practice.
- Abdominal radiography or ultrasonography every 3–5 months to enhance early detection of urolith recurrence and prevention of the need for repeated surgery.
- Small uroliths are easily removed by voiding urohydropropulsion or catheter retrieval.

PREVENTION/AVOIDANCE

- A high-moisture (canned) diet formulated to prevent formation of calcium oxalate uroliths may help prevent recurrence.
- Foods for older dogs that are lower in protein, phosphorus, and calcium, and which do not promote acidic urine are usually associated with decreased calcium and phosphorus excretion. Hill's Prescription canned g/d is one example.
- Because of the high moisture content of canned foods and their tendency to promote dilute urine, canned diets are more effective than dry diets in preventing recurrence.
- Avoid excessive acidification or alkalinization of urine.



MISCELLANEOUS

SYNONYMS

Apatite uroliths

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Table 1

Calcium Phosphate Uroliths submitted to the Minnesota Urolith Center (MUC) in 2013.

	Dog (n = 66,310)	Cat (n = 15,602)
Calcium phosphate carbonate form (CPC)	0.49%	0.08%
Calcium phosphate apatite form (CAP)	0.10%	0.15%
Calcium hydrogen phosphate 2H ₂ O (Brushite)	0.23%	0.04%

UROLITHIASIS, CYSTINE



BASICS

OVERVIEW

- Formation of uroliths, composed of cystine in the urinary tract.
- Occurs with cystinuria, an inborn error of metabolism caused by defective tubular reabsorption of cystine, ornithine, lysine, and arginine (COLA) leading to cystine urolith formation.
- Cystine is freely filtered by glomeruli; most is actively reabsorbed in the proximal tubules.
- Impaired intestinal absorption of these amino acids has not been associated with any nutritional deficiency states in dogs, presumably because they are non-essential amino acids.
- Unless protein intake is severely restricted, cystinuric dogs have no detectable abnormalities associated with amino acid loss. Excessive loss of arginine in urine predisposes cats to hyperammonemic encephalopathy. Some cystinuric dogs may have carnitinuria.
- Cystinuric dogs have been classified into three different types: Type 1 autosomal recessive SLC3A1 mutations found in Newfoundlands, Landseer, and Labrador retrievers; Type 2 autosomal dominant SLC7A9 identified in Australian cattle dogs and European Miniature Pinschers, and Type 3, which has sex limited inheritance and has been identified in Mastiff and related breeds, Scottish Deerhound, and Irish Terriers.
- Because not all cystinuric dogs and cats form uroliths, cystinuria is a predisposing rather than a primary cause of cystine urolithiasis. Cystine is relatively insoluble in acid urine; becomes more soluble in alkaline urine.
- A genetic missense mutation of the SLC3A1 Gene has recently been identified in one cat with cystine uroliths.

SIGNALMENT

- Dogs—primarily adult (mean age 5 years; range 3 months–14 years) males but may also affect females. It occurs in excess of 80 breeds, including dachshunds, English bulldogs, Newfoundlands, Labrador retrievers, Chihuahuas, pit bulls, and French bulldogs. May be detected in male and female Newfoundland and Labradors < 1 year of age.
- Cats—primarily adult (mean age at diagnosis, 3.5 years; range, 4 months–12 years) males and females; most common the domestic shorthair and Siamese breeds.

SIGNS

- Depend on location, size, and number of uroliths; affected animals may be asymptomatic.
- Urocystoliths—include pollakiuria, dysuria, and hematuria.

• Urethroliths—include pollakiuria, dysuria, and sometimes voiding of small smooth uroliths. Complete outflow obstruction may result in post-renal azotemia that may progress to uremia.

• Nephroliths—typically asymptomatic; may be associated with manifestations of hydronephrosis and renal insufficiency.

CAUSES & RISK FACTORS

- Cystinuria is a risk factor.
- Breed predisposition.
- In young and middle-aged dogs with previous history of cystine urolithiasis—recurrence within 6–12 months following surgery unless prophylactic therapy is given.
- Urolith formation—enhanced by acidic, concentrated urine, incomplete and infrequent micturition.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Uroliths mimic other causes of pollakiuria, dysuria, hematuria, and/or outflow obstruction.
- Differentiate from other types of uroliths by urinalysis, radiography, and quantitative analysis of voided or retrieved uroliths.

CBC/BIOCHEMISTRY/URINALYSIS

- Cystine crystals are six-sided; insoluble in acetic acid.
- Positive urine cyanide-nitroprusside test.

OTHER LABORATORY TESTS

- Urinary amino acid profiles—reveal abnormal quantities of cystine and, in some dogs and cats, ornithine, lysine, arginine, and other amino acids.
- Quantitative mineral analysis of uroliths.
- DNA test.

IMAGING

- Radiography—the radiodensity of cystine uroliths is similar to that of struvite and silica, less than that of calcium oxalate and calcium phosphate, and greater than that of ammonium urate; when large enough, cystine uroliths can be detected by survey radiography.
- Ultrasonography—can detect cystine uroliths; does not provide reliable information about the radiodensity or shape.

DIAGNOSTIC PROCEDURES

Urethrocytostoscopy—used to detect cystine urethroliths and urocystoliths.



TREATMENT

- In dogs: Medical dissolution of uroliths by combination of *N*-(2-mercaptopropionyl)-glycine (2-MPG) and dietary therapy; Hill's

Prescription Diet Canine u/d reduces urinary excretion of cystine, promotes formation of alkaline urine, and reduces urine concentration; it is used in conjunction with 2-MPG for urolith dissolution and is often effective alone in preventing recurrence of cystine uroliths.

• In one study, castration reduced recurrence of cystine uroliths in dogs identified with Type 3, sex limited inheritance.

• In cats: Diets designed for renal insufficiency and geriatric cats may be suitable to minimize formation. Give enough potassium citrate (40–75 mg/kg PO q12h) to maintain a urine pH of 7.5. Choose a moist formulation diet to help reduce urine concentration. Dissolution with 2-MPG has been studied in a small number of cats at an oral dose of 12–20 mg/kg q12h. Frequency of recurrence was minimized in these cats without adverse side effects.

• In dogs, and cats, remove urocystoliths unable to be dissolved by voiding urohydropropulsion, basket retrieval, lithotripsy, or surgery.



MEDICATIONS

DRUG(S)

Urine Alkalinizers

• For patients that have acidic urine despite dietary therapy and control of urease-positive urinary tract infections.

• Data from cystinuric humans suggest that dietary sodium may enhance cystinuria; thus potassium citrate may be preferable to sodium bicarbonate as a urine alkalinizer. Give enough potassium citrate (40–75 mg/kg PO q12h) to maintain a urine pH of 7.5.

Thiol-Containing Drugs

• 2-MPG decreases urine concentration of cystine by combining with cysteine to form cysteine-2-MPG, which is more soluble than cystine.

• With status as an orphan drug, Thiola™ is only available from the distributor Retrophin. Generic 2-MPG (Tiopronin) may be obtained from compounding pharmacies. In dogs: 2-MPG may be given at a dosage of 15–20 mg/kg PO q12h to dissolve canine cystine uroliths in conjunction with dietary therapy. In our hospital, mean dissolution time was 78 days (range, 11–211 days).

• 2-MPG may be given at a lower dosage (5–10 mg/kg PO q12h) to prevent recurrent canine cystine uroliths.

• In cats: 2-MPG has been studied in a small number of cats at an oral dose of 12–20 mg/kg q12h. Frequency of recurrence was minimized in these cats without adverse side effects.

UROLITHIASIS, CYSTINE

(CONTINUED)

- Drug-induced adverse events associated with 2-MGP are uncommon in dogs; they include reversible Coombs'-positive spherocytic anemia, thrombocytopenia, glomerular proteinuria, myopathy, aggressiveness, and increased hepatic enzyme activity.
- 2-MPG should be used with caution in cats, as the efficacy and safety of 2-MPG has not been thoroughly evaluated in normal or cystinuric cats.

**FOLLOW-UP**

- Minimize recurrence with dietary management or 2-MPG.

- Monitor urolith dissolution at 30-day intervals by urinalysis, survey or contrast radiography, or ultrasonography.
- Although cystine uroliths tend to recur, recurrence does not affect all cystinuric dogs and cats.
- In some older dogs, the rate of recurrence declines as a consequence of a reduction in the magnitude of cystinuria.

**MISCELLANEOUS****ABBREVIATION**

- 2-MPG = *N*-(2-mercaptopropionyl)-glycine

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UROLITHIASIS, STRUVITE—CATS



BASICS

DEFINITION

Struvite uroliths and struvite urethral plugs have physical and etiopathogenic differences; thus, these terms should not be used as synonyms. Struvite uroliths are polycrystalline concretions composed primarily of magnesium ammonium phosphate and small quantities of matrix. Struvite feline urethral plugs commonly are composed of large quantities of matrix mixed with crystals (especially magnesium ammonium phosphate). Some urethral plugs are composed primarily of organic matrix, sloughed tissue, blood, and/or inflammatory reactants.

PATOPHYSIOLOGY

- See Urolithiasis, Struvite—Dogs.
- The most commonly encountered form of naturally occurring feline urethral plugs contains relatively large quantities of matrix in addition to minerals, especially struvite. Risk factors associated with formation of MAP crystals contained in urethral plugs are similar to those associated with formation of struvite uroliths. Prevention or control of these risk factors should minimize the recurrence of the struvite component of urethral plugs. Specific causes and composition of urethral plug matrix have not yet been classified. One hypothesis is that plug matrix follows the onset of urinary tract infections or other inflammatory disorders such as idiopathic cystitis.

SYSTEMS AFFECTED

Renal/Urologic—upper and lower urinary tract

INCIDENCE/PREVALENCE

- The prevalence of feline struvite uroliths submitted to the Minnesota Urolith Center declined from 78% in 1981 to 33% in 2002, but then increased to 48% in 2005. Struvite uroliths comprised 46% of feline uroliths in 2013. In comparison, uroliths comprised primarily of calcium oxalate increased from approximately 2% in 1981 to 55% in 2002, but then decreased to 40% in 2005. Calcium oxalate comprised 41% of feline uroliths in 2013. These dramatic changes in the frequency of occurrence of the mineral composition of feline uroliths parallel changes in the composition of manufactured diets.
- Currently, struvite makes up approximately 50% of all types of uroliths in the feline lower urinary tract. Of these, 95% are sterile.
- Struvite has been detected in approximately 8% of feline nephroliths.
- Since 1981, struvite has remained the most common (~90%) mineral in matrix-crystalline urethral plugs.

SIGNALMENT

Species

Cat (see Urolithiasis, Struvite—Dogs)

Mean Age and Range

- Mean age at time of diagnosis is approximately 7 years (range, < 1–22 years).
- Sterile struvite uroliths do not affect immature cats; infection-induced struvite may occur in immature cats:

Predominant Sex

- Struvite uroliths are more common in female cats (55%) than in males (45%).
- Struvite urethral plugs primarily affect males.

SIGNS

General Comments

- Affected cats may be asymptomatic.
- Depend on location, size, number, and cause of uroliths.

Historical Findings

- Typical signs of urocystoliths include pollakiuria, dysuria, perirenia, and hematuria.
- Typical signs of urethroliths include pollakiuria, perirenia, dysuria, and sometimes voiding of small, smooth uroliths.
- Signs of post-renal azotemia (e.g., anorexia and vomiting) are found in some cats with outflow obstruction.
- Manifestations of renal insufficiency (polyuria and polydipsia) are found in some cats with nephroliths.
- Signs typical of outflow obstruction (e.g., dysuria, large painful urinary bladder, and signs of post-renal azotemia) are found in cats with struvite urethral plugs.

Physical Examination Findings

- A thickened, firm, contracted bladder wall is found in some cats with urocystoliths.
- Detection of urocystoliths by palpation is unreliable because it is insensitive.
- Urethral plugs or urethroliths may be detected by examination of the distal penis and penile urethra.
- Outflow obstruction results in an enlarged urinary bladder and signs of post-renal azotemia.

CAUSES

See "Pathophysiology"

RISK FACTORS

- For formation of sterile struvite uroliths, risk factors include mineral composition, energy content, and moisture content of diets; urine-alkalinizing metabolites in diets; quantity of diet consumed; ad libitum versus meal-feeding schedules; formation of concentrated urine; and retention of urine.
- Probable risk factors for infection-induced struvite urolithiasis—include urinary tract infection with urease-producing microbial pathogens, abnormalities in local host defenses that allow bacterial urinary tract infections (including perineal urethrostomies), and the quantity of urea (the substrate of urease) excreted in urine.
- The normal small diameter of the distal urethra of male cats

predisposes them to obstruction with plugs and urethroliths.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Uroliths mimic other causes of pollakiuria, dysuria, perirenia, hematuria, and/or outflow obstruction.
- Differentiate struvite uroliths and urethral plugs from other types of uroliths by signalment, urinalysis, urine culture, radiography, ultrasonography, cystoscopy, and quantitative analysis of voided or retrieved uroliths or plugs.

CBC/BIOCHEMISTRY/URINALYSIS

- Complete outflow obstruction may cause post-renal azotemia (e.g., high serum urea nitrogen, creatinine, and phosphorus).
- Magnesium ammonium phosphate crystals typically appear as colorless, orthorhombic (having three unequal axes intersecting at right angles), coffin-like prisms. They often have three to eight sides.

OTHER LABORATORY TESTS

- Pretreatment quantitative bacterial urine cultures (preferably with specimen obtained by cystocentesis) yield bacterial urinary tract infections in only ~1–3% of affected 2- to 7-year-old patients.
- Quantitative mineral analysis is the accepted standard of practice for uroliths and urethral plugs retrieved during voiding, by voiding urohydropropulsion, by aspiration into a urinary catheter, or by cystoscopy.
- Bacterial culture of inner portions of uroliths retrieved from patients with urease-positive microbes cultured from urine may be of value.

IMAGING

Radiography

- Struvite uroliths—radiodense; may be detected by survey radiography; some struvite urethral plugs may be detected by survey radiography.
- The size and number of uroliths are not a reliable index of probable efficacy of dissolution therapy.
- Contrast urethrocystography helps identify the site(s) of urethral obstruction and urethral strictures.

Ultrasonography

- Detects location and approximate size and number of uroliths. However, tends to overestimate stone size and underestimate stone number.
- Does not indicate degree of radiodensity or shape of uroliths.

DIAGNOSTIC PROCEDURES

Cystoscopy reveals location, number, size, and shape of urethroliths and urocystoliths.

PATHOLOGIC FINDINGS

Urethral plugs may contain red blood cells, white cells, transitional epithelial cells, bacteria, and/or viruses in addition to matrix and minerals.

UROLITHIASIS, STRUVITE—CATS

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

- Retrograde urohydropropulsion to eliminate urethral stones, lavage to remove urethral plugs.
- Voiding urohydropropulsion to eliminate bladder and urethral stones, and/or surgery require short periods of hospitalization.
- Medical dissolution of struvite uroliths is an outpatient strategy.

DIET

- Treatment of sterile struvite uroliths with an appropriate diet (prototype diet is Hill's Prescription Diet Feline s/d) typically results in dissolution within 2–4 weeks of therapy. It has become the treatment standard of practice.
- Infection-induced struvite urocystoliths may be dissolved by feeding a calculolytic diet and an appropriate antimicrobial.
- Continue diet therapy for 1 month after survey radiographic evidence of urolith dissolution.
- Struvite crystalluria may be minimized by feeding magnesium-restricted urine-acidifying diets.
- Canned (moist) foods help to reduce urine concentration of calculogenic metabolites and promote increased frequency of normal voiding.

CLIENT EDUCATION

- If dietary management is used, limit access to other foods and treats.
- Short-term (weeks to months) treatment with a calculolytic diet (Hill's Feline s/d) and antibiotics as needed is effective in dissolving infection-induced struvite uroliths.
- Owners of cats with infection-induced struvite urocystoliths must comply with dosage schedule for antibiotic therapy.
- Avoid feeding calculolytic diets to immature cats.

SURGICAL CONSIDERATIONS

- Ureteroliths cannot be dissolved. Consider surgery for persistent ureteroliths associated with morbidity.
- Urethroliths cannot be medically dissolved. Consider voiding urohydropropulsion to remove urethroliths or urethral plugs. Alternatively, move urethroliths into the bladder by retrograde urohydropropulsion.
- Immovable urethroliths, recurrent urethral plugs, or strictures of the distal urethra may require perineal urethrostomy.
- Consider laser lithotripsy for urocystoliths and/or urethroliths.
- Consider surgical correction if uroliths are obstructing urine outflow and/or if correctable abnormalities predisposing to recurrent urinary tract infection are identified by radiography or other means.
- Uroliths and urethral plugs should be localized before considering surgical correction.
- Radiographs should be obtained immediately following surgery to verify that all uroliths were removed.



MEDICATIONS

DRUG(S)

- Dietary dissolution of infection-induced urocystoliths or requires oral administration of appropriate antibiotics, chosen on the basis of bacterial culture and antimicrobial susceptibility tests. Give antibiotics at therapeutic dosages until the urinary tract infection is eradicated and there is no radiographic evidence of uroliths.
- Buprenorphine may be considered to alleviate clinical signs of discomfort; suggested empirical dose is 15 µg/kg via buccal transmucosal administration q8–12h as needed. Tolteridine may be considered as an anticholinergic and antispasmodic to minimize hyperactivity of the bladder detrusor muscle and urge incontinence; the suggested empirical dose is 0.05 mg /kg PO q12h.

CONTRAINDICATIONS

Do not give urine acidifiers to azotemic patients or immature cats.

PRECAUTIONS

Azotemic patients are at increased risk for adverse drug events.



FOLLOW-UP

PATIENT MONITORING

Check rate of urolith dissolution at monthly intervals by urinalysis, urine culture, survey or contrast radiography, or ultrasonography.

PREVENTION/AVOIDANCE

- Recurrent sterile struvite uroliths in cats may be prevented by using acidifying, magnesium-restricted diets or urine acidifiers. Do not administer urine acidifiers with acidifying diets.
- Consider use of a modified high-moisture, magnesium-restricted, acidifying diet that has not been supplemented with sodium (Prescription Diet c/d Multicare Feline) to minimize recurrence of struvite and/or calcium oxalate crystalluria and uroliths.
- For patients whose urine has been acidified, carefully monitor them for calcium oxalate crystalluria. Change management protocol if persistent calcium oxalate crystalluria develops.
- In patients at risk for both struvite and calcium oxalate crystalluria, focus on preventing calcium oxalate uroliths. Struvite uroliths can be medically dissolved; recurrent calcium oxalate uroliths cannot be dissolved.
- Infection-induced struvite urolithiasis can be prevented by eradicating and controlling urinary tract infections. Use of magnesium-restricted, acidifying diets is not required if the urease-positive microbes can be eradicated.

POSSIBLE COMPLICATIONS

- Urocystoliths may pass into and obstruct the urethra of male cats, especially if the patient is persistently dysuric. Urethral obstruction may be managed by retrograde urohydropropulsion.
- An indwelling transurethral catheter increases the risk for iatrogenic bacterial urinary tract infection and/or urethral stricture.

EXPECTED COURSE AND PROGNOSIS

In our hospital, the mean time for dissolution of feline sterile urocystoliths was 1 month (range, 2 weeks–5 months). The mean time for dissolution of infection-induced struvite urocystoliths was 10 weeks (range, 9–12 weeks).



MISCELLANEOUS

ASSOCIATED CONDITIONS

Any disease that predisposes to bacterial urinary tract infection.

AGE-RELATED FACTORS

Infection-induced struvite is the most common urolith in immature cats. Sterile struvite is rare in immature cats.

SYNOMYMS

- Feline lower urinary tract disease
- Feline urologic disease
- FUS

SEE ALSO

- Lower Urinary Tract Infection chapters
- Nephrolithiasis
- Urolithiasis, Struvite—Dogs

ABBREVIATIONS

- FUS = feline urologic syndrome
- MAP = magnesium ammonium phosphate

Suggested Reading

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Consulting Editor Carl A. Osborne



Client Education Handout
available online

UROLITHIASIS, STRUVITE—DOGS



BASICS

DEFINITION

Formation of polycrystalline concretions (i.e., uroliths, calculi, or stones) composed of MAP (a.k.a. as struvite) in the urinary tract.

PATHOPHYSIOLOGY

Infection-Induced Struvite

- Urine must be supersaturated with MAP for struvite uroliths to form. MAP supersaturation of urine may be associated with several factors, including urinary tract infections with urease-producing microbes, alkaline urine, genetic predisposition, and diet. • If animals are affected by urinary tract infections caused by urease-producing microbes (especially species of *Staphylococcus*, *Proteus*, and *Ureaplasma*) and their urine contains sufficient urea, the result is a unique combination of concomitant elevations in the concentrations of ammonium (NH_4^+), phosphate (PO_4^{3-}), and carbonate (CO_3^{2-}) in an alkaline environment. These conditions favor formation of uroliths containing struvite ($\text{MgNH}_4\text{PO}_4 \cdot 6\text{H}_2\text{O}$), calcium apatite [$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH}_2)$], and carbonate apatite [$\text{Ca}_{10}(\text{PO}_4)_6\text{CO}_3$]. • Consumption of dietary protein in excess of the daily requirement for anabolism results in formation of urea from catabolism of amino acids. • The magnitude of hyperammonuria, hypercarbonaturia, and alkaluria mediated by microbial urease depends on the quantity of urea (the substrate of urease) in urine. • Abnormal urinary excretion of minerals as a result of enhanced glomerular filtration rate, reduced tubular reabsorption, or enhanced tubular secretion is not required for initiation and growth of infection-induced struvite uroliths; however, metabolic and anatomic abnormalities may indirectly induce struvite uroliths by predisposing to urinary tract infections.

Sterile Struvite

- Dietary or metabolic factors may be involved in the genesis of sterile struvite uroliths in dogs.
- Microbial urease is not involved in formation of sterile struvite uroliths.

SYSTEMS AFFECTED

Renal/Urologic

GENETICS

- The high incidence of struvite uroliths in some breeds of dogs such as miniature schnauzers suggests a familial tendency. We hypothesize that susceptible miniature schnauzers inherit some abnormality of local host defenses of the urinary tract that increases their susceptibility to urinary tract infection. • Sterile struvite uroliths were found in a family of English cocker spaniels.

INCIDENCE/PREVALENCE

Struvite uroliths account for approximately 40% of stones affecting the canine lower

urinary tract and 33% of stones affecting the upper urinary tract.

GEOGRAPHIC DISTRIBUTION

Ubiquitous

SIGNALMENT

Species

Dog (see Urolithiasis, Struvite—Cats)

Breed Predilections

- Miniature schnauzer, Shih Tzu, Bichon Frise, miniature poodle, cocker spaniel, and Lhasa apso. • Any breed may be affected.

Mean Age and Range

- Mean age, 6 years (range < 1 to > 19 years).
- Most uroliths in immature (< 12 months old) dogs are infection-induced struvite.

Predominant Sex

More common in females (~85%) than males (~15%), which may be related to the greater propensity of females to develop bacterial UTI.

SIGNS

General Comments

- Some dogs are asymptomatic. • Signs depend on location, size, and number of uroliths.

Historical Findings

- Typical signs of urocystoliths include pollakiuria, dysuria, and hematuria; sometimes small, smooth uroliths are voided.
- Typical signs of urethroliths include pollakiuria and dysuria; sometimes small, smooth uroliths are voided. • Nephroliths may be associated with manifestations of renal insufficiency. Obstruction to urine outflow with bacterial urinary tract infection may result in generalized pyelonephritis and septicemia.

Physical Examination Findings

- Uroliths may be palpated in the urinary bladder and urethra (by rectal exam).
- Obstruction of the urethra may cause enlargement of the urinary bladder.
- Obstruction of a ureter may cause enlargement of the associated kidney.
- Complete urine outflow obstruction combined with bacterial infection may cause ascending urinary tract infection, signs of renal failure, and signs of septicemia.

CAUSES

- Urinary tract disorders that predispose to infections with urease-producing bacteria, fungal pathogens, or ureaplasma in patients whose urine contains a large quantity of urea.
- Specific causes of sterile struvite uroliths are unknown.

RISK FACTORS

- Exogenous or endogenous exposure to high concentrations of glucocorticoids predispose to bacterial urinary tract infection.
- Abnormal retention of urine. • Alkaline urine decreases the solubility of struvite.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Uroliths mimic other causes of pollakiuria, dysuria, hematuria, and/or outflow obstruction. • Differentiate from other types of uroliths by signalment, rectal exam, urinalysis, urine culture, radiography, and quantitative analysis of voided or retrieved uroliths.

CBC/BIOCHEMISTRY/URINALYSIS

- Complete outflow obstruction can cause post-renal azotemia (e.g., high BUN, creatinine, and phosphorus). • Magnesium ammonium phosphate crystals typically appear as colorless, orthorhombic (having three unequal axes intersecting at right angles), coffin-like prisms. They may have three to six or more sides and often have oblique ends.

OTHER LABORATORY TESTS

- Quantitative bacterial culture of urine, preferably collected by cystocentesis.
- Bacterial culture of inner portions of infection-induced struvite uroliths.
- Quantitative mineral analysis of uroliths retrieved during voiding, by voiding urohydropropulsion, by aspiration into a urinary catheter, or by cystoscopy.

IMAGING

- Struvite uroliths are radiodense and may be detected by survey radiography.
- Ultrasonography—can detect uroliths, but provides no information about their density or shape. • Determine precise location, size, and number of uroliths; the size and number are not a reliable index of probable efficacy of dissolution therapy.



TREATMENT

APPROPRIATE HEALTH CARE

- Retrograde urohydropropulsion to move urethral stones and reestablish urethral patency, voiding urohydropropulsion to eliminate bladder stones. • Shock-wave lithotripsy and/or surgery require short periods of hospitalization. • Medical dissolution of struvite uroliths is an outpatient strategy.

DIET

- Infection-induced and sterile struvite urocystoliths and nephroliths may be dissolved by feeding a calculolytic food (Hill's Prescription Diet Canine s/d). • Continue calculolytic diet therapy for 1 month beyond survey radiographic evidence of urolith dissolution. • Avoid use of the protein-restricted diet in patients with protein-calorie malnutrition. The calculolytic diet is designed

UROLITHIASIS, STRUVITE—DOGS

(CONTINUED)

for short-term (weeks to months) dissolution therapy, rather than long-term (months to years) prophylactic therapy. If used, monitor the patient for evidence of protein malnutrition. Avoid prolonged feeding of the calculolytic diet to immature dogs.

CLIENT EDUCATION

- If dietary management is used, limit access to other foods and treats.
- Short-term treatment with a calculolytic food and administration of antibiotics has been effective in dissolving struvite uroliths.
- Comply with dosage schedule for antibiotic and diet therapy.

SURGICAL CONSIDERATIONS

- Ureteroliths cannot be dissolved; consider surgery or shock-wave (ESWL) lithotripsy for persistent ureteroliths associated with morbidity.
- Urethroliths cannot be medically dissolved; consider voiding urohydropropulsion if the urethroliths are likely to pass through the entire length of the urethra. Alternatively, consider lithotripsy or move urethroliths into the bladder by retrograde urohydropropulsion.
- Immovable urethroliths may require urethrotomy or urethrostomy.
- Nephroliths causing outflow obstruction or associated with non-functioning kidneys cannot be dissolved medically.
- Consider surgical correction if uroliths are obstructing urine outflow and/or if correctable abnormalities predisposing to recurrent urinary tract infection are identified by radiography or other means.



MEDICATIONS

DRUG(S)

- Dietary dissolution of infection-induced urocystoliths or nephroliths requires oral administration of appropriate antibiotics, chosen on the basis of quantitative bacterial culture and antimicrobial susceptibility tests. Give antibiotics at therapeutic dosages until there is no radiographic evidence of uroliths and there is laboratory confirmation of eradication of urinary tract infection.
- Patients with infection-induced struvite urocystoliths associated with persistent bacterial infection with urease-producing bacteria and refractory to dietary and antibiotic dissolution may be given AHA (Lithostat, Mission Pharmacal, 12.5 mg/kg PO q12h). AHA is a urease inhibitor that blocks hydrolysis of urea to ammonia.

CONTRAINDICATIONS

AHA is teratogenic and should not be given to pregnant dogs.

PRECAUTIONS

- Diet-induced polyuria will reduce the concentration of antimicrobial drugs in urine; consider this fact when calculating antimicrobial dosages.
- Prolonged administration of AHA at higher doses

induces abnormalities in bilirubin metabolism in some dogs.

- Higher doses of AHA may induce a reversible hemolytic anemia.



FOLLOW-UP

PATIENT MONITORING

Monitor rate of urolith dissolution at monthly intervals by urinalysis, urine culture, ultrasonography, and/or survey or contrast radiography.

PREVENTION/AVOIDANCE

- Infection-induced struvite urolithiasis may be prevented by eradicating and controlling infections by urease-producing bacteria.
- Recurrent sterile struvite uroliths may be prevented by use of acidifying, magnesium-restricted diets (Hill's Prescription Diet Canine c/d) or urine acidifiers.
- Monitor patients whose urine has been acidified for calcium oxalate crystalluria. Change management protocol if persistent calcium oxalate crystalluria develops.
- In patients at risk for both struvite and calcium oxalate crystalluria, focus on prevention of calcium oxalate uroliths—struvite uroliths can be medically dissolved if they recur; recurrent calcium oxalate uroliths cannot be dissolved.

POSSIBLE COMPLICATIONS

- Benefits and risks are associated with feeding struvitolytic diets. Not all patients qualify for dietary medical management, including those with (1) abnormal fluid accumulation, (2) azotemic primary renal failure, and (3) predispositions to pancreatitis (especially miniature schnauzers with hyperlipidemia).
- Urocystoliths may pass into and obstruct the urethra of male dogs, especially if the patient is persistently dysuric. Urethral obstruction may be managed by retrograde urohydropropulsion or lithotripsy.
- Dysuria may be minimized by antimicrobial treatment of bacterial urinary tract infections and oral administration of anticholinergic drugs.
- Dogs that do not consume their daily requirement of the calculolytic diet may develop varying degrees of protein calorie malnutrition. This can be prevented by proper calculation of the daily dietary requirement and adjustment in the quantity of food fed on the basis of serial physical examination.
- Diet-associated polyuria will result in voiding increased urine volume. This may be associated with varying degrees of urinary incontinence in neutered female dogs with a predisposition to estrogen-responsive incontinence.

EXPECTED COURSE AND PROGNOSIS

- In our hospital, the mean time for dissolution of infection-induced urocystoliths in dogs was approximately 3 months (range 2 weeks–7 months). The mean time for dissolution of infection-induced struvite

nephroliths in dogs was 6 months (range 2–10 months). The mean time for dissolution of sterile struvite urocystoliths in dogs was 6 weeks (range 4–12 weeks).

- Compliance with dietary recommendations is suggested by a reduced concentration of urea in serum (approximately 10 mg/dL), and a low urine specific gravity (1.004–1.014).
- If uroliths increase in size during dietary management or do not begin to decrease in size after approximately 4–8 weeks of appropriate medical management, alternative methods should be considered. Difficulty in inducing complete dissolution of uroliths by creating urine under-saturated with struvite should prompt consideration that (1) the wrong mineral component was identified, (2) the nucleus of the uroliths has a different mineral composition than other portions of the urolith, and (3) the owner is not complying with therapeutic recommendations.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Any disease that predisposes to bacterial urinary tract infection.

AGE-RELATED FACTORS

Infection-induced struvite is the most common form of urolith in immature dogs. The uroliths develop as a result of microbial UTI.

PREGNANCY/FERTILITY/BREEDING

- AHA is teratogenic.
- The calculolytic food is not designed to sustain pregnancy.

SYNOMYS

- Phosphate calculi
- Infection stones
- Urease stones
- Triple-phosphate stones

ABBREVIATIONS

- AHA = acetohydroxamic acid
- ESWL = extracorporeal shock wave lithotripsy
- MAP = magnesium ammonium phosphate
- UTI = urinary tract infection

Suggested Reading

Osborne CA, Lulich JP, Bartges JW, et al. Canine and feline urolithiasis: Relationship of etiopathogenesis to treatment and prevention. In: Osborne CA, Finco DR, eds., *Canine and Feline Nephrology and Urology*. Baltimore: Williams & Wilkins, 1995, pp. 798–888.

Authors Carl A. Osborne, Jody P. Lulich, and Eugene E. Nwaokorie

Consulting Editor Carl A. Osborne



Client Education Handout
available online

UROLITHIASIS, URATE



BASICS

DEFINITION

Uroliths composed of uric acid, sodium urate, or ammonium urate

PATHOPHYSIOLOGY

- Impaired conversion of uric acid to allantoin causes high concentration of uric acid in serum and urine.
- Patients with portosystemic shunts may develop ammonium urate uroliths because of impaired hepatic metabolism of uric acid and ammonia.

GENETICS

Dalmatians have a breed predisposition to forming urate urolithiasis.

INCIDENCE/PREVALENCE

Approximately 5–8% of uroliths retrieved from dogs and cats

SIGNALMENT

Species

Dog and cat

Breed Predilections

Dalmatians, English bulldogs, and breeds at risk for portosystemic shunts (e.g., Yorkshire terriers).

Mean Age and Range

- Mean age in patients without portosystemic shunts is 3.5 years (range, 0.5 to > 10 years).
- Mean age in patients with portosystemic shunts is < 1 year (range, 0.1 to > 10 years).

Predominant Sex

- More common in male dogs without portosystemic shunts.
- No sex predilection in dogs with portosystemic shunts or cats.

SIGNS

Historical Findings

Hematuria, dysuria, pollakiuria. Possible hepatic encephalopathy in patients with portosystemic shunts.

Physical Examination Findings

- Urethral obstruction
- No signs in some patients
- Stunted growth and copper-colored irises (cats) in patients with portosystemic shunts

CAUSES

Rule out portosystemic shunt

RISK FACTORS

- High purine intake (glandular meat)
- Persistent aciduria in a predisposed animal



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other causes of lower or upper urinary tract disease

CBC/BIOCHEMISTRY/URINALYSIS

- Aciduria, urate crystalluria, azotemia in patients with urinary outflow obstruction.
- Low BUN and microcytosis in patients with portosystemic shunts; reduced production of urea by the liver may mask hypoglycemia, hypoalbuminemia, and increased hepatic enzyme activities in patients with more severe hepatic dysfunction.

OTHER LABORATORY TESTS

Liver function tests such as bile acids have abnormal results in patients with portosystemic shunts.

IMAGING

- Urate uroliths may be radiolucent; may need intravenous pyelogram to detect nephroliths or double contrast cystography to detect urocystoliths. Microhepatitis in patients with portosystemic shunts.
- Ultrasonography may reveal small uroliths and a portosystemic shunt.

DIAGNOSTIC PROCEDURES

Liver biopsy; bile acids, blood ammonia

PATHOLOGIC FINDINGS

In patients with portosystemic shunts, liver biopsy may reveal hepatic atrophy and/or dysplasia.



TREATMENT

APPROPRIATE HEALTH CARE

Urethral or ureteral obstruction may require inpatient treatment. Urate uroliths can be dissolved on outpatient basis.

NURSING CARE

Fluid therapy to correct dehydration

ACTIVITY

Usually not restricted, except after surgery

DIET

For dissolution and prevention, a high moisture, low-purine, urine-alkalinizing diet.

CLIENT EDUCATION

Recurrence of uroliths is possible. Therefore a plan to minimize recurrence should be developed.

SURGICAL CONSIDERATIONS

- Cystotomy, urethrotomy, nephrotomy, percutaneous cystolithotomy, or cystoscopy and retrieval or laser lithotripsy to remove uroliths.
- Portosystemic shunt ligation.



MEDICATIONS

DRUG(S)

Allopurinol (15 mg/kg PO q12h), a xanthine oxidase inhibitor, for dissolution (see Figure 2).

CONTRAINdications

Glucocorticoids and other immunosuppressive drugs may promote hyperuricosuria.

Endogenous Purines
Dietary Purines
↓
Purine Pool

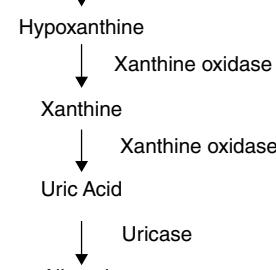


Figure 1.

PRECAUTIONS

Allopurinol is contraindicated in animals with renal failure and is not effective in animals with portosystemic shunts.

POSSIBLE INTERACTIONS

Skin eruption with use of allopurinol and ampicillin.



FOLLOW-UP

PATIENT MONITORING

See Figure 3.

PREVENTION/AVOIDANCE

High-moisture, low-purine, urine-alkalinizing diet

POSSIBLE COMPLICATIONS

- Urethral obstruction
- Uroliths likely to recur if no preventive measures

EXPECTED COURSE AND PROGNOSIS

- Medical dissolution takes an average of 4 weeks, if there is good compliance.
- Medical dissolution usually not successful with portosystemic shunt.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Portosystemic shunt

PREGNANCY/FERTILITY/BREEDING

Low-protein/purine diet is not recommended for pregnant or lactating animals.

Suggested Reading

Bartges JW, Osborne CA, Felice LJ. Canine xanthine uroliths: Risk factor management. In: Kirk RW, Bonagura JD, eds., Current Veterinary Therapy XI. Philadelphia: Saunders, 1992, pp. 900–905.

Osborne CA, Lulich JP, Thumchai R, et al. Diagnosis, medical treatment, and prognosis

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UROLITHIASIS, URATE

(CONTINUED)

of feline urolithiasis. *Vet Clin North Am Small Anim Pract* 1996; 26:589–628.

Author Joseph W. Bartges
Consulting Editor Carl A. Osborne



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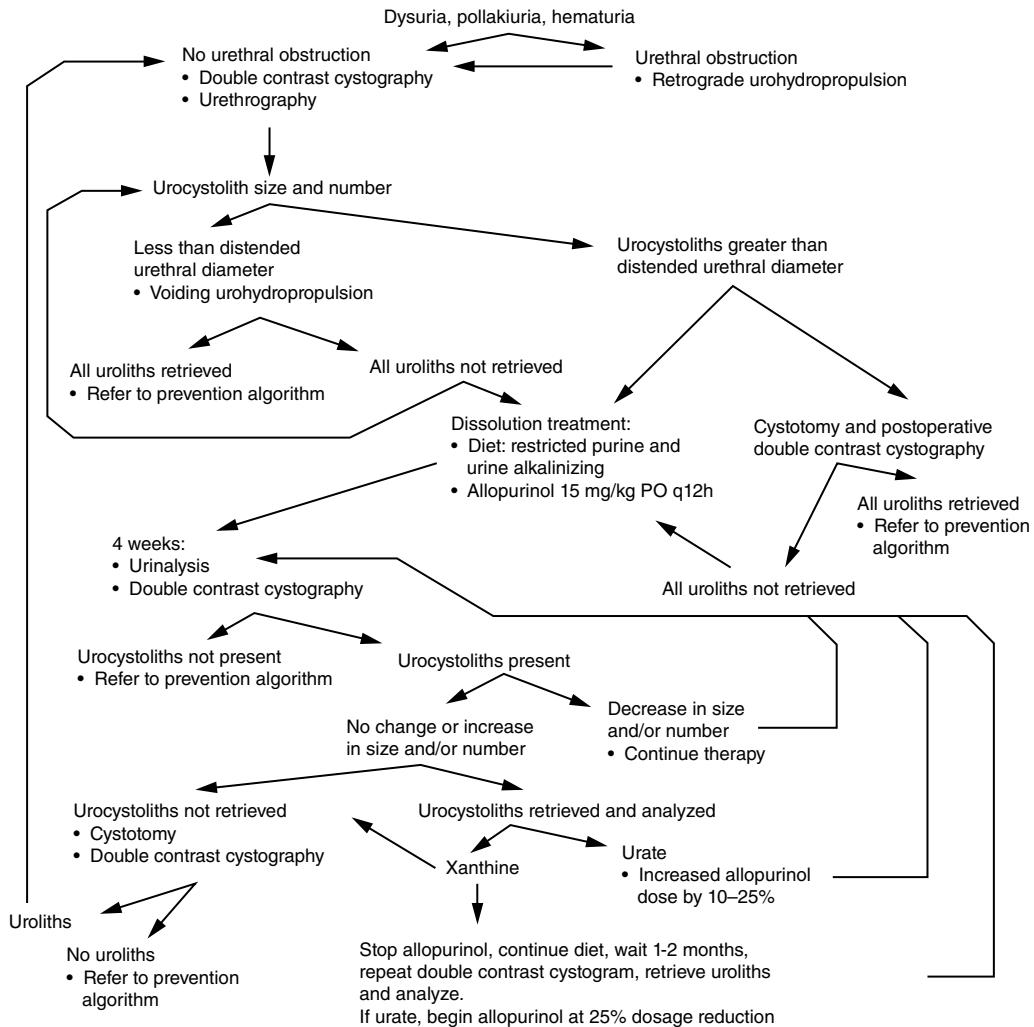


Figure 2.

Algorithm for treatment of urate urocystolithiasis.

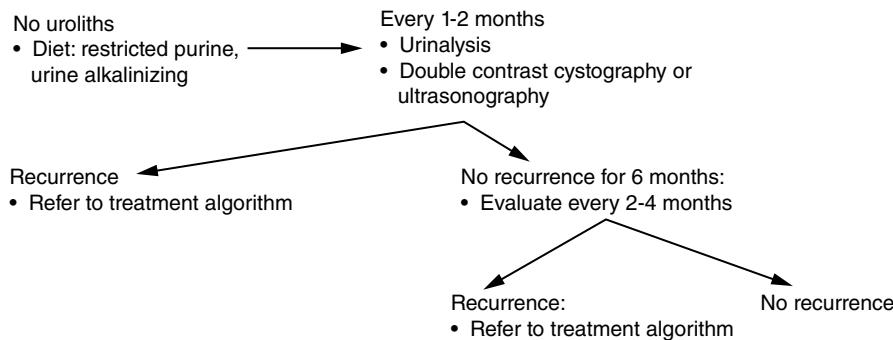


Figure 3.

Algorithm for prevention of urate urocystolithiasis.

UROLITHIASIS, XANTHINE



BASICS

OVERVIEW

- Xanthine, a degradation product of purine metabolism, is converted to uric acid by the enzyme xanthine oxidase. Naturally occurring (enzyme deficiency) or drug-induced (allopurinol) impairment of xanthine oxidase ultimately results in hyperxanthinemia and xanthinuria. • In naturally occurring xanthinuria, a familial or congenital defect in xanthine oxidase activity is likely. A breed predisposition has not been identified in cats (number = 392 submitted to the Minnesota Urolith Center (MUC) 1981–2014). In Cavalier King Charles spaniels, an autosomal recessive mode of inheritance has been postulated to occur. Xanthine nephrolithiasis in a dachshund associated with renal failure has been reported. • Acquired xanthinuria is a common complication of treatment of urate urolithiasis or leishmaniasis with allopurinol. High purine diets increase the risk of xanthinuria in patients treated with allopurinol. • Xanthine is the least soluble of the purines excreted in urine.

SIGNALMENT

- Dog and cat. Naturally occurring xanthinuria is more common in cats than in dogs. • In dogs, allopurinol-induced xanthinuria may affect any breed, age, or gender. Naturally occurring xanthinuria and xanthine uroliths have been observed in young Cavalier King Charles spaniels. • In cats, xanthine uroliths affect adult males (66%) and females (33%) (mean age at diagnosis 3.3 years; range 2 months–13 years). Most common in the domestic shorthair and domestic longhair breeds.

SIGNS

- Dependent on location, size, and number of uroliths. • Pollakiuria, dysuria, hematuria and voiding of small, smooth, yellow uroliths. Complete outflow obstruction may result in azotemia. • May be asymptomatic. Nephroliths may be associated with hydronephrosis and renal insufficiency.

CAUSES & RISK FACTORS

- Xanthinuria • Canine breed predisposition include Cavalier King Charles spaniels and dachshunds. • Cats: uroliths often recur unless prophylactic therapy is initiated.
- Retrospective data from the MUC shows that approximately 11% of cats had > 1 occurrence of xanthine uroliths. Urolith formation enhanced by acid urine pH, highly concentrated urine, and incomplete and infrequent micturition. • In animals given excessive allopurinol, xanthinuria is enhanced by failure to appropriately restrict dietary purine precursors.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Uroliths mimic other causes of pollakiuria, dysuria, hematuria, and/or outflow obstruction. • Differentiate from other types of uroliths, especially ammonium urate, by urinalysis, radiography, and quantitative analysis of retrieved uroliths.

CBC/BIOCHEMISTRY/URINALYSIS

Xanthine crystals cannot be distinguished from ammonium urate or amorphous urates by light microscopy. All these crystals are usually brown or yellow-brown and may form spherules of varying size.

OTHER LABORATORY TESTS

- Infrared spectroscopy, X-ray diffraction, or other quantitative techniques are required to differentiate xanthine from ammonium urate, sodium urate, and uric acid. • High-pressure liquid chromatography of urine to detect xanthine, hypoxanthine, and other purine metabolites.

IMAGING

- Radiography—Similar to that of soft tissue. Cannot be reliably detected by survey radiography. • Ultrasonography, double contrast cystography, and intravenous urography aid in detecting uroliths and their location.

OTHER DIAGNOSTIC PROCEDURES

- May be detected by urethrocytostoscopy.
- Uroliths for analysis may be retrieved by aspiration via a transurethral catheter or voiding urohydropropulsion.

TREATMENT

- Medical protocols that consistently promote dissolution of xanthine uroliths have not been developed. • Remove small urocystoliths by voiding urohydropropulsion. • Surgery remains the most reliable method to remove larger active uroliths from the lower urinary tract. • Minimize further growth of existing uroliths by reducing dietary risk factors. Discontinue or reduce allopurinol medication dosages. • Pending further studies in cats with naturally occurring xanthine uroliths, consider canned renal-failure diets to increase urine volume, minimize purine precursors, and minimize formation of acid urine.
- Consider perineal urethrostomies for recurrent urethral obstruction in male cats.



MEDICATIONS

DRUG(S)

Urine Alkalinizers

- Consider in patients that have acid urine despite dietary therapy. • A sufficient quantity

of potassium citrate or sodium bicarbonate should be given to sustain a urine pH of 7.0–7.5.

Allopurinol

- When treating urate urolithiasis in dogs, adjust dosage of allopurinol in context of magnitude of concentration of urine, uric acid, and quantity of dietary purines (see Urolithiasis, Urate). • In dogs, allopurinol-induced uroliths may dissolve by discontinuing allopurinol therapy but continuing a low purine diet.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Do not give allopurinol to cats or dogs with naturally occurring xanthine uroliths.

FOLLOW-UP

- Monitor dissolution at 30-day intervals by urinalysis, contrast radiography or ultrasonography. • Recurrence does not occur in all xanthinuric cats and dogs.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Urate urolithiasis • Nephrolithiasis

SEE ALSO

- Crystalluria • Urolithiasis, Urate

Suggested Reading

Bartges JW, Osborne CA, Felice LJ. Canine xanthine uroliths: Risk factor management. In: Kirk RW, Bonagura JD, eds., Current Veterinary Therapy XI. Philadelphia: Saunders, 1992, pp. 900–905.

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Authors Carl A. Osborne and Joseph W. Bartges

Consulting Editor Carl A. Osborne

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UTERINE INERTIA



BASICS

OVERVIEW

Failure to expel fetuses of normal size and with normal presentation and posture through a normal birth canal at the normal end of gestation.

Primary Uterine Inertia

- Multifactorial—failure to establish a normal, progressive myometrial contraction pattern.
- Seen in large-breed dogs with one to two puppies in the litter—failure to initiate parturition at term.
- Occurs with large litter sizes—overstretching of the uterus.

Secondary Uterine Inertia

- Occurs following initiation of parturition where some or all of the litter is not expelled.
- Can be secondary to dystocia or large litter.

SIGNALMENT

Female cat and dog of any age

SIGNS

- Primary—failure to initiate parturition at the end of gestation; dam is typically asymptomatic except for possible vaginal discharge following placental separation; fetal heart rates decline with delay in intervention.
- Secondary—contractions cease despite normal contractions initially; may deliver part of litter and then stop; fetal heart rates decline with delay in intervention.

CAUSES & RISK FACTORS

- Primary—inadequate stimulation from fetuses to initiate cascade of events leading to parturition (small litters); abnormal or inadequate hormones or receptors; systemic disease; obesity; tocolytic administration; hypocalcemia; uterine infection; inadequate or unbalanced nutrition.
- Secondary—follows exhaustion of uterine muscle during normal parturition of large litters; occurs during dystocia after prolonged periods of uterine contraction and eventual uterine fatigue; can occur with uterine torsion and trauma.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Primary—inaccurate predicted parturition date; false pregnancy; non-viable pregnancy.
- Secondary—normal parturition; parturition already complete.

CBC/BIOCHEMISTRY/URINALYSIS

- Normocytic, normochromic anemia (normal in pregnancy).
- Hypercholesterolemia (normal in pregnancy).
- May have low total calcium or low iCa.
- Hypoglycemia may be seen in some bitches but is not thought to play a significant role in uterine inertia.

OTHER LABORATORY TESTS

Serum progesterone < 2 ng/mL for 48 hours prior to parturition in most cases.

IMAGING

- Ultrasonography findings—fetal heart rates sustained < 160–170 indicate stress and need for intervention; separation of the placenta from the uterus—need for immediate intervention to optimize survival of litter.
- Radiographic findings—evaluate for presence; size; and any abnormalities of presentation, position, and posture of fetus(es).

DIAGNOSTIC PROCEDURES

Digital vaginal examination to evaluate for presence of fetus within caudal birth canal and abnormal anatomy causing narrowed birth canal.



TREATMENT

- Inpatient—if live fetus(es) are present and fetal stress is documented, the best option for survival is immediate c-section; surgery is the only option for primary uterine inertia when fetal survival is desired.
- Fluid therapy as needed for hydration.
- Medical—for secondary uterine inertia with non-obstructive dystocia and no evidence of fetal distress.



MEDICATIONS

DRUG(S)

- 10% calcium gluconate (1 mL/5 kg SC q4-6h or 0.2 mL/kg IV)—if hypocalcemia documented.
- 2.5–5% dextrose-containing fluids if hypoglycemic.
- Oxytocin not typically effective as the sole treatment for true uterine inertia cases; use 15–30 minutes after calcium treatment; 0.5–4 IU/dog SC or IM; 0.5–1 IU/cat SC or IM; do not administer to cases of obstructive dystocia.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Cardiac arrhythmia with calcium treatment, monitor electrocardiogram and discontinue treatment if arrhythmia noted. Continuous ECG recommended with IV calcium administration.
- Contractions may resume with calcium treatment and rehydration alone.
- Delaying surgery while pursuing medical management may decrease fetal survival rate.
- Uterine rupture (rare).



FOLLOW-UP

PATIENT MONITORING

- Follow iCa levels in hypocalcemic cases; calcium supplementation indicated while

lactating for cases with eclampsia.

- Monitor dam's temperature and character of vaginal discharge daily for 5–7 days following dystocia or C-section—concern for metritis.

- Tocodynamometry to monitor contractions and fetal wellbeing during parturition (WhelpWise, Veterinary Perinatal Specialties, Wheatridge, CO, 303-423-3429).

PREVENTION/AVOIDANCE

- Optimize breeding management to help increase litter size in cases of primary inertia due to small litter.
- Advise only breeding bitches in good body condition and monitor nutrition during pregnancy.
- Utilize tocodynamometry to identify secondary uterine inertia early; allows prompt augmentation of contractions.
- Remove animals with repeated primary uterine inertia from breeding stock.

POSSIBLE COMPLICATIONS

- Death of viable fetuses if too much time elapses before intervention.
- Primary inertia thought to be heritable in some breeds of dogs and cats.

EXPECTED COURSE AND PROGNOSIS

- Primary uterine inertia—may recur on subsequent pregnancies; elective C-section can optimize fetal survival rate.
- Secondary uterine inertia—will not necessarily recur if due to fetal factors such as large litter size or dystocia due to malpresentation.



MISCELLANEOUS

ASSOCIATED CONDITIONS

SEE ALSO

- Dystocia • Eclampsia

ABBREVIATION

iCa = ionized calcium

Suggested Reading

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Pretzer SD. Medical management of canine and feline dystocia. Theriogenology 2008, 70:332–336.

Author Milan Hess

Consulting Editor Sara K. Lyle

UTERINE TUMORS



BASICS

OVERVIEW

- Rare tumors arising from the uterine smooth muscle and epithelial tissues.
- Comprise 0.3–0.4% of tumors in dogs and 0.2–1.5% in cats.
- Dogs—usually benign; leiomyomas, 85%–90%; leiomyosarcoma, 10%; other types (e.g., carcinoma, fibroma, fibrosarcoma, lipoma, plasmacytoma, hemangiosarcoma) rare.
- Cats—usually malignant (adenocarcinoma); include leiomyoma, leiomyosarcoma, fibrosarcoma, fibroma, lipoma, and Müllerian tumor (adenosarcoma).
- Metastasis—may occur with malignant forms.

SIGNALMENT

- Dog and cat.
- No breed predilection reported.
- Middle-aged to older animals usually affected.
- Birt-Hogg-Dube syndrome in German shepherd dogs has been associated with uterine leiomyomas, renal cystadenocarcinomas, and nodular dermatofibrosis.

SIGNS

- Dogs—often clinically silent and discovered incidentally; vaginal discharge; pyometra, infertility; abdominal organ compression or secondary metastatic signs.
- Cats—vaginal discharge (may be hemorrhagic); abnormal estrous cycles; polyuria; polydipsia; vomiting; abdominal distention, infertility, uterine prolapse; signs related to metastatic disease.

CAUSES & RISK FACTORS

- Intact sexual status (hormonal influence)
- Mutated BHD gene in German shepherds



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pyometra
- Other mid-caudal abdominal masses

CBC/BIOCHEMISTRY/URINALYSIS

No specific abnormalities

OTHER LABORATORY TESTS

N/A

IMAGING

- Abdominal radiography—may detect a mid-caudal abdominal mass.
- Thoracic radiography—recommended; assess for distant pulmonary metastasis.
- Ultrasonography—may reveal uterine mass.
- Abdominal CT/MRI—further delineation of mass, assess for metastatic disease.

DIAGNOSTIC PROCEDURES

- Cytologic evaluation—however, tumors might be poorly exfoliative.
- Histopathologic examination—necessary for definitive diagnosis.



TREATMENT

Ovariohysterectomy—treatment of choice



MEDICATIONS

DRUG(S)

Doxorubicin, cisplatin, carboplatin, epirubicin—rational choices for palliation of malignant or metastatic disease.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Doxorubicin—carefully monitor patients with underlying cardiac disease; consider pretreatment and serial echocardiograms and ECG.
- Cisplatin—do not use in dogs with preexisting renal disease; do not use without appropriate and concurrent diuresis; do not use in cats (fatal).
- Chemotherapy may be toxic; seek advice if unfamiliar with these agents.



FOLLOW-UP

PATIENT MONITORING

- Malignant—consider thoracic and abdominal radiographs every 3 months.

- CBC, biochemical profile, and urinalysis (if using cisplatin)—perform before each chemotherapy treatment.

EXPECTED COURSE AND PROGNOSIS

Prognosis—excellent (cure) if benign; guarded if malignant; poor if metastases present; after chemotherapy, unknown.



MISCELLANEOUS

ASSOCIATED CONDITIONS

BHD syndrome in German shepherd dogs has been associated with uterine leiomyomas.

ABBREVIATIONS

- BHD = Birt-Hogg-Dube
- CT = computed tomography
- ECG = electrocardiogram
- MRI = magnetic resonance imaging

Suggested Reading

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Author Heather M. Wilson-Robles

Consulting Editor Timothy M. Fan

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UVEAL MELANOMA—CATS



BASICS

OVERVIEW

- Also called feline diffuse iris melanoma.
- The most common intraocular tumor in cats. • Usually arise from the anterior iridal surface with extension to the ciliary body and choroid. • Tend to be flat and diffuse, not nodular (unlike intraocular melanomas in dogs). • Initially has a benign clinical and histologic appearance. • Unique feature—may develop metastatic disease up to several years later. • Metastatic rate may be up to 63%, though another study found metastatic lesions in 3 of 37 feline ocular melanoma cases (8.1%). • Secondary glaucoma may increase the risk for metastasis.

SIGNALMENT

- No sex or breed predisposition. • Average age is 9.5 years, although can affect any adult cat.

SIGNS

Historical Findings

- Iris color change. • Secondary glaucoma leading to mydriasis or buphthalmia, resulting in blindness.

Physical Examination Findings

- Iris surface—thickened, irregular, usually pigmented, though can be non-pigmented.
- Lesions—focal to diffuse; usually flat; slowly progressive; may involve one or both eyes.
- Advanced disease—often see pigmented tumor cells in the aqueous; homogeneously thickened iris. • May note drainage angle infiltration, which may result in secondary glaucoma.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Freckles on the surface of the iris that do not appear to change over time—may be benign pigmented lesions; more likely melanocytoma, a benign lesion.
- Heterochromia irides—congenital, non-progressive alteration in iridal pigmentation. • Diffuse iridal color change that results from chronic anterior uveitis. Differs from uveal melanoma by the history of chronic anterior uveitis. • Iris atrophy—the anterior iris stroma is lost, increasing visualization of the heavily pigmented posterior iris tissue. Iris thinning is seen as full-thickness holes in the iris or as retroillumination defects in the iris when light is bounced off the tapetum back through the iris. • Limbal melanomas—benign behavior; usually focal, superiorly located, flat to slightly raised limbal masses that do not invade the uveal tract unless they are very large.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

IMAGING

- Thoracic radiographs and abdominal ultrasonography for extensive lesions—help determine presence and extent of metastatic disease. • Recommended presurgically and every 6 months after the diagnosis if histopathologic diagnosis indicates extensive disease.

DIAGNOSTIC PROCEDURES

- Complete ophthalmic examination, including tonometry and gonioscopy.
- Fine-needle aspiration of the iridal surface (“vacuuming”)—diagnostic value questionable; not beneficial for staging.
- Iridal biopsy—may be performed, not beneficial for staging the disease.
- Melanocytes in the iridocorneal angle and ciliary vessels suggest metastasis may have occurred, but these may not be evident for years later.



TREATMENT

- Varies with age of cat, extent and speed of progression, ophthalmologist's preference, and client's level of concern about the potential for malignancy. • Old cat with slow progression—consider only periodic examinations and serial photography to monitor the progress of the lesion(s). • Younger cat with rapidly progressive disease—consider enucleation.
- Small, isolated, freckle-like lesions have been apparently successfully treated with laser (diode) photoablation, although controlled or long-term follow-up studies are lacking.
- Mild to moderate diffuse iridal involvement—most ophthalmologists prefer a conservative approach of periodic examinations and serial photography to monitor the growth progress of the lesion(s). Enucleation is an alternative if progression can be documented or the owner is highly concerned about the potential for malignancy.
- Extensive iridal involvement resulting in changes in pupil shape or mobility, extra-iridal extension, invasion into the drainage angle, or secondary glaucoma—enucleation is suggested. • Cats with iridal thickening and iridocorneal angle involvement, with and without glaucoma, however, had similar survival times when compared with unaffected age-matched control cats.
- Advanced lesions consisting of infiltrative iris involvement including the posterior epithelium and ciliary body had decreased survival times, presumably as a result of metastatic disease. • When enucleating, use a gentle technique; in humans enucleation has been associated with metastasis.



MEDICATIONS

DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- IOP—quarterly monitoring if surgical options are declined; mild IOP elevation may be treated with oral or topical carbonic anhydrase inhibitors (e.g., dorzolamide or brinzolamide at 1 drop to affected eye q8h, or methazolamide at approximately 6.25 mg per cat PO q12–24h); secondary glaucoma due to melanoma is best controlled by enucleation.
- Common metastasis sites—liver, lungs, regional lymph nodes; monitor periodically.

EXPECTED COURSE AND PROGNOSIS

- One long-term study shows that patients with early iris melanoma have no increased risk of life-threatening metastasis compared to controls, but patients with advanced lesions have dramatically shortened survival times.
- Lesions—focal, multifocal to diffuse; usually flat; pigmentation over months to years (i.e., variable); may involve one or both eyes.
- Advanced disease—often see pigmented tumor cells in the aqueous; homogeneously thickened iris causing abnormal pupil shape and change in pupil mobility. • Prognosis—guarded, even with enucleation; metastasis may not become apparent for several years or may be diagnosed on necropsy.



MISCELLANEOUS

SYNOMYMS

- Diffuse iris melanoma • Iris melanoma

ABBREVIATION

- IOP = intraocular pressure

Suggested Reading

Dubielzig RR. Ocular neoplasia in small animals. Vet Clin North Am Small Anim Pract 1990, 20:837–848.

Schaffer EH, Gordon S. Feline ocular melanoma. Clinical and pathologic-anatomic findings in 37 cases. Tierarzt Prax 1993, 21(3):255–264.

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UVEAL MELANOMA—DOGS



BASICS

OVERVIEW

- Melanomas of the anterior uvea (e.g., iris and ciliary body) and posterior uvea (choroid). • Most common primary intraocular neoplasm in dogs. • Usually benign and unilateral; often destructive to the eye but also can be very slow-growing. • Most often affects the anterior uvea. In a retrospective study of 1842 enucleated eyes with uveal melanoma, 79.2% were benign and 20.8% malignant. • Anterior uveal—4% rate of vascular metastasis to lungs and viscera, but rare for malignant uveal melanoma to metastasize. • Choroidal—rarely metastasize.

SIGNALMENT

- No breed or sex predilection • Anterior uveal—average age 8–10 years • Choroidal melanoma—average age 6.5 years
- Range—2 months to 17 years

SIGNS

Anterior Uveal

- Pigmented scleral or corneal mass.
- Pigmented mass visible in the anterior chamber or posterior to the pupillary margin.
- Irregular pupil. • Uveitis. • Glaucoma.
- Hyphema. • No vision loss—unless mass obstructs the pupil or glaucoma has developed.

Choroidal

- Often missed because of tumor location; usually an incidental finding. • Posterior segment mass on funduscopy. • Very slow growing; rarely require enucleation. • Rare tumor.

CAUSES & RISK FACTORS

- Idiopathic. • Potential transformation of flat, pigmented iris freckles into melanomas.
- Young Labrador retrievers—presumed autosomal recessive inheritance.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Non-neoplastic uveal proliferations—iris freckles are not raised. • Diffuse iris hyperpigmentation secondary to chronic uveitis, particularly in golden retrievers (golden retriever pigmentary uveitis/golden retriever uveitis) and in boxers. • Ocular melanosis in cairn terriers. • Uveal cysts—transilluminate and may move freely within the eye, unlike melanomas. • Granulomatous masses. • Iris bombe. • Ocular perforation with uveal prolapse. • Other ocular neoplastic conditions, especially conjunctival melanoma, which could be misinterpreted as extra-scleral extension of uveal melanoma. Conjunctival

melanoma is usually malignant and behaves aggressively in dogs, making it essential to differentiate it from uveal melanoma.

- Outward scrolling of pupillary margin owing to uveitis (ectropion uvea).

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal

OTHER LABORATORY TESTS

N/A

IMAGING

Ocular ultrasonography—may help determine the extent of the mass.

DIAGNOSTIC PROCEDURES

- Slit-lamp biomicroscopy—determine size and location of mass. • Transillumination of mass. • Tonometry. • Indirect ophthalmoscopy—with or without concomitant scleral indentation.
- Gonioscopy—evaluate drainage angle for tumor extension. • Ocular ultrasonography—if cornea opaque and cannot visualize deeper ocular structures, or suspect ciliary body mass hidden by iris.

PATHOLOGIC FINDINGS

- Usually restricted to the enucleated globe; biopsy not practical in most patients. • Two cell types usually seen—plump cells filled with melanin, spindle cells. • Benign appearance and low mitotic index (< 2 mitotic figures per 10 high power fields) common. • Mitotic index—most reliable criterion for malignancy; usually 4 mitotic figures per 10 high power fields in clinically malignant tumors. • When submitting eyes for histologic evaluation, request bleached tissue sections and mitotic index. • Best if veterinary ocular pathologist evaluates globe histologically.



TREATMENT

- Usually benign, may opt to monitor every 3–6 months. • Young Labrador retrievers—aggressive growth, need surgery. • Counsel the client about enucleation; this surgery often causes the client emotional distress.
- Emphasize that the condition is unilateral, sparing the fellow eye, and that one-eyed animals function very well. • Indications for enucleation—size of the mass increases rapidly; eye cannot be salvaged; mass spreads diffusely within the eye; visual function significantly impaired; extra-ocular invasion; secondary complications (e.g., glaucoma, signs of pain, and hemorrhage). Note: glaucoma is painful (headache), but owner often does not realize this. • Enucleation technique—use gentle surgical technique to prevent showering of tumor cells into the vascular circulation; avoid tension on optic chiasm, as could blind fellow eye; exenterate the entire orbital contents, if extra-scleral

extension is noted. • Other surgical treatments—infrequently used; sector iridectomy and iridocyclectomy of discrete small masses. • Laser treatment of small iris tumor. • Melanoma vaccine efficacy unknown; vaccine likely ineffective for patients without enucleation. Consider vaccine if malignant melanoma is present, to try to prevent metastasis. Cost is a potential deterrent.



MEDICATIONS

DRUG(S) OR COMPLEMENTARY

ALTERNATIVE MEDICATION

Reseveratrol, a potent antioxidant, inhibits uveal tumor growth in two animal models (mouse and human cell line) of uveal melanoma, but when sourced from the grapeskin, it should be avoided in dogs due to potential toxicity. Grapeseed extract is a safe alternative that may be beneficial to support ocular health of affected dogs.

CONTRAINdicATIONS/POSSIBLE
INTERACTIONS

N/A



FOLLOW-UP

- Postoperative thoracic and abdominal radiography or ultrasonography—at 6 and 12 months if the mitotic index is high or the patient has extra-scleral, vascular, or optic nerve extension. • Evaluate the enucleation site for tumor recurrence.



MISCELLANEOUS

Suggested Reading

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Author Terri L. McCalla

Consulting Editor Paul E. Miller

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UVEODERMATOLOGIC SYNDROME (VKH)



BASICS

OVERVIEW

- Rare syndrome similar to Vogt-Koyanagi-Harada syndrome in humans.
- Chronic granulomatous inflammatory condition of unknown etiology.
- Affects the eyes, skin, and meninges.
- Clinical signs reflect melanin as the target of inflammation.

PATOPHYSIOLOGY

- Likely an autoimmune process against antigenic components of melanocytes, suspected tyrosinase and related proteins; involves T-cells and macrophages (especially ocular lesions), B-cells, and macrophages.
- Cell-mediated hypersensitivity and antimelanin antibodies demonstrated in humans; similar mechanisms postulated for dogs.

SYSTEMS AFFECTED

- Ophthalmic
- Skin/Exocrine
- Nervous (rarely)

SIGNALMENT

- Dog
- Akita, Samoyed, Siberian husky, Alaskan malamute, and chow chow predisposed
- Other breeds and mixed breeds reported
- Suspected heritability
- No sex predilection
- Mean age of onset 6 months–6 years

SIGNS

- Ophthalmic signs almost always precede dermatologic signs.
- Sudden onset uveitis (photophobia, conjunctival inflammation, pain).
- Secondary changes include glaucoma, cataracts, bullous retinal detachment, and progression to blindness.
- Concurrent or subsequent leukoderma of the nose, lips, and eyelids.
- Depigmented nasal planum may develop crusting and ulceration.
- Concurrent or subsequent striking leukotrichia of the muzzle and periorbital regions.
- Footpads, scrotum, vulva, anus, and oral cavity (hard palate) may also depigment.
- Neurologic symptoms (meningoencephalitis) possible, but very rare.

CAUSES & RISK FACTORS

- Exact cause is unknown.
- Most likely an autoimmune disorder.
- Skin trauma or infectious agent (e.g., virus) are possible triggers.
- Exposure to sunlight can exacerbate the symptoms.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pemphigus foliaceus
- Pemphigus erythematosus
- Discoid lupus erythematosus
- Systemic lupus erythematosus
- Mucocutaneous pyoderma (severe)
- Vitiligo
- Neoplasia—epitheliotropis

lymphoma

- Numerous inflammatory and infectious dermatoses can cause depigmentation.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

ANA—negative

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Skin biopsy necessary for diagnosis, especially when correlated with ocular disease.
- Interpretation of tissue by a dermatopathologist strongly recommended.
- Ophthalmologic consultation strongly recommended.

PATHOLOGIC FINDINGS

Lichenoid dermatosis consisting of mostly histiocytic inflammation; macrophages containing granular melanin pigment; pigmentary incontinence.



TREATMENT

- Aggressive and rapid initiation of immunosuppressive therapy is recommended to prevent formation of posterior synechiae and secondary glaucoma, cataracts, or blindness.
- Retinal exams are the most important means of monitoring progress; improvement in dermatologic lesions may not reflect continued retinal pathology.
- Bilateral enucleation can improve patient comfort and attitude when eye condition worsens and medical treatment is unsuccessful.
- Management by a veterinary ophthalmologist is strongly recommended.



MEDICATIONS

DRUG(S)

- Initial high doses of prednisone (1.1–2.2 mg/kg PO q12–24h) and azathioprine (1.5–2.5 mg/kg PO q24h); the dosages and frequencies should be tapered to q48h for chronic use.
- Azathioprine may be discontinued after a few months of therapy, but prednisone may be necessary indefinitely.
- Cases may improve with initial use of prednisone alone, but delaying aggressive therapy with azathioprine risks irreversible progression of disease.
- Topical or subconjunctival steroids and cycloplegics may be indicated if anterior uveitis is present.
- Refractory cases may require use of systemic cyclosporine.

CONTRAINDICATIONS/POSSIBLE

INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Potential side effects of prednisone and azathioprine—anemia, leukopenia, thrombocytopenia, elevated serum alkaline phosphatase levels, vomiting, and pancreatitis.
- Biweekly serum chemistries and complete blood counts including platelet counts at first; less often as drug dose and frequency are tapered.
- Weekly or biweekly examinations including retinal evaluations initially. Retinal exams are an important means of monitoring the disease; improvement in dermatologic lesions may not mirror improvement in retinal lesions.
- Tapering of drugs should be based on improvement of ocular lesions.
- Severe opportunistic infections with organisms not typically considered pathogenic may occur with combination of cyclosporine and other immunosuppressive agents.

EXPECTED COURSE AND PROGNOSIS

- Generally good for dermatologic symptoms.
- Guarded to poor for vision unless treatment is quickly instituted and is effective.
- Some breeds (e.g., Akita or Siberian husky) may respond less well.



MISCELLANEOUS

SEE ALSO

- Dermatoses, Depigmenting Disorders
- Lupus Erythematosus, Cutaneous
- Lupus Erythematosus, Systemic
- Lymphoma, Cutaneous Epitheliotropic
- Pemphigus

ABBREVIATION

- ANA = antinuclear antibody
- VKH = Vogt-Koyanagi-Harada syndrome

INTERNET RESOURCES

- <http://www.veterinarianpartner.com/Content.plx?P=A&A=1714&S=0&EVetID=3001459>

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VAGINAL DISCHARGE



BASICS

DEFINITION

Any substance emanating through the vulvar labia

PATHOPHYSIOLOGY

- Dependent on underlying cause of vaginal discharge.
- Discharge may originate from uterus, vagina, vestibule, clitoris, clitoral sinus, perivulvar dermis, or urinary tract.

SYSTEMS AFFECTED

- Reproductive
- Renal
- Skin
- Urinary

INCIDENCE/PREVALENCE

- Unknown as there are many causes.
- Considered a common reason for seeking veterinary care.

SIGNALMENT

- Healthy bitch < 6–12 months of age (prepubertal)—juvenile (puppy) vaginitis and congenital anomalies more common.
- Non-pregnant bitch that has undergone at least one estrous cycle—normal estrus, persistent estrus (cystic ovarian disease or granulosa cell tumor); pyometra; neoplasia.
- Bitch bred in the last 30–70 days—normal parturition (50–70 days) or abortion (< 50 days).
- Bitch that has recently whelped—normal lochia or postpartum metritis more common; subinvolution of placental sites.
- Ovariectomized bitch—vaginal stricture or estrogen-responsive urinary incontinence more common; neoplasia.

SIGNS

Historical Findings

- Discharge from the vulva.
- Licking, scooting, and spotting.
- Attracting male dogs.
- Parturition—with postpartum discharge.
- Recent estrus—with pyometra.
- Hemorrhagic discharge > 8 weeks postpartum—subinvolution of placental sites.
- Vomiting, anorexia—may be seen with metritis and pyometra.

Physical Examination Findings

- Vaginal discharge that may be serosanguinous, purulent, lochial, hemorrhagic, mucoid, or urinous.

CAUSES

Normal Physiologic Conditions

- Proestrus
- Estrus
- Diestrus
- Late pregnancy
- Parturition
- Normal lochia

Pathologic Conditions

- Cystic ovarian disease (persistent estrus).
- Brucella canis*.
- Metritis.
- Pyometra.
- Retained placenta or fetuses.
- Subinvolution of placental sites (hemorrhagic discharge postpartum ≥ 8 weeks).
- Neoplasia—uterus, vagina, urinary tract (including transmissible venereal tumor), ovary (granulosa cell tumor/persistent estrus).
- Vaginitis.
- Estrogen-responsive urinary incontinence.
- Coagulopathy.

- Congenital defects of the distal genital tract—intersex conditions, imperfect embryologic fusion of the Müllerian ducts (vagina), joining of the genital folds (vestibule) and genital swellings (vulvar lips), ectopic ureters.

RISK FACTORS

- Prophylactic antibiotics—may alter normal vaginal flora and predispose to secondary infection.
- Exogenous estrogen—predispose to pyometra in the intact bitch.
- Exogenous androgens—may cause clitoral hypertrophy.
- Exogenous or endogenous progesterone—predispose to pyometra or stump pyometra.
- Obesity—excess skin folds around vulva.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Healthy intact bitch < 6–12 months of age—juvenile vaginitis (prepubertal), normal estrous cycle, urogenital trauma or neoplasia, foreign body, coagulopathy, ectopic ureter(s), congenital abnormalities of the perineum or distal genital tract, intersex conditions, urinary tract disease.
- Non-pregnant bitch that has undergone at least one estrous cycle—normal estrus, persistent estrus (cystic ovarian disease or granulosa cell tumor); pyometra; neoplasia.
- Bitch bred in the last 30–70 days—abortion, pyometra, normal parturition (> 57 days from breeding), fetal/embryonic death, split heat, *Brucella canis* infection.
- Bitch that has recently whelped—lochia (normal up to 6–8 weeks postpartum), subinvolution of placental sites (hemorrhagic discharge ≥ 8 weeks postpartum), postpartum metritis, vaginal trauma, retained placenta or fetus.
- Ovariectomized bitch—vaginal stricture, foreign body, neoplasia, polyps, stump pyometra due to exogenous or endogenous progesterone, exogenous estrogens (exposure to owner's hormone replacement therapy), perivulvar dermatitis, ovarian remnant syndrome, estrogen-responsive urinary incontinence.

CBC/BIOCHEMISTRY/URINALYSIS

- Regenerative anemia—may be normal in pregnancy or during estrus.
- Leukocytosis with a left shift—pyometra or postpartum metritis.
- Elevated BUN and creatinine—pyometra.
- Isosthenuria—with polyuria and polydipsia associated with pyometra.
- Urinalysis—may indicate urinary tract infection.

OTHER LABORATORY TESTS

- Progesterone—determine if bitch is in luteal phase, which increases likelihood of pyometra. Progesterone, 17-hydroxyprogesterone may be secreted in animals with adrenal cortex disease (ACTH stim test; Clinical Endocrinology Service, University of Tennessee; (865)

974-5638). • *Brucella canis* serology—screen with rapid slide agglutination test (D-Tec® CB, Zoetis; (888)963-8471); agar gel immunodiffusion test confirmatory (Cornell University Diagnostic Laboratory, (607)253-3900); bacterial culture of whole blood or lymph node aspirate.

IMAGING

Radiography

- Detect enlarged uterus or ovary, pregnancy.
- Evidence of fetal death—presence of gas around fetus or misalignment and/or collapse of fetal skeleton.

Ultrasonography

- Determine contents of uterus, free fluid in the uterus is characteristic of pyometra, hydrometra, and mucometra.
- Pregnancy diagnosis and embryonic/fetal wellbeing: heartbeat may be seen as early as the 20th day of diestrus, heart rate < 180 bpm indicates fetal stress.
- Masses—neoplasia, granulomas, cystic ovarian disease or granulosa cell tumor, or foreign body; saline distention of the vagina may help visualization.

Contrast Radiography—Vaginogram/Urethrogram/Cystogram/IVP

- Identify abnormal conformation or structure (i.e., neoplasia or foreign body) within the vagina.
- Rule-out vestibulovaginal strictures, rectovaginal and urethrovaginal fistulas.
- Rule-out differentials and help localize the problem.
- Pronounced folds (rugae) of vagina during estrus will cause filling defects (normal).

DIAGNOSTIC PROCEDURES

Vaginal Cytology

- Determine nature of discharge—*inflammatory, hemorrhagic*.
- Evaluate epithelial cells for cornification—cornification present under the influence of estrogen.
- Always performed in order to interpret vaginal cultures.

Vaginal Culture and Sensitivity

- Performed prior to other diagnostic procedures.
- Use guarded swab to sample cranial vagina.
- Most common organisms in the microbiome (commensals and potential pathogens) are *E. coli*, *Streptococcus* spp., *Pasteurella* spp., and *Staphylococcus* spp.

- Other organisms which can be commensals include *Mycoplasma* spp., *Enterobacter* spp., *Pseudomonas* spp., *Klebsiella* spp.
- Reminder: the vagina is not a sterile environment and culture of normal bitches results in growth of normal vaginal flora; use of vaginal cytology and other diagnostic tools is essential for interpretation of culture results.
- Normal microbiome consists of numerous opportunistic pathogens, e.g., *E. coli* and *Mycoplasma* spp.

Vaginoscopy

- Rigid cystourethroscope or ureteroscope; pediatric gastroscope or proctoscope; or flexible endoscope used to visualize vagina.

VAGINAL DISCHARGE

(CONTINUED)

- Identify source of vaginal discharge—uterine, vaginal, vestibular, or urethral.
- Visualize anomalies, persistent hymen, neoplasia, foreign body, trauma, abscess, and evaluate the vaginal and vestibular mucosa.
- Use of specialized scope to flush uterus if indicated.
- Removal of foreign body or biopsy of vaginal mass.

Other

- Digital examination of vestibule, vaginovestibular junction, and distal vagina.
- Biopsy and histopathology of mass lesions.
- Cystocentesis—urine culture and sensitivity.
- Clotting profile.



TREATMENT

- Based on diagnosis
- No treatment for normal causes of vaginal discharge
- Usually treated on outpatient basis except pyometra.
- Also refer to individual disease chapters.

SURGICAL CONSIDERATIONS

- Pyometra may be medically or surgically (OHE) managed.
- Ovariectomy or OHE is treatment of choice for neoplastic conditions.
- Cystic ovarian disease can be medically managed or ovariectomy/OHE performed.
- Removal of foreign body or surgical excision of mass(es).
- Surgical excision or radiation therapy are options for TVT.



MEDICATIONS

DRUG(S) OF CHOICE

- Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) for uterine evacuation (myometrial contractions) and luteolysis—dinoprost (Lutalyse®)
- 50–100 $\mu\text{g}/\text{kg}$ SC q8–24h daily till progesterone level < 2.0 ng/mL and uterus is cleared of fluid; cloprostolen (Estrumate®)
- 1–5 $\mu\text{g}/\text{kg}$ SC q24h.
- Antibiotic—choice based on guarded cranial vaginal culture and sensitivity.
- Dopamine agonist—may be used in addition to $PGF_{2\alpha}$ for luteolysis via suppression of the luteotropic hormone prolactin—bromocriptine (10 $\mu\text{g}/\text{kg}$ PO) or cabergoline (5 $\mu\text{g}/\text{kg}$ PO) q8–24h until serum progesterone level < 2.0 ng/mL .
- Supportive care including intravenous fluids as indicated.

CONTRAINDICATIONS

Certain antibiotics may be contraindicated during pregnancy and nursing.

PRECAUTIONS

- Prostaglandin $F_{2\alpha}$ —side effects include panting, vomiting, defecation/diarrhea, and possibly hypotension. Side effects last

30–40 minutes and decrease gradually with subsequent doses, quickly metabolized in lungs.

- Dopamine agonists—side effects include vomiting and nausea; can be controlled with antiemetics.
- Strict monitoring of patients being managed medically for pyometra as patient may become endotoxemic or septicemic and require emergency OHE.
- Stabilize patient prior to anesthetic induction for surgical management of pyometra.

ALTERNATIVE DRUG(S)

Aglepristone (Alizin®; 10 mg/kg SC, 2 doses given 24 hours apart)—progesterone receptor antagonist that may be used alone or concurrently with prostaglandin therapy for treatment of pyometra (currently not available in the United States).



FOLLOW-UP

PATIENT MONITORING

Pyometra

- Recheck serum progesterone until < 2.0 ng/mL .
- Recheck ultrasound after progesterone < 2.0 ng/mL to monitor clearance of uterine fluid.
- Recheck CBC and chemistry to monitor systemic health.

SIPS

- Monitor PCV—depending on amount of blood loss.

PREVENTION/AVOIDANCE

- Puppy vaginitis—delay elective OHE until after first estrous cycle in cases of juvenile vaginitis; may avoid chronic vaginitis.
- Avoid exogenous steroids (estrogens, progestins, androgens).

POSSIBLE COMPLICATIONS

Endotoxemia and septicemia may occur with pyometra or metritis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Pyometra and cystic endometrial hyperplasia

AGE-RELATED FACTORS

- Increased risk for pyometra after each estrous cycle.
- Neoplasia more common in older bitches.

ZOONOTIC POTENTIAL

- *Brucella canis*—fluids and fetal tissue during abortion are highly contaminated with organisms.
- Immunocompromised people are at highest risk. Animal caretakers and pathologists are at risk due to high exposure.

PREGNANCY/FERTILITY/BREEDING

- Pyometra—grave prognosis for future fertility in bitches diagnosed with pyometra in conjunction with CEH, better prognosis (successful pregnancies have been reported) if overt signs of CEH not present and bitch is bred and becomes pregnant on next estrous cycle.
- Neoplasia—poor prognosis for future fertility.
- TVT—sexually transmitted disease; breeding should be avoided.
- *Brucella canis*—sexually transmitted disease and grave prognosis for resolution of disease and normal fertility; should not be used for breeding.

SEE ALSO

- Abortion, Spontaneous (Early Pregnancy Loss)—Cats
- Abortion, Spontaneous (Early Pregnancy Loss)—Dogs
- Brucellosis
- Ovarian Remnant Syndrome
- Ovulatory Failure
- Pyometra
- Retained Placenta
- Sexual Development Disorders
- Subinvolution of Placental Sites
- Transmissible Venereal Tumor
- Vaginal Malformations and Acquired Lesions
- Vaginitis

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- CEH = cystic endometrial hyperplasia
- OHE = ovariohysterectomy
- PCV = packed cell volume
- TVT = transmissible venereal tumor

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Client Education Handout
available online

VAGINAL HYPERPLASIA AND PROLAPSE



BASICS

OVERVIEW

- Protrusion of spherical or donut-shaped mass from vulva during proestrus or estrus, rarely during gestation, parturition, or after administration of estrogenic drugs. • Type I—slight eversion of vaginal floor cranial to the urethral orifice but no protrusion through vulva. • Type II—vaginal tissue prolapses through vulvar opening (tongue-shaped mass). • Type III—donut-shaped eversion of the entire circumference of vaginal wall, including the urethral orifice, seen ventrally on the prolapsed tissue. • Exaggerated response of vaginal mucosa to estrogen, some affected animals have follicular cysts.
- Despite the name, the change seen histopathologically is edema rather than hyperplasia or hypertrophy if occurring during proestrus or estrus. • Severe prolapse—may occlude urethra and prevent normal urination. • True vaginal prolapse without hyperplasia or edema occurs rarely postpartum and may include uterine body and horns.

SIGNALMENT

- Young (most 18–22 months, range 6 months to 4.6 years), large-breed bitches.
- Predisposed breeds—large and brachycephalic breeds (boxer, mastiff, English bulldog, Saint Bernard); Labrador and Chesapeake Bay retrievers; German shepherd; springer spaniel; walker hound; Airedale terrier; American pit bull terrier. • Hereditary component probable—increased incidence in some family lines.

SIGNS

Historical Findings

- Onset of proestrus or estrus. • Although rare, can be seen during diestrus or at parturition (8–12% of cases occur at parturition); or after administration of estrogenic drugs. • Licking of vulvar area.
- Failure to allow copulation. • Dysuria.
- Previous occurrence.

Physical Examination Findings

- Protrusion of round, tongue-shaped, or donut-shaped tissue mass from the vulva.
- Vaginal examination—locate lumen and urethral orifice; types I and II: vaginal lumen is dorsal to the prolapse; type III: lumen is central to the prolapse; urethral orifice is ventral to the prolapse with all three types.
- Tissue may be dry or necrotic.

CAUSES & RISK FACTORS

- Estrogen stimulation • Genetic predisposition • Dystocia • Increased abdominal pressure



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Vaginal polyp—differentiated by vaginal examination. • Vaginal neoplasia—transmissible venereal tumor and leiomyoma; differentiated by signalment, stage of cycle, and vaginal examination. • Clitoral hypertrophy; differentiated by physical examination.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Biopsy (old bitch)—differentiate from neoplasia



TREATMENT

- Outpatient; unless urethral obstruction.
- Breeding—possible by artificial insemination (discuss potential heritability).
- Prolapsed tissue—keep clean and lubricated with sterile water-soluble lubricant.
- Elizabethan collar and clean indoor environment—minimize tissue trauma.
- Instruct client to monitor patient's ability to urinate. • If urethral obstruction present, place indwelling urinary catheter.
- Regression—usually begins in late estrus; should be resolved during early diestrus.
- Recurrence rate—66–100% at next estrous cycle.

SURGICAL CONSIDERATIONS

- Ovariohysterectomy—prevents recurrence; may hasten resolution. • Severe condition—requires surgical reduction or resection; identify and catheterize urethra, 25% recurrence at next cycle after surgery. • With dystocia, cesarean section required, ovariohysterectomy may be necessary.
- Surgical amputation of the prolapsed tissue in an awake, standing bitch has been described. • When occurring during pregnancy, both resection of prolapse and surgical reduction with accompanying hysterectomy have been successfully reported. Vaginal delivery with concurrent vaginal prolapse has been reported; close monitoring for obstructive dystocia is recommended.



MEDICATIONS

DRUG(S)

GnRH (2.2 µg/kg IM) or hCG (1,000 IU IM)—if breeding not planned that cycle; may

hasten ovulation and resolution by a couple of days; not effective if given after ovulation (progesterone > 8–10 ng/mL).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Avoid progestational drugs, they can induce pyometra.



FOLLOW-UP

PATIENT MONITORING

Monitor health of prolapsed tissue and the ability to urinate.

PREVENTION/AVOIDANCE

Ovariohysterectomy—recommended owing to genetic component and likelihood of recurrence.

POSSIBLE COMPLICATIONS

Type III—may affect urethra and prevent normal urination.

EXPECTED COURSE AND PROGNOSIS

- Medical treatment—prognosis for recovery good, except with urethral involvement.
- Surgical intervention for type III—prognosis good.



MISCELLANEOUS

ABBREVIATIONS

- GnRH = gonadotropin-releasing hormone
- hCG = human chorionic gonadotropin

INTERNET RESOURCES

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VAGINAL MALFORMATIONS AND ACQUIRED LESIONS



BASICS

DEFINITION

Altered anatomic architecture due to congenital anomalies (imperforate hymen, dorsoventral septum, hymenal constriction, rectovaginal fistula, segmental aplasia, cysts, conformational defects of the vulva) and acquired conditions (vaginal hyperplasia, foreign bodies, strictures, adhesions, fistulas, and neoplasia).

PATOPHYSIOLOGY

Congenital

- Normal embryologic development—the paired paramesonephric (Müllerian) ducts fuse to form the uterine body, cervix, and vagina; urogenital sinus forms the vestibule, urethra, and urinary bladder; hymen (composed of the epithelial linings of the paramesonephric ducts and urogenital sinus and an interposed layer of mesoderm) normally disappears by birth.
- Errors during embryonic development—imperforate hymens; dorsoventral septae; hymenal constrictions (including vestibulovaginal stenoses); vaginal diverticulum (double vagina, vaginal pouch); cysts.

Acquired

- Vaginal scarring—response to trauma (mating, dystocia, sexual abuse) or inflammation; with mature scarring, may note adhesions or strictures, which narrow the diameter of the vagina.
- Vaginal hyperplasia (dogs)—result of an exaggerated response of the vaginal mucosa to estrogen; effect produced is edema rather than hyperplasia or hypertrophy.
- Neoplastic processes—extraluminal leiomyoma most common; usually old patients; no effect of ovarian status on occurrence.

SYSTEMS AFFECTED

- Reproductive—principal effect: interference with natural mating and whelping; frequent concurrent problem: vaginitis.
- Renal/Urologic—ascending urinary tract infections not uncommon; may note urinary incontinence in conjunction with congenital malformations of the hymenal area; interrelationship not understood and is not universally accepted.
- Skin/Exocrine—usually see perivulvar dermatitis secondary to vaginitis, recessed vulva (redundant perivulvar folds or hypoplastic vulva), or urinary incontinence.

GENETICS

Congenital—heritable component may be suspected; no direct evidence.

INCIDENCE/PREVALENCE

- Incidence (congenital)—unknown; conditions may be asymptomatic, especially if the female is never used for breeding.

- Prevalence (vaginal septa)—in one study, reported as 0.03% of all cases seen.

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Congenital—none identified.
- Vaginal hyperplasia—breeds more prone: large and brachycephalic breeds (boxer, mastiff, English bulldog, Saint Bernard); Labrador and Chesapeake Bay retrievers; German shepherd; springer spaniel; walker hound; Airedale terrier; American pit bull terrier.

Mean Age and Range

- Congenital lesion (e.g., imperforate hymen, stenosis, septa)—young (< 2 years of age) intact or spayed females.
- Vaginal hyperplasia—young (< 2 years of age) intact females.
- Acquired lesion (adhesions and strictures)—post-pubertal females of any age.
- Neoplasia—mean age, 10 years; ovarian status has no effect.

SIGNS

Historical Findings

- Vulvar discharge
- Excessive licking of vulva
- Frequent or inappropriate urination
- Stranguria or dyschezia
- Urinary incontinence
- Attractive to males
- Refuses mating
- Mass at vulvar labia

Physical Examination Findings

- Usually normal.
- Evidence of vaginal discharge or perivulvar dermatitis common.
- Recessed or hypoplastic vulva occasionally seen.

CAUSES

- Congenital
- Inflammatory
- Hormonal
- Traumatic
- Neoplastic



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Vaginitis—concurrent with many malformations; differentiated by vaginoscopy and positive contrast vaginography.
- Urinary tract infection—differentiated by vaginal cytology and concurrent urinalysis on a sample collected by cystocentesis.
- Pyometra—differentiated by CBC, biochemistry profiles, and abdominal ultrasonography.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC and biochemistry—usually normal.
- Urinalysis—may show evidence of a secondary ascending urinary tract infection.

IMAGING

Positive-Contrast Vaginography

- Defines vaginal vault to the cervix, urethra, cranial vestibule, and urinary bladder.
- Defines the cervical canal and uterine lumen in intact patient during estrus.
- Identifies strictures, septae, persistent hymens, masses,

rectovaginal fistulas, urethrovaginal fistulas, vaginal rupture, and diverticulae.

- Patients should be fasted for 24 hours; give enema 2 hours before the procedure.
- Place patient under sedation or general anesthesia.
- Pass a balloon-tipped Foley catheter in the vestibule; inflate balloon; infuse aqueous iodinated contrast media (1 mL/kg); avoid overdistension and underdistension.
- Vestibulovaginal stenoses: ratio of the maximal height of the vagina to the smallest height of the vestibulovaginal junction—normal > 0.35, mild 0.26–0.35, moderate 0.20–0.25, severe < 0.20.
- Urinary incontinence—may require excretory urography to rule-out ectopic ureters or an intrapelvically positioned bladder neck; urethrocystoscopy.

Abdominal Ultrasonography

- Much of the vagina is not accessible owing to the bony pelvis.
- Cranial vaginal masses may occasionally be imaged.
- Aid visualization by infusing saline into the vagina before examination; helps differentiate luminal from transmural or extraluminal lesions.

DIAGNOSTIC PROCEDURES

- Order in which procedures are performed is important; they are listed here in the recommended order.
- Vaginal culture—identify secondary infections; guarded culturette recommended to avoid contamination from the vestibule and caudal vagina (see Vaginal Discharge; Vaginitis).
- Vaginal cytology—identifies stage of the estrous cycle; reveal inflammatory or neoplastic cells (see Breeding, Timing).
- Digital examination of the vestibule and caudal vagina—measure the diameter; identify caudal strictures or masses; note the size and conformation of the vulva; patient standing with abdomen supported (sedation) or in recumbency (anesthesia).
- Vaginoscopy—identify strictures, adhesions, septa, diverticula, masses, and foreign bodies; may use a variety of specula; a long (16–20 cm), hollow, rigid-type (e.g., infant proctoscope) with either a fiber-optic or halogen light source recommended; match the speculum's diameter to size of the patient; post-cervical fold (normal) obscures visualization of the external os of the cervix; rigid cystoscopes (used for transcervical insemination) adequate for many anomalies, need vaginal distension (under general anesthesia) with saline or air to visualize some anomalies or lesions.
- Imaging—when results of previous procedures suggest an anatomic abnormality; vaginography and/or ultrasonography.

PATHOLOGIC FINDINGS

Congenital

- Imperforate hymen—thin fenestrated membrane, dorsoventral band(s), or a thick membrane at the vestibulovaginal junction;

(CONTINUED)

VAGINAL MALFORMATIONS AND ACQUIRED LESIONS

simplest, most common defect; remainder of the genital tract normal. • Dorsoventral septum—oriented dorsoventrally in the vagina, cranial to the vestibulovaginal junction; may note a double cervix (most common variant); double vagina, or divided uterine fundus (rare). • Hymenal constriction or vestibulovaginal stenosis—moderate to severe constriction at the vestibulovaginal junction. • Vaginal hypoplasia, or vaginal aplasia—vagina, cervix, uterus, vulva may be absent or hypoplastic.

Acquired

- Strictures and adhesions—may be identified anywhere in the vagina or vestibule; result of prior trauma and/or inflammation; persistent vaginitis, refusal to mate, dystocia, or problems with micturition are common sequelae. • Vaginal hyperplasia and prolapse.
- Vaginal neoplasia—usually leiomyoma, usually extraluminal in the wall of the vestibule; leiomyosarcomas; transmissible venereal tumors; lipomas; mast cell tumors; epidermoid carcinomas; squamous cell carcinomas; fibromas; fibrosarcomas; and invasive urinary tract carcinomas reported.
- Foreign bodies—plant material, sticks, and swabs occasionally found.



TREATMENT

APPROPRIATE HEALTH CARE

- Usually outpatient, until nature of the defect is ascertained. • Inpatient—for positive contrast vaginography.

NURSING CARE

Manual dilation (bougienage)—digitally or with a smooth rigid object; may attempt in patients that have an imperforate hymen or mild vestibulovaginal stenosis; may be performed in a sedated patient gradually over a course of several treatments; may be performed in an anesthetized patient at one time to maximal dilation; variable success; typically leads to reduction, but not complete resolution, of clinical signs; unlikely to resolve moderate or severe stenoses.

SURGICAL CONSIDERATIONS

- Resection, transection, excision—many minor congenital (e.g., imperforate hymen, small dorsoventral septa) and acquired lesions (small strictures or adhesions in the caudal portion of the vagina or masses).
- Episiotomy—usually required for adequate surgical access. • T-shaped vaginoplasty—described for vestibulovaginal stenoses; resection appears to provide the best odds of resolution, although results are variable.
- Complete ring resection—vaginal stenosis.
- Vulvoplasty—excessive vulvar fold (redundant perivulvar skin fold) with or

without increased perivulvar fat deposition; recessed vulva; reserved for patients with concurrent chronic vaginitis, vaginovulvar discharge, perivulvar dermatitis.

- Transendoscopic laser ablation—one report for correcting a dorsoventral septum in an English bulldog that subsequently bred and delivered four pups vaginally.
- Ovariohysterectomy—patient has no breeding value; exhibits signs only during estrus. • Vaginal ablation (vaginectomy cranial to the external urethral orifice) and ovariohysterectomy—patient has no breeding value; concurrent severe, refractory vaginitis at all stages of the estrous cycle; severe vaginal stenosis; broad-based vaginal tumors.



MEDICATIONS

DRUG(S) OF CHOICE

- Concurrent vaginitis—common; usually resolves with correction of the anatomic defect; for severe condition, hasten resolution with appropriate local and antibiotic therapy (see Vaginitis). • Stenotic lesions—corticosteroids (prednisone: 1 mg/kg PO q 24h) used in conjunction with manual dilation in an attempt to prevent recurrence; high recurrence rates with or without steroids.



FOLLOW-UP

PREVENTION/AVOIDANCE

Congenital lesions—possibly inherited, but not confirmed; for a familial line with a high number of affected individuals, recommend sterilization of affected individuals and their sire and dam.

POSSIBLE COMPLICATIONS

- Dystocia, urinary tract infections, incontinence, and vaginitis—with vaginal malformations; with patients that fail to respond to treatment. • Strictures and adhesions—may be postoperative complications of surgical procedures aimed at correcting abnormalities.

EXPECTED COURSE AND PROGNOSIS

- Depends on the severity of the lesion and the degree of inflammation after treatment.
- Prognosis after treatment for imperforate hymens, short dorsoventral bands, or caudal strictures or adhesions—fair to good for improvement of clinical signs; fair to guarded for complete resolution of signs and normal fertility. • Prognosis for hymenal constrictions, vaginal hypoplasia or severe cranial strictures or adhesions—guarded to poor for complete resolution of signs and normal fertility; with concurrent severe

vaginitis, the best recommendation is vaginal ablation.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Urinary tract infections • Vaginitis
- Urinary incontinence

AGE-RELATED FACTORS

- Congenital—more likely in young bitches of any ovarian status. • Vaginal hyperplasia—more likely in young intact bitches.
- Neoplasia of the vagina or vestibule—more likely in old bitches of any ovarian status.

PREGNANCY/FERTILITY/BREEDING

- Some patients may be bred by artificial insemination; the possibility for a vaginal delivery is unlikely without correction of the anomaly. • Warn owner that an elective cesarean section may be required.

SEE ALSO

- Breeding, Timing • Transmissible Venereal Tumor • Vaginal Discharge • Vaginal Hyperplasia and Prolapse • Vaginal Tumors • Vaginitis

INTERNET RESOURCES

Seim HB. Surgeon's Corner: Vulvoplasty. Clinician's Brief. <http://www.cliniciansbrief.com/article/surgeon-s-corner-vulvoplasty>

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VAGINAL TUMORS



BASICS

OVERVIEW

- Second most common reproductive tumor, comprising 2.4–3% of all tumors in dogs.
- Dogs—86% benign smooth muscle tumors, often pedunculated (e.g., leiomyoma, fibroleiomyoma, and fibroma); lipoma, transmissible venereal tumor, mast cell tumor, squamous cell carcinoma, leiomyosarcoma, hemangiosarcoma, osteosarcoma, or extension of primary urinary tract carcinomas also reported.
- Dogs—may be an incidental finding at necropsy.
- Cats—extremely rare; usually of smooth muscle origin.
- Hormonal influence—may play a role in the development of leiomyomas, fibromas, or polypoid tumors.

SIGNALMENT

- Dog—mean age, 10.2–11.2 years, boxers, nulliparous bitches.
- Cat—no data available.

SIGNS

Dogs

- Extraluminal—slow-growing perineal mass; vulvar discharge; dysuria; pollakiuria; vulvar licking; dystocia.
- Intraluminal—mass protruding from the vulva (often at estrus); vulvar discharge; stranguria; dysuria; tenesmus.

Cats

- Firm mass
- Constipation

CAUSES & RISK FACTORS

- Intact sexual status (hormonal influence)
- Nulliparous bitches more commonly affected



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Vaginal prolapse
- Urethral neoplasia
- Uterine prolapse
- Clitoral hypertrophy
- Vaginal polyp
- Vaginal abscess/granuloma
- Vaginal hematoma

CBC/BIOCHEMISTRY/URINALYSIS

No consistent abnormalities

OTHER LABORATORY TESTS

N/A

IMAGING

- Thoracic radiography—recommended; assess for pulmonary metastatic disease.
- Abdominal radiography—may detect cranial extension of a mass.
- Ultrasonography, vaginography, and urethrocystography—may help delineate mass.
- CT/MRI—definitive delineation of tumor, assess for surgical feasibility, assess for metastatic disease.

DIAGNOSTIC PROCEDURES

- Vaginoscopy with cytologic examination of an aspirate—may help determine cell type.
- Biopsy with histopathologic examination—often necessary for definitive diagnosis.

PATHOLOGIC FINDINGS

- Intraluminal—vestibular wall; protruding into the vulva; may occur singularly or as multiple masses.
- Extraluminal—vestibular roof; causing a bulging of the perineum.



TREATMENT

- Surgical excision and concurrent ovariohysterectomy—treatment of choice.
- Postoperative radiotherapy—may be of benefit for sarcoma and incompletely resected benign tumors.



MEDICATIONS

DRUG(S)

- Postoperative therapy—no standard established.
- Doxorubicin, cisplatin, or carboplatin—rational choice to palliate malignant or metastatic disease.
- Piroxicam may be useful especially for those dogs with primary urinary tumors extending into the vagina and carcinomas.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Doxorubicin—carefully monitor with underlying cardiac disease; consider pretreatment and serial echocardiograms and ECG.
- Cisplatin—do not use in cats (fatal); do not use in dogs with renal disease; always use appropriate and concurrent diuresis.
- Chemotherapy may be toxic; seek advice if you are unfamiliar with chemotherapeutic drugs.

- Piroxicam should not be used with other NSAIDs or prednisone and should be avoided in animals with underlying renal or hepatic disease. Should not be used in conjunction with cisplatin.



FOLLOW-UP

PATIENT MONITORING

- Thoracic and abdominal radiography—consider every 3 months if tumor is malignant.
- CBC (doxorubicin, cisplatin, carboplatin), biochemical profile (cisplatin, piroxicam), urinalysis (cisplatin, piroxicam)—perform before each chemotherapy treatment.

EXPECTED COURSE AND PROGNOSIS

- Prognosis—good with complete excision; guarded if incomplete excision; poor with metastatic disease; poor with carcinoma or squamous cell tumor.
- Recurrence—15% (leiomyoma) without concurrent ovariohysterectomy.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Cats—reported concurrent cystic ovaries and mammary gland adenocarcinoma.

ABBREVIATIONS

- CT = computed tomography
- ECG = electrocardiogram
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug

Suggested Reading

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VAGINITIS



BASICS

DEFINITION

Inflammation of the vagina

PATHOPHYSIOLOGY

- Juvenile vaginitis: unknown, possibly due to imbalances of juvenile vaginal mucosal glandular epithelium.
- Primary adult-onset vaginitis: *Brucella canis* or canine herpesvirus.
- Secondary adult-onset vaginitis: sequela to congenital anomaly, vaginal atrophy post-OHE, drug therapy, foreign body, neoplasia, urinary tract infection, urinary incontinence, systemic disease such as diabetes mellitus.

SYSTEMS AFFECTED

Reproductive

INCIDENCE/PREVALENCE

- 0.7% incidence in one study
- Primary vaginitis—very rare

SIGNALMENT

Species

Primarily dog

Mean Age and Range

- Juvenile vaginitis: less than 1 year of age, ranging from 8 weeks to 1 year, prepubertal animals.
- Adult-onset vaginitis: over 1 year of age, ranging from 1 to 16 years of age.

SIGNS

Historical Findings

Juvenile Vaginitis

- May have no significant history
- Vulvar discharge—seen most often following urination
- Vaginal irritation
- Crusting of the hair coat in the vulvar region
- Scooting
- Excessive vulvar licking
- Perivulvar pruritus
- Inability to housetrain

Adult-Onset Vaginitis

- Vulvar discharge
- Excessive vulvar licking
- Pollakiuria
- Pain during urination
- PU/PD
- Pruritus
- Urinary incontinence
- Infertility

Physical Examination Findings

- Vulvar discharge: mucoid to purulent, scant to copious.
- Vulvar hyperemia.
- Vestibular hyperemia.
- Perivulvar dermatitis.
- Digital examination—strictures and hymens identified at vaginovestibular junction, granular irregularity of mucosa, especially wall opposite urethral papilla.
- Vaginoscopy—diffuse hyperemia of vaginal and vestibular mucosa, prominent lymphoid follicles, luminal exudates, erythema of the urethral papilla or clitoral fossa; presence of foreign body, neoplasia, or congenital abnormalities.

CAUSES

- Prepubertal vagina.
- Infantile vulva.
- Urinary tract infection.
- Urinary or fecal incontinence.
- Foreign body.
- Neoplasia—TVT, leiomyoma
- Bacterial: *Brucella canis*, *E. coli*, *Streptococcus* spp., *Staphylococcus intermedius*, *Pasteurella* spp., *Chlamydia*, *Pseudomonas* spp., *Mycoplasma* spp.

E. coli, *Streptococcus* spp., *Staphylococcus intermedius*, *Pasteurella* spp., *Chlamydia*, *Pseudomonas* spp., *Mycoplasma* spp.

- Viral—canine herpesvirus.
- Congenital anomalies including vaginovestibular strictures, inverted vulva.
- Vaginal trauma.
- Vaginal hematoma.
- Vaginal abscess.
- Systemic disease—diabetes mellitus.
- Zinc toxicity.
- Exogenous or endogenous androgens.

RISK FACTORS

- Alteration of normal vaginal flora by exogenous antibiotic administration.
- Clitoral hypertrophy secondary to exogenous or endogenous (hermaphrodites) androgens.
- Inverted or recessed vulva.
- Obesity.
- Abnormal conformation.
- Vaginal trauma.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Normal—hemorrhagic or serosanguinous discharge during proestrus and may continue into estrus.
- Normal—slight purulent exudates may be normal in early diestrus; neutrophils and non-cornified epithelial cells seen on cytologic examination.
- Normal mucus discharge during pregnancy.
- Normal—postpartum discharge for up to 6–8 weeks; odorless dark brown or hemorrhagic discharge; substantial amounts are normal for up to 4 weeks.
- Subinvolution of the placental sites—hemorrhagic discharge lasting longer than ≥ 8 weeks postpartum.
- Cystourethritis.
- Foreign body.
- Pyometra.
- Metritis.
- Retained placenta(s).
- Clitoral hypertrophy.
- Embryonic or fetal death.
- Urine or feces contamination secondary to congenital anomaly or acquired condition.
- Perivulvar dermatitis.
- Urine contamination with ectopic ureter.
- Incontinence secondary to “hypoestrogenism.”
- Sexual differentiation disorder.
- Vaginal neoplasia.
- Vaginal trauma.
- Vaginal hematoma.
- Vaginal abscess.
- Ovarian neoplasia.
- Zinc toxicity.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually within normal limits.
- Adult onset: may indicate urinary tract infection, hematuria, or systemic disease such as diabetes mellitus to pinpoint underlying cause.
- Urinalysis may indicate dilute urine in young puppies (normal finding).

OTHER LABORATORY TESTS

- *Brucella canis* serology: rapid slide agglutination test (D-Tec CB; Zoetis, (888) 963-8471); agar gel immunodiffusion test (Cornell University Diagnostic Laboratory, (607) 253-3900); bacterial culture of whole blood or lymph node aspirate.
- Serum progesterone concentration—to determine if patient is in estrus or in the luteal phase (≥ 2 ng/mL).

patient is in estrus or in the luteal phase (≥ 2 ng/mL).

IMAGING

Ultrasonography

- Rule-out uterus as source of any vaginal discharge.
- Detection of masses: neoplasia, granuloma, or foreign body; saline distention of the vagina may help visualization.

Contrast Radiography—Vaginogram /Urethrogram/Cystogram/IVP

- Identify abnormal conformation or structure (e.g., neoplasia or foreign body) within the vagina.
- Rule-out vestibulovaginal strictures, rectovaginal and urethrovaginal fistulas.
- Rule-out differentials and help localize the problem.

DIAGNOSTIC PROCEDURES

Vaginal Culture and Sensitivity

- Performed prior to other diagnostic procedures.
- Use guarded swab to sample cranial vagina.
- 74% of adult-onset cases positive for bacterial growth, of which 64% were pure cultures.
- Most common organisms are *E. coli*, *Streptococcus* spp., and *Staphylococcus intermedius*.
- Other organisms include *Mycoplasma*, *Pasteurella*, *Pseudomonas* spp., *Chlamydia*.
- Reminder: the vagina is not a sterile environment and culture of normal bitches results in growth of normal vaginal flora; use of vaginal cytology and other diagnostic tools is essential for interpretation of culture results.

Vaginal Cytology

- Always performed in conjunction with vaginal culture.
- Juvenile vaginitis: usually polymorphonuclear leukocytes ± bacteria.
- Adult-onset vaginitis: usually indicative of septic inflammation.
- Evaluate epithelial cells for cornification—cornification present under the influence of estrogen.
- Determine nature of discharge—inflammatory, blood, presence of fecal material.

Vaginoscopy

- Rigid cystourethroscope, ureteroscope, pediatric gastroscope, proctoscope, or flexible endoscope used to visualize vagina.
- Visualization of anomalies: persistent hymen, neoplasia, foreign body, trauma, abscess, and evaluation of the vaginal mucosa.
- Identify source of vaginal discharge—uterine, vaginal, vestibular, or urethral.
- Removal of foreign body or biopsy of vaginal mass.
- The vaginal wall can be thin in ovariectomized bitches—exercise care when using rigid cystourethroscope and ureteroscope.

Other

- Digital vaginal examination—may be best diagnostic tool for identifying strictures in posterior tract.
- Biopsy and histopathology of vaginal mass.
- Urine culture and sensitivity—identify ascending/concurrent infections.

VAGINITIS



TREATMENT

APPROPRIATE HEALTH CARE

- Correction/removal of underlying cause.
- Most often treated as outpatient. • Surgical management may be necessary to remove foreign bodies or masses or for correction of structural anomalies. • Prevention of self mutilation—use of Elizabethan collars.

ACTIVITY

Not altered

DIET

Not altered

CLIENT EDUCATION

General

- *Brucella canis*—positive patients should be isolated. Euthanasia recommended due to zoonotic potential and lack of effective treatment. • Exogenous estrogens and androgens must be removed from the environment.

Juvenile Vaginitis

- Generally resolves without treatment. Advise patience. • Should resolve after first estrous cycle, if not before. Patient may need to go through one estrous cycle prior to elective OHE.

Adult-Onset Vaginitis

- Usually occurs secondary to underlying cause. • Generally resolves after correction of inciting cause. • If no primary cause can be identified, high likelihood of spontaneous recovery without treatment.

SURGICAL CONSIDERATIONS

- Correction of structural anomaly • Removal of foreign body • Removal of vaginal mass
- Episiotomy • Vaginectomy may be performed in refractory cases.



MEDICATIONS

DRUG(S) OF CHOICE

Juvenile Vaginitis

- No treatment for bitches in uncomplicated cases. • Antibiotic therapy warranted in patients with excessive discomfort (pain or excessive vulvar licking) and/or urinary tract infections. • Antibiotic selection based on culture and sensitivity.

Adult-Onset Vaginitis

- Systemic antibiotic selection based on positive cranial vaginal culture and sensitivity; treat for 4 weeks. • NSAIDs may be used to help decrease inflammation.
- Anti-inflammatory dose of corticosteroids may be helpful in decreasing inflammation and discomfort, but side effects are less desirable and may result in subsequent infection. • DES—for idiopathic or recurrent

vaginitis in spayed bitches; helps to reestablish normal mucosal integrity, increases vaginal epithelial cornification, normalization of vaginal vault, use lowest effective dose; 0.5 mg PO for dogs less < 9 kg or 1 mg PO for dogs > 9 kg q24h for 7 days, then taper dose over 2–4 weeks and maintain at lowest effective dose for potential lifelong therapy.

CONTRAINDICATIONS

- Antibiotic therapy in patients may result in alteration of normal flora and development of infection secondary to treatment. • Vaginal douches with antibiotic/antiseptic agents may be irritating to the vaginal mucosa and worsen the condition. • Corticosteroid administration may worsen concurrent urinary tract infection.

PRECAUTIONS

Estrogen administration may increase risk of pyometra in intact animals.

POSSIBLE INTERACTIONS

Effects of hydrocortisone may be potentiated with concurrent estrogen therapy.

ALTERNATIVE DRUG(S)

- Juvenile vaginitis may be treated with DES to induce estrus in refractory cases, but long-term effects are not documented.
- Moist towelettes/baby wipes may be used to clean the perivulvar area.



FOLLOW-UP

PATIENT MONITORING

Juvenile Vaginitis

- Reevaluate if symptoms become more severe or intolerable. • Reevaluate after first estrous cycle.

Adult-Onset Vaginitis

- Recheck if symptoms do not resolve after removal of underlying cause. • Reculture 5–7 days after cessation of antibiotic therapy or if symptoms continue despite therapy.

PREVENTION/AVOIDANCE

- Delay elective OHE until after first estrous cycle in juvenile vaginitis cases • Avoid using antibiotics in unwarranted cases • Maintain good body weight and condition • Avoid vaginal douching • Avoid exogenous androgen therapy.

EXPECTED COURSE AND PROGNOSIS

- Juvenile vaginitis—onset at 6 weeks to 6–12 months of age; duration of days to months but typically intermittent; usually resolves with time or after first estrous cycle.
- Adult-onset—normally resolves after removal/treatment of inciting cause; antibiotic therapy may hasten resolution in warranted cases, NSAIDs may help resolve inflammation.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Perivulvar dermatitis

AGE-RELATED FACTORS

Juvenile vaginitis may be present in prepubertal dogs, usually < 1 year of age.

ZOONOTIC POTENTIAL

Brucella canis—uncommon cause of vaginitis but should be ruled out.

PREGNANCY/FERTILITY/BREEDING

- Vaginitis during pregnancy is rare but may result in ascending infection and subsequent abortion. Resolution of vaginitis should result in a good prognosis for fertility if underlying cause does not affect fertility prognosis.
- Structural anomalies such as persistent hymen may prevent natural matings to occur, or could predispose to a dystocia if artificially inseminated. • Scarring secondary to trauma may result in excessive fibrous tissue and decreased distensibility of the vagina.

SEE ALSO

- Brucellosis • Metritis • Pyometra
- Retained Placenta • Sexual Development Disorders • Subinvolution of Placental Sites
- Vaginal Malformations and Acquired Lesions

ABBREVIATIONS

- DES = diethylstilbestrol • OHE = ovariohysterectomy • NSAID = nonsteroidal anti-inflammatory drug • PU/PD = polyuria/polydipsia • TVT = transmissible venereal tumor • UTI = urinary tract infection

Suggested Reading

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Author Julie T. Cecere

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Acknowledgment The author and editors acknowledge the prior contributions of Leeah R. Chew and Beverly J. Purswell.



Client Education Handout
available online

VASCULAR RING ANOMALIES



BASICS

OVERVIEW

Right Aortic Arch

- Entrapment of the esophagus by a persistent right fourth aortic arch on the right and dorsally, the base of the heart and pulmonary artery ventrally, and ductus or ligamentum arteriosum on the left and dorsally.
- Causes megaesophagus cranial to the obstruction at the base of the heart.

Double Aortic Arch

- Entrapment of the esophagus by a functional aortic arch on the right, an atretic aortic arch on the left, the base of the heart and pulmonary artery ventrally, and ductus or ligamentum arteriosum on the left and dorsally.
- Causes megaesophagus cranial to the obstruction at the base of the heart; also causes some tracheal compression.

SIGNALMENT

- Dogs and cats
- Seen most commonly in German shepherds, Irish setters, Great Dane, and Boston terriers

SIGNS

- Regurgitation of undigested solid food in animals < 6 months old.
- Malnourishment in many animals.
- Time between eating and regurgitation varies.
- Signs of aspiration pneumonia (e.g., cough, tachypnea or dyspnea) in some animals.

CAUSES & RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Congenital megaesophagus
- Stricture, diverticulum, or esophageal foreign body
- Esophageal motility disorder in Shar-Peis

CBC/BIOCHEMISTRY/URINALYSIS

- Results usually normal
- High white blood cells in some animals with aspiration pneumonia

OTHER LABORATORY TESTS

N/A

IMAGING

- Thoracic radiography—shows food-filled cranial esophagus or signs of aspiration pneumonia in some animals.
- Contrast esophagography—confirms megaesophagus extending to the heart base.
- Fluoroscopy—may be used to differentiate esophageal motility disorders.
- Angiography—may be needed to differentiate between specific vascular ring anomalies.

OTHER DIAGNOSTIC PROCEDURES

Esophagoscopy can be used to differentiate esophageal motility disorders.



TREATMENT

- Surgical correction of the vascular entrapment is indicated—can be performed thoroscopically in some cases.
- Medical management of concurrent aspiration pneumonia may be necessary.
- Feeding procedures for megaesophagus may also be necessary for a prolonged period.
- Supportive care with oxygen may be needed in animal with aspiration pneumonia.



MEDICATIONS

DRUG(S)

Broad-spectrum antibiotics, such as enrofloxacin (2.5 mg/kg q12h) and amoxicillin (10–15 mg/kg q12h) should be instituted in animals with aspiration pneumonia.

CONTRAINdicATIONS/POSSIBLE

INTERACTIONS

N/A



FOLLOW-UP

EXPECTED COURSE AND PROGNOSIS

- Prognosis for resolution of the problem, even after surgery, is guarded although some can have resolution of clinical signs.
- Complications of malnourishment and aspiration pneumonia are common and severe.
- Esophageal function is often permanently compromised.



MISCELLANEOUS

Suggested Reading

Bonagura JD, Lehmkuhl LB. Congenital heart disease. In: Fox PR, Sisson D, Moise NS, eds., Textbook of Canine and Feline Cardiology, 2nd ed. Philadelphia: Saunders, 1999, pp. 471–535.

Parks, MK. Park's Pediatric Cardiology for Practitioners 6th ed. Philadelphia: Elsevier Saunders 2014: 307–313.

Author Jean M. Betkowski

Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

Acknowledgment The author and editors acknowledge the prior contributions of Carroll Loyer.

VASCULITIS, CUTANEOUS



BASICS

DEFINITION

Inflammation of blood vessel walls

PATHOPHYSIOLOGY

Primarily type III (immune complex), but type I and type II reactions possible.

SYSTEMS AFFECTED

- Skin/Exocrine
- Renal/Urologic—some greyhounds

GENETICS

- Familial pyogranuloma and vasculitis of Scottish terriers possibly autosomal dominant
- Proliferative arteritis in St. Bernards; unknown mode of inheritance

SIGNALMENT

Species

Dog and cat (rare)

Breed Predilections

Any age breed or sex may be affected; Chinese Shar-Pei, dachshund, collie, Shetland sheepdog, German shepherd dog, and rottweiler predisposed

SIGNS

Historical Findings

Anorexia, depression, pyrexia possible

Physical Examination Findings

- Focal alopecia with scarring and scaling (especially vaccine-induced/lesions over location of vaccination).
- Necrosis and punctate ulcers, palpable purpura, hemorrhagic bullae or urticaria.
- Acrocyanosis.
- Extremities (paws, pinnae, lips, tail, and oral mucosa) may be painful.
- Pitting edema of the extremities, polyarthropathy, and myopathy possible.

CAUSES

- Idiopathic
- Drug-induced
- Vaccine-induced
- Adverse food reaction
- Tick-borne diseases (e.g., *Rickettsia rickettsii*)
- Infectious
- Underlying metabolic process (e.g., diabetes)
- Auto-immune
- Neoplasia



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- See "Causes"
- Deep pyoderma
- Ear margin seborrhea
- Chemical and thermal burn
- Hypersensitivity reaction
- Dermatomyositis
- Cryoglobulinemia
- Toxic epidermal necrolysis
- Erythema multiforme
- Eosinophilic dermatitis
- Systemic lupus erythematosus
- Bullous pemphigoid
- Pemphigus vulgaris
- Sepsis

CBC/BIOCHEMISTRY/URINALYSIS

Normal unless due to underlying metabolic process or infection.

OTHER LABORATORY TESTS

- Serologic testing for parasitic and infectious disease in high-risk areas.
- Immunodiagnostic—ANA titer, Coombs' test, and cold agglutinin tests.

DIAGNOSTIC PROCEDURES

- Skin scrapings—demodicosis.
- Biopsy of early lesion—submit to a dermatopathologist; findings depend on the underlying cause but usually include neutrophilic (leukocytoclastic/non-leukocytoclastic), lymphocytic, eosinophilic, or granulomatous mixed cells in and around the vessels; vascular necrosis and fibrin thrombi may be prominent; perivascular hemorrhage and edema may occur.
- Representative cultures (e.g., blood, urine, skin) if suspicious of infectious issues.
- Titers for rickettsial infections.
- Immunoassay for fungal organisms.

PATHOLOGIC FINDINGS

- May vary according with stage and etiology.
- Intramural inflammation of vessels, endothelial cell swelling, pale collagen, faded hair follicles, hemorrhage, and edema of surrounding tissue.



TREATMENT

APPROPRIATE HEALTH CARE

- Underlying disease—first priority in clinical management.
- No systemic abnormalities—treat as outpatient.
- Systemic disease—inpatient care recommended.

NURSING CARE

Adequate wound care may be necessary for cases with severe and extensive ulceration.

ACTIVITY

- No limitation unless infectious agent suspected.
- Isolate if contagious or zoonotic agent suspected.

CLIENT EDUCATION

- Inform client that the prognosis is guarded until a cause is found.

SURGICAL CONSIDERATIONS

Individual (focal) lesions may be surgically excised. Otherwise, dependent on underlying etiology.



MEDICATIONS

DRUG(S) OF CHOICE

- The underlying disease process should be identified and appropriately treated; if drugs or drug-like substances are suspected, they should be discontinued.
- First-line therapy while awaiting histopathology results, if no drug reaction is suspected—antibiotics.
- Immune-mediated disease with concurrent vasculitis—prednisolone (0.5–4 mg/kg q24h and taper according to response).
- Pentoxifylline 10–20 mg/kg PO q8h.

- Cyclosporine may be considered.

- Tetracycline and niacinamide each 500 mg q8h for dogs > 10 kg or 250 mg PO q8h for dogs < 10 kg or doxycycline 5 mg/kg PO q12h with niacinamide as with tetracycline.

PRECAUTIONS

- Do not use any medications suspected of causing hypersensitivity.
- Do not administer tetracycline/doxycycline to pregnant or young animals.

ALTERNATIVE DRUGS

- Chlorambucil 0.1–0.2 mg/kg every 1–2 days PO initially and taper according to response.
- Azathioprine 1–2 mg/kg every 1–2 days PO initially and taper according to response.
- Dapsone (1 mg/kg PO q24h) or sulfasalazine (15–22 mg/kg PO q8–12h).



FOLLOW-UP

PATIENT MONITORING

- Monitor appropriately during treatment of specific etiology.
- Pentoxifylline—may decrease blood pressure; may cause excitation; monitor blood pressure if concerned.
- Doxycycline or tetracycline—possible increased liver enzymes, possible esophageal strictures in cats (doxycycline); monitor liver chemistries.
- Patients receiving prednisolone, azathioprine, chlorambucil, sulfasalazine, or dapsone—monitor appropriately with CBC, chemistry screen, and urinalysis.
- Sulfasalazine or dapsone—may decrease tear formation; Schirmer tear test every 2 weeks initially and then routinely.
- Immuno-suppressive therapies should be reduced to the lowest possible therapeutic dose.

POSSIBLE COMPLICATIONS

Sepsis and death from primary cause and/or sequelae if severe.

EXPECTED COURSE AND PROGNOSIS

If no underlying disease is found, vasculitis may be difficult to treat and the prognosis is guarded.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

- Corticosteroids, sulfasalazine, tetracycline/doxycycline, and dapsone—do not use in pregnant animals.
- All drugs should be used with caution in pregnant and breeding animals.

ABBREVIATION

ANA = antinuclear antibody

Suggested Reading

Innara, M. Cutaneous vasculitis. Vet Clin North Am Small Anim Pract 2013, 43:113–134.

Author Karen A. Kuhl

Consulting Editor Alexander H. Werner

VASCULITIS, SYSTEMIC



BASICS

OVERVIEW

- Blood vessel inflammation caused by endothelial injury or extension of adjacent inflammation or infection.
- Endothelial damage by infectious agent, parasite infestation, endotoxin, or immune complex deposition initiates local inflammation, neutrophil accumulation, and complement activation. Neutrophils release lysosomal enzymes, leading to necrosis of vessel wall, thrombosis, and hemorrhage. In humans and dogs with polyarteritis nodosa, intimal proliferation and vessel wall degeneration and necrosis predominate and lead to hemorrhage, thrombosis, and necrosis of involved vessels and adjacent tissues in most patients.
- Non-dermal vasculitis (e.g., renal, hepatic, and serosal surfaces of body cavities) may be the mechanism leading to development of clinically apparent signs of systemic disease (e.g., polyarthritis and proteinuria) without causing obvious external lesions.

SIGNALMENT

Dog and cat

SIGNS

Historical Findings

- Provocative drug (e.g., penicillin, sulfonamides, streptomycin, and hydralazine) given to sensitized animal.
- Recent vaccination history.
- Exposure to ticks.
- Poor dirofilariasis prophylaxis in endemic area.

Physical Examination Findings

- Swelling.
- Ulceration.
- Necrosis of affected skin, especially mucous membranes, mucocutaneous junctions, pinnae edges, and footpads.
- Systemic signs reflecting organ involvement (e.g., hepatic, renal, and CNS).
- Systemic signs of illness (e.g., lethargy, lymphadenopathy, pyrexia, vague signs of pain, and weight loss).
- Juvenile polyarteritis in beagles characterized by recurring episodes of fever ($> 40^{\circ}\text{C}$) and neck pain persisting for 3–7 days.
- Cutaneous lesions of polyarteritis nodosa (subcutaneous nodules—less common in dogs than in people).
- Signs associated with underlying infectious or immune-related disease (e.g., thrombocytopenia and polyarthropathy).
- Ophthalmologic examination—anterior uveitis, sclera injection, hyphema.

CAUSES & RISK FACTORS

Infectious

- Parasitic—*Dirofilaria immitis*, *Angiostrongylus vasorum*, *Leishmania* spp., *Babesia gibsoni*.
- Viral—e.g., feline infectious peritonitis and canine coronavirus infection.
- Rickettsial—e.g., Rocky Mountain spotted fever and ehrlichiosis.
- Bacterial—sepsis

Immune-Related

- Systemic lupus erythematosus
- Rheumatoid arthritis-like arthropathy
- Lupus-like drug reaction
- Type III hypersensitivities (e.g., to food, sulfonamides, fenbendazole, and penicillin)
- Juvenile polyarteritis in beagles
- Wegener's granulomatosis (rare)
- Polyarteritis nodosa
- Neoplasia
- Uremia



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cutaneous signs developing after administration of medication implicate drug reaction (usually not immediate, may develop after days or weeks).
- Vasculitis associated with polyarthropathy and pyrexia implicates immune or infectious cause.
- Cold hemagglutinin disease suggested by distribution of cyanotic or necrotic lesions (nose, ears, toes, tail tip, prepuce) and history of exposure to cold.

CBC/BIOCHEMISTRY/URINALYSIS

Results depend on underlying disease.

OTHER LABORATORY TESTS

- Serologic tests may aid diagnosis of infectious (i.e., rickettsial, *Leishmania*) disease.
- ANA titer positive in patients with SLE, may also be positive in patients with other systemic illnesses.
- Occult heartworm test positive in patient with dirofilariasis.
- Angiostrongylus* infestation diagnosed by fecal examination and cytologic examination of tracheal wash.

IMAGING

Radiographs help diagnose dirofilariasis and *Angiostrongylus* infection.

DIAGNOSTIC PROCEDURES

- Skin biopsy specimen from edge of developing lesion may be diagnostic for vasculitis but may not reveal cause.
- Immunofluorescence test of skin biopsy specimen may rule-out pemphigus and pemphigoid diseases.
- If allergic response is suspected, resolution of signs upon discontinuation of suspect medication or food supports diagnosis.



TREATMENT

- Usually resolution of underlying condition and supportive care.
- If untreatable or unknown underlying condition—glucocorticoid, immunosuppressive (e.g., cyclophosphamide, azathioprine), and other drugs (e.g., dapsone and sulfasalazine) are occasionally effective, but clinical trials of efficacy have not been reported in animals.



MEDICATIONS

DRUG(S)

- Infectious or immune-related—treat underlying disease (see specific condition); supportive care.
- Lupus-like drug reactions—discontinue drug; supportive care.
- Type III hypersensitivity—discontinue drug; supportive care.
- Polyarteritis nodosa—glucocorticoids and cyclophosphamide (unknown value).
- "Idiopathic" vasculitis—if other causes have been ruled-out, administer dapsone (1 mg/kg PO q8h for 14 days, then 1 mg/kg PO q12h for 14 days, then 1 mg/kg PO q24h; may eventually be decreased to q48h to maintain remission); alternative—sulfasalazine (45 mg/kg PO q8h). Neither drug's effectiveness is well documented. Pentoxifylline has been used in limited numbers of cases at doses of 25–35 mg/kg PO q12h. Immunosuppressive doses of corticosteroids may be helpful in idiopathic cases.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Do not administer sulfasalazine to patients sensitive to sulfonamides.
- Pentoxifylline is a methylxanthine derivative and may reduce blood pressure.



FOLLOW-UP

- Patients undergoing treatment with dapsone—monitor CBC and liver enzymes for side effects (e.g., hemolytic anemia, methemoglobinemia, and hepatopathy).
- Patients undergoing treatment with sulfasalazine—monitor for keratoconjunctivitis sicca, blood dyscrasias, and hepatopathy.



MISCELLANEOUS

SEE ALSO

- Lupus Erythematosus, Systemic
- Vasculitis, Cutaneous

ABBREVIATIONS

- ANA = antinuclear antibody
- CNS = central nervous system
- SLE = systemic lupus erythematosus

V

Suggested Reading

- Innera M. Cutaneous vasculitis in small animals. Vet Clin North Am Small Anim Pract 2013; 43:113–134.
Son WC. Idiopathic canine polyarteritis in control beagle dogs from toxicity studies. J Vet Sci 2004; 5(2):147–150.

Author Francis W.K. Smith, Jr.

Consulting Editors Larry P. Tilley and Francis W.K. Smith, Jr.

VENTRICULAR ARRHYTHMIAS/SUDDEN DEATH IN GERMAN SHEPHERDS



BASICS

OVERVIEW

Inherited disorder resulting in ventricular arrhythmias in otherwise healthy young German shepherd dogs. The phenotypic spectrum is wide with some affected dogs having infrequent single premature ventricular complexes while other dogs have frequent and rapid ventricular tachycardia that is associated with sudden death. The pattern of inheritance is complex, depending heavily on background genetics. Siblings of German shepherd dogs that have died suddenly should be tested for this disorder.

SIGNALMENT

- Most dogs develop arrhythmias at approximately 12 weeks of age (identified as young as 6 weeks of age). The number and severity of the arrhythmias tend to peak between the ages of 5 and 9 months of age. By approximately 18–24 months of age most dogs have only a few arrhythmias. • Male and female dogs are afflicted equally.

SIGNS

- Signs are very rare (e.g., in > 500 dogs examined only 1 had syncope) because the dangerous ventricular tachycardia is non-sustained until in some dogs it degenerates into ventricular fibrillation resulting in death (usually between 5 and 9 months of age).
- Arrhythmias often detected during routine examination before neutering. • Death is associated with sleep, rest after exercise, or excitement after sleep particularly in the early morning.

CAUSES & RISK FACTORS

- The genetic mutation(s) responsible for this disorder has not been identified. • Multiple electrophysiologic abnormalities have been identified—early and delayed afterdepolarizations, heterogeneous and altered action potential duration, ion channel current density, calcium cycling, and sympathetic innervation have been documented. • Ventricular tachycardia tends to be most frequent with slow heart rates (drug-induced [e.g., phenylephrine, fentanyl] or during sleep).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Rule out myocarditis.

CBC/BIOCHEMISTRY/URINALYSIS

Results of routine laboratory tests are within normal ranges.

OTHER LABORATORY TESTS

Troponin concentration—to rule out myocarditis. Dogs with inherited arrhythmias have normal troponin levels.

IMAGING

- Thoracic radiographs normal.
- Echocardiography—echocardiograms of individual dogs are usually normal.

DIAGNOSTIC PROCEDURES

24-Hour Ambulatory Electrocardiogram (Holter Recording)

- Required for diagnosis and classification of the severity. • Arrhythmias identified most commonly are polymorphic ventricular tachycardia that is rapid (rates > 400 bpm) with single premature complexes that are most commonly of a left ventricular origin pattern (negative in lead II). Although non-sustained rapid polymorphic ventricular tachycardia is the most characteristic, approximately 15% of dogs will have monomorphic slower and more sustained ventricular tachycardia. • Some dogs will have thousands of singles with no ventricular tachycardia; extensive periods of ventricular bigeminy have been found in others. • After 6 months of age, the runs of ventricular tachycardia are more common after pauses.

PATHOLOGIC FINDINGS

- Routine gross and histopathologic examination is within normal limits.



TREATMENT

- Limited studies have shown that pacing the heart to keep the heart rate higher than 120 bpm decreased the frequency of the arrhythmias; however, it did not prevent sudden death. • Implantation of cardioverter defibrillators might be helpful, but the proper programming of these devices in young dogs is complicated. • Avoid drugs that slow the heart rate. • Anesthesia is not contraindicated in these dogs so long as anticholinergic drugs are used to prevent bradycardia during the age range when the arrhythmias exist. • Treatment is required only for dogs with ventricular tachycardia. Afflicted dogs with only premature ventricular complexes do not die. However, if a young dog is identified with this disorder, repeated Holter monitoring is advised to be sure that the phenotype of that particular dog does not include ventricular tachycardia (e.g., the peak affectedness of that dog has not yet occurred).



MEDICATIONS

DRUG(S)

- The ventricular arrhythmias usually are easily suppressed with lidocaine at 2 mg/kg IV. • Control of the arrhythmias with oral medication is more problematic. • Sotalol alone can be proarrhythmic and should not be used alone. • Sotalol at 2–3 mg/kg PO q12h combined with mexiletine at 4–8 mg/kg PO q8h suppresses the ventricular

arrhythmias, but the response in individual dogs is highly variable.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Avoid drugs that slow the heart rate until the dogs are older than 18–24 months of age.
- Drugs that slow or prolong the action potential duration such as sotalol, phenylephrine, or fentanyl are proarrhythmic.



FOLLOW-UP

PATIENT MONITORING

- Repeat Holter monitoring to assess drug efficacy is highly advised. • After 18–24 months of age the Holter monitoring is again repeated. If the number of ventricular ectopic complexes is < 2,000 singles with no ventricular tachycardia, the dog's risk of death is very low and the medications may be stopped. • Although an occasional dog will have a dramatic drop in the arrhythmia count and severity during treatment, most do not. Therefore, the absence of arrhythmias on Holter recordings after 18–24 months of age indicates a change in the disorder rather than an antiarrhythmic effect. • Lifelong treatment is not required.

EXPECTED COURSE AND PROGNOSIS

- Approximately 50% of affected dogs with > 10 runs of ventricular tachycardia/24 hours will die suddenly before 1 year of age. If a dog does not have ventricular tachycardia identified by 24-hour electrocardiographic monitoring, the probability of death is very low. • If a young German shepherd dog with frequent ventricular tachycardia does not die, it will live. Although this statement is ironic at best, even severely affected dogs that have reached the age of 2 years with documented absence of arrhythmia have lived a normal lifespan > 12 years.



MISCELLANEOUS

AGE-RELATED FACTORS

Because identification of affected dogs depends on the determination of arrhythmias before the age of 1 (ideally 4–9 months) to 2 years (at most), afflicted dogs can easily be missed because the only clinical sign is sudden death with no evidence of a cause found on routine post-mortem examination.

Suggested Reading

Kraus MS, Gelzer ARM, Moise S. Treatment of cardiac arrhythmias and conduction disturbances. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., Manual of Canine and Feline Cardiology, 5th ed. St. Louis, MO: Saunders Elsevier, 2015 (in press).

Author N. Sydney Moise

Consulting Editors Larry P Tilley and Francis W.K. Smith, Jr.

VENTRICULAR FIBRILLATION

**BASICS****DEFINITION**

Ventricular rhythm associated with loss of organized ventricular activity resulting in cardiac muscle fibrillation.

ECG Features

- Rapid, chaotic, irregular rhythm with bizarre waves or oscillations. Oscillations may be large (coarse fibrillation) or small (fine fibrillation).
- No P waves.
- No QRS complexes.

PATHOPHYSIOLOGY

Loss of organized ventricular activity results in acute and profound drop in cardiac output, usually followed by death.

SYSTEMS AFFECTED

- Cardiovascular
- All organ systems affected by loss of perfusion

GENETICS

N/A

INCIDENCE/PREVALENCE

Unknown

SIGNALMENT**Species**

Dog and cat

Breed Predilections

None

Mean Age and Range

Unknown, but probably more common in old animals

SIGNS**Historical Findings**

- Severe systemic illness or cardiac disease in many patients
- Previous cardiac arrhythmias in some patients

Physical Examination Findings

- Cardiac arrest
- Collapse
- Death

CAUSES

- Anoxia
- Aortic stenosis
- Autonomic imbalances, especially high sympathetic tone or administration of catecholamines
- Cardiac surgery
- Drug reactions—e.g., anesthetic agents, especially halothane and ultrashort-acting barbiturates, digoxin
- Electrical shock
- Electrolyte and acid-base imbalances
- Hypothermia
- Myocardial injury
- Myocarditis
- Shock

RISK FACTORS

Any severe systemic illness or heart disease

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

Rule out ECG artifact. Reapply ECG clips and ensure good skin contact and adequate alcohol applied to leads. Check pulse.

CBC/BIOCHEMISTRY/URINALYSIS

Abnormalities generally relate to the underlying metabolic problem that causes ventricular fibrillation.

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

PATHOLOGIC FINDINGS

N/A

**TREATMENT****APPROPRIATE HEALTH CARE**

- Rapidly fatal rhythm requiring immediate, aggressive treatment.
- Patient will probably die without electrical cardioversion.

Direct Current Defibrillation

- Immediate defibrillation is recommended when the duration of cardiopulmonary arrest caused by ventricular fibrillation is 4 minutes or less; otherwise, a 2-minute cycle of chest compressions before defibrillation is recommended. The dose of energy for initial defibrillation is 2–4 J/kg (biphasic defibrillator) or 4–6 J/kg (monophasic defibrillator).
- If an initial shock is not successful, CPR is resumed for 2 minutes before defibrillation is attempted again. A 50% escalation in the energy delivered may be considered for subsequent defibrillation attempts.
- If no access to electrical defibrillator, administer a precordial thump. Apply a sharp blow with your open fist to the chest wall over the heart. Rarely successful, but you have nothing to lose.

NURSING CARE

Treat any problems such as hypothermia, hyperkalemia, and acid-base disorders.

CLIENT EDUCATION

If the patient is converted back to a sinus rhythm, warn the owner that the patient is at high risk for recurrence of the arrhythmia in the immediate post-resuscitation period.

SURGICAL CONSIDERATIONS

N/A

**MEDICATIONS****DRUG(S) OF CHOICE**

- Institute CPR.
- Epinephrine—the low dose (0.01 mg/kg) of epinephrine is recommended because high-dose therapy has not been associated with increased survival. A shortcut to calculate low-dose epinephrine volume for administration is 0.1 mL/10 kg. The dose may be repeated at 3- to 5-minute intervals.
- Vasopressin—there is evidence that this drug may be equivalent to or even superior to epinephrine in some situations. The dose of vasopressin is 0.8 units/kg (dogs and cats), and the dose may be repeated at 3- to 5-minute intervals.
- Once animal is successfully converted, administer intravenous lidocaine or amiodarone to lower the risk of refibrillation or development of ventricular tachycardia.
- Lidocaine—the dose of lidocaine is 2 mg/kg (dogs, IV, IO, IT), and a shortcut to calculate

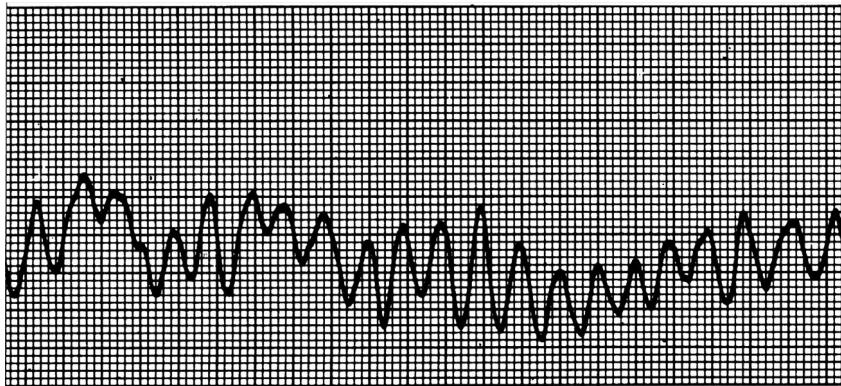


Figure 1.

Coarse ventricular fibrillation. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

VENTRICULAR FIBRILLATION

(CONTINUED)

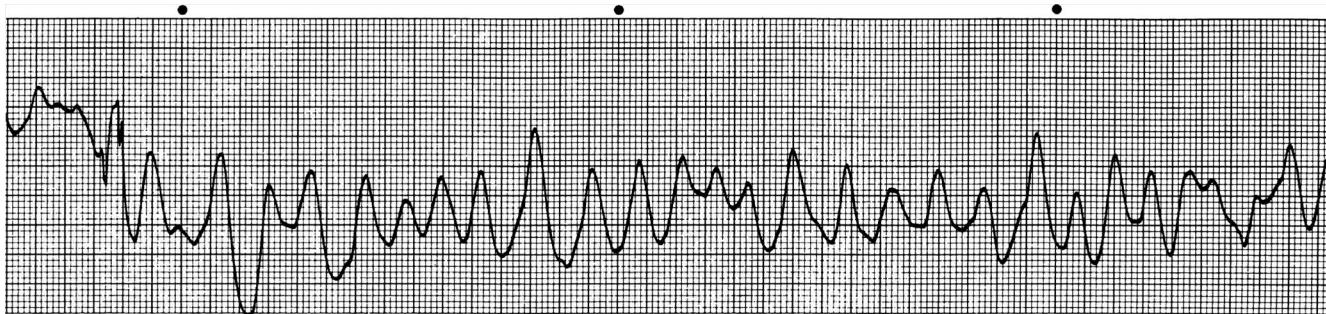


Figure 2.

Ventricular flutter-fibrillation in a cat with severe myocardial damage from an 11-story fall. The complexes are very wide, bizarre, tall, and rapid. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

the dose for the 2% (20 mg/mL) solution is 1 mL/10 kg.

- Amiodarone—the dose of amiodarone is 5–10 mg/kg (dogs, IV), and it is diluted in 5% dextrose before administration.

Hypotension is a common occurrence during amiodarone administration.

PRECAUTIONS

Lidocaine raises the fibrillation threshold but makes defibrillation more difficult.

ALTERNATIVE DRUG(S)

Chemical conversion can be attempted if no access to electrical defibrillator. Administer 1 mEq potassium/kg and 6 mg acetylcholine/kg IC; rarely successful.



FOLLOW-UP

PATIENT MONITORING

- CBC, urinalysis, biochemistry profile, arterial blood gases, and acid-base status.
- If primary cardiac disease is suspected—echocardiogram and thoracic radiographs.
- Monitor ECG closely and frequently.

PREVENTION/AVOIDANCE

Careful monitoring of critically ill patients to prevent and correct acid-base disturbances, hypotension, and hypoxemia.

POSSIBLE COMPLICATIONS

- Death
- DIC and multiorgan failure

EXPECTED COURSE AND PROGNOSIS

Most patients die because of either the arrhythmia or the underlying disease.



MISCELLANEOUS

AGE-RELATED FACTORS

None

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

Cardiopulmonary Arrest

ABBREVIATIONS

- CPCR = cardiopulmonary cerebral resuscitation
- DIC = disseminated intravascular coagulation
- ECG = electrocardiogram
- IC = intracardiac
- IL = intralingual
- IT = intratracheal

Suggested Reading

Cole SG, Otto CM, Hughes D:

Cardiopulmonary cerebral resuscitation in small animals: a clinical practice review, part I. J Vet Emerg Crit Care 2002, 12:261–267.

Cole SG, Otto CM, Hughes D:

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VENTRICULAR PREMATURE COMPLEXES



BASICS

DEFINITION

Single cardiac impulse initiated within the ventricles instead of the sinus node.

ECG Features

- QRS complexes typically wide and bizarre
- P waves dissociated from the QRS complexes

PATHOPHYSIOLOGY

Mechanisms include increased automaticity, reentry, and delayed afterdepolarizations.

SYSTEMS AFFECTED

Cardiovascular—secondary effects on other systems because of poor perfusion.

GENETICS

Polygenic in German shepherd dogs—inherited ventricular arrhythmia.

INCIDENCE/PREVALENCE

Unknown

SIGNALMENT

Species

Dog and cat

Breed Predilections

- Common in large-breed dogs with cardiomyopathy, especially boxers (arrhythmogenic right ventricular cardiomyopathy) and Doberman pinschers.
- Inherited ventricular arrhythmia in German shepherds.
- Common in cats with cardiomyopathy; occasionally seen in cats with hyperthyroidism.

Mean Age and Range

Seen in all age groups

SIGNS

Historical Findings

- Weakness
- Exercise intolerance
- Syncope
- Sudden death
- Often asymptomatic

Physical Examination Findings

- Irregular rhythm associated with pulse deficits; may auscult splitting of the first or second heart sound.
- May be normal if arrhythmia is intermittent and absent during examination.
- May observe signs of CHF (e.g., cough, dyspnea) or murmur, depending on the cause of arrhythmia.

CAUSES

- Cardiomyopathy
- Congenital defects (especially subaortic stenosis)
- Chronic valve disease
- Gastric dilation and volvulus
- Traumatic myocarditis (dogs)
- Digitalis toxicity
- Hyperthyroidism (cats)
- Cardiac neoplasia
- Myocarditis
- Pancreatitis

RISK FACTORS

- Hypokalemia
- Hypomagnesemia
- Acid-base disturbances
- Hypoxia



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Supraventricular premature beats with bundle branch block.
- Look for P waves associated with the wide QRS complexes; an atrial premature complex with aberrant conduction has an associated P wave.
- An atrial premature complex is usually followed by a non-compensatory pause in which the R-R interval of the two sinus complexes enclosing an APC is less than the R-R interval of three consecutive sinus complexes.
- A ventricular premature complex is usually followed by a compensatory pause in which the R-R interval of two sinus complexes enclosing a VPC is greater than or equal to the R-R interval of three consecutive sinus complexes.

CBC/BIOCHEMISTRY/URINALYSIS

- Hypokalemia and hypomagnesemia predispose animals to ventricular arrhythmias and blunt the response to class I antiarrhythmic drugs (e.g., lidocaine, procainamide, mexiletine, and quinidine).
- High amylase and lipase if condition is secondary to pancreatitis.

OTHER LABORATORY TESTS

- High T₄ (cats) if condition is secondary to hyperthyroidism.
- Increased cardiac troponin I, a biomarker for possible acute myocardial injury may suggest an underlying cardiac condition.

IMAGING

Echocardiography may reveal structural heart disease.

DIAGNOSTIC PROCEDURES

Long-term ambulatory (Holter) recording of the ECG to detect transient ventricular arrhythmias in patients with unexplained syncope or weakness.

PATHOLOGIC FINDINGS

Vary with underlying cause



TREATMENT

APPROPRIATE HEALTH CARE

Generally outpatient basis

ACTIVITY

Restrict if the arrhythmia is accompanied by clinical signs or evidence of structural heart disease.

CLIENT EDUCATION

Alert owner to potential for the arrhythmia worsening and syncope or sudden death.

SURGICAL CONSIDERATIONS

- Continuous ECG monitoring recommended while anesthetized.

- Premedicating the patient with acepromazine (0.02–0.05 mg/kg) raises the threshold for ventricular fibrillation.
- Mask inductions not recommended; sympathetic release during mask induction can aggravate arrhythmia.
- Avoid anticholinergics unless bradycardia develops.



MEDICATIONS

DRUG(S) OF CHOICE

General Comments

- Correct any hypokalemia or hypomagnesemia.
- Drug therapy in the absence of clinical signs—controversial; studies in humans with asymptomatic VPCs and myocardial infarction demonstrated a high incidence of sudden death when treatment was initiated with class I antiarrhythmic agents; no similar studies have been conducted in veterinary patients.
- The author generally does not prescribe antiarrhythmic drugs unless there is evidence of clinical signs of low cardiac output (e.g., episodic weakness or syncope) or the belief that the patient is at high risk of sudden death, based on presence of R on T phenomenon or breed association with VPCs and sudden death (e.g., boxers and Doberman pinschers).
- If antiarrhythmic therapy is initiated in an attempt to lower the risk of sudden death, the author usually chooses a beta-blocker or sotalol; no studies have been done to confirm efficacy of beta-blockers for prevention of sudden death in dogs or cats.

Dogs

- Patient not in CHF or hypotensive—initiate therapy with a beta-blocker such as propranolol (0.2–1 mg/kg PO q8h), atenolol (0.2–1 mg/kg q12h), or metoprolol (0.2–1 mg/kg PO q8–12h) or class III agent sotalol (1–3.5 mg/kg PO q12h).
- Patient in CHF or hypotensive—initiate therapy with a class I antiarrhythmic agent such as mexiletine (5–8 mg/kg PO q8h) or procainamide (8–20 mg/kg PO q6–8h).
- Combine a class I antiarrhythmic drug with a beta-blocker or sotalol if arrhythmia persists; especially in boxers.
- Sotalol monotherapy may have proarrhythmic effect in German shepherds.

Cats

Atenolol (6.25–12.5 mg PO q12h)

V

CONTRAINDICATIONS

Avoid atropine, catecholamines (e.g., epinephrine and dopamine) until arrhythmia is controlled.

PRECAUTIONS

- Use beta-blockers cautiously in animals with CHF; they initially depress myocardial contractility.
- Use digoxin cautiously; it can potentially aggravate ventricular arrhythmias.

VENTRICULAR PREMATURE COMPLEXES

(CONTINUED)

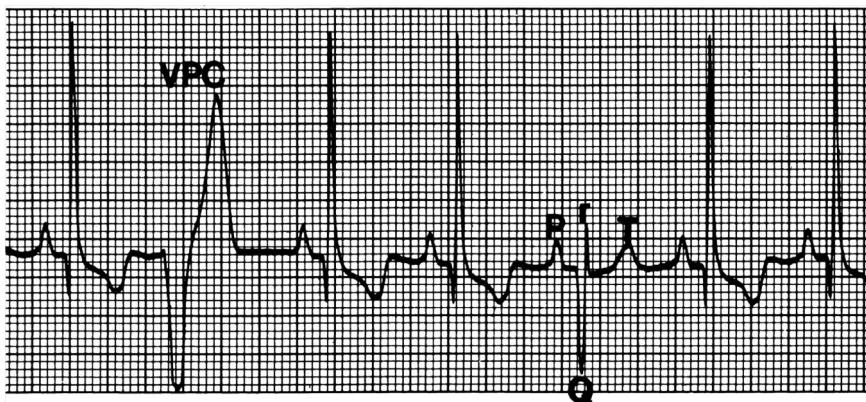


Figure 1.

VPC and a fusion complex (fifth complex) in a dog with myocarditis from pancreatitis. A fusion complex is the simultaneous activation of the ventricle by impulses coming from the SA node and the ventricular ectopic foci. The QRS complex is intermediate in form. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

- Drugs that prolong the action potential (e.g., sotalol) may worsen arrhythmia in German shepherds with inherited ventricular arrhythmia.

POSSIBLE INTERACTIONS

Quinidine and amiodarone raise serum digoxin levels.

ALTERNATIVE DRUG(S)

- Consider amiodarone (5–10 mg/kg PO q12h) for refractory arrhythmias in dogs (generally reserved for ventricular tachycardia); may not want to use in Doberman pinschers.
- Consider sotalol (10–20 mg/cat PO q12h) or procainamide (3–8 mg/kg PO q6–8h) for cats that do not tolerate beta-blockers.

**FOLLOW-UP****PATIENT MONITORING**

- Holter monitoring preferred for monitoring severity of the arrhythmia and efficacy of antiarrhythmic therapy; the goal of antiarrhythmic therapy is to reduce the frequency of ventricular ectopy by > 85%.
- Serial ECGs are not as useful as Holter monitoring—VPCs and paroxysmal ventricular tachycardia can occur sporadically through the day.
- Serum digoxin levels in patients receiving that medication.

PREVENTION/AVOIDANCE

Correct predisposing factors such as hypokalemia, hypomagnesemia, myocardial hypoxia, and digoxin toxicity.

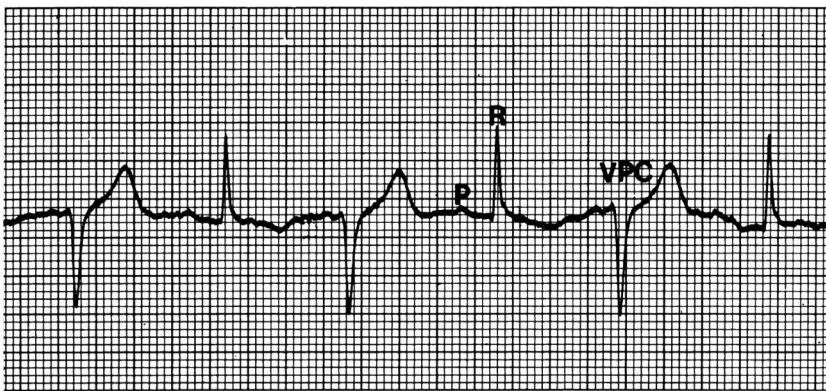


Figure 2.

Ventricular bigeminy. Every other complex is a VPC from the same focus. Each is coupled (interval the same between it and the adjacent sinus complex) to the preceding normal complex. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

POSSIBLE COMPLICATIONS

Syncope, sudden death

EXPECTED COURSE AND PROGNOSIS

- If cause is metabolic—condition may resolve with good prognosis.
- If condition is associated with cardiac disease—prognosis is guarded; VPCs may increase the risk of sudden death.

**MISCELLANEOUS****SEE ALSO**

- Chagas Disease (American Trypanosomiasis)
- Digoxin Toxicity
- Myocarditis
- Ventricular Tachycardia

ABBREVIATIONS

- APC = atrial premature complex
- CHF = congestive heart failure
- ECG = electrocardiogram
- T4 = thyroxine
- VPC = ventricular premature complex

Suggested Reading

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Client Education Handout
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VENTRICULAR SEPTAL DEFECT



BASICS

DEFINITION

An anomalous communication between the two ventricles. The defect may be in the inlet, outlet, muscular, or membranous septum. Most VSDs in small animals are perimembranous, such that the defect is subaortic and has a right ventricular orifice that is beneath the septal leaflet of the tricuspid valve.

PATHOPHYSIOLOGY

- A VSD results in a pulmonary systemic shunt—direction and volume of the shunt are determined by the size of the defect, the relationship of the pulmonary and systemic vascular resistances, and the presence of other anomalies.
- Most VSDs in dogs and cats are small and therefore restrictive (i.e., sufficiently small that the difference between left and right ventricular pressures is maintained). Moderate-sized VSDs are only partially restrictive and result in various degrees of right ventricular hypertension. Large VSDs have an area that is as large as or larger than the open aortic valve; they are non-restrictive, so that left and right ventricular pressures are necessarily equal. Only moderate and large defects impose a pressure load upon the right ventricle.
- In a patient with normal resistance to right ventricular ejection, the direction of the shunt is left to right, which increases pulmonary venous return and imposes a volume load on the left atrium and ventricle. With large shunts, left ventricular congestive failure can develop.
- Unless the defect is of moderate size or large, the right ventricle is spared.

SYSTEMS AFFECTED

- Respiratory—if pulmonary edema develops.
- Cardiovascular—a large shunt can result in pulmonary vascular disease, pulmonary hypertension, and shunt reversal (i.e., Eisenmenger's syndrome). This is uncommon in small animals; if shunt reversal occurs, it usually does so early in life.

GENETICS

Breed predispositions recognized; genetic transmission has not been established.

INCIDENCE/PREVALENCE

One of the most common congenital cardiac malformations in cats, comprising 15% of cases with congenital cardiac defects in one study. Less common in dogs, occurring in 10% of cases with congenital cardiac defects in one study.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat

Breed Predilections

English bulldog, English springer spaniel, basset hound, Akita, West Highland white terrier, Lakeland terrier

Mean Age and Range

Most defects detected during routine examination of puppies and kittens.

Predominant Sex

N/A

SIGNS

Historical Findings

- Usually asymptomatic.
- Clinical signs of left ventricular failure include dyspnea, exercise intolerance, syncope, and cough.

Physical Examination Findings

- A restrictive VSD results in a systolic murmur that typically is loud, band-shaped, and heard best over the right hemithorax. There may be a softer, midsystolic murmur of functional pulmonic stenosis heard over the left heart base. A diastolic decrescendo murmur results if the VSD undermines anatomic support of the aortic valve, causing aortic regurgitation. Patients with right-to-left shunts generally do not have murmurs.
- Split-second heart sound in some patients.
- Femoral pulses usually normal.
- Mucous membranes—pink, unless pulmonary hypertension causes a right-to-left shunt and arterial hypoxemia.
- Tachycardia, dyspnea, and crackles may be evident if left ventricular failure occurs.

CAUSES

Congenital; may have a genetic basis



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other congenital cardiac malformations that cause systolic murmurs include atrioventricular valve dysplasia, aortic or pulmonary stenosis, and complex malformations such as tetralogy of Fallot.
- The “to-and-fro” murmur that results when aortic valve regurgitation complicates a VSD must be distinguished from the continuous murmur of patent ductus arteriosus.
- Generally, diagnosis of congenital cardiac malformations requires echocardiographic evaluation including Doppler studies.

CBC/BIOCHEMISTRY/URINALYSIS

- Results usually normal.
- Uncommon right-to-left shunting results in compensatory erythrocytosis.
- Patients with severe CHF may have prerenal azotemia.

OTHER LABORATORY TESTS

N/A

OTHER LABORATORY TESTS

Thoracic Radiography

- Radiographic appearance is determined by the size and direction of the shunt. Thoracic

radiographs may be normal if the VSD is small. Larger defects cause various degrees of left or even generalized cardiac enlargement. Pulmonary hyperperfusion with prominence of the main pulmonary artery segment may be apparent. CHF is manifest as pulmonary edema.

- Patients with right-to-left shunts have right-sided cardiomegaly; the pulmonary arteries are large proximally but distally attenuated, and the pulmonary veins are small because of reduced pulmonary perfusion.

Echocardiography

- Two-dimensional echocardiographic study may demonstrate left atrial enlargement with left ventricular dilation and hypertrophy. Systolic myocardial function is usually preserved. Right ventricular hypertrophy is apparent only if the defect is moderate-sized or large or if the VSD is one aspect of a complex malformation such as tetralogy of Fallot. Careful study usually demonstrates the defect. Evaluate echocardiographic images critically; the artifact of “septal drop-out” is very common.
- The diagnosis is confirmed by Doppler interrogation of the interventricular septum. If the defect is restrictive, spectral Doppler reveals a high-velocity systolic jet. The shunt may be seen directly by color-flow Doppler. Contrast echocardiography may help in the diagnosis of a right-to-left VSD.
- Infrequently, VSDs spontaneously close. The mechanism of closure is usually adherence of a part of the septal tricuspid valve leaflet to the interventricular septum resulting in the echocardiographic appearance of “septal aneurysm.” Spontaneous closure of VSDs has been documented. Occasionally, a “septal aneurysm” is an incidental echocardiographic finding.

Cardiac Catheterization

Selective cardiac catheterization allows visualization of the defect by contrast angiography and calculation of the shunt fraction (QP/QS) and pulmonary vascular resistance.

OTHER DIAGNOSTIC PROCEDURES

Electrocardiographic Findings

- Evidence of left atrial enlargement, left ventricular hypertrophy, or even right ventricular hypertrophy in some animals.
- Right ventricular enlargement pattern in most animals that have a right-to-left shunt because of pulmonary vascular disease or pulmonic stenosis.

V

PATHOLOGIC FINDINGS

Size of the defect determines the degree of chamber enlargement and hypertrophy; pulmonary edema and possibly ascites are seen in patients with CHF.

VENTRICULAR SEPTAL DEFECT

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

Clinical signs are related to CHF; most patients can be treated as outpatients.

NURSING CARE

N/A

ACTIVITY

Restrict if animal has CHF; need not restrict asymptomatic patients with small defects.

DIET

Moderate sodium restriction recommended for patients with CHF.

CLIENT EDUCATION

Definitive surgical correction is not widely available; if CHF develops, it is terminal, even with palliative care.

SURGICAL CONSIDERATIONS

- Only a minority of VSDs are sufficiently large to warrant repair.
- Consider definitive surgical repair of the defect during cardiopulmonary bypass for defects associated with large shunt. Cardiopulmonary bypass is presently performed at a small number of veterinary centers. Consider pulmonary artery banding as a palliative procedure for patients with moderate or large shunts and CHF.
- Some VSDs are amenable to transcatheter closure using purpose-designed metallic occluder devices.



MEDICATIONS

DRUG(S) OF CHOICE

Furosemide, enalapril, pimobendan, and, in some circumstances, digoxin—recommended for animals with CHF (see Congestive Heart Failure, Left-Sided).

CONTRAINDICATIONS

Vasodilators—contraindicated or used only with great caution in patients with complex malformations that include stenotic lesions.

PRECAUTIONS

ACE inhibitors and digoxin must be used cautiously if patient has renal dysfunction.



FOLLOW-UP

PATIENT MONITORING

Periodic echocardiographic or radiographic evaluation suggested for patients without clinical signs.

PREVENTION/AVOIDANCE

Breeding affected animals is not recommended.

POSSIBLE COMPLICATIONS

- Left ventricular congestive failure
- Bacterial endocarditis • Pulmonary hypertension • Arrhythmias

EXPECTED COURSE AND PROGNOSIS

- Patients with small shunts may have a normal lifespan; isolated, restrictive VSDs usually do not cause clinical signs.
- Concurrent anomalies such as pulmonic stenosis or aortic insufficiency worsen the prognosis.
- Patients with overt CHF may live 6–18 months with medical treatment.
- The development of pulmonary hypertension and shunt reversal is uncommon but generally associated with a poor prognosis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- VSD may be one component of complex malformations such as tetralogy of Fallot.
- Most VSDs are perimembranous and subaortic. Therefore, aortic valve insufficiency resulting from a poorly supported aortic valve complicates the condition in some patients.
- In cats, VSD may be associated with an atrial septal defect and atrioventricular valve abnormalities as part of a complete atrioventricular septal defect (endocardial cushion defect).

AGE-RELATED FACTORS

The murmur of VSD becomes apparent shortly after birth, when pulmonary vascular resistance drops.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

High risk in patients with large defects; breeding affected animals is not recommended.

SYNOMYS

Interventricular septal defect

SEE ALSO

- Congestive Heart Failure, Left-Sided
- Tetralogy of Fallot

ABBREVIATIONS

- ACE = angiotensin converting enzyme
- CHF = congestive heart failure • VSD = ventricular septal defect

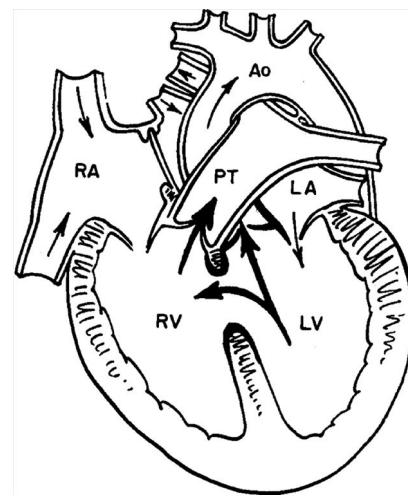


Figure 1.

Ventricular septal defect. In this schematic, the defect results in an unobstructed communication and therefore, right ventricular hypertrophy and pulmonary hypertension are shown. Left-to-right shunting is shown. RA = right atrium, LA = left atrium, RV = right ventricle, LV = left ventricle, AO = aorta, PT = pulmonary trunk. (From: Roberts W. Adult Congenital Heart Disease. Philadelphia: F.A. Davis, 1987, with permission.)

Suggested Reading

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Client Education Handout
available online

VENTRICULAR STANDBY (ASYSTOLE)



BASICS

DEFINITION

Absence of ventricular complexes on the ECG or absence of ventricular activity (electrical-mechanical dissociation).

ECG Features

- Ventricular asystole can result from severe sinoatrial block or arrest or by third-degree AV block without a junctional or ventricular escape rhythm; ECG features include:
- P waves present if patient has complete AV block (Figure 1)
- P waves absent during asystole if patient has severe sinoatrial block or arrest
- No QRS complexes
- Electrical-mechanical dissociation—a recorded ECG cardiac rhythm (P-QRS-T) and no effective cardiac output or palpable femoral pulse.

PATOPHYSIOLOGY

Ventricular asystole represents cardiac arrest; if the ventricular rhythm is not restored in 3–4 minutes, irreversible brain injury can occur.

SYSTEMS AFFECTED

- Cardiovascular
- All organ systems affected by loss of perfusion

GENETICS

N/A

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dog and cat

Breed Predilections

None

Mean Age and Range

Unknown

SIGNS

Historical Findings

- Severe systemic illness or cardiac disease in many patients
- Other cardiac arrhythmias in some
- Syncope

Physical Examination Findings

- No ventricular pulse can be palpated
- Cardiac arrest
- Collapse
- Death

CAUSES

- Complete AV block with absence of ventricular or junctional escape rhythm.
- Severe sinus arrest or block.
- Hyperkalemia (Figure 2).

RISK FACTORS

- Any severe systemic illness (e.g., severe acidosis and hyperkalemia) or heart disease.
- Hypoadrenocorticism causing hyperkalemia.
- Urinary tract rupture or obstruction, resulting in hyperkalemia.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Rule out ECG artifact; reapply ECG clips and make sure skin contact is good and adequate alcohol is applied to leads.

CBC/BIOCHEMISTRY/URINALYSIS

Severe hyperkalemia possible cause

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Systemic blood pressure—readable pressure absent

PATHOLOGIC FINDINGS

N/A



TREATMENT

APPROPRIATE HEALTH CARE

- Asystole is a frequently fatal rhythm requiring immediate aggressive treatment.
- Artificial pacing with a transvenous pacemaker may succeed if myocardium is mechanically responsive.
- DC electrical conversion is not effective unless the rhythm can first be converted to ventricular fibrillation with medications.

NURSING CARE

Treat any treatable problems such as hypothermia, hyperkalemia, and acid-base disorders.

ACTIVITY

N/A

DIET

N/A

CLIENT EDUCATION

None

SURGICAL CONSIDERATIONS

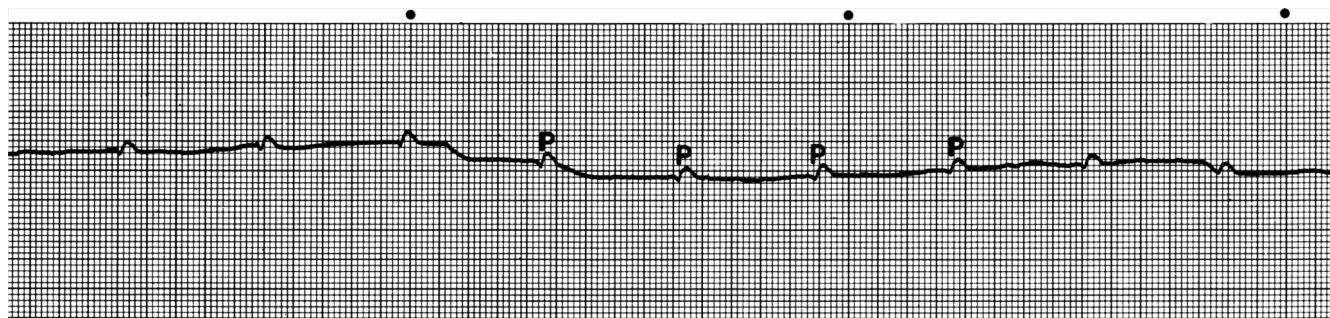
None



MEDICATIONS

DRUG(S) OF CHOICE

- Institute cardiopulmonary resuscitation.
- Epinephrine 0.2 mg/kg IV, IT, or IL (double the dose for IT administration and deliver with equal volume of saline).
- Atropine 0.05 mg/kg IV, IT, or IL (double the dose for IT administration and deliver with equal volume of saline).
- Sodium bicarbonate 1 mEq/kg IV for each 10 minutes of cardiac arrest.
- Dexamethasone and dopamine may be helpful in patients with electrical-mechanical dissociation.



V

Figure 1.

Ventricular asystole in a dog with severe complete AV block. Only P waves (atrial activity) are present; there is no ventricular activity. (Lead II, 50 mm/second, 1 cm = 1 mV.) (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

VENTRICULAR STANDSTILL (ASYSTOLE)

(CONTINUED)

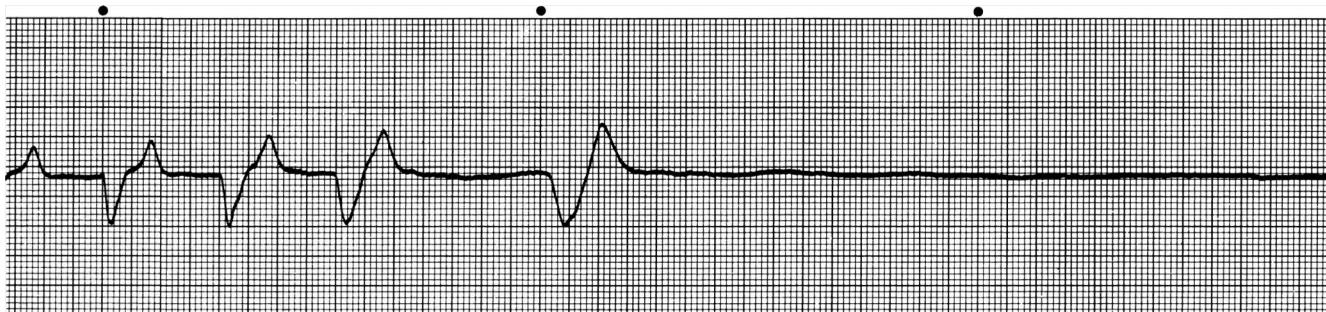


Figure 2.

Ventricular asystole in a cat with severe hyperkalemia (11 mEq/L) from urethral obstruction. No P waves or QRS complexes are seen after four wide and bizarre QRS complexes (atrial standstill with delayed ventricular conduction). (Lead II, 50 mm/sec, 1 cm = 1 mV.) (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

CONTRAINdications

Drugs that depress sinus node or AV node conduction in patients with sinus arrest or heart block (e.g., beta-blockers, calcium channel blockers, digoxin).

PRECAUTIONS

None

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

Calcium gluconate—patients with ventricular standstill and hyperkalemia.

**FOLLOW-UP****PATIENT MONITORING**

- If animal is resuscitated—evaluate CBC, biochemical analysis, and urinalysis.
- If animal survives and primary cardiac disease is suspected—an echocardiogram and thoracic radiographs.
- ECG—closely and frequently.

PREVENTION/AVOIDANCE

Careful monitoring of critically ill patients to prevent and correct acid-base disturbances, hypotension, and hypoxemia.

POSSIBLE COMPLICATIONS

- Death
- DIC and multiorgan failure

EXPECTED COURSE AND PROGNOSIS

Usually die. If sinus rhythm reestablished, prognosis still usually guarded to poor as not uncommon to arrest again.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

None

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

None

SYNONYM

Ventricular asystole

SEE ALSO

- Atrioventricular Block, Complete (Third Degree)

- Cardiopulmonary Arrest
- Sinus Arrest and Sinoatrial Block

ABBREVIATIONS

- AV = atrioventricular
- DIC = disseminated intravascular coagulation
- ECG = electrocardiogram
- IL = intralingual
- IT = intratracheal

Suggested Reading

Kraus MS, Gelzer ARM, Moise S. Treatment of cardiac arrhythmias and conduction disturbances. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., Manual of Canine and Feline Cardiology, 5th ed. St. Louis: Saunders Elsevier, 2015 (in press).

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VENTRICULAR TACHYCARDIA



BASICS

OVERVIEW

Ventricular tachycardia may occur in structurally normal hearts (hereditary arrhythmias) or may occur due to myocardial abnormalities associated with cardiomyopathy, significant valvular disease, or myocarditis. To date, there is no medical therapy available that is known to prevent sudden death in animals afflicted with ventricular tachyarrhythmias.

ECG Features

- Three or more ventricular premature contractions in a row.
- May be intermittent (paroxysmal) or sustained; heart rate usually > 150 bpm with a regular or irregular rhythm.
- QRS complexes—typically wide and bizarre.
- If P waves visible—dissociated from the QRS complexes.
- Breed-specific ECG changes—VT in boxers is characteristically positive in the ventrocaudal leads (leads II, III, and aVF) or display a “left bundle branch block pattern.” VT in Doberman pinschers and German shepherds has both polymorphic and monomorphic characteristics.

PATHOPHYSIOLOGY

Potentially life-threatening arrhythmia because it can degenerate into ventricular fibrillation, resulting in sudden death. Usually signifies underlying myocardial disease or metabolic/electrolyte derangement; mechanisms include increased automaticity, reentry, and triggered activity.

SYSTEMS AFFECTED

Cardiovascular system, with secondary effects on other systems because of poor perfusion.

GENETICS

- Arrhythmogenic right ventricular cardiomyopathy (ARVC) in boxer dogs and dilated cardiomyopathy with VT in Doberman pinschers are both inherited as autosomal dominant traits.
- There is an association with a striatin mutation with the development of DCM in boxers. Striatin is desmosomal protein (scaffolding protein) that has been associated with ARVC in humans. In addition, the Wnt signaling pathway is now implicated in boxer dogs with ARVC. In brief, Wnt signaling pathways play essential roles in cell behavior, survival, and proliferation.
- There is a mutation in Doberman pinschers in the *PDK4* gene. However, there are more than 20 different mutations in humans that can cause DCM.
- Ventricular arrhythmias and sudden cardiac death are hereditary in German shepherd dogs; mode of inheritance is polygenic due to

an abnormality in a major gene with modifiers.

- In the Maine Coon and Ragdoll cat a mutation in the myosin binding protein C (MYBPC3) has been identified. However, the Ragdoll mutation is different from the Maine Coon mutation as it is located in a different region of the gene.
- Testing positive for the genetic defect does not mean all animals will express the phenotype of the disease.

INCIDENCE/PREVALENCE

Common arrhythmia in dogs; uncommon in cats

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dogs and cats

Breed Predilections

Commonly seen in large-breed dogs with cardiomyopathy, especially boxers and Doberman pinschers. German shepherd dogs with sudden cardiac death.

Mean Age and Range

- All age groups if not breed-specific VT.
- Boxers with arrhythmogenic cardiomyopathy usually present at 4–6 years of age, frequency and severity of the arrhythmia usually increases over time.
- Doberman pinschers with occult cardiomyopathy typically develop ventricular arrhythmias beginning at 3–6 years of age, but it also can occur much later in life; frequency and severity of the arrhythmia usually increases over time.
- German shepherds develop ventricular arrhythmias at 12–16 weeks of age and the frequency and severity of the arrhythmias increases until 24–30 weeks of age. After 8 months of age the arrhythmia severity stabilizes or starts to decrease.

SIGNS

Historical Findings

- Syncope
- Weakness
- Exercise intolerance
- Sudden death
- May be asymptomatic

Physical Examination Findings

- May be normal if arrhythmia is paroxysmal and absent during examination.
- Paroxysmal or sustained tachycardia may be auscultated.
- Femoral pulses may have variable pulse intensity or are weak during runs of VT.
- Signs of congestive heart failure or murmur may be present, depending on cause of arrhythmia.

CAUSES

- Cardiomyopathy
- Congenital defects (especially subaortic stenosis)

- Chronic degenerative valve disease
- Traumatic or infectious myocarditis
- Cardiac neoplasia
- Gastric dilation and volvulus
- Splenic neoplasia/ hemorrhage
- Hyperthyroidism (cats)
- Digitalis toxicity
- Pancreatitis

RISK FACTORS

- Hypokalemia, hyperkalemia
- Hypomagnesemia
- Acid-base disturbances
- Hypoxemia
- Neoplasia (e.g., cardiac or splenic hemangiosarcoma)
- Anemia



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Supraventricular tachycardia with bundle branch block. If P waves can be identified, look for association between P waves and QRS complexes. If there is a consistent PR interval, then the rhythm is supraventricular with bundle branch block. If there is no association between P waves and QRS complexes, the rhythm is probably ventricular tachycardia. If P waves cannot be identified due to a fast rate (P buried in preceding T wave), lidocaine administration may result in slowing of the VT rate and P waves may be identified if present. Termination of a tachyarrhythmia after administration of lidocaine supports diagnosis of ventricular tachycardia. If no effect with lidocaine, esmolol administration may result in slowing of a supraventricular tachycardia with bundle branch block, so that P waves associated with QRS complexes can be identified.

CBC/BIOCHEMISTRY/URINALYSIS

- Hypokalemia and hypomagnesemia predispose animal to ventricular tachycardia and blunt response to class I antiarrhythmic drugs (e.g., lidocaine, procainamide, mexiletine, and quinidine).
- High amylase and lipase if arrhythmia is secondary to pancreatitis.
- Inflammatory changes may occur on CBC such as increased neutrophil count if arrhythmias secondary to myocarditis.

OTHER LABORATORY TESTS

- Increased troponin (cTnI) with myocarditis. Cardiac troponin is a highly sensitive and specific biomarker of myocardial injury.
- High T₄ (cats) if arrhythmia is secondary to hyperthyroidism.
- Lyme or tick titers in myocarditis.
- Genetic testing if suspect DCM as the cause for VT:
 - Striatin mutation can be tested for in boxers.
 - There is one genetic mutation that can be

VENTRICULAR TACHYCARDIA

(CONTINUED)

tested for in Doberman pinschers—mutation in the *PDK4* gene.

- Genetic testing if suspect HCM in cats:
 - In the Maine Coon and Ragdoll genetic testing can be performed. There is a mutation in the cardiac myosin binding protein C gene (*MYBPC3*).
- Increased TLI (trypsin-like immunoreactivity) and PLI (pancreatic lipase immunoreactivity) if suspect pancreatitis is a cause for the VT.

IMAGING

Echocardiography may reveal presence of underlying structural heart disease.

DIAGNOSTIC PROCEDURES

ECG

Long-term ambulatory (Holter) or event recording of the ECG—for detection of intermittent ventricular arrhythmias in patients with unexplained syncope or weakness.

PATHOLOGIC FINDINGS

Vary with underlying cause



TREATMENT

APPROPRIATE HEALTH CARE

- Most patients with intermittent VT can safely be evaluated for underlying diseases (echocardiogram, lab work) and it is ideal to establish a true baseline of the arrhythmia quantity and quality by a 24-hour Holter prior to initiating therapy.
- If an animal is unstable (lateral recumbent, weak, or has frequent syncope), immediate intravenous treatment in a hospital setting with continuous ECG monitoring may be required. Once the arrhythmia is controlled and patient is hemodynamically stable, oral medication should be instituted. A follow-up 24-hour Holter is required to test efficacy and possible pro-arrhythmic effects of antiarrhythmic therapy.

NURSING CARE

Varies with underlying cause

ACTIVITY

- Generally speaking, there is no known benefit to exercise restriction.
- Boxer dogs tend to have an increased incidence of VT during excitement, so in some cases owners should know what specific situations to avoid.

DIET

N/A

CLIENT EDUCATION

Alert the owner to the potential for sudden death.

SURGICAL CONSIDERATIONS

- When possible, determine the cause of the arrhythmia and treat it prior to inducing general anesthesia.

- Assess if VT is correctable with a test dose of lidocaine; if it is, treat as necessary with lidocaine, either using IV boluses or CRI.
- Premedication with acepromazine (0.02–0.05 mg/kg) raises the threshold for ventricular fibrillation.
- Avoid pro-arrhythmic drugs such as alpha-2 agonists (xylazine and medetomidine) and thiopental.
- Mask inductions are not recommended in inadequately sedated patients with ventricular arrhythmias because increased sympathetic tone during mask induction will aggravate the arrhythmia.
- Continuous ECG monitoring while animal is anesthetized.



MEDICATIONS

DRUG(S) OF CHOICE

Correct any hypokalemia or hypomagnesemia, if possible, prior to instituting medical therapy.

Dogs

Acute Life-Threatening VT

- Administer lidocaine slowly in 2 mg/kg IV boluses (up to 8 mg/kg total) to convert to sinus rhythm; follow with lidocaine CRI, 30–80 µg/kg/minute.
- If lidocaine fails—administer procainamide slowly in 2 mg/kg IV boluses (up to 20 mg/kg total) to convert to sinus rhythm; follow with procainamide infusion at 20–50 µg/kg/minute or 8–20 mg/kg IM q6h.
- In cases of refractory VT lidocaine and procainamide CRIs can be combined.
- If the patient does not respond to lidocaine or procainamide, administer slow IV boluses of esmolol (a short-acting beta-blocker) at 0.05–0.1 mg/kg q5 minutes to a cumulative dose of 0.5 mg/kg, or as a 50–200 µg/kg/minute CRI.
- Combination of esmolol with procainamide may cause a significant drop in cardiac output and hypotension.

Chronic VT in a Stable Patient

- Sotalol (1–2 mg/kg PO q12h).
- Mexiletine monotherapy is not very effective, but combination of mexiletine (5–8 mg/kg PO q8h) with a beta-blocker such as atenolol (0.25–0.5 mg/kg PO q12h) or sotalol (1–2 mg/kg PO q12h) may be more effective for refractory VT, especially in boxer dogs.
- In German shepherd dogs the combination of mexiletine and sotalol is the most effective. Sotalol monotherapy should be avoided due to its proarrhythmic effects in this breed.

Cats

- Use lidocaine cautiously and only for sustained ventricular tachycardia; neurotoxicity (seizures) is common in cats. Use one-tenth of the dosage used for dogs.

- Atenolol (6.25–12.5 mg PO q12h) is preferred in cats.

CONTRAINdications

Avoid atropine, catecholamines (e.g., epinephrine, dopamine), until arrhythmia is controlled.

PRECAUTIONS

- Use beta-blockers cautiously in animals with CHF. Monitoring by echocardiogram is recommended to check for worsening of myocardial function due to beta blockade.
- Sotalol when used as a sole agent and other drugs that prolong the action potential duration may worsen VT in German shepherd dogs with inherited ventricular arrhythmias.

POSSIBLE INTERACTIONS

Quinidine and amiodarone raise digoxin levels.

ALTERNATIVE DRUG(S)

- For extremely refractory life-threatening VT in dogs consider amiodarone, 10 mg/kg q12h for 1 week (loading dose), then 5 mg/kg q24h (maintenance dose). Although amiodarone is a potent antiarrhythmic drug, its benefits must be balanced against its slow onset to action and adverse effects, which include hepatic toxicity, gastrointestinal disturbances, and blood dyscrasias in dogs. Caution is advised when considering amiodarone therapy because of its adverse effects. Signs of toxicity include anorexia, vomiting, lethargy, and hepatic enzyme elevation. Amiodarone hepatopathy is reversible after reduction of dosage or discontinuation of the drug. Overt clinical signs of toxicity resolve within a few days of stopping amiodarone. Hepatic enzyme activity gradually returns to normal within 3 months after amiodarone is discontinued or the dosage is reduced.
- Monitoring of serial serum chemistries is recommended, since increases in liver enzyme activities usually precede the onset of clinical signs of amiodarone toxicity. Liver enzymes should be measured after 7 days of drug loading and once monthly during maintenance therapy.
- Consider sotalol (10–20 mg/cat q12h) for refractory arrhythmias in cats.



FOLLOW-UP

PATIENT MONITORING

- Holter monitoring is preferred for monitoring severity of the arrhythmia and efficacy of antiarrhythmic therapy; the goal of antiarrhythmic therapy is to reduce the frequency of ventricular ectopy by > 85%.
- Serial ECGs and telemetry can be used cautiously—not as useful as Holter monitoring because ventricular premature complexes and paroxysmal ventricular

(CONTINUED)

VENTRICULAR TACHYCARDIA

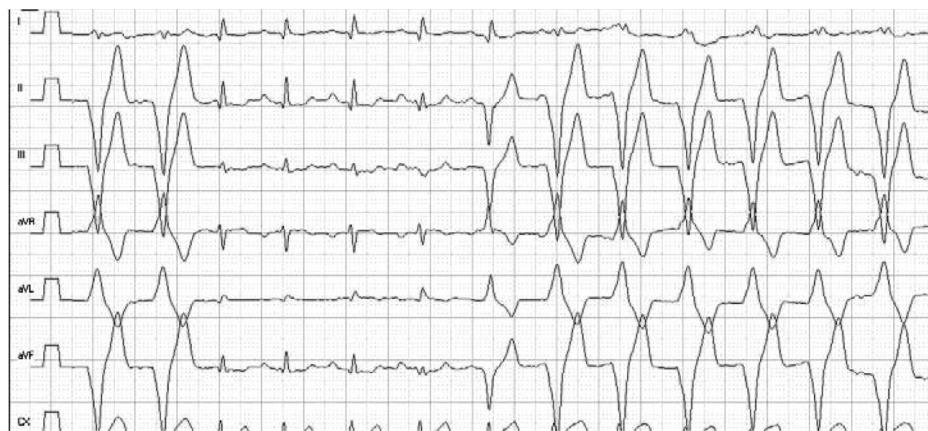


Figure 1.

Ventricular tachycardia. 6-lead ECG demonstrating the wide and bizarre QRS complexes that occur at the beginning and end of the ECG. Ventricular tachycardia should be treated as soon as possible. Acid-base and electrolyte abnormalities should always be corrected.

tachycardia can occur sporadically through the day.

- To avoid digoxin toxicity, serum digoxin levels should be measured after 1 week, 8–10 hours post-pill in patients receiving that medication due to its narrow therapeutic range (0.5–1.5 ng/mL).

PREVENTION/AVOIDANCE

- Correct predisposing factors such as hypokalemia, hypomagnesemia, myocardial hypoxia, and digoxin toxicity.
- In boxer dogs, limit significant stress or excitement as the increase in sympathetic tone may exacerbate the arrhythmia.

POSSIBLE COMPLICATIONS

- Syncope
- Sudden death

EXPECTED COURSE AND PROGNOSIS

- If cause is metabolic—condition may resolve with a good prognosis.
- If condition is associated with cardiac disease—prognosis is guarded because the underlying heart disease is likely chronic and progressive and therefore the arrhythmias may also worsen over time; presence of significant VT increases the risk of sudden death.
- If VT associated with hemangiosarcoma (cardiac or splenic)—the long-term outcome is grave due to the poor prognosis of the underlying disease.
- Approximately 50% of German shepherds with more than 10 runs of ventricular tachycardia/24 hours die suddenly.
- If German shepherd dogs reach the age of 18 months, the probability of sudden death decreases.
- Unlike boxers with ARVC, Doberman pinschers with VT and DCM may die suddenly during their first syncopal episode.



MISCELLANEOUS ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Chagas Disease (American Trypanosomiasis)
- Digoxin Toxicity
- Myocarditis
- Ventricular Arrhythmias/Sudden Death in German Shepherds
- Ventricular Premature Complexes

ABBREVIATIONS

- ARVC = arrhythmogenic right ventricular cardiomyopathy
- CHF = congestive heart failure
- DCM = dilated cardiomyopathy
- ECG = electrocardiogram
- T₄ = thyroxine
- VT = ventricular tachycardia

Suggested Reading

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V



Client Education Handout
available online

VERTEBRAL COLUMN TRAUMA



BASICS

DEFINITION

- Vertebral column trauma is caused by the application of exogenous forces to vertebrae, intervertebral discs, tendons and ligamentous support structures, and the spinal cord.
- The clinical signs may include hyperesthesia, limb paresis and/or general proprioceptive ataxia, para- or tetraplegia, loss of nociception, urinary retention, and fecal incontinence.

PATHOPHYSIOLOGY

- In the normal vertebral column, passive (bones, ligaments), active (tendons, muscles), and neural systems are responsible for stability.
- Compression, lateral bending, torsion, and sheer forces may result in failure of these systems, leading to vertebral column fracture or subluxation.
- In some instances, significant spinal cord injury can be present without instability or fracture. Traumatic disc herniation, penetrating injuries associated with the vertebral canal, and post-traumatic vascular myopathy are scenarios by which this may occur.
- Most commonly, animals are evaluated after vertebral column trauma due to the presence of SCI.
- SCI occurs because of primary and secondary mechanisms.
- Primary injury results from mechanical events such as spinal cord compression and contusion.
- Secondary injury is the biochemical cascade that follows primary events, which consist of oxidative stress, inflammation, excitotoxicity, vascular injury, and other processes.

SYSTEMS AFFECTED

- Nervous
- Musculoskeletal
- Others possible due to exogenous trauma

INCIDENCE/PREVALENCE

- Vertebral fractures and luxations represented 6% of all feline myelopathies and 7% of all canine neurology cases in two single center studies.
- The incidence of traumatic SCI without fracture/luxation is unknown.

GEOGRAPHIC DISTRIBUTION

Data not available

SIGNALMENT

Species

Dog and cat

Breed Predilections

Limited data on vertebral fracture/luxation suggest medium- and large-breed dogs are commonly affected.

Mean Age and Range

One retrospective report on vertebral trauma indicated that affected dogs and cats were young (median 2 years of age; range 0.25–15 years).

Predominant Sex

Males appear overrepresented.

SIGNS

General Comments

- The majority of dogs with vertebral column trauma have SCI.
- Concurrent peripheral (e.g., brachial plexus trauma) or central nervous system injuries (e.g., head trauma) can occur.
- Abnormalities associated with other body systems are frequently identified.

Historical Findings

- Acute onset paresis and ataxia or para-/tetraplegia.
- Clinical signs suggestive of hyperesthesia (vocalization, reluctance to move, arched back).
- Lethargy and poor appetite.

Neurologic Examination Abnormalities

- SCI is usually classified as C1–C5, C6–T2, T3–L3, L4–Cd5, multifocal, or diffuse based on neurologic examination.
- Focal SCI is most common.
- Gait abnormalities—in > 90% of animals; may include general proprioceptive ataxia, paresis, and loss of voluntary movement.
- Abnormalities in spinal reflexes and postural reactions are common and reflect the spinal cord segment(s) injured.
- Regional hyperesthesia.
- Animals with severe SCI may have absent nociception.
- The absence of deep nociception is a negative prognostic indicator, with the proportion of animals ambulating following thoracolumbar vertebral fracture/luxation traditionally placed at < 5%.

Physical Examination Abnormalities

- Pulmonary contusions and rib fractures
- Pelvic and appendicular bone fractures
- Cutaneous wounds
- Traumatic brain injury
- Abdominal organ injury

CAUSES

- Automobile accident is the most common cause of vertebral column trauma.
- Other etiologies include fall (frequent in cats), animal bites and gunshot wounds.

RISK FACTORS

Animals housed outdoors, those walked off lead, and those unsecured in the cabs of pickup trucks are likely overrepresented.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other neurologic diseases such as disc herniation, fibrocartilagenous embolic myopathy, meningo(myelitis, discospondylitis, and vertebral column neoplasia, should be considered.
- Orthopedic injuries such as appendicular fracture or ligamentous injuries may occasionally be mistaken for vertebral column trauma.

CBC/BIOCHEMISTRY/URINALYSIS

- Abnormalities may be present if significant injury has occurred to other body systems.
- Anemia, findings consistent with

dehydration, elevated creatinine kinase, and hematuria are all commonly seen.

IMAGING

Radiography

- 70% sensitive and highly specific for detecting vertebral fracture/luxation.
- Vertebral radiographs do not permit visualization of the spinal cord and have poor soft tissue detail.

Myelography

- Can define extradural spinal cord compression; has been used in decision making for surgical approaches after SCI.
- Invasive, does not allow direct visualization of spinal cord parenchyma, and lacks the tissue detail of advanced imaging studies.
- May not detect lateralized spinal cord compression as effectively as advanced imaging modalities.

Advanced Imaging

- CT—gold standard for evaluating the bones of the vertebral column and may also be used to visualize mineralized disc material and extradural hemorrhage.
- MRI—can be utilized to visualize the bony vertebral column, but provides more soft tissue detail than CT; it is the only means to exclude certain differential diagnoses, such as fibrocartilagenous embolic myopathy, and provides prognostic information concerning recovery.

DIAGNOSTIC PROCEDURES

- CSF—often unremarkable; in some severe cases, CSF total protein, nucleated count, and red blood cell count may be increased.
- CSF abnormalities with SCI are not etiology-specific.
- CSF is collected as an adjunct and not as a substitute to advanced imaging.

PATHOLOGIC FINDINGS

- Gross findings may include evidence of vertebral luxation/fracture, extradural hemorrhage, disc extrusion, spinal cord swelling, dural/subarachnoid erythema/hemorrhage, and myelomalacia.
- Histopathologic abnormalities within the spinal cord may include necrosis, demyelination, zones of spinal cord infarction, parenchymal hemorrhage, and axonal spheroids.



TREATMENT

APPROPRIATE HEALTH CARE

- Emergency intensive care management is recommended for all animals immediately following injury.
- Surgical management may be needed if imaging suggests significant spinal cord compression or vertebral column instability.
- Medical management may be selected for animals that lack evidence of instability/compression.

(CONTINUED)

VERTEBRAL COLUMN TRAUMA

NURSING CARE

- Prior to imaging, animals should be immobilized on a back board.
- Animals with imaging that suggests vertebral column instability should be immobilized until surgical stabilization.
- Non-ambulatory dogs require padded bedding, frequent turning, and urinary bladder evacuation.
- Fluid therapy is required in the event of dehydration.
- Physical rehabilitation consisting of range of motion exercises, electrical muscle stimulation, active weight bearing, and underwater treadmill may be beneficial. Physical rehabilitation that involves significant mobilization should only be performed after vertebral column instability is addressed.

ACTIVITY

- Strict exercise restriction for 4 weeks for all animals that have received vertebral column surgery. Animals with fractures and instability may require 6–8 weeks of rest.
- Animals that are medically managed and lack vertebral column instability/fracture may require shorter periods of rest.

CLIENT EDUCATION

Outcome is generally believed to be good for animals that have traumatic SCI with intact nociception, so long as appropriate therapy is selected.

SURGICAL CONSIDERATIONS

- Surgery is recommended for animals with advanced imaging that supports significant spinal cord compression or vertebral column instability (e.g., subluxation, violation of multiple vertebral unit compartments).
- Spinal stapling, pins and methylmethacrylate, and various plates can be used to stabilize the vertebral column.
- Decompression may be needed with or without stabilization in cases where there is significant extradural hemorrhage or disc material.

**MEDICATIONS****DRUG(S) OF CHOICE**

- *Opioid analgesics* are commonly used to relieve hyperesthesia associated with trauma (tramadol 3–5 mg/kg PO q8–6h).
- *Nonsteroidal anti-inflammatory drugs* provide analgesia and anti-inflammatory effects, which may be beneficial. Carprofen is commonly used at 2.2 mg/kg PO q12h.
- *Alpha receptor antagonists* can relax the internal urethral sphincter and facilitate urinary voiding in upper and lower motor neuron bladder dysfunction. Prazosin can be administered at 1 mg/15 kg PO q8–12h.
- *Muscarinic agonists* stimulate detrusor contractility and may permit urine voiding in dogs with lower motor neuron bladder. Bethanechol chloride is delivered at 5–15 mg/dog PO q8–12h.

CONTRAINDICATIONS

- *Glucocorticoids* continue to be commonly used in veterinary medicine for vertebral column trauma. While high-dose methylprednisolone sodium succinate provided within 8 hours of injury has been shown to be beneficial in some human SCI clinical trials, most human SCI centers have ceased providing this intervention as it is fraught with adverse events and does not robustly enhance recovery.
- MPSS and other glucocorticoids have not been shown to be beneficial in dogs with SCI, although research has been largely retrospective. Adverse effects are commonly recognized in the setting of canine disc-associated SCI.

PRECAUTIONS

- NSAIDs may result in gastric ulcers in animals that have SCI.
- Glucocorticoids may cause gastric ulceration, vomiting, colonic ulceration, and urinary tract infections (especially dexamethasone).
- Alpha-antagonists may result in hypotension and gastrointestinal signs.
- Muscarinic agonism is not suggested in animals with upper motor neuron bladder dysfunction that are not receiving alpha blockade. Muscarinic agonists can result in excessive salivation, defecation, urination, and bradycardia.

POSSIBLE INTERACTIONS

Glucocorticoids and NSAIDs should not be combined as this increases the risk of gastrointestinal adverse effects.

ALTERNATIVE DRUG(S)

- Experimental medical strategies for SCI work via many mechanisms, including neuroprotection, induction of plasticity, and regeneration.
- Clinical trials evaluating small molecules and cellular therapies are ongoing.

**FOLLOW-UP****PATIENT MONITORING**

- Daily physical examination-based scoring of SCI with a validated scale is strongly suggested to monitor progression.
- The modified Frankel scale, Texas Spinal Cord Injury Scale, and 14-point pelvic limb motor score are three validated systems used in dogs.

PREVENTION/AVOIDANCE

Indoor animals have lower risk of exogenous SCI.

POSSIBLE COMPLICATIONS

- Chronic ataxia/paresis as well as failure to regain voluntary ambulation are possible.
- Some animals may have urinary/fecal incontinence, especially if they are non-ambulatory.
- Non-ambulatory animals are at risk for skin ulcers and urinary tract infection.

EXPECTED COURSE AND PROGNOSIS

- Animals with intact nociception have a good prognosis for ambulatory recovery if appropriate treatment is undertaken.
- Animals with absent nociception that have vertebral fracture or luxation have a very poor prognosis for regaining voluntary ambulation (< 5%), but literature on this topic is limited.
- Dogs without fracture/luxation that lack nociception may have poorer outcome than dogs with non-traumatic disc herniation, but data limited on this subset of dogs with traumatic SCI.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Animals that have traumatic SCI often have injury to other body systems.

AGE-RELATED FACTORS

Younger animals appear more commonly affected.

PREGNANCY/FERTILITY/BREEDING

SCI may affect ability to achieve pregnancy and carry fetuses to term.

SYNONYMS

Traumatic myelopathy

SEE ALSO

- Myelopathy—Paresis/Paralysis—Cats
- Neck and Back Pain • Paralysis

ABBREVIATIONS

- CSF = cerebrospinal fluid
- CT = computed tomography
- MPSS = methylprednisolone sodium succinate
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug
- SCI = spinal cord injury

Suggested Reading

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Consulting Editor Joane M. Parent

V

VESICOURACHAL DIVERTICULA



BASICS

OVERVIEW

- A common congenital anomaly of the urinary bladder that occurs when a portion of the urachus (i.e., a fetal conduit that allows passage of urine from the bladder to the placenta) located at the bladder vertex fails to close; the result is a blind diverticulum of variable size that protrudes from the bladder vertex.
- Other characteristics include congenital microscopic diverticula (microscopic lumens that may persist at the bladder vertex).
- Acquired macroscopic diverticula develop after the onset of concurrent but unrelated acquired lower urinary tract diseases; presumably, urethral obstruction or detrusor hyperactivity induced by inflammation causes high intraluminal pressure and subsequent enlargement of microscopic diverticula.
- Congenital macroscopic diverticula, most likely caused by impaired urine outflow, develop before or soon after birth and persist indefinitely.

SIGNALMENT

- Dog and cat.
- Frequently encountered in cats with acquired lower urinary tract diseases; twice as common in male cats as in female cats.
- No breed or age predisposition.

SIGNS

- Depend on concomitant disorders predisposing to formation of macroscopic vesicourachal diverticula.
- Hematuria, dysuria, pollakiuria, or signs of urethral obstruction in some patients with concurrent acquired lower urinary tract diseases.

CAUSES & RISK FACTORS

- Persistent congenital microscopic diverticula—cause unknown.
- Congenital microscopic diverticula—risk factors for acquired macroscopic diverticula.
- Diseases associated with increased bladder intraluminal pressure (e.g., bacterial urinary tract infection, uroliths, urethral plugs, and idiopathic disease)—risk factors for acquired macroscopic diverticula.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Persistent (or patent) urachus; very uncommon)—characterized by inappropriate

loss of urine through the umbilicus.

- Persistent urachal ligaments are non-patent fibrous remnants of the urachus, connecting the bladder vertex to the umbilicus.
- Urachal cysts are focal accumulations of fluid in isolated segments of the urachus. They may be aseptic or septic.

CBC/BIOCHEMISTRY/URINALYSIS

- Abnormal findings are related to the underlying disorder that causes vesicourachal diverticula, unless complicated by concurrent acquired lower urinary tract diseases.
- Abnormal findings related to secondary urinary tract infection.

IMAGING

- Congenital and acquired macroscopic diverticula—best identified by positive-contrast urothrocystography.
- Radiographs obtained with the bladder completely then partially distended with contrast medium may facilitate detection of small diverticula.

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

- Extramural macroscopic diverticula appear as convex or conical luminal projections from the bladder vertex.
- Intramural microscopic diverticula appear as transitional epithelium-lined lumens persisting at the bladder vertex from the level of the submucosa to subserosa.



TREATMENT

- Many macroscopic diverticula in cats (and probably dogs) are acquired and self-limiting if the underlying disease is eliminated.
- Direct treatment efforts toward eliminating underlying cause(s) of lower urinary tract disease.
- Consider diverticulectomy if a macroscopic diverticulum persists in a patient with persistent or recurrent bacterial urinary tract infection despite appropriate antimicrobial therapy.



MEDICATIONS

DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

If bacterial urinary tract infection persists or recurs despite proper antimicrobial therapy, the status of the diverticulum should be reevaluated by contrast radiography.

PREVENTION/AVOIDANCE

Avoid diagnostic procedures or treatments that alter normal host urinary tract defenses and predispose to urinary tract infection.

POSSIBLE COMPLICATIONS

Persistent congenital macroscopic diverticula are risk factors for recurrent bacterial urinary tract infection.

EXPECTED COURSE AND PROGNOSIS

- Congenital microscopic diverticula are usually clinically silent unless complicated by concurrent lower urinary tract disease.
- Acquired macroscopic diverticula typically heal in 2–3 weeks after amelioration of clinical signs of lower urinary tract disease.
- Diverticulectomy and appropriate antimicrobial therapy usually associated with resolution of recurrent urinary tract infections in patients with persistent congenital macroscopic diverticula.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Persistent congenital macroscopic diverticula are potential risk factors for recurrent bacterial urinary tract infections.
- Acquired macroscopic diverticula are typically encountered in patients with concurrent lower urinary tract diseases.

SEE ALSO

- Feline Idiopathic Lower Urinary Tract Disease
- Lower Urinary Tract Infection chapters

Suggested Reading

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Authors John M. Kruger and Carl A.

Osborne

Consulting Editor Carl A. Osborne

VESTIBULAR DISEASE, GERIATRIC—DOGS



BASICS

DEFINITION

Acute onset non-progressive disturbance of the peripheral vestibular system in older dogs.

PATHOPHYSIOLOGY

- Unknown.
- Suspected abnormal flow of the endolymphatic fluid in the semicircular canals of the inner ear secondary to disturbance in production, circulation, or absorption of the fluid.
- Possible intoxication of the vestibular receptors or inflammation of the vestibular portion of the vestibulocochlear nerve (cranial nerve VIII).
- Often incorrectly referred to as a stroke, geriatric vestibular disease is neither central in location nor suspected to be vascular or ischemic in origin.

SYSTEMS AFFECTED

Nervous—peripheral vestibular system

GENETICS

N/A

INCIDENCE/PREVALENCE

Common, sporadic, acquired disease of older dogs

SIGNALMENT

Species

Dog

Breed Predilections

- None reported
- Seems to occur more frequently in medium to large breeds

Mean Age and Range

Geriatric; patients usually > 8 years old

Predominant Sex

N/A

SIGNS

General Comments

- Signs of acute onset peripheral vestibular dysfunction usually unilateral but occasionally bilateral.
- If vestibular signs are severe, do not incorrectly attribute the signs (especially the gait) to a central (i.e., CNS) location.

Historical Findings

- Sudden onset of imbalance, disorientation, reluctance to stand, and (usually) head tilt and irregular eye movements.
- May be preceded or accompanied by nausea and vomiting.

Physical Examination Findings

- Head tilt—mild to marked; directed toward the side of the lesion; occasionally disease is bilateral with erratic side-to-side head movements either without a head tilt or with a mild tilt in direction of the more severely affected side.

- Abnormal (resting) nystagmus common in early stages; either horizontal or rotatory with the fast phase always in the direction opposite to the head tilt; with bilateral disease, abnormal nystagmus usually mild or not present and physiologic nystagmus or conjugate eye movements diminished to absent.

- Mild to marked disorientation and vestibular ataxia with tendency to lean or fall in the direction of the head tilt.
- Strength and proprioception normal; with severe disease, patient may be reluctant to stand and may have other issues (e.g. hip dysplasia), making assessment of gait difficult; with bilateral disease, may have base-wide stance.

CAUSES

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Primarily distinguished from other causes of vestibular deficits by the acute onset and usually rapid improvement without specific treatment.
- Otitis media and interna—may have concurrent ipsilateral facial nerve (cranial nerve VII) paresis or paralysis, deafness, and/or Horner's syndrome; otitis externa with ruptured tympanic membrane may be present with otitis media and interna.
- Ototoxic drugs—eliminated by history.
- Trauma—may cause similar acute changes; differentiated by history, results of physical examination.
- Hypothyroid neuropathy—usually not as acute in onset or as severe; may be associated with clinical signs of hypothyroidism and possible cranial nerve VII deficit.

CBC/BIOCHEMISTRY/URINALYSIS

- Generally normal.
- Hemoconcentration secondary to dehydration may be present.
- Unrelated concurrent disorders (e.g., renal and hepatic disease) associated with geriatric state may cause laboratory abnormalities.

OTHER LABORATORY TESTS

N/A

IMAGING

- Usually none required.
- Radiographs of tympanic bullae: normal radiographs do not rule out bulla disease.
- CT or MRI (preferred over radiographs)—may be required to rule out other causes such as otitis media and interna.

DIAGNOSTIC PROCEDURES

- Brainstem auditory evoked response—to assess cochlear portion of cranial nerve VIII; may help to evaluate for otitis media and interna since only the vestibular portion of

cranial nerve VIII is affected with geriatric vestibular disease.

- Deafness may, however, be present as an unrelated aging change.

PATHOLOGIC FINDINGS

None reported



TREATMENT

APPROPRIATE HEALTH CARE

- Mild disease—usually can manage as outpatient.
- Severe disease—patients that cannot ambulate or require intravenous fluid support should be hospitalized during the initial stages.

NURSING CARE

- Treatment supportive, including rehydration by intravenous fluids if required.
- Keep recumbent patients warm and dry using soft, absorbent bedding and, if required, urinary catheter.
- Severe disease—physical therapy, including passive manipulation of limbs and moving body to alternate sides, may be required initially.

ACTIVITY

Restrict activity as required by the degree of disorientation and vestibular ataxia.

DIET

- No modification usually required.
- Nausea, vomiting, and severe disorientation—initially withhold oral intake then supervised feeding.

CLIENT EDUCATION

Reassure client that although the initial signs can be alarming and incapacitating, the prognosis for rapid improvement and recovery is excellent.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

- Sedatives—for severe disorientation and ataxia; diazepam (2–10 mg/dog PO or IV q8h), acepromazine (0.02–0.05 mg/kg IM, SC, IV to maximum of 2 mg).
- Antiemetic drugs or drugs against motion sickness—questionable benefit; dimenhydrinate (4–8 mg/kg PO, IM, IV q8h), meclizine HCl (25 mg PO q24h).
- Glucocorticoids—not recommended since do not alter the course of the disease; may exacerbate concurrent issues (e.g., dehydration).
- Antibiotics—recommended when otitis media and interna cannot be ruled-out; trimethoprim-sulfa (15 mg/kg PO q12h or

VESTIBULAR DISEASE, GERIATRIC—DOGS

(CONTINUED)

30 mg/kg PO q12–24h); first-generation cephalosporin (e.g., cephalexin 10–30 mg/kg PO q6–12h); amoxicillin/clavulanic acid (12.5 mg/kg PO q12h).

CONTRAINDICATIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Neurologic examination of outpatient—repeat 2–3 days later to confirm stabilization and initial improvement.
- Discharge inpatient when able to ambulate and resume eating and drinking.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Fluid and electrolyte imbalances and decompensation of renal insufficiency (if exists) may follow vomiting and/or insufficient fluid and food intake.
- Pressure sores/abrasions.

EXPECTED COURSE AND PROGNOSIS

- Improvement of clinical signs usually starts within 72 hours with resolution of vomiting

and improvement of nystagmus and vestibular ataxia.

- Head tilt and ataxia—significant improvement usually occurs over 7–10 days; if no improvement other causes of peripheral vestibular disease should be pursued; mild head tilt may persist.
- Most patients return to normal within 2–3 weeks.
- Recurrence—repeat episodes of geriatric vestibular disease can occur on the same or opposite side but are uncommon; brief return of signs may occur with stress (e.g., anesthesia).



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

Geriatric dogs affected (mean age suggested 12.5 years)

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Benign idiopathic canine peripheral vestibular disease

- Canine idiopathic vestibular disease/syndrome
- Idiopathic canine peripheral vestibular disease
- Old dog vestibular syndrome

SEE ALSO

- Head Tilt
- Otitis Media and Interna

ABBREVIATIONS

- CNS = central nervous system
- CT = computed tomography
- MRI = magnetic resonance imaging

Suggested Reading

de Lahunta A, Glass EN, Kent M. Veterinary Neuroanatomy and Clinical Neurology, 4th ed. St. Louis, MO: Saunders Elsevier, 2015, pp. 348–349.

Dewey CW. A Practical Guide to Canine and Feline Neurology, 2nd ed. Ames, IA: Wiley-Blackwell, 2008, pp. 272–273.

Garosi L. Head tilt and nystagmus. In: Platt SR, Garosi LS, eds., Small Animal Neurological Emergencies. London, UK: Manson Publishing, 2012, pp. 253–263.

Author Susan M. Cochrane

Consulting Editor Joane M. Parent



Client Education Handout
available online

VESTIBULAR DISEASE, IDIOPATHIC—CATS



BASICS

DEFINITION

Acute onset non-progressive disturbance of the peripheral vestibular system of cats.

PATHOPHYSIOLOGY

- Unknown.
- Suspected abnormal flow of the endolymphatic fluid in the semicircular canals of the inner ear, secondary to a disturbance in the production, circulation, or absorption of the fluid.
- Possible intoxication of the vestibular receptors or inflammation of the vestibular portion of the vestibulocochlear nerve (cranial nerve VIII).

SYSTEMS AFFECTED

Nervous—peripheral vestibular system

INCIDENCE/PREVALENCE

- Sporadic acquired disease
- None reported

SIGNALMENT

Species

Cat

Mean Age and Range

Any age; rare in cats < 1 year of age

SIGNS

General Comments

Limited to signs associated with peripheral vestibular disturbance.

Historical Findings

Sudden onset of severe disorientation, falling, rolling, leaning, vocalizing, and crouched posture; tendency to panic when picked up.

Physical Examination Findings

- Head tilt—always toward the side of the lesion; occasionally disease is bilateral with wide, side-to-side excursions of the head either without a head tilt or with a mild tilt toward the more severely affected side.
- Resting nystagmus—usually horizontal, but may be rotatory with the fast phase always in direction opposite to the head tilt; with bilateral disease, the abnormal nystagmus is usually mild or not present, and physiologic nystagmus or conjugate eye movements are diminished to absent.
- Vestibular ataxia with tendency to roll and fall toward the side of the head tilt.
- Preservation of strength and normal proprioception; with bilateral disease, patient may be reluctant to ambulate, preferring to stay in a crouched posture and possible wide-based stance.

CAUSES

- Unknown.
- Previous upper respiratory tract infection—suspected in some patients; relationship not confirmed; in limited necropsy data no evidence of inflammation.

RISK FACTORS

May be an increase in cases in the summer and early fall, possibly after outbreaks of upper respiratory disease; disease can occur throughout the year.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Diagnosis made on the basis of acute onset peripheral vestibular signs that improve rapidly without specific treatment.
- Otitis media and interna (e.g., bacterial, parasitic)—may have concurrent ipsilateral facial nerve (cranial nerve VII) paresis or paralysis, Horner's syndrome, deafness, ruptured tympanic membrane, otitis externa, and/or radiographic changes in tympanic bulla; signs usually not self-limiting.
- Nasopharyngeal polyp(s)—may cause unilateral or, much less commonly, bilateral peripheral vestibular signs; may have concurrent tympanic bulla involvement; signs usually not as acute and severe at onset and are not self-limiting.
- Blue-tailed lizard ingestion—southeastern United States; thought to produce a similar acute, unilateral, peripheral vestibular syndrome; vomiting, salivation, irritability, and trembling also noted; most patients recover without specific treatment.
- Aminoglycoside toxicity, especially streptomycin—may cause acute unilateral or bilateral peripheral vestibular syndrome and/or hearing loss; differentiated by history of drug use.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

IMAGING

- None usually necessary.
- Radiographs of tympanic bullae: normal radiographs do not rule-out bulla disease.
- CT or MRI—occasionally required to rule out other causes such as otitis media and interna and nasopharyngeal polyp(s).

DIAGNOSTIC PROCEDURES

Brainstem auditory evoked response—may help rule-out other causes (e.g., otitis media and interna; nasopharyngeal polyp); with idiopathic vestibular disease hearing not

affected since disease limited to the vestibular portion of cranial nerve VIII.

PATHOLOGIC FINDINGS

None reported



TREATMENT

APPROPRIATE HEALTH CARE

- Usually outpatient.
- Inpatient—severely affected patient may require hospitalization for supportive care.

NURSING CARE

- Mild disease—treatment supportive only.
- Severe disease—may require intravenous or subcutaneous fluids; maintain patient in quiet, well-padded cage.

ACTIVITY

Restricted according to the degree of disorientation and ataxia.

DIET

Patient may initially be reluctant to eat and drink because of disorientation and/or nausea.

CLIENT EDUCATION

Reassure client that, despite initial alarming and often incapacitating signs, the prognosis for rapid and complete recovery is excellent.



MEDICATIONS

DRUG(S) OF CHOICE

- Sedatives—for severe disorientation and rolling; diazepam (1–5 mg/cat PO q8–12h) and acepromazine (0.02–0.05 mg/kg IM, SC, IV).
- Antiemetic drugs and drugs against motion sickness—questionable benefit; e.g., meclizine HCl 12.5 mg PO q24h.
- Glucocorticoids—not recommended since do not alter course of the disease.
- Antibiotics—recommended if otitis media and interna cannot be ruled out; trimethoprim-sulfa (15 mg/kg PO q12h); first-generation cephalosporin (e.g., cephalexin 10–30 mg/kg PO q6–12h); amoxicillin/clavulanic acid (Clavamox 62.5 mg/cat PO q12h, Clavaseptin 12.5 mg/kg PO q12h).



FOLLOW-UP

PATIENT MONITORING

- Neurologic examination of outpatient—repeat in approximately 72 hours to confirm stabilization and initial improvement.

VESTIBULAR DISEASE, IDIOPATHIC—CATS

(CONTINUED)

- Inpatient—discharge patient when able to ambulate and resume eating and drinking.

EXPECTED COURSE AND PROGNOSIS

- Marked improvement, especially in resting nystagmus within 72 hours, with progressive improvement of gait and head tilt.
- Patients usually normal within 2–3 weeks.
- Head tilt—final sign to resolve; mild residual tilt may remain.

- If signs do not improve rapidly, other causes of vestibular disease should be pursued.
- Rarely recurs.

**MISCELLANEOUS****ABBREVIATIONS**

- CT = computed tomography
- MRI: magnetic resonance imaging

Suggested Reading

Garosi L. Head tilt and nystagmus. In: Platt SR, Garosi LS, eds., *Small Animal Neurological Emergencies*. London, UK: Manson Publishing 2012, pp. 253–263.

Author Susan M. Cochrane

Consulting Editor Joane M. Parent



Client Education Handout available online

VITAMIN D TOXICOSIS



BASICS

DEFINITION

Hypercalcemic disorder resulting from ingestion of vitamin D rodenticide preparations, excessive dietary and vitamin supplementation, ingestion of congeners of vitamin D metabolites used for treatment of psoriasis and other immune-mediated human disorders, or diets high in vitamin D.

PATOPHYSIOLOGY

- Cholecalciferol is metabolized to 25-hydroxycholecalciferol in the liver. 25-hydroxycholecalciferol is metabolized to several metabolites in the kidney, including calcitriol, the most potent metabolite in terms of enhancing calcium absorption from the gut and calcium resorption from bones under physiologic conditions.
- 1,25-Dihydroxycholecalciferol is the active metabolite of cholecalciferol under physiologic conditions. • Under toxic conditions, 25-hydroxycholecalciferol is the predominant circulating and active metabolite. • Calcipotriol (Dovonex), a congener of calcitriol, does not require activation; has immediate but limited action due to a short half-life (100 minutes).
- 25-Hydroxycholecalciferol, calcitriol, and calcipotriol increase absorption of calcium from the gut, stimulate bone resorption, and enhance calcium absorption in renal distal tubules, resulting in hypercalcemia (serum calcium > 12.5 mg/dL). • Serum phosphorus is also increased (> 8 mg/dL). • The outcome is metastatic and dystrophic mineralization of soft tissues, resulting in pathophysiology of the affected organs.

SYSTEMS AFFECTED

- Cardiovascular—mineralization, arrhythmias. • Gastrointestinal—anorexia; mineralization; emesis; hematemesis; constipation; increased gastric acid secretion.
- Musculoskeletal—demineralization; muscle tremors. • Nervous—seizures or depression.
- Renal/Urologic—calcification, proximal tubular necrosis, and renal failure.
- Respiratory—mineralization; dyspnea.

INCIDENCE/PREVALENCE

- Cholecalciferol rodenticide toxicosis—most common cause of vitamin D poisoning in dogs and cats. • Vitamin D₃ poisoning from excessive vitamin D₃ in a commercial dog food in January of 2000, April of 2006, and October of 2010 led to pet food recalls.
- Calcipotriol ointment (Dovonex; 50 µg calcipotriol/g) antipsoriasis medication—leading cause of vitamin D congener toxicity in dogs. • Suckling pups and kittens can be poisoned through milk. • Overall incidence of vitamin D toxicity is unknown.

SIGNALMENT

Species

- Dogs and cats • Other species, particularly exotics

Mean Age and Range

All ages affected; younger dogs (< 6 months) and cats are the most sensitive.

SIGNS

General Comments

- Calcipotriol (Dovonex)—signs develop within 6–12 hours post-ingestion
- Cholecalciferol rodenticides—signs develop within 12–36 hours post-ingestion

Historical Findings

- Inactivity • Vomiting • CNS depression
- Weakness • Anorexia • Polydipsia
- Polyuria • Diarrhea • Melena
- Hematemesis • Loss in body weight
- Constipation • Seizures • Muscle tremors

Physical Examination Findings

- Depression • Vomiting • Diarrhea
- Hematemesis • Hematochezia • Polyuria
- Polydipsia • Renal pain on palpation
- Gastrointestinal hemorrhage • Abdominal pain • Hypersalivation • Oropharyngeal erosive lesions • Bradycardia; ventricular premature contractions • Dyspnea

CAUSES

- Cholecalciferol rodenticides (0.075%)—Quintox, Rampage, Ortho Rat-B-Gone, Ortho Mouse-B-Gone, others; clinically normal dogs and cats have developed hypercalcemia at 0.5 mg/kg bw; signs have occurred in dogs and cats at 0.1 mg/kg bw.
- Calcipotriol: Ingesting 1.8–3.6 µg/kg BW is toxic to dogs. • Diet: In dogs, daily ingestion of vitamin D₃ in excess of the recommended dietary maximum of 1.43 kIU/1,000 kcal of ME causes chronic toxicosis. • In cats, chronic intake of diets containing more than the recommended maximum vitamin D₃ concentrations of 2.5 kIU/1,000 kcal ME is toxic. • In the 2006 dog food outbreak, dietary concentrations of vitamin D₃ were found between 1.51 and 2.67 kIU/1,000 kcal ME.

RISK FACTORS

- Preexisting renal, gastrointestinal, cardiac, lung, or CNS diseases • Dehydration
- Neoplasia • Primary hyperparathyroidism
- Hypoadrenocorticism • Granulomatous diseases (e.g., blastomycosis) • Juvenile hypercalcemia • Age—young animals are most susceptible • Feline idiopathic hypercalcemia



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other hypercalcemic disorders, including lymphosarcoma and other malignancies, hypoadrenocorticism, chronic renal failure, primary hyperparathyroidism, and

granulomatous lesions in soft tissues. Vitamin D and congener toxicosis can be differentiated from these diseases because it suppresses intact parathyroid hormone. In other conditions, iPTH is either normal or increased. • Juvenile hypercalcemia.

- Anticoagulant rodenticide and NSAID toxicity—due to hematemesis and melena.

CBC/BIOCHEMISTRY/URINALYSIS

- Calcium—hypercalcemia (total serum calcium > 12.5 mg/dL, ionized calcium > 6.0 mg/dL). Hypercalcemia is immediate (2–3 hours) and transient (will decline to normal within 24 hours post-ingestion) with calcipotriol ingestion. In cholecalciferol rodenticide toxicity, hypercalcemia is evident 12 hours post-ingestion and persists for weeks if not treated. • Hyperphosphatemia (> 8 mg/dL), may precede hypercalcemia.
- Hypokalemia. • Azotemia. • Hyposthenuria, proteinuria, and glucosuria. • Metabolic acidosis. • Calcipotriol—other abnormalities include hypoalbuminemia, increased ALP, ALT, and AST activity, thrombocytopenia, prolonged APTT, and increased fibrinogen concentration.

OTHER LABORATORY TESTS

- Currently there are no confirmatory tests for calcipotriol intoxication. Serum 25-hydroxy vitamin D and calcitriol are normal. • In acute, one-time ingestions, serum 25-hydroxy vitamin D concentration is increased at least 10 times normal (normal ranges: dogs, 60–215 nmol/L; cats, 65–170 nmol/L) in cholecalciferol toxicosis. • In chronic intoxications, serum 25-hydroxy vitamin D concentrations can increase from 1.5 to 5 times above normal values. • Serum 1,25 dihydroxy vitamin D is only transiently increased and is of limited diagnostic value.
- The total calcium-to-total phosphorus ratio in renal cortex of deceased dogs is in the range of 0.4–0.9 for all vitamin D-related intoxications. • Renal cortical 25-hydroxy vitamin D concentration > 80 nmol/L supports a diagnosis of cholecalciferol toxicosis. • Biliary 25-hydroxy vitamin D concentration > 100 nmol/L supports a diagnosis of cholecalciferol toxicosis.
- Decreased iPTH (normal in dogs is 3–17 pmol/L and for cats is 0–4 pmol/L).
- Normal Na/K ratio.

IMAGING

Ultrasonography—renal, gastric wall, lung hyperechogenicity

V

DIAGNOSTIC PROCEDURES

- ECG—may show bradycardia, sinus tachycardia, ventricular premature complexes.
- Endoscopy—may reveal erosive/hemorrhagic gastric mucosa.

PATHOLOGIC FINDINGS

- Diffuse mineralization of gastric wall and intestines; hemorrhage in gastric mucosa; mineralization of the soft palate, salivary

VITAMIN D TOXICOSIS

(CONTINUED)

glands, other soft tissues. • Necrosis and mineralization of myocardium (especially the atria) and large blood vessels; myocardial degeneration. • Mineralization of glomerular mesangium and capsule, and renal tubular basement membranes. • Tubular necrosis. • Mineralization of lungs.



TREATMENT

APPROPRIATE HEALTH CARE

- Calcipotriol—emergency treatment is recommended; prognosis is guarded, and hospitalization is required.
- Cholecalciferol—once clinical signs show (usually 24–36 hours post-ingestion), gastric decontamination is not worthwhile.
- Hospitalization with close observation in all cases for at least 48 hours post-ingestion.

NURSING CARE

- Correct dehydration and electrolyte imbalances (hypokalemia). • Enhance calciuresis with fluid therapy—strongly recommended for all patients. • Peritoneal dialysis with a calcium-free dialysate—for severe azotemia and hypercalcemia. • Blood transfusion—if anemia is severe or in case of hypovolemia. • Antibiotic therapy—to prevent secondary bacterial infection because of broken defense barrier in gut. • Parenteral alimentation—recommended to rest the gut and to overcome anorexia.

DIET

Offer low-calcium, low-phosphorus diets.

CLIENT EDUCATION

- Caution client to keep all rodenticide products in places that are inaccessible to pets.
- Caution client to secure all medications where pets cannot reach them. • Warn client that vitamin D toxicity is a severe and costly disease to treat with prolonged therapy and hospitalization.



MEDICATIONS

DRUG(S) OF CHOICE

- Pamidronate disodium—to treat hypercalcemia • Salmon calcitonin—to treat hypercalcemia

Decontamination of Gastrointestinal Tract

- Must for calcipotriol ingestions; highly toxic. • Within 2 hours of vitamin D ingestion. • Emetic and activated charcoal followed by osmotic cathartics. • Dogs—apomorphine 0.02–0.04 mg/kg IV, IM, SC, or subconjunctivally. • Cats—xylazine 0.4–0.5 mg/kg IV. • Activated charcoal powder (1–4 g/kg) combined with a saline cathartic (magnesium or sodium sulfate, 250 mg/kg)—PO or by gastric tube.

Hypercalcemia Reduction

- Pamidronate disodium 1.3–2.0 mg/kg in 0.9% sodium chloride slow IV over 2–4 hours; repeat once in 3–4 days for large ingestions; do not combine with salmon calcitonin. • Salmon calcitonin 4–6 IU IM or SC every 6 hours till calcium concentration stabilizes; limited efficacy and patients may become refractory. • Prednisolone—dogs and cats: 2–6 mg/kg IM or PO q12h.
- Furosemide—dogs, 2–6 mg/kg; cats, 1–4 mg/kg SC, IV, or IM q8–12h.

Seizure Control

Diazepam 0.5 mg/kg IV, repeat as necessary

Control of Clinically Significant Ventricular Arrhythmias

Lidocaine—dogs, 2–4 mg/kg IV over 1 minute, repeat up to 8 mg/kg; cats, use cautiously at 0.25–0.5 mg/kg IV slowly.

Gastrointestinal Protection

- Sucralfate 0.25–1 g PO q6–8h.
- Famotidine 0.5–1 mg/kg IV, IM, PO q12h.

Antiemetics

Maropitant 1 mg/kg SQ q24h.

PRECAUTIONS

- Supratherapeutic doses of pamidronate disodium may worsen renal failure. • Salmon calcitonin—associated with side effects: anorexia, anaphylaxis, and emesis. Rarely used. • Xylazine—may aggravate respiratory depression and result in vagal-mediated slowing of the heart rate. • Prolonged prednisolone therapy may result in adrenocortical suppression; taper doses gradually over a 2–4-week treatment period.



FOLLOW-UP

PATIENT MONITORING

- Following pamidronate therapy—serum calcium and BUN at 24, 48, and 72 hours following exposure; if hypercalcemia is present, fluid diuresis is recommended; if hypercalcemia still present, repeat pamidronate infusion 72 or 96 hours after the first infusion and monitor serum calcium and BUN q48h. • Following calcitonin therapy—serum calcium and BUN; monitor q24h and continue adjusting dose until calcium returns to normal (24–48 hours for calcipotriol, or 2–4 weeks for cholecalciferol). • Calcipotriol causes short-term hypercalcemia (24–48 hours) with massive soft tissue mineralization; requires long-term aggressive fluid and supportive therapy.
- Cholecalciferol-induced hypercalcemia is persistent, requiring long-term management and supportive care (2–4 weeks).

PREVENTION/AVOIDANCE

- Keep rodenticides and medications out of reach of pets. • Avoid diets high in vitamin D.

POSSIBLE COMPLICATIONS

- Chronic renal failure—inability to concentrate urine. • Secondary bacterial infection from injury in the gut. • Subclinical renal, cardiovascular, and gastrointestinal injury—due to mineralization.

EXPECTED COURSE AND PROGNOSIS

- Calcipotriol—guarded prognosis unless aggressive therapy is immediate due to peracute nature of condition and associated massive soft tissue mineralization.
- Cholecalciferol—depends on severity and duration of hypercalcemia; if hypercalcemia is unresponsive or severe mineralization occurs before therapy is initiated, prognosis is poor.



MISCELLANEOUS

AGE-RELATED FACTORS

Distinguish from normal juvenile hypercalcemia.

PREGNANCY/FERTILITY/BREEDING

Teratogenic effects—calcipotriol and vitamin D have antiproliferative effects and potential for teratogenesis.

SYNONYMS

- Calcipotriol toxicosis • Cholecalciferol toxicosis • Dovonex toxicosis • Vitamin D congeners toxicosis

ABBREVIATIONS

- ALP = alanine phosphatase • ALT = alanine aminotransferase • APTT = activated partial thromboplastin time • AST = aspartate aminotransferase • CNS = central nervous system • ECG = electrocardiogram • iPTH = intact parathyroid hormone • ME = metabolizable energy • NSAID = nonsteroidal anti-inflammatory drug

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Author Wilson K. Rumbeha
Consulting Editor Lynn R. Hovda

VOMITING, ACUTE



BASICS

DEFINITION

- Forceful, neurologically mediated reflex expulsion of gastric contents from the oral cavity.
- Acute vomiting is defined as vomiting of short duration (< 5–7 days) and variable frequency.

PATHOPHYSIOLOGY

• A complex set of reflex activities under central neurologic and hormonal control involving the coordination of GI, abdominal, and respiratory musculature.

- Often preceded by prodromal signs of nausea.
- In the first stage there is increased saliva production with bicarbonate to lubricate the esophagus and neutralize gastric acid.
- This is followed by decreased gastric and esophageal motility and increased retrograde motility of the proximal small intestine.
- Stage 2 consists of retching, which is forceful contractions of the abdominal muscles and diaphragm with a resultant negative intrathoracic pressure and positive intra-abdominal pressure to facilitate moving gastric contents orally.
- In stage 3 the gastric contents are expelled. There is a change in the intrathoracic pressure from negative to positive via the force generated by the abdominal and diaphragm muscles.

Concurrently, respiration is inhibited and the nasopharynx and glottis close to prevent aspiration.

- Stimulation of stretch receptors, chemoreceptors, and osmoreceptors located throughout the GI tract, hepatobiliary system, genitourinary system, peritoneum, and pancreas are examples of neural activation. (Duodenum has the most receptors.)
- The humoral stimuli are mediated through the chemoreceptor trigger zone; with a more permeable blood-brain barrier.
- Cats have poorly developed CTZ dopaminergic receptors and therefore respond poorly to apomorphine or D2 dopaminergic receptor antagonists such as metoclopramide.
- Higher centers can lead to psychogenic vomiting, and input from the vestibular apparatus (e.g. motion sickness, vestibular disease) can stimulate the emetic center.

SYSTEMS AFFECTED

- Cardiovascular—hypovolemia, causing tachycardia, pale mucous membranes, and weak pulses; hypokalemia can cause arrhythmias.
- Gastrointestinal—reflux esophagitis.
- Metabolic—electrolyte and acid-base abnormalities (e.g. hypokalemia, hyponatremia, hypochloremia, metabolic alkalosis), prerenal azotemia, and dehydration.
- Nervous—lethargy.
- Respiratory—aspiration pneumonia, rhinitis from vomitus refluxed into the nasopharynx.

GENETICS

No genetic basis

INCIDENCE/PREVALENCE

Increased incidence in younger animals with dietary indiscretion

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

No age, breed, or sex predisposition

Species

Dog and cat

SIGNS

Historical Findings

- Variable vomiting of food and/or fluid. It is essential to differentiate between vomiting and regurgitation when obtaining the history.
- Ingestion of foreign material.
- Variable lethargy and appetite loss; may see diarrhea and/or melena.

Physical Examination Findings

- May include dehydration, (e.g., dry mucous membranes, reduced skin turgor, sunken eyes, pale mucous membranes, tachycardia, weak pulses), fluid-filled bowel loops, excessive gut sounds, abdominal pain (localized [e.g., foreign body, pancreatitis, pyelonephritis, hepatic disease] vs. diffuse [e.g., peritonitis, severe enteritis]), or abdominal mass (e.g., foreign body, intussusception, torsed viscus).
- May note diarrhea or melena on rectal examination.
- May see fever with infectious and inflammatory causes.
- May be unremarkable.

CAUSES

- Adverse food reactions—most frequent cause of acute vomiting; indiscretions (eating rapidly, ingestion of foreign material); intolerances (e.g. sudden diet change, allergies).
- Drugs—antibiotics, anti-inflammatory drugs (corticosteroids, NSAIDs), chemotherapeutics, digitalis, narcotics, xylazine.
- GI inflammation—*infectious enteritis*: viruses (parvo, distemper, corona virus), bacteria (*Salmonella*, *Campylobacter*, *Helicobacter* spp.); hemorrhagic gastroenteritis.
- Gastroduodenal ulcers.
- GI obstruction—foreign bodies, intussusception, neoplasia, volvulus, ileus, constipation, mucosal hypertrophy.
- Systemic disease—uremia, hepatic failure, sepsis, acidosis, electrolyte imbalance (hypokalemia, hypocalcemia, hypercalcemia).
- Abdominal disorders—pancreatitis, peritonitis, pyometra.
- Endocrine disease—hypoadrenocorticism, diabetic ketoacidosis.
- Neurologic disease—vestibular disturbances, meningitis, encephalitis, CNS trauma.
- Parasitism—ascariids, *Giardia*, *Physaloptera*, *Ollulanus tricuspis* (cats), salmon poisoning (dogs).
- Toxins—lead, ethylene glycol, zinc, mycotoxins, household plants.
- Miscellaneous—anaphylaxis, heat stroke, motion sickness, pain, fear.

RISK FACTORS

- Dietary indiscretion
- Sudden changes to diet



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiating Similar Signs

- Vomiting usually includes hypersalivation, retching, and forceful contractions of the abdominal muscles and diaphragm.
- Must always be differentiated from regurgitation, which is the passive expulsion of fluid or food from the esophagus or pharyngeal cavity, and dysphagia (difficulty in swallowing), which is observed during eating or drinking.
- Animals that are vomiting may have disorders that additionally cause regurgitation, and frequent vomiting can lead to reflux esophagitis and regurgitation.

Differentiating Causes

- If no signs of serious vomiting (e.g., dehydration, lethargy, fever, anorexia, or abdominal pain), can assess with a thorough history and physical examination alone.
- When indications of serious vomiting exist, when frequency intensifies, or when signs do not resolve over 2–3 days, obtain a minimum database (including CBC, biochemical analysis, urinalysis, and survey abdominal radiographs) in an attempt to find the primary cause.

CBC/BIOCHEMISTRY/URINALYSIS

- In non-severe vomiting, the hemogram, biochemical profile, and urinalysis are typically unremarkable unless the animal is dehydrated.
- Anemia with panhypoproteinemia seen with severe gastric ulceration and bleeding.
- Dehydration—may see hemoconcentration (high PCV and total protein).
- May see a stress leukogram.
- Infectious or inflammatory causes—may see an inflammatory leukogram.
- Acute hepatopathies—may see elevated liver enzymes and serum bilirubin.
- Pancreatitis—may see elevated lipase, amylase, and liver enzymes.
- Hyponatremia, hyperkalemia, hypoglycemia, and azotemia suggest hypoadrenocorticism.
- Hyperglycemia with glucosuria and ketonuria indicates ketoacidotic diabetic mellitus.

OTHER LABORATORY TESTS

Additional blood tests for specific diseases when indicated (e.g., blood lead level, ethylene glycol assay, ACTH stimulation testing for hypoadrenocorticism, and canine pancreatic lipase immunoreactivity (cPL) or feline pancreatic lipase immunoreactivity (fPL) testing for pancreatitis).

IMAGING

- Survey abdominal radiographs are often unremarkable, but radiodense foreign bodies, segmental ileus, or gastric distension indicating volvulus or outflow obstruction may be observed; serosal detail may be lost (“ground glass” appearance) with pancreatitis or peritonitis; a mass effect or haziness in the

VOMITING, ACUTE

(CONTINUED)

right cranial quadrant or persistent gas in the descending duodenum may indicate pancreatitis. • Can use contrast radiography to evaluate for radiolucent foreign bodies, obstruction, intussusception, or volvulus. • Can use abdominal ultrasonography to visualize an obstruction, an intussusception, or pancreatitis.

DIAGNOSTIC PROCEDURES

Endoscopy may be useful to assess for gastroduodenal ulceration and gastric and proximal duodenal foreign bodies.

PATHOLOGIC FINDINGS

Dependent on etiology



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient if vomiting non-serious
- Hospitalize if severe vomiting

NURSING CARE

• Fasting the animal is not warranted unless the vomiting is intractable and the risk of aspiration pneumonia is increased. • Patients with frequent episodes of vomiting should be treated initially by keeping the animal NPO and administering intravenous crystalloid fluids.

ACTIVITY

Animals should have limited activity until the vomiting has stopped.

DIET

• If vomiting resolves, initially offer small amounts of water or ice cubes, and if vomiting does not recur, follow with an easily digestible, low-fat, intestinal diet or single-protein and single-carbohydrate-source diet such as non-fat cottage cheese or skinless white chicken and rice in a 1:3 ratio. • If vomiting does not recur, wean the patient back onto the normal diet over 4–5 days.

CLIENT EDUCATION

Owners should be educated on the risks of giving their pet table scraps and to refrain from feeding high-fat treats. They should limit the pet's access to the trash and monitor the pet while it plays with toys to prevent ingestion of foreign bodies.

SURGICAL CONSIDERATIONS

Surgery should be considered for obstructions of any kind as well as for peritonitis or volvulus.



MEDICATIONS

DRUG(S) OF CHOICE

- May use antiemetics in patients with severe vomiting causing electrolyte and/or acid-base disturbances or reflux esophagitis.
- Several antiemetics are available for both

dogs and cats—phenothiazine derivatives that act at the CTZ and emetic center include chlorpromazine (0.5 mg/kg SC q8h) and metoclopramide, a dopamine antagonist and motility modifier that acts at the CTZ and on local receptors in the gut (0.2–0.5 mg/kg PO or SC q6–8h, or 1–2 mg/kg/day as a CRI); H₁-receptor antagonists acting on the CTZ can be used in motion sickness (e.g., diphenhydramine 2–4 mg/kg PO, IM q6–8h) for dogs only; maropitant, a neurokinin-1 antagonist (1 mg/kg SC q24h or 2 mg/kg PO q24h). • Patients with ulceration—can use H₂-receptor antagonists such as ranitidine (1–2 mg/kg PO, SC, IV q12h) and famotidine (0.5–1 mg/kg PO, SC, IV q12h), proton pump inhibitors such as omeprazole (0.7–1 mg/kg PO q12–24h), and/or gastric mucosal protectants such as sucralfate (250 mg/cat PO q6–12h, 250–1,000 mg/dog PO q6–12h) as a slurry. • Fever or mucosal injury (hematemesis, melena)—antibiotics may be indicated (e.g., ampicillin, enrofloxacin).

CONTRAINdications

• Use phenothiazines with caution in dehydrated patients because of possible hypotension from their alpha-receptor antagonist effect; they also may lower the seizure threshold and should be avoided in epileptics. • Do not use anticholinergics; they can cause gastric atony and intestinal ileus, which could exacerbate vomiting. • Do not use prokinetics such as metoclopramide and cisapride in patients with GI obstruction • Maropitant should be used with caution in patients with hepatic disease and preferably for a maximum of 5 days.

PRECAUTIONS

Use antiemetics cautiously; they may suppress vomiting and mask progressive disease or hamper an important means of monitoring response to primary therapy.

POSSIBLE INTERACTIONS

Anticholinergics and opioids may negate the effect of metoclopramide.

ALTERNATIVE DRUG(S)

- Cisapride • Famotidine • Dolasetron
- Pantoprazole



FOLLOW-UP

PATIENT MONITORING

• If frequency of vomiting increases or the animal has systemic evidence of disease: hospitalize for treatment and obtain appropriate diagnostics. • If vomiting persists beyond 7 days despite conservative therapy, pursue appropriate testing for chronic vomiting.

PREVENTION/AVOIDANCE

- Animals should be fed a highly digestible fat-restricted diet. • Owners should attempt

to control indiscriminate eating and monitor for foreign body ingestion.

POSSIBLE COMPLICATIONS

- Aspiration pneumonia • Esophagitis
- Dehydration • See "Systems Affected"

EXPECTED COURSE AND PROGNOSIS

• Recovery from non-serious vomiting is usually rapid and spontaneous. • Feeding of a highly digestible, fat-restricted diet will frequently control non-serious vomiting. • GI foreign bodies have a good prognosis after endoscopic retrieval or surgical removal.



MISCELLANEOUS

ASSOCIATED CONDITIONS

See "Systems Affected"

AGE-RELATED FACTORS

Young animals are more likely to ingest foreign objects and acquire viral, bacterial, and parasitic disease.

ZOONOTIC POTENTIAL

Some species of *Giardia*, *Salmonella*, and *Campylobacter* are zoonotic.

PREGNANCY/FERTILITY/BREEDING

Misoprostol, a synthetic prostaglandin E1 analogue used most often in treatment or prevention of gastric ulceration associated with nonsteroidal anti-inflammatory drugs, is contraindicated in pregnant animals.

SYNONYM

Emesis

SEE ALSO

- Diarrhea, Acute • Gastroduodenal Ulceration/Erosion

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- CNS = central nervous system • CTZ = chemoreceptor trigger zone • GI = gastrointestinal • NSAID = nonsteroidal anti-inflammatory drug • PCV = packed cell volume

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Simpson KW. Diseases of the stomach. In: Ettinger SJ, Feldman EC, eds., Textbook of Veterinary Internal Medicine, 7th ed. St. Louis, MO: Elsevier, 2010, pp. 1504–1526.

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Client Education Handout
available online

VOMITING, CHRONIC



BASICS

DEFINITION

Persistent vomiting lasting longer than 5–7 days or vomiting that occurs intermittently several days/week. This condition is usually non-responsive to symptomatic treatment.

PATHOPHYSIOLOGY

- Vomiting occurs when the vomiting center, located within the medulla oblongata, is activated by the humoral or neural pathway.
- There are four main components to the vomiting reflex: (1) visceral receptors within the GI tract; (2) vagal and sympathetic afferent neurons; (3) CRTZ; and (4) vomiting center.
- The humoral pathway is mediated via activation of the CRTZ and is affected by uremic toxins, liver disease, digoxin toxicity, endotoxemia, apomorphine, and other bloodborne triggers.
- The neural pathway is mediated via activation of the vomiting center and is affected by disorders associated with obstruction, distension, or inflammation of the gastrointestinal tract.
- All causes of vomiting (including the vestibular apparatus and cerebrum) are ultimately mediated via the vomiting center.

SYSTEMS AFFECTED

- Endocrine/Metabolic—dehydration, electrolyte and acid-base imbalances.
- Cardiovascular—hypovolemia or electrolyte and acid-base imbalances can cause arrhythmias.
- Gastrointestinal—gastroesophageal reflux, esophagitis, and subsequent esophageal stricture.
- Respiratory—aspiration pneumonia.
- Neurologic—altered mentation.

SIGNALMENT

- Dog and cat.
- Young animals are more likely to ingest foreign bodies; linear foreign bodies are more common in cats.
- Confirmed or suspected breed predispositions—brachycephalic breeds are prone to pyloric outflow obstruction secondary to mucosal hypertrophy; Basenji, German shepherd, and Shar-Pei are prone to inflammatory bowel disease; rottweiler are prone to eosinophilic IBD; Airedale terrier prone to pancreatic carcinoma; beagle, Bedlington terrier, cocker spaniel, Doberman pinscher, Labrador retriever, Skye terrier, and standard poodle are prone to chronic hepatitis. Yorkshire terrier predisposed to intestinal lymphangiectasia.

SIGNS

Historical Findings

- Vomiting of food, clear or bile-stained fluid, hematemesis, decreased appetite or anorexia,

pica, melena, polydipsia, and abdominal distension are typical of gastric disease.

- Diarrhea and profound weight loss are more characteristic of intestinal disease.
- Signs such as weakness, polyuria, or jaundice relate to other underlying metabolic diseases.

Physical Examination Findings

- Weight loss and poor hair coat may indicate chronic malnutrition.
- Abdominal palpation may reveal abdominal distention, pain, thickened bowel loops, lymphadenopathy, or mass effects.
- Tacky mucous membranes and prolonged skin tenting if dehydration is present; pale membranes if patient is anemic.
- Oral examination may reveal uremic ulcerations or sublingual string foreign bodies.
- Rectal examination may detect diarrhea, hematochezia, or melena.

CAUSES

Esophageal Disease

- Hiatal hernia (more commonly associated with regurgitation)
- Gastroesophageal reflux (more commonly associated with regurgitation)

Infectious Disease

- *Helicobacter*-related gastritis
- Histoplasmosis
- Pythiosis
- Small intestinal bacterial overgrowth
- Gastric parasites—*Physaloptera* spp.
- Intestinal parasitism

Metabolic Diseases

- Renal disease
- Hepatobiliary disease
- Hypoadrenocorticism
- Chronic pancreatitis
- Diabetic ketoacidosis (DKA)
- Metabolic acidosis
- Electrolyte abnormalities—hypo-/hyperkalemia, hyponatremia, hypercalcemia

Inflammatory Bowel Disease

- Lymphocytic, plasmacytic, eosinophilic, or granulomatous
- Gastritis, enteritis, or colitis

Obstructive GI Disease

- Foreign body
- Congenital pyloric stenosis
- Chronic pyloric hypertrophic gastropathy
- Intussusception

Neoplastic Disease

- GI lymphoma, adenocarcinoma, fibrosarcoma, gastrointestinal stromal cell tumor
- Pancreatic adenocarcinoma
- Gastrin-secreting tumor (gastrinoma)
- Systemic mastocytosis

Neurologic

- Cerebral edema
- CNS tumors
- Encephalitis/meningoencephalitis
- Vestibular disease

Motility Disorders

- Post-gastric dilatation
- Post-surgical—gastric, duodenal
- Electrolyte imbalances
- Ileus (see chapter, Ileus, for underlying causes)

Miscellaneous

- Drug-induced (e.g., NSAIDs, glucocorticoids, chemotherapeutics, antibiotics, antifungals)
- Food intolerance/allergy
- Toxicity

Additional Causes in Cats

- Parasitic—dirofilariasis, *Ollulanus tricuspis*
- Inflammatory—cholecystitis, cholangiohepatitis
- Metabolic—hyperthyroidism
- Functional—constipation/obstipation

RISK FACTORS

Breed-associated disease (see "Signalment")



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Vomiting must first be differentiated from regurgitation.
- Regurgitation is a passive retrograde movement of fluid or undigested food into the oronasal cavity that has not yet reached the stomach and occurs without an abdominal component, thus localizing disease to the esophagus.
- Vomiting is a centrally mediated reflex often preceded by prodromal signs of restlessness, nausea, salivation, and repeated swallowing.
- Vomiting patients may also regurgitate because of secondary esophagitis.
- Vomit of food or partially digested food is more common with primary gastric disease, while vomitus of bile is more likely intestinal in origin.

CBC/BIOCHEMISTRY/URINALYSIS

- CBCs are often unremarkable with primary gastric disease.
- Chronic GI bleeding can cause a nonregenerative anemia, often with characteristics of iron deficiency (microcytosis, hypochromasia, thrombocytosis).
- Acute GI bleeding can cause either regenerative or nonregenerative anemia, depending on severity and duration.
- Nonregenerative anemia may also occur secondary to chronic metabolic or inflammatory diseases.
- IBD, chronic pancreatitis, cholangiohepatitis, and cholecystitis may cause neutrophilic leukocytosis and monocytosis.
- Eosinophilia can occur from eosinophilic gastroenteritis, adrenocortical insufficiency, and GI parasitism.
- Thrombocytopenia has been reported with IBD.

VOMITING, CHRONIC

(CONTINUED)

- Dehydration increases the packed cell volume and total protein.
- Biochemistry provides diagnostic and therapeutic information; normal results rule-out metabolic disease as the underlying etiology with the exception of hypoadrenocorticism that can have normal electrolytes.
- Electrolyte and acid-base imbalances reflect severity of losses and can help to localize disease.
- Hypochloremic metabolic alkalosis, often with hypokalemia, indicates substantial loss of gastric content, most consistent with a gastric outflow obstruction.
- Hyperkalemia in the vomiting patient suggests hypoadrenocorticism or oliguric/anuric renal failure; occasionally, enteritis caused by trichuriasis or bacterial infection (salmonellosis) mimics hypoadrenocorticism.
- Metabolic acidosis is common in patients with dehydration, renal failure, DKA, and severe gastroenteritis with diarrhea.
- Increased liver enzyme activity, hypoalbuminemia, hyperbilirubinemia, hypoglycemia, or low urea nitrogen concentration indicates hepatic disease.
- Persistent hyperglycemia and glucosuria is consistent with diabetes mellitus.
- Hyperglobulinemia may indicate chronic inflammation or infection.
- Hypoalbuminemia, lymphopenia, and hypomagnesemia occur secondary to a protein-losing enteropathy caused by infiltrative intestinal diseases such as lymphocytic plasmacytic gastroenteritis, neoplasia, histoplasmosis, or primary intestinal lymphangiectasia.
- Hypcholesterolemia may also be seen with lymphangiectasia.
- Urinalysis is used to rule out non-GI causes of chronic vomiting such as renal failure and DKA.
- Acidic urine in the hypokalemic, hypochloremic, alkaliotic patient indicates substantial loss of gastric content as would occur with gastric outflow obstruction.

OTHER LABORATORY TESTS

- ACTH stimulation test is used to confirm hypoadrenocorticism. A resting cortisol test $< 2 \mu\text{g}/\text{dL}$ should be followed with an ACTH stimulation test to confirm hypoadrenocorticism.
- Pancreatic lipase immunoreactivity assay may help confirm pancreatitis together with supportive history and physical exam findings and ultrasound.
- Bile acid concentration (pre- and postprandial) is used to help confirm hepatobiliary dysfunction.
- Fecal testing for gastrointestinal parasitism.

IMAGING

- Survey radiographs of the abdomen help identify foreign bodies, GI distension with fluid or gas, and displacement, malposition,

shape, and/or size changes of abdominal organs.

- Survey radiographs of the thorax are used to evaluate for pulmonary metastases, gross esophageal abnormalities, or infectious disease.
- A gastrogram or upper GI series can be used to identify foreign bodies, GI wall masses or infiltrative disease, mucosal ulceration, delayed gastric emptying, and motility disorders; however, the procedure is relatively insensitive for detection of mucosal ulceration.
- Abdominal ultrasonography helps identify parenchymal abnormalities of the liver, gallbladder, kidneys, pancreas, GI tract, and mesenteric lymph nodes.
- CT and MRI further evaluate for parenchymal abnormalities of abdominal organs.

DIAGNOSTIC PROCEDURES

- Gastroduodenoscopy—allows direct inspection of the gastric and intestinal lumen to identify gross mucosal lesions and foreign bodies and provides a minimally invasive method of biopsy to evaluate for microscopic disease. Limitations of endoscopy include the working length of the endoscope (unable to access the jejunum in large-breed dogs) and depth of the biopsies.
- Laparoscopy or exploratory laparotomy is used for more extensive diagnostic and therapeutic procedures.



TREATMENT

- Specific treatment should be aimed at eliminating the underlying cause in conjunction with supportive therapy.
- If vomiting is intractable, stop oral intake of food and water for 12–24 hours or until the vomiting episodes are better controlled with antiemetics.
- Use crystalloid fluid therapy to replace deficits and to provide for maintenance and ongoing losses.
- If acid-base status is unknown or if hypochloremic metabolic alkalosis is present, use 0.9% sodium chloride.
- If metabolic acidosis is present, use lactated Ringer's solution.
- Supplement potassium if hypokalemia is present; 20 mEq of KCl/L of fluid can be safely added for replacement and maintenance; use higher concentrations if severe hypokalemia is present.
- Debilitated patients and those in poor nutritional condition may need supplemental parenteral or enteral nutrition.
- Dietary therapy for patients with suspected food allergy or with IBD should use an elimination diet containing a single, novel protein source or a hydrolyzed diet.
- Blood transfusion in severely anemic patients with evidence of active GI bleeding.

- Use surgical treatment if uncontrolled hemorrhage, obstruction, or perforation is suspected.



MEDICATIONS

DRUG(S)

- Antisecretory drugs such as H₂-receptor blockers (e.g., famotidine, ranitidine) or proton-pump inhibitors such as omeprazole (more potent)—famotidine 0.5–1 mg/kg PO, IV, or SC q12h; ranitidine 1–2 mg/kg PO, IV q12h; omeprazole 0.7–1.5 mg/kg PO q12–24h.
- Protectants such as sucralfate (0.5–1 g/dog PO q8–12h; 0.25 g/cat PO q8–12h) to accelerate gastric mucosal healing; can be used with antisecretory drugs for patients with evidence of upper GI bleeding (e.g., hematemesis or melena).
- Antibiotics—indicated for treatment of *Helicobacter*-associated gastritis, SIBO, and as an adjunct to corticosteroids in the treatment of IBD.
- Suggested treatment of *Helicobacter*-associated gastritis—amoxicillin 20 mg/kg PO q8h plus omeprazole 0.7–1.5 mg/kg PO q24h and metronidazole 10 mg/kg PO q12h for 21 days; clarithromycin 7.5 mg/kg PO q12h can be used with amoxicillin and metronidazole (as above) as an alternative therapy for cats.
- Metronidazole—may be used at 10 mg/kg PO q12h in conjunction with corticosteroids to treat IBD, although evidence of direct benefit of this approach is currently lacking.
- Antibiotic-responsive enteropathy (tylosin-responsive enteropathy)—tylosin is the drug of choice administered at 5–10 mg/kg q24h for 8–12 weeks. Alternative option is metronidazole (10 mg/kg q12h for 8–12 weeks) although tylosin is felt to be superior for this disorder.
- Use corticosteroids in conjunction with dietary changes to treat biopsy-confirmed IBD; azathioprine, chlorambucil, or cyclosporine can also be used in patients with poor response to corticosteroids alone or to decrease the dosage of steroids required to control symptoms. Avoid the use of more than 2 immunomodulatory drugs given concurrently.
- Prokinetic drugs (e.g., metoclopramide, cisapride or erythromycin) are used to treat delayed gastric emptying not associated with obstructive disease.
- Pyrantel pamoate is effective for *Physaloptera*; fenbendazole is effective for *Ollulanus*.
- Iron supplementation for animals with chronic GI bleeding that develop microcytic hypochromic anemia.
- Surgery and/or chemotherapy for neoplasia, depending on the tumor type and location.
- Paraneoplastic hypersecretion of gastric acid, as occurs with mastocytosis and

(CONTINUED)

VOMITING, CHRONIC

- gastrin-secreting pancreatic tumors, is best treated with antisecretory drugs (e.g., omeprazole) to diminish gastritis, gastric ulcer, and chronic vomiting.
- Reserve antiemetics for patients with persistent vomiting unresponsive to treatment of the underlying disease. Maropitant is a neurokinin-1 receptor antagonist suppressing vomiting at the CRTZ, vomiting center, and vagal afferents; maropitant 1 mg/kg SC q24h, 2 mg/kg PO q24h. Phenothiazines (e.g., chlorpromazine) work at both the CRTZ and vomiting center; chlorpromazine 0.5 mg/kg SC, IM q6–8h.
 - Prokinetic drugs (e.g., metoclopramide)—metoclopramide also blocks the dopaminergic 2 receptors at the CRTZ, but this effect is far weaker in cats compared to dogs; metoclopramide 0.2–0.5 mg/kg IV, IM, PO q6–8h; metoclopramide can also be administered as a continuous rate infusion of 1–2 mg/kg/24h in hospitalized patients.
 - Vomiting caused by chemotherapy is best treated with ondansetron 0.5–1 mg/kg IV, PO given 30 minutes before chemotherapy.

PRECAUTIONS

- Do not give α -adrenergic blockers such as chlorpromazine to dehydrated patients as they can cause hypotension.
- Use antiemetics with caution, as they can mask the underlying problem.
- Metoclopramide can cause lethargy, restlessness, agitation, and other behavioral changes, particularly in cats.
- Corticosteroids are immunosuppressive and are a risk factor for development of GI

ulceration; use caution when treating IBD with corticosteroids at high dosages or for long periods.

- Azathioprine and chlorambucil are myelotoxic; monitor CBCs for neutropenia and thrombocytopenia every 2 weeks for the first month of treatment and monthly thereafter.
- Cyclosporine can exacerbate vomiting and diarrhea when used at high dosages; use with caution in patients with renal disease.
- Do not use anticholinergics as antiemetics, as they can exacerbate vomiting by causing gastric atony and gastric retention.
- Metoclopramide and cisapride are contraindicated in patients with GI obstruction.

POSSIBLE INTERACTIONS

Ranitidine interferes with hepatic metabolism of theophylline, phenytoin, and warfarin, and should not be used concurrently with these drugs. Avoid use of cimetidine because it is a weak H₂-receptor antagonist and is a potent inhibitor of the cytochrome P450 enzyme pathway.

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

Helicobacter heilmannii and *H. felis* may have zoonotic potential; they have been isolated from humans with chronic gastritis, most of whom have had close contact with dogs or cats.

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- CNS = central nervous system
- CRTZ = chemoreceptor trigger zone
- CT = computed tomography
- DKA = diabetic ketoacidosis
- GI = gastrointestinal
- IBD = inflammatory bowel disease
- MRI = magnetic resonance imaging
- NSAID = nonsteroidal anti-inflammatory drug
- SIBO = small intestinal bacterial overgrowth

Suggested Reading

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**Client Education Handout
available online**

VON WILLEBRAND DISEASE



BASICS

DEFINITION

- Primary hemostatic defect caused by a quantitative or functional deficiency of vWF.
- Clinical expression varies from a mild to severe bleeding diathesis.

PATHOPHYSIOLOGY

- vWF is an adhesive plasma protein required for normal platelet binding at sites of small vessel injury. In addition, plasma vWF is a carrier protein for coagulation factor VIII.
- A lack of vWF impairs platelet adhesion and aggregation, especially at sites of high shear stress. The largest molecular weight (MW) forms of vWF demonstrate highest reactivity in supporting platelet-collagen interactions.

SYSTEMS AFFECTED

- vWF deficiency may cause spontaneous hemorrhage, prolonged post-traumatic hemorrhage, and ultimately blood loss anemia.
- Spontaneous hemorrhage—typically manifests as bleeding from mucosal surfaces.

GENETICS

- An autosomal trait; both males and females express and transmit the defect with equal frequency.
- Expression pattern of severe forms (Types 2 and 3 vWD) is recessive; milder form (Type 1 vWD) appears to be recessive or incomplete dominant.

INCIDENCE/PREVALENCE

- The most common hereditary hemostatic defect in dogs.
- Rarely reported in cats.

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Breed Predilections

- Three type classifications are found in dogs; a single type predominates within each affected breed.
- Type 1 vWD (mild to moderate signs): quantitative protein deficiency. Low vWF:Ag with proportionate reduction in vWF function. Type 1 is the most common classification.
 - Breeds: Airedale, Akita, basset hound, Bernese mountain dog, dachshund, Doberman pinscher, German shepherd, golden retriever, greyhound, Irish wolfhound, Manchester terrier, miniature pinscher, Pembroke Welsh corgi, poodle, and sporadic cases in any breed and mixed-breed dogs.
- Type 2 vWD (severe signs): quantitative and functional protein defect; low vWF:Ag with disproportionate lack of activity due to absence of high MW multimers.
 - Breeds: German wirehaired and shorthaired pointers.

- Type 3 vWD (severe signs): complete lack of plasma vWF.

- Breeds: Chesapeake Bay retriever, Dutch Kooiker, Scottish terrier, Shetland sheepdog, and sporadic cases in any breed.

Mean Age and Range

- Severe (Types 2 and 3 vWD) typically manifests by 3–6 months of age.
- Milder forms typically demonstrate abnormal bleeding after surgery or trauma, or in association with another condition that impairs hemostasis.

SIGNS

Physical Examination Findings

- Hemorrhage from mucosal surfaces: epistaxis, gastrointestinal hemorrhage, hematuria, vaginal hemorrhage, gingival hemorrhage.
- Prolonged bleeding after surgery or trauma.
- Blood loss anemia if prolonged hemorrhage.

CAUSES

Heredity vWD is caused by mutations that impair vWF synthesis, release, or stability.

RISK FACTORS

Acquired disease conditions or drug therapy that impair platelet function may exacerbate clinical signs of vWD.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Thrombocytopenia (the first rule-out for any patient with abnormal hemorrhage).
- Acquired coagulation factor deficiency (often associated with liver disease, vitamin K deficiency, or DIC).
- Acquired platelet function defects (often associated with drug therapy, uremia, hyperproteinemia).
- Hereditary coagulation factor deficiencies.
- Hereditary platelet function defects.

CBC/BIOCHEMISTRY/URINALYSIS

- Regenerative anemia develops after blood loss.
- Platelet count is normal unless the patient has experienced acute, massive bleeding.

OTHER LABORATORY TESTS

- Coagulation screening tests (ACT, APTT, PT, TCT, fibrinogen)—normal.
- Clinical diagnosis based on specific measurement of plasma vWF concentration (vWF:Ag).
 - vWF:Ag < 50% indicates vWF deficiency, but clinical signs of abnormal bleeding typically develop in animals with vWF:Ag < 25%.
 - Types 1 and 2 vWD are characterized by low vWF:Ag, whereas Type 3 vWD is defined as the complete absence of detectable protein (vWF:Ag < 0.1%).

- Types 1 and 2 vWD are differentiated based on functional and/or structural vWF analyses.

- vWF:CBA is a functional measure of vWF/collagen affinity. Type 2 vWD dogs have a relative lack of vWF:CBA compared to vWF:Ag, resulting in a protein concentration to function ratio > 2:1. Type 1 vWD dogs have proportionate protein concentration and function.

- vWF multimer structure is visualized on Western blots. Type 2 vWD dogs lack the highest MW forms.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- BMBT and the platelet function analyzer-100 are point-of-care screening tests whose endpoints are prolonged in patients with platelet aggregation defects, and vWF deficiency. Prolongation is nonspecific and may accompany severe thrombocytopenia, anemia, or changes in blood viscosity.
- BMBT (expected values 2–4 minutes): typical values for Type 1 vWD = 5–10 minutes, Types 2 and 3 vWD > 12 minutes.
- PFA-100 closure times (expected ADP/collagen closure time < 120 seconds): typical values for Type 1 vWD = 150–300 seconds, Types 2 and 3 vWD > 300 seconds.

PATHOLOGIC FINDINGS

Hemorrhage is the only associated abnormality. Morbidity and mortality are caused by blood loss or hemorrhage into critical sites (i.e., CNS, respiratory tract).



TREATMENT

- Transfusion of fresh whole blood, fresh plasma, fresh frozen plasma, and cryoprecipitate will supply vWF.
- Component therapy (fresh frozen plasma at 10–12 mL/kg) or cryoprecipitate (unit definition and dosage vary by source) is best for surgical prophylaxis and non-anemic patients, to prevent red cell sensitization and volume overload.
- Patients with severe vWD may require repeated transfusion (q6–12h) to control or prevent hemorrhage.

SURGICAL CONSIDERATIONS

- Preoperative transfusion should be given just before the procedure. Peak vWF is obtained immediately after transfusion, with values falling to baseline by 24 hours after a single dose.
- Cage rest and close monitoring (serial Hct and examination of surgical site) for 24 hours after surgery are ideal to confirm adequate hemostasis. Management of severe vWD typically requires at least one postoperative transfusion.

(CONTINUED)

VON WILLEBRAND DISEASE**MEDICATIONS****DRUG(S) OF CHOICE**

- Desmopressin acetate (DDAVP) is a vasopressin analog that can be given preoperatively to dogs with mild to moderate Type 1 vWD to enhance surgical hemostasis. Dosage is 1 µg/kg SC; given 30 minutes before surgery.
- Response is variable; transfusion should be available if DDAVP alone does not prevent bleeding.

CONTRAINDICATIONS

Avoid drugs with anticoagulant or antiplatelet effects: NSAIDs, sulfonamide antibiotics, heparin, coumadin, plasma expanders, estrogen, cytotoxic drugs.

**FOLLOW-UP****PATIENT MONITORING**

Observe closely for hemorrhage associated with trauma or surgical procedures.

PREVENTION

- Screen dogs preoperatively to determine baseline vWF:Ag in breeds or lines with high prevalence of vWD. The risk of abnormal bleeding is greatest for vWF:Ag < 25%.
- Clinically affected dogs should not be bred. Carriers of vWD can be identified based on low vWF:Ag (< 50%); however, values for carrier and clear dogs may overlap at the low end of normal range (50–70% vWF:Ag). At present, commercial tests (VetGen) to detect specific vWF mutations in DNA are available for several breed-variants of vWD. Dogs that are heterozygous for a specific mutation are considered vWD “carriers” and homozygotes are considered vWD “affected.”

- Selective breeding practices can reduce or eliminate vWD from an affected pedigree. Breeding two clear parents is ideal because all offspring are expected to be vWD clear. Breeding one clear and one carrier parent may be acceptable, with the clear pups produced from these matings used for subsequent breeding. Carrier-to-carrier matings are inadvisable because they are most likely to produce clinically affected offspring.

EXPECTED COURSE AND PROGNOSIS

- Most dogs with mild to moderate vWD have good quality of life and require minimal or no special treatment.
- Dogs with more severe forms require transfusion for surgery and should be transfused if supportive care fails to control a spontaneous bleed. Most of these dogs can be maintained comfortably in pet homes.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- The development of any disease condition that impairs platelet function may exacerbate the bleeding tendency of vWD. Common conditions include thrombocytopenia, endocrinopathy (hypothyroidism, hypocortisolism), hyperproteinemia, and uremia.
- Acquired vWD occurs in humans with aortic stenosis, and features of Type 2 vWD have been reported in Cavalier King Charles spaniels with mitral valve disease.

PREGNANCY/FERTILITY/BREEDING

See “Prevention” for breeding recommendations.

SYNOMYS

vWF protein was formerly referred to as factor VIII-related antigen.

ABBREVIATIONS

- ACT = activated clotting time
- APTT = activated partial thromboplastin time
- BMBT = buccal mucosal bleeding time
- DDAVP = deamino-8-d-arginine vasopressin
- DIC = disseminated intravascular coagulation
- MW = molecular weight
- NSAID = nonsteroidal anti-inflammatory drug
- PT = prothrombin time
- TCT = thrombin clotting time
- vWF = von Willebrand factor
- vWF:Ag = von Willebrand factor antigen
- vWF:CBA = von Willebrand factor collagen binding assay

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**Client Education Handout
available online**

WEIGHT LOSS AND CACHEXIA



BASICS

DEFINITION

- *Weight loss* refers to unintended loss of body weight. Relative to prior stable body weight, acute loss of 10% or chronic loss of 15% is considered clinically important.
- *Cachexia* refers to a state of severe weight loss and tissue wasting secondary to underlying disease, such as cancer, heart failure, or severe inflammatory conditions. In addition to fat loss, cachectic patients lose a significant amount of lean body mass, especially skeletal muscle.
- *Sarcopenia* refers to a disproportionate loss of skeletal muscle and LBM. Sarcopenia can occur without loss of body weight. Sarcopenia may occur secondary to disease or may be age-related.
- LBM loss, such as occurs in cachexia and sarcopenia, contributes to debilitation including weakness, fatigue, and shortness of breath.
- In cats and dogs, loss of lean body mass is a significant risk factor for mortality.
- Weight loss or below-normal body condition is associated with shorter survival in cardiac and cancer patients.

PATHOPHYSIOLOGY

Weight Loss

- Weight loss may occur due to decreased intake or increased energy expenditure, including metabolic waste, resulting in negative energy balance.
- Decreased or insufficient intake can be caused by poor appetite secondary to systemic disease, oral disease, or anosmia; or by inadequate access to nutrients that can occur if access to food is restricted.
- Decreased intake of nutrients can be caused by dysphagia, vomiting or regurgitation.
- Malabsorption syndromes are important causes of weight loss.
- Reduced energy intake or absorption in otherwise healthy animals leads to compensatory changes in metabolism, such as reduced energy metabolism and a shift toward lipid-based energy utilization.

Cachexia

- Cachexia, with loss of fat and LBM, occurs secondary to acute or chronic inflammatory diseases, such as cancer, cardiac disease, renal failure, diabetes, sepsis, chronic fever, etc.
- Features that differentiate cachexia from simple weight loss include activation of inflammatory cytokines, activation of the ubiquitin-proteosome system and metabolic dysregulation resulting in increased energy metabolism.
- Cachexia is associated with increases in IL-6, TNF- α , and other pro-inflammatory cytokines; norepinephrine, epinephrine and cortisol; increased oxidative stress; and

decreased anabolic factors such as IGF-1 and DHEA.

- Inflammatory changes result in dysregulation of appetite, insulin resistance, and increased muscle protein breakdown. Inflammatory cytokines activate the ubiquitin-proteosome system and impair tissue synthesis.
- Increased basal metabolic rate and metabolic inefficiencies contribute to tissue wasting. Secondary anorexia or withholding of food aggravates protein-calorie malnutrition.
- Provision of nutrition to cachectic patients without addressing the underlying disease or metabolic dysregulation is rarely successful in correcting the loss of body tissues.

SYSTEMS AFFECTED

- All body systems may be affected by weight loss depending on the underlying disease and severity of illness.
- Cachexia can result in muscle weakness, fatigue and respiratory compromise.

SIGNALMENT

Dog and cat, especially prominent in aging animals.

SIGNS

Historical Findings

- Clinical signs in patients with weight loss may include normal, increased, decreased, or absent appetite, fever, or other signs of systemic illness.
- A comprehensive dietary history is important to determine nutrient intake, dietary type and quantity offered and consumed, and any changes.
- Historical information on patient's daily activity, environment, pregnancy, appetite, or signs of gastrointestinal disease (e.g., vomiting, diarrhea, stool color/consistency, dysphagia, regurgitation) can help assess calorie expenditure or indicate malabsorption.
- Other historical findings may be indicative of underlying diseases, such as polyuria, polydipsia, changes in attitude, lameness or exercise intolerance.

Physical Examination Findings

- Physical examination must include body weight, a body condition score and an assessment of muscle wasting.
- In obese animals, loss of LBM may occur despite excess body fat so these should be evaluated separately.
- Body weight should be compared against historical data to determine percent weight change.
- BCS is a semiquantitative assessment of body composition and correlates well with body fat.
- Muscle wasting is assessed by palpating over the scapulae, skull, and wings of the ilia, as well as palpation of the gluteal and vastus muscles. This is usually scored subjectively on a 4-point scale.
- Additional evaluation should be aimed at detecting any abnormality that may be

associated with an underlying disease (see "Causes").

CAUSES

Dietary Causes

- Insufficient quantity or quality of food
- Low-calorie or low-protein diet
- Competition in a multi-pet household

Anorexia/Pseudoanorexia

- Inability to smell, prehend, or chew food
- Dysphagia
- Nausea
- Regurgitation
- Vomiting

Maldigestive and Malabsorptive Disorders

- Inflammatory bowel disease
- Intestinal neoplasia (lymphoma, carcinoma, sarcoma)
- Lymphangiectasia
- Severe intestinal parasitism
- Age related decreases in digestive function
- Exocrine pancreatic insufficiency

Metabolic Disorders

- Organ failure—cardiac, hepatic, or renal failure
- Hypoadrenocorticism
- Hyperthyroidism (especially cats)
- Cancer
- Increased catabolism—fever, infection, inflammation, cancer

Excessive Nutrient Loss

- Protein-losing enteropathy
- Protein-losing nephropathy
- Diabetes mellitus
- Extensive skin lesions (e.g., burns)

Neuromuscular Disease

- Lower motor neuron disease
- CNS disease—usually associated with anorexia or pseudoanorexia

Physiologic Increased Use of Calories

- Increased physical activity
- Prolonged or extreme cold environment
- Pregnancy or lactation

RISK FACTORS

- Age
- See "Causes"



DIAGNOSIS

- Diagnosis is by evaluation of BCS and muscle wasting. Loss of LBM can occur without significant weight change (sarcopenia).
- Body weight should be compared to historic weight if available after adjusting for under- or over-hydration.
- Once loss of weight or LBM is confirmed, seek underlying cause.

DIFFERENTIAL DIAGNOSIS

- See "Causes."
- Determine if weight loss is associated with increased, normal or decreased calorie intake and absorption of nutrients.

(CONTINUED)

- Determine what the patient's appetite was at the onset of weight loss as any condition can lead to anorexia if it persists long enough for the patient to become debilitated.
- Fever suggests an underlying infectious or inflammatory cause.
- Absence of fever is more consistent with metabolic causes of weight loss such as cardiac, renal, or hepatic failure.

CBC/BIOCHEMISTRY/URINALYSIS

- Laboratory tests may be indicative of underlying disease.
- No laboratory tests reliably measure protein/calorie malnutrition, but the following may be observed:
 - Low hematocrit, elevated alkaline phosphatase, and/or low urea nitrogen with normal to elevated serum creatinine.

OTHER LABORATORY TESTS

- Determined by most likely differential diagnoses on the basis of findings of the history, physical examination, and initial database.
- Perform serologic FeLV and FIV tests in cats with weight loss of unknown cause.
- Measure serum T₄ concentration in any cat > 5 years old with weight loss of unknown cause.
- Examine serial fecal centrifugation flotations and direct smears to exclude intestinal parasitism.
- In endemic areas, or in pets with a history of travel, rule-out infectious (parasitic, protozoal, viral, and fungal) diseases.
- Specific organ function tests as indicated by historical, physical examination, and initial database findings. Examples include serum TLI for exocrine pancreatic insufficiency; ACTH stimulation test for hypoadrenocorticism; pre- and postprandial serum bile acids for hepatobiliary disease; and urine protein:creatinine ratio if protein-losing nephropathy is suspected.

IMAGING

Thoracic, abdominal, or other radiographs, ultrasound, or echocardiography may be indicated, depending on other clinical findings and suspected underlying causes.

DIAGNOSTIC PROCEDURES

- Vary depending on initial diagnostic findings and the suspected underlying cause of weight loss. See chapter(s) for specific diseases.
- If indications for exploratory laparotomy exist—consider placing a feeding tube at that time.

**TREATMENT**

- The most important treatment principles are to treat the underlying cause of the weight loss and provide appropriate nutritional support.
- Inadequate calorie and protein intake is common among hospitalized patients.

- Calorie needs should be calculated at resting energy requirements ($70\text{Kcal} \cdot \text{kg}^{0.75}$). When feeding is initiated, begin by delivering 25% of RER on day 1 and gradually increase over 3–5 days to achieve RER. Monitor body weight and response, and gradually increase as tolerated. While animals do need to increase their body weight, overfeeding too quickly can result in metabolic problems associated with refeeding syndrome.
- Unless contraindicated, protein intake should be increased above maintenance levels to encourage retention or restoration of LBM.

ORAL NUTRITION

- If the patient is physically able to ingest, digest and absorb nutrients, this is the preferred route.*
- To increase voluntary food intake, offer palatable food several times daily; offer the patient's usual food; offer moist food unless the patient prefers dry food; offer food warmed to body temperature.
- Unless contraindications exist, consider using diets formulated to be high in protein and fat calories. Examples include "critical care" therapeutic diets as well as performance and growth diets. Kitten foods may be suitable for adult cats, and cat foods may be suitable for canine patients.
- Long-chain omega-3 fatty acids EPA and DHA can reduce inflammatory mediators. Consider diets enriched with EPA and DHA for cachectic patients, or those with inflammatory conditions. Examples include therapeutic diets for arthritis, dermatologic and neoplastic conditions. Alternatively, supplement with high EPA fish oil capsules at 1 g fish oil/4.5 kg body weight.
- If underweight patients refuse therapeutic diets (e.g., renal diet, cardiac diet), try an alternate brand, add broth or other flavorants, or consider homemade. Adequate intake of a maintenance diet is preferred over inadequate intake of a therapeutic diet.
- Appetite stimulants may be tried on a short-term basis (see "Medications").
- Forced feeding is rarely effective and is not recommended.

ENTERAL NUTRITION

- If the patient is unable or unwilling to ingest food, but can digest and absorb nutrients, this is the preferred route.*
- Enteral feeding as far proximal in the GI tract as the patient can tolerate is preferred.
- Nasoesophageal tubes (5–8Fr) can be used until patients are able to undergo anesthesia for placement of a larger tube. Due to small tube size, only liquid diets can be used.
- Esophagostomy (12–14Fr for cats, 20–24Fr for dogs) or gastrostomy tubes (18–24Fr) can be placed fairly quickly using a choice of techniques.
- Jejunostomy tubes or gastro-jejunostomy tubes (5–8Fr) are more difficult to place and manage, and require liquid diets fed via chronic infusion. These may be appropriate for patients with intractable vomiting or

severe compromise of the esophagus and stomach.

PARENTERAL NUTRITION

- If the patient is unable to tolerate enteral feedings, this is the preferred route.*
- Total (central) parenteral nutrition requires a dedicated central venous access line, which must be placed and maintained aseptically to reduce complications.
- Metabolic complications and refeeding syndromes are more common in catabolic and cachectic patients.
- Protein in parenteral admixtures should provide 15–25% of calories for dogs and 25–35% of calories for cats. The remaining calories may be provided by glucose or a combination of glucose and lipids, with up to 70% of the non-protein calories from lipid. Vitamins and electrolytes can be provided separately.
- Patients should be fed about 50% of RER on the first day, gradually increasing over 2 days to achieve RER. Patients must be monitored carefully for metabolic (hyperglycemia, hyperlipidemia) and electrolyte (hyper- or hypokalemia, hypophosphatemia, hyper- or hyponatremia, hypomagnesemia) complications.

**MEDICATIONS****DRUG(S) OF CHOICE**

- Depend on the underlying cause of the weight loss; see specific chapter for each condition.
- Appetite stimulants may be useful in addition to medications targeted at the underlying condition; adjust selection or dosage based on underlying disease:
 - Benzodiazepines: diazepam (0.1–0.2 mg/kg PO q12–24h in dogs; 0.05–0.10 mg/kg IV q24h dog/cat); oxazepam (1.25–2.5 µg/cat PO q12–24h; 0.3–0.4 g/kg PO q12–24h for dogs); midazolam (2–5 mg/kg IV for cats); flurazepam (0.1–0.2 mg/kg PO q12–24h for cats).
 - Mirtazapine (1.88 mg/cat PO q24–48h to 3.5 mg/cat (1/4 of a 15 mg tablet) PO q72h). The dose in dogs is 3.75 mg q24h in animals weighing < 7 kg; 7.5 mg q24h in dogs weighing 7–14 kg; 15 mg q24h in dogs weighing 14–27 kg; 30 mg q24h in dogs > 27 kg. The drug is available in 15 mg and 30 mg tablets.
 - Propofol (1–2 mg/kg IV for dogs).
 - Anabolic agents: stanozolol (1–2 mg PO q 12–24h); boldenone (5 mg SC or IV).

CONTRAINdicATIONS

See drug label for specifics

PRECAUTIONS

- Appetite stimulants should only be used for a limited period (days). Recognize that appetite stimulants do not treat the

WEIGHT LOSS AND CACHEXIA

(CONTINUED)

underlying cause of the animal's anorexia and may hamper the assessment of the patient's therapeutic response to concurrently administered drugs.

- Monitor food intake to assure adequate intake.

POSSIBLE INTERACTIONS

Many medications used for underlying causes can cause anorexia and/or nausea.

ALTERNATIVE DRUG(S)

- Megestrol acetate to inhibit inflammatory mediators, promote appetite and weight gain.
- Clenbuterol to enhance muscle mass.
- Long chain omega-3 fatty acids to reduce inflammation.



FOLLOW-UP

PATIENT MONITORING

- See specific condition for follow-up regarding underlying cause.
- Monitor body weight and body condition score closely.
- Appetite and food intake should be monitored closely to ensure nutritional needs are being met.

POSSIBLE COMPLICATIONS

- See specific underlying cause.
- If using assisted (tube) feeding: GI intolerance with vomiting and/or diarrhea; tube displacement or regurgitation leading to aspiration; peritonitis; metabolic disturbances including hyperglycemia, hypophosphatemia, hypokalemia or hypomagnesemia.

- If using parenteral feeding: sepsis; thrombosis; thrombophlebitis; metabolic disturbances including hyperglycemia, hyperlipidemia, azotemia, hyperammonemia, hypophosphatemia, hypokalemia, or hypomagnesemia.



MISCELLANEOUS

ASSOCIATED CONDITIONS

See "Causes"

AGE-RELATED FACTORS

Loss of LBM is more common in geriatric patients

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Lactation can be associated with weight loss due to increased calorie expenditure.

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone
- BCS = body condition score
- CNS = central nervous system
- DHA = docosahexaenoic acid
- DHEA = dehydroepiandrosterone
- EPA = Eicosapentaenoic acid
- FeLV = feline leukemia virus
- FIV = feline immunodeficiency virus
- GI = gastrointestinal
- IGF-1 = insulin-like growth factor I
- IL-6 = interleukin-6
- LBM = lean body mass

- RER = resting energy requirements
- TLI = trypsin-like immunoreactivity
- TNF = tumor necrosis factor

INTERNET RESOURCES

To find a veterinary nutritionist qualified to assist in formulating homemade therapeutic or maintenance diets: <http://www.ACVN.org>.

Suggested Reading

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Client Education Handout
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WEST NILE VIRUS INFECTION



BASICS

OVERVIEW

- An acute to inapparent viral disease with neurologic manifestations caused by West Nile virus, a member of the family Flaviviridae, genus *Flavivirus*. The geographic distribution of the virus is North, Central, South America, Africa, Asia, southern Europe, and Australia (Kunjin virus).
- Natural route of infection is through the bite of numerous species of mosquitoes depending upon geographic location. Infection produces a low-level viremia that is undetectable by day 6 post-infection. Viremia levels insufficient for dogs to be an amplifying host. Antibody detectable by day 7 post-infection.

SIGNALMENT

- Natural infections not limited by species or age.
- Seroprevalence varies with geographic region (3–38%).

SIGNS

- High percentage of dogs show no clinical signs—no experimentally infected dogs have shown clinical signs.
- Incubation period 2–4 days post-infection.
- Febrile response 40.3–42.2°C (104–108°F) 3–6 days post-infection.
- In the rarely affected dogs, common signs are ataxia, depression, anorexia, tremors, conscious proprioceptive deficits, seizures, weakness, flaccid paralysis.

CAUSES & RISK FACTORS

- Neurologic disease caused by West Nile virus.
- Outdoor dogs much greater odds of being seropositive than indoor dogs. High seroprevalence in coyotes supports outdoor risk factor.
- Stray dogs greater odds of being seropositive than owned dogs.
- Lineage 1 virus more neurovirulent (all North American isolates) than lineage 2 (Africa).
- Yearly fluctuation of infections linked to density of mosquito populations.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- On an individual basis, the signs of WNV-induced neurologic disease are indistinguishable from signs associated with various “arbovirus” infections, e.g., EEE, VEE, La Crosse.
- Other considerations—rabies, canine distemper, neosporosis, toxoplasmosis, pseudorabies, encephalomyocarditis virus.

CBC/BIOCHEMISTRY/URINALYSIS

- Generally normal.
- Serial sampling may show drop in leukocytes but may remain within normal.

IMAGING

Electroencephalogram

DIAGNOSTIC PROCEDURES

- Low viremia levels make detection of agent in acute phase highly unlikely. Test of choice if an attempt is made is RT-PCR for WNV specifically or for arboviruses in general.
- Acute and convalescent serum samples should be collected for IgM ELISA test and/or virus neutralization assays.
- For post-mortem testing—RT-PCR and/or immunohistochemistry.

PATHOLOGIC FINDINGS

- Gross lesions not present in limited number of dogs necropsied (one case with epicarditis).
- Histologic lesions in brain—mild, multifocal, non-suppurative meningoencephalitis (lymphocytic to lymphohistiocytic perivasacular infiltrates predominantly in gray matter).



TREATMENT

Supportive therapy directed at reducing neurologic signs.



MEDICATIONS

- Antiviral drugs have not been tested for efficacy.

- Antipyretics to reduce fever.
- Antiseizure medication.



FOLLOW-UP

PREVENTION/AVOIDANCE

Vaccines although available for equines have not been approved for dogs.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- West Nile virus can infect numerous species including humans; however, the insect vector is generally necessary for transmission. The viremia is too low in infected dogs to serve as host for infecting feeding mosquitoes.
- Care should be taken if necropsy is done, as infectious viral particles may be presented in tissue samples.

RISK TO OTHER ANIMALS

Virus is not transmitted from the infected dog to other animals. Clinical case of WNV should be noted as indicative of infected mosquitoes in the area.

ABBREVIATIONS

- EEE = eastern equine encephalitis
- ELISA = enzyme-linked immunosorbent assay
- RT-PCR = reverse transcriptase polymerase chain reaction
- VEE = Venezuelan equine encephalitis
- WNV = West Nile virus

INTERNET RESOURCES

<http://npic.orst.edu/pest/mosquito/wnv.html> (links to many other sites)

Suggested Reading

Njaa BL. Emerging viral encephalitides in dogs and cats. Vet Clin Small Anim 2008, 38:863–878.

Author Edward J. Dubovi

Consulting Editor Stephen C. Barr

WHIPWORMS (TRICHURIASIS)



BASICS

OVERVIEW

- The whipworm, *Trichuris*, occurs in the cecum of dogs (*T. vulpis*) and cats (*T. felis*). Feline trichuriasis is rare in the United States.
- Life cycle is direct; infection is acquired by ingestion of larvated eggs; infective eggs can persist in the environment for months to years.
- Infection can be asymptomatic or cause bloody diarrhea and large bowel inflammation.
- Clinical signs can occur before patency, i.e., before eggs are shed in feces; prepatent period is approximately 70–90 days.
- No extra-intestinal migration occurs.

SIGNALMENT

- Dogs, cats of any age, breed, and sex
- Rarely seen in cats in the United States

SIGNS

- Range from asymptomatic to severe.
- Intermittent large bowel diarrhea often containing mucus and fresh blood (hematochezia).
- Bloody diarrhea with dehydration, anemia, and weight loss in severe cases.
- Signs can occur before eggs detectable in feces.
- Acute to chronic debilitation.

CAUSES & RISK FACTORS

- Ingestion of infective (larvated) eggs from environment contaminated with feces of infected dog.
- Eggs accumulate in environment and remain infective for months to years, especially in soil and dirt runs in moist, shady areas.
- Return of dog to an environment contaminated with infective eggs after anthelmintic treatment will result in reinfection.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Bacterial (spirochaetal) infections of cecum.
- Hookworm infection—identify eggs in feces; signs include anemia, pale mucous

W

membranes, and melena rather than fresh blood in feces.

- Inflammatory bowel disease.
- Gastrointestinal ulcers.
- Dietary indiscretion.
- Capillarid infections (*Pearsonema*, *Eucoleus*)—eggs similar in appearance but smaller with roughened surface; infect urinary or respiratory tracts, respectively, rather than GI tract; usually asymptomatic.
- Secondary pseudohypoaldrenocorticism in severe trichuriasis with metabolic acidosis, hyponatremia, hyperkalemia, and dehydration; normal ACTH stimulation response in trichuriasis.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal; hyponatremia, hyperkalemia, and metabolic acidosis can occur in very severe cases.

OTHER LABORATORY TESTS

ACTH stimulation test in severe cases with electrolyte disturbances to differentiate trichuriasis from hypoadrenocorticism.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Centrifugal flotation of feces in sugar solution (s.g. > 1.2) preferred method.
- Differentiate *Trichuris* eggs (brown, ovoid or lemon-shaped with prominent bipolar plugs, smooth shell, single cell within egg, ~90 × 45 µm) from similar capillarid eggs (smaller, roughened shell surface).



TREATMENT

- Outpatient treatment with anthelmintic for most cases.
- Severe cases with dehydration and electrolyte disturbances require inpatient fluid therapy plus anthelmintic.



MEDICATIONS

DRUG(S)

- Fenbendazole 50 mg/kg PO q24h for 3 days; repeat monthly 3 times; extra-label use in cats.

- Febantel/praziquantel/pyrantel pamoate—label dose PO in dogs.
- Milbemycin oxime 0.5 mg/kg PO q30 days in dogs.
- Moxidectin/imidacloprid, label dose in dogs.



FOLLOW-UP

PATIENT MONITORING

Repeat fecal examination for trichurid eggs and/or retreat with anthelmintic at 3 weeks and at 3 months following initial treatment or once a month for 3 months to detect and eliminate recently matured adults.

PREVENTION/AVOIDANCE

- Prompt removal and disposal of feces to prevent environmental contamination with infective eggs.
- Anthelmintic treatment of infected dogs to prevent shedding of eggs and contamination of environment.

EXPECTED COURSE AND PROGNOSIS

Good prognosis following treatment and implementation of preventive measures.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Relatively rare cases of human infection with *T. vulpis* have been diagnosed based on morphologic differences between eggs of the human whipworm, *T. trichiura*, and those of *T. vulpis*.

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone
- GI = gastrointestinal

INTERNET RESOURCES

<http://www.capcvet.org>

Suggested Reading

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Author Matt Brewer

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WOLFF-PARKINSON-WHITE SYNDROME



BASICS

DEFINITION

- Ventricular preexcitation occurs when impulses originating in the sinoatrial node or atrium activate a portion of the ventricles prematurely through an accessory pathway without going through the AV node; the remainder of the ventricles are activated normally through the usual conduction system.
- WPW syndrome consists of ventricular preexcitation with episodes of paroxysmal supraventricular tachycardia (Figures 1 and 2).

ECG Features of Ventricular Preexcitation

- Normal heart rate and rhythm.
- Normal P waves.
- Short PR interval (dogs, < 0.06 second; cats, < 0.05 second).
- Widened QRS (small dogs, > 0.05 second; large dogs, > 0.06 second; cats, > 0.04 second), often with slurring or notching of the upstroke of the R wave (delta wave).

ECG Features of Ventricular Preexcitation with WPW Syndrome

- Extremely rapid heart rate (dogs, often > 300 bpm; cats, approaching 400–500 bpm).
- P waves may be difficult to recognize.
- QRS complexes may be normal, wide with delta wave, or very wide and bizarre, depending on the circuit.
- Conduction is usually 1:1 (i.e., 1 P wave for every QRS complex).

PATHOPHYSIOLOGY

- Can be associated with congenital or acquired cardiac defects in dogs or cats.
- May be associated with hypertrophic cardiomyopathy in cats.
- Hemodynamic compromise during episodes of supraventricular tachycardia with WPW syndrome.

- WPW syndrome results from a developmental abnormality of the atrioventricular groove. During normal cardiogenesis, direct continuity between the atrial and ventricular myocardium is lost by growth of the annulus fibrosis. Defects in the annulus leave muscular connections called accessory pathways or Kent bundles between the atria and ventricular myocardium. By bypassing the AV node, these pathways can lead to preexcitation of the ventricles.
- The accessory pathways typically have an “all or none” conduction properties. They may only conduct from the atria to the ventricles (called anterograde or antegrade conduction), only from the ventricles to the atria (called retrograde conduction), or in both directions.

SYSTEMS AFFECTED

Cardiovascular

INCIDENCE/PREVALENCE

Unknown

SIGNALMENT

Species

Dog and cat

SIGNS

Historical Findings

- None in patients with ventricular preexcitation
- Syncope in patients with WPW syndrome

Physical Examination Findings

- None in animals with ventricular preexcitation
- Rapid heart rate in animals with WPW syndrome

CAUSES

Congenital Heart Disease

- Congenital defect limited to the conduction system
- Atrial septal defect in dogs or cats
- Tricuspid valvular dysplasia in dogs

Acquired Heart Disease

- Hypertrophic cardiomyopathy in cats



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Ventricular preexcitation—differentiate from other causes of short PR intervals (e.g., fever, hyperthyroidism, and anemia); these conditions do not cause delta waves.
- Narrow complex WPW syndrome—differentiate from other supraventricular arrhythmias (e.g., atrial tachycardia, atrial flutter, and atrial fibrillation); WPW syndrome is most easily recognized after conversion to normal heart rate and rhythm.
- Alternating WPW syndrome should not be confused with ventricular bigeminy.
- Wide complex WPW syndrome must be differentiated from ventricular tachycardia.
- Short PR interval may be correlated with a normal QRS complex if the anomalous pathway bypasses the AV node and connects to the bundle of His (i.e., Lown-Ganong-Levine syndrome).

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

Normal

IMAGING

Echocardiography may show structural heart disease

DIAGNOSTIC PROCEDURES

Electrocardiography

PATHOLOGIC FINDINGS

- Pathologic findings vary with underlying cause
- Possibility of no organic heart lesions

CV₆LU

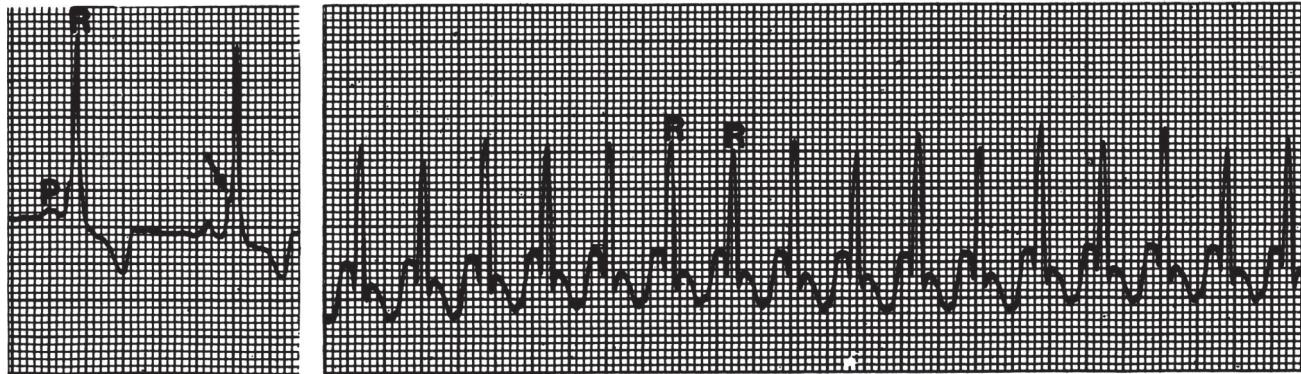


Figure 1.

Wolff-Parkinson-White syndrome (canine). Ventricular preexcitation represented by the short PR interval, wide QRS complex, and delta wave (arrow) in CV₆LU. Paroxysms of supraventricular tachycardia are represented in the long lead II rhythm strip. (From: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)

WOLFF-PARKINSON-WHITE SYNDROME

(CONTINUED)

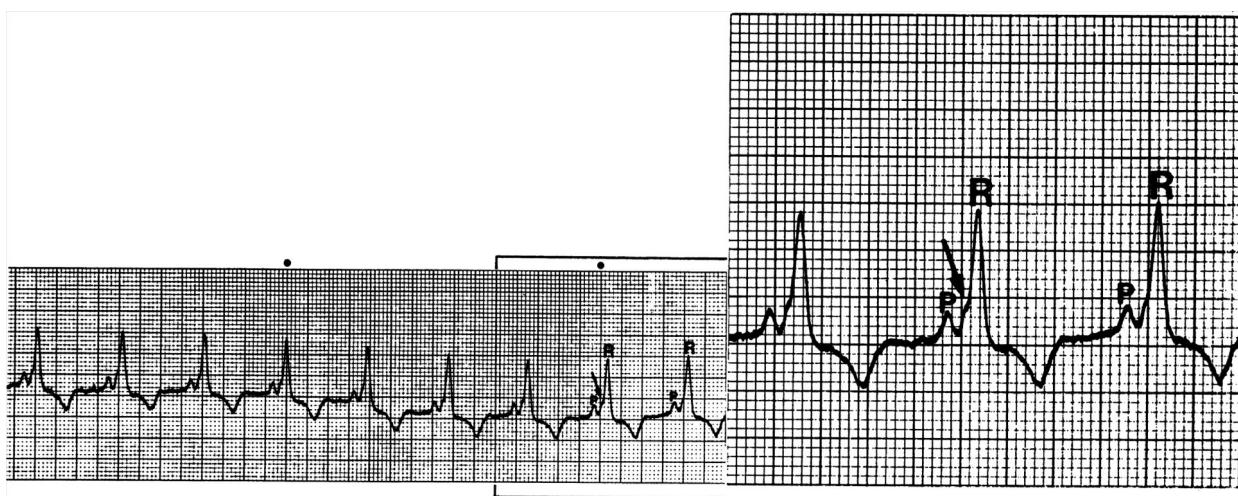


Figure 2.

Ventricular preexcitation in a cat with episodes of fainting. The P waves are normal, the PR interval is short, and the QRS complex is wide; delta waves (arrow) are present. (From: Tilley LP Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.)



TREATMENT

APPROPRIATE HEALTH CARE

- Ventricular preexcitation without tachycardia—no treatment needed.
- WPW syndrome requires conversion by ocular or carotid sinus pressure, direct current shock (the most effective treatment), or drugs.

ACTIVITY

May need to be limited with WPW until supraventricular tachycardias are controlled.

CLIENT EDUCATION

WPW—explain the need to identify and treat the underlying cause in addition to therapy for supraventricular tachycardia.

SURGICAL CONSIDERATIONS

Catheter ablation with radiofrequency current—a relatively recent technique that allows accessory pathways to be destroyed or ablated by a transvenous catheter positioned at the site of the pathway; can be preferred alternative to lifelong therapy with drugs.



MEDICATIONS

DRUG(S) OF CHOICE

- A variety of drugs are used in humans; opinions differ on agents of choice.
- Lidocaine IV bolus (2 mg/kg) followed by IV drip (25–75 mg/kg/min CRI—dogs only).
- Esmolol (dogs and cats, 50–100 mg/kg bolus; 50–200 mg/kg/min CRI).
- Propranolol (cats, 2.5–5 mg PO q8–12h; dogs, 0.2–1 mg/kg PO q8h) or atenolol (cats, 6.2–12.5 mg PO q24h; dogs, 0.25–1 mg/kg PO q12h).

W

- Diltiazem may be effective (cats, 1–2.5 mg/kg PO q8h; dogs, 0.5–1.5 mg/kg PO q8h).
- Procainamide IV may be used acutely because it decreases conduction over the accessory pathway and is safe if anterograde accessory pathway conduction is present in atrial fibrillation.

CONTRAINDICATIONS

- Digitalis, verapamil, and propranolol may be contraindicated—by slowing conduction through the AV node, these drugs may favor conduction through the anomalous pathways.
- Cats—propranolol and atenolol are the drugs of choice.



FOLLOW-UP

PATIENT MONITORING

Serial ECG

POSSIBLE COMPLICATIONS

None expected

EXPECTED COURSE AND PROGNOSIS

Depends on severity of the underlying cause; most WPW patients respond to therapy for supraventricular tachycardia—favorable prognosis.



MISCELLANEOUS

ABBREVIATIONS

- AV = atrioventricular
- ECG = electrocardiogram
- WPW = Wolff-Parkinson-White

INTERNET RESOURCES

www.vetgo.com/cardio.

Suggested Reading

- Al-Khatib SM, Pritchett ELC. Clinical features of Wolff-Parkinson-White syndrome. *Am Heart J* 1999, 138:403–413.
Hill BL, Tilley LP. Ventricular preexcitation in seven dogs and nine cats. *JAVMA* 1985, 187:1026–1031.

Kittleson MD. Electrocardiography. In Kittleson MD, Kienle RD, eds., *Small Animal Cardiovascular Medicine*. St. Louis: Mosby, 1998, pp. 72–94.

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Tilley LP, Smith FW. *Essentials of Electrocardiography. Interpretation and Treatment*, 4th ed. Ames, IA: Wiley Blackwell Publishing, 2016 (in preparation).

Wright KN. Assessment and treatment of supraventricular tachyarrhythmias. In Bonagura JD, ed., *Kirk's Current Veterinary Therapy XIII*. Philadelphia: Saunders, 2000, pp. 726–729.

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XYLITOL TOXICOSIS



BASICS

OVERVIEW

- Xylitol—a 5-carbon sugar alcohol used as a sweetener; present in some sugar-free gums, candies, toothpastes, mouthwashes, vitamins, liquid medications, and baked goods. It is also available as a granulated powder for cooking and baking.
- Ingestion by dogs can cause vomiting, weakness, ataxia, seizures, hypokalemia, hypophosphatemia/hyperphosphatemia, and hypoglycemia due to excess insulin release.
- Mild to moderate elevations of ALT can be seen within 4 hours of ingestion.
- Hepatic failure with high liver enzymes, hyperbilirubinemia, and coagulopathy may occur at dosages > 0.5 g/kg.
- Dosages of > 0.075–0.1 g/kg of xylitol may cause hypoglycemia.

SIGNALMENT

- Dogs—no breed, age, or sex predilection
- Cats—toxicity not established

SIGNS

- May develop within 15–30 minutes of exposure; with sugar-free gums, hypoglycemia may be delayed up to 12 hours.
- Vomiting common.
- Progressive lethargy, weakness, ataxia, collapse, and seizures.
- Hepatic failure may be accompanied by vomiting and widespread hemorrhage including petechiae, ecchymosis, and gastrointestinal and abdominal bleeding.
- Clinical signs of hypoglycemia may not be evident prior to onset of hepatic failure.

CAUSES & RISK FACTORS

Ingestion of xylitol or xylitol-containing products



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Hypoglycemia

- Insulin overdose
- Sulfonylurea antihyperglycemic agents
- Insulinoma (pancreatic β -cell tumor)

Acute Hepatic Failure

- Acetaminophen
- Aflatoxin
- Blue-green algae
- Amanita and similar hepatotoxic mushrooms
- Iron
- Sago palms (*Cycad* spp.)
- Leptospirosis

CBC/BIOCHEMISTRY/URINALYSIS

- Hypoglycemia
- Hypokalemia
- Hypophosphatemia or hyperphosphatemia
- Increased ALT, AST, SAP—may be delayed up to 24–48 hours
- Bilirubinemia
- Thrombocytopenia

OTHER LABORATORY TESTS

- Prolonged PT/PTT
- Increased FDP, D-dimers and/or decreased fibrinogen

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

- Severe hepatic necrosis
- Widespread hemorrhage



TREATMENT

- Decontamination—emesis if patient is asymptomatic; activated charcoal not likely to be beneficial.
- Monitor at 1–2-hour intervals for hypoglycemia and hypokalemia and correct as needed.
- Monitor for hepatic changes.



MEDICATIONS

DRUG(S)

- Dextrose—0.5–1 g/kg IV followed by a 2.5–5% CRI—consider starting with dosages of > 0.1 g/kg.
- Potassium chloride—supplement in fluids if potassium value < 2.5 mmol/L.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

None



FOLLOW-UP

- Monitor glucose levels for at least 24 hours.
- Monitor hepatic enzymes, bilirubin, PT/PTT, and platelets for at least 72 hours.
- Prognosis good for uncomplicated hypoglycemia with mild-to-moderate elevations of ALT; guarded to poor if severe hepatic necrosis occurs especially if hyperphosphatemia is present.



MISCELLANEOUS

SEE ALSO

- Hepatic Failure, Acute
- Hypoglycemia
- Poisoning (Intoxication) Therapy

ABBREVIATIONS

- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- FDP = fibrin degradation products
- PT = prothrombin time
- PTT = partial thromboplastin time
- SAP = alkaline phosphatase

INTERNET RESOURCES

- <http://www.aspapro.org/sites/pro/files/xylitol.pdf>
- <http://www.petpoisonhelpline.com/2013/11/theres-xylitol/>

Suggested Reading

Murphy L A, Coleman AE. Xylitol toxicosis in dogs. *Vet Clin North Am Small Anim Pract* 2012, 42(2):307–312.

Xia Z, Cai L, He Y, et al. Xylitol poisoning of dogs is associated with increased glycogenolysis, coagulopathy, and oxidative stress. *Toxicol Environ Chem* 2013, 95(2):337–343.

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ZINC TOXICOSIS



BASICS

OVERVIEW

- Toxicity results from the ingestion of zinc-containing material.
- Causes gastrointestinal inflammation and hemolytic anemia; may cause multiple organ failure (e.g., renal, hepatic, pancreatic, and cardiac), DIC, and cardiopulmonary arrest.

SIGNALMENT

Most frequently reported in young, small-sized dogs (i.e., < 12 kg); can occur in all species of all sizes.

SIGNS

- Anorexia
- Vomiting
- Diarrhea
- Lethargy
- Pale or icteric mucous membranes
- Hemoglobinemia
- Hemoglobinuria
- Orange-tinted feces
- Tachycardia

CAUSES & RISK FACTORS

- There are a variety of zinc compounds with different bioavailabilities: zinc carbonate and zinc gluconate (dietary supplements), zinc chloride (deodorants), zinc pyrithione (shampoos), zinc acetate (throat lozenges), zinc oxide (sunblock, Desitin, calamine lotion), zinc sulfide (paints), metallic zinc (coins).
- Toxic doses have not been well defined.
- Brass: alloy of copper and zinc.
- Toxicities result from ingestion of zinc-containing material: U.S. pennies minted after 1982 (most common source), nuts, bolts, staples, galvanized metal (e.g., nails), pieces from board games, zippers, miscellaneous toys, jewelry.
- Organic forms of zinc (e.g., zinc oxide) generally cause only gastrointestinal inflammation.
- Acidic environment within the stomach promotes rapid leaching of zinc from the ingested substance, allowing for zinc to be absorbed.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Numerous causes of gastrointestinal upset: viral, bacterial, parasitic, immune mediated.
- Numerous causes of hemolysis: immune-mediated hemolytic anemia, Babesia, onion and garlic toxicosis, mothball toxicosis (naphthalene), caval syndrome, acetaminophen, coral snake venom, pit viper venom, brown recluse spider venom, mushrooms, overhydration, skunk spray.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemolytic anemia, with possible Heinz body formation.
- Regeneration will occur if there is enough time: high nucleated RBC counts, basophilic stippling, polychromasia, elevated reticulocytes.
- Target cells.
- Spherocytosis—mild and often inconsistent.
- Leukocytosis with a neutrophilia.

- Hemoglobinemia.
- Bilirubinemia.
- High liver enzymes AST, ALP; less common are elevations in GGT and ALT.
- Elevated pancreatic enzymes—amylase and lipase—may indicate multiple organ failure.
- Proteinuria.
- Pigmenturia (hemoglobin, bilirubin).
- Azotemia (high BUN and creatinine)—not common.

OTHER LABORATORY TESTS

- Serum zinc levels often exceed 5 ppm (approximate normal range: 0.70–2 ppm for dogs and cats).
- Blood must be collected in non-zinc-contaminated blood tubes.
- Coagulation panel—may indicate DIC (prolonged PT and PTT, hypofibrinogenemia, thrombocytopenia, and high FDPs).
- Frequent monitoring of PCV is indicated because the decline in PCV can be rapid.

IMAGING

- Abdominal imaging—*may* reveal metallic object(s) in the gastrointestinal tract.
- Often the zinc object has passed (via vomit or feces) by the time the patient is admitted.

DIAGNOSTIC PROCEDURES

ECG—may reveal arrhythmias and ST-segment abnormalities.



TREATMENT

- Rapid removal of the zinc object by endoscopy or laparotomy/gastrotomy—imperative.
- Intravenous fluid therapy—maintain hydration and diuresis—acute renal failure is a serious sequela.
- Severe intravascular hemolysis—may require blood transfusion(s)/packed RBCs, oxygen-carrying substances (Oxyglobin).
- Inform client about the hazards of ingesting zinc-containing objects (especially US pennies minted after 1982).



MEDICATIONS

DRUG(S)

- Chelation therapy may *not* be warranted once the source of the excess zinc is removed—zinc levels drop fairly rapidly (over a few to several days) via excretion into bile, pancreatic secretions, and urine.
- CaEDTA—100 mg/kg diluted in 5% dextrose SC, divided into 4 doses per day (treatment as for lead poisoning) if clinical improvement or reduced blood zinc is not accomplished by removal of zinc objects.
- Penicillamine—110 mg/kg/day PO divided 6–8h for 5–14 days (treatment as for lead poisoning)—generally less frequently used than CaEDTA.
- Heparin—150 U/kg SC q6h; for DIC.
- H2-receptor antagonists (e.g., cimetidine, ranitidine, famotidine), proton pump inhibitors (e.g., omeprazole), and

antacids used alone or in combination—may help reduce stomach acidity and the rate of release of zinc.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Avoid aminoglycoside antibiotics and other potential nephrotoxins—risk of acute renal failure.



FOLLOW-UP

PATIENT MONITORING

- ECG—monitor for evidence of arrhythmias and ST-segment alterations.
- Coagulation profile, PCV, RBC, amylase, lipase, BUN, creatinine, ALP, AST, and ALT—monitor for the first 72 hours after zinc removal.
- Monitor serum zinc levels.

EXPECTED COURSE AND PROGNOSIS

- Multiple organ failure (e.g., kidney, liver), DIC, pancreatic disease, cardiopulmonary arrest—potential outcomes.
- Rapid removal of the source of zinc may provide progressive improvement over 48–72 hours; complete recovery possible.



MISCELLANEOUS

SEE ALSO

Poisoning (Intoxication) Therapy

ABBREVIATIONS

- ALP = alkaline phosphatase
- ALT = alanine aminotransferase
- AST = aspartate aminotransferase
- DIC = disseminated intravascular coagulation
- ECG = electrocardiogram
- GGT = gamma-glutamyltransferase
- PCV = packed cell volume
- PT = prothrombin time
- PTT = partial thromboplastin time
- RBC = red blood cells

Suggested Reading

Dziwenka MM, Coppock R. Zinc. In: Plumlee KH, ed., Clinical Veterinary Toxicology. St. Louis, MO: Elsevier Mosby, 2004, pp. 221–230.

Gurnee CM, Drobatz KJ. Zinc intoxication in dogs: 19 cases (1991–2003). J Am Vet Med Assoc 2007, 230(8):1174–1179.

Talcott PA. Zinc poisoning. In: Peterson ME, Talcott PA, eds., Small Animal Toxicology, 3rd ed. St. Louis, MO: Elsevier Saunders, 2013, pp. 847–851.

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APPENDIX I

NORMAL REFERENCE RANGES FOR LABORATORY TESTS

Table I-A

<i>Test</i>	<i>Units</i>	<i>Dogs</i>	<i>Cats</i>
WBC	$10 \times 3/\text{mm}^3$	6.0–17.0	5.5–19.5
RBC	$10 \times 6/\text{mm}^3$	5.5–8.5	6.0–10
Hemoglobin	g/dL	12.0–18.0	9.5–15
Hematocrit	%	37.0–55.0	29–45
Mean corpuscular volume	fL	60.0–77.0	41.0–54
Mean corpuscular hemoglobin	pg	19.5–26	13.3–17.5
Mean corpuscular hemoglobin concentration	%	32.0–36.0	31–36
Platelet count (automated)	$10 \times 3/\text{mm}^3$	200–500	150–600
Platelet count (manual)	$10 \times 3/\text{mm}^3$	164–510	230–680
Neutrophils	%	60–77	35–75
	Absolute	3,000–11,500	2,500–12,500
Bands	%	0–3	0–3
	Absolute	0–510	0–585
Lymphocytes	%	12–30	20–55
	Absolute	1,000–4,800	1,500–7,000
Monocytes	%	3–10	1–4
	Absolute	180–1,350	0–850
Eosinophils	%	2–10	2–12
	Absolute	1,000–1,250	0–1,500
Basophils	%	0–1	0–1
	Absolute	0–100	0–100
Reticulocyte count	%	0.5–1.5	0.0–1.0
Corrected	%	0.0–1.0	0.0–1.0
Absolute	/mm ³	0–80,000	0–50,000

From Abbott Cell Dyn 3500; IDEXX Veterinary Services.

It is important to realize that normal values vary among individual laboratories.

Table I-B

<i>Test</i>	<i>Units</i>	<i>Dogs</i>	<i>Cats</i>
Blood urea nitrogen (BUN)	mg/dL	7–27	15–34
Creatinine	mg/dL	0.4–1.8	0.8–2.3
Cholesterol	mg/dL	112–328	82–218
Glucose	mg/dL	60–125	70–150
Alkaline phosphatase (ALP)	IU/L	10–150	0–62
Alanine aminotransferase (ALT)	IU/L	5–60	28–76
Aspartate aminotransferase (AST)	IU/L	5–55	5–55
Total protein	g/dL	5.1–7.8	5.9–8.5
Albumin	g/dL	2.6–4.3	2.4–4.1
Globulin	g/dL	2.3–4.5	3.4–5.2
Albumin–globulin ratio		0.75–1.9	0.6–1.5
Sodium	mEq/L	141–156	147–156
Potassium	mEq/L	4.0–5.6	3.9–5.3
Sodium–potassium ratio		27–40	> 27.0
Chloride	mEq/L	105–115	111–125

NORMAL REFERENCE RANGES FOR LABORATORY TESTS (CONTINUED)

Table I-B

<i>Test</i>	<i>Units</i>	<i>Dogs</i>	<i>Cats</i>
Total CO ₂	mEq/L	17–24	13–25
Anion gap	mEq/L	12–24	13–27
Calcium	mg/dL	7.5–11.3	7.5–10.8
Phosphorus	mg/dL	2.1–6.3	3.0–7.0
Total bilirubin	mg/dL	0–0.4	0.0–0.4
Direct bilirubin	mg/dL	0.0–0.1	0.0–0.1
Indirect bilirubin	mg/dL	0–0.3	0.0–0.3
Lactate dehydrogenase (LDH)	IU/L	50–380	46–350
Creatine kinase (CK or CPK)	IU/L	10–200	64–440
Gamma glutamyl transferase (GGT)	IU/L	0–10	1–7
Uric acid	mg/dL	0–2	0–1
Amylase	IU/L	500–1,500	500–1,500
Lipase	U/L	100–500	10–195
Magnesium	mEq/L	1.8–2.4	1.8–2.4
Triglycerides	mg/dL	20–150	20–90
Bile acids:			
Fasting	μmol/L	0.0–5.0	0.0–5.0
Post-prandial	μmol/L	< 25	< 15
Random	μmol/L	< 25	< 15
Total iron	μg/dL	33–147	33–134
Unsaturated iron binding capacity	μg/dL	127–340	105–205
Total iron binding capacity	μg/dL	282–386	169–325

From Hitachi Chemistry Analyzer model 747 IDEXX Veterinary Services.

It is important to realize that normal values vary among individual laboratories.

Table I-C

Conversion table for hematologic units				
<i>Analyte</i>	<i>Example Values</i>		<i>Conversion Factors</i>	
	<i>Traditional</i>	<i>SI*</i>	<i>Traditional to SI</i>	<i>SI to Traditional</i>
Hemoglobin	15.0 g/dL	150 g/L	10	0.1
HCT or PCV	45%	0.45 L/L	0.01	100
Erythrocytes	$6.0 \times 10^6/\text{mm}^3$	$6.0 \times 10^{12}/\text{L}$	10^6	10^{-6}
MCV	75 μ ³	75 fL	No change	No change
MCH	25 μg	25 pg	No change	No change
MCHC	33 g/dL	330 g/L	10	0.1
WBC	$15.0 \times 10^3/\text{mm}^3$	$15.0 \times 10^9/\text{L}$	10^6	10^{-6}
Platelets	$250 \times 10^3/\text{mm}^3$	$250 \times 10^9/\text{L}$	10^6	10^{-6}

*Système International d'Unités.

Modified from Appendices. In: Bonagura JD, ed., Kirk's Current Veterinary Therapy XIII. Philadelphia: Saunders, 2000, p. 1209 (with permission).

NORMAL REFERENCE RANGES FOR LABORATORY TESTS (CONTINUED)

Table I-D

Conversion table for clinical biochemical units			
Analyte	Traditional Unit (with Examples)	Conversion Factor	SI Unit (with Examples)
Alanine aminotransferase	0–40 U/L	1.00	0–40 U/L
Albumin	2.8–4.0 g/dL	10.0	28–40 g/L
Alkaline phosphatase	30–150 U/L	1.00	30–150 U/L
Ammonia	10–80 µg/dL	0.5871	5.9–47.0 µmol/L
Amylase	200–800 U/L	1.00	200–800 U/L
Aspartate aminotransferase	0–40 U/L	1.00	0–40 U/L
Bile acids (total)	0.3–2.3 µg/mL	2.45	0.74–5.64 µmol/L
Bilirubin	0.1–0.2 mg/dL	17.10	2–4 µmol/L
Calcium	8.8–10.3 mg/dL	0.2495	2.20–2.58 mmol/L
Carbon dioxide	22–28 mEq/L	1.00	22–28 mmol/L
Chloride	95–100 mEq/L	1.00	95–100 mmol/L
Cholesterol	100–265 mg/dL	0.0258	2.58–5.85 mmol/L
Copper	70–140 µg/dL	0.1574	11.0–22.0 µmol/L
Cortisol	2–10 µg/dL	27.59	55–280 nmol/L
Creatine kinase	0–130 U/L	1.00	0–130 U/L
Creatinine	0.6–1.2 mg/dL	88.40	50–110 µmol/L
Fibrinogen	200–400 mg/dL	0.01	2.0–4.0 g/L
Folic acid	3.5–11.0 µg/L	2.265	7.93–24.92 nmol/L
Glucose	70–110 mg/dL	0.05551	3.9–6.1 mmol/L
Iron	80–180 µg/dL	0.1791	14–32 µmol/L
Lactate	5–20 mg/dL	0.1110	0.5–2.0 mmol/L
Lead	150 µg/dL	0.04826	7.2 µmol/L
Lipase, Sigma-Tietz (37°C)	≤ 1 ST U/dL	280	≤ 280 U/L
Lipase, Cherry-Crandall (30°C)	0–160 U/L	1.00	0–160 U/L
Lipids (total)	400–850 mg/dL	0.01	4.0–8.5 g/L
Magnesium	1.8–3.0 mg/dL	0.4114	0.80–1.20 mmol/L
Mercury	≥ 1.0 µg/dL	49.85	≤ 50 nmol/L
Osmolality	280–300 mOsm/kg	1.00	280–300 mmol/kg
Phosphorus	2.5–5.0 mg/dL	0.3229	0.80–1.6 mmol/L
Potassium	3.5–5.0 mEq/L	1.0	3.5–5.0 mmol/L
Protein (total)	5–8 g/dL	10.0	50–80 g/L
Sodium	135–147 mEq/L	1.00	135–147 mmol/L
Testosterone	4.0–8.0 mg/mL	3.467	14.0–28.0 nmol/L
Thyroxine	1–4 µg/dL	12.87	13–51 nmol/L
Triglyceride	10–500 mg/dL	0.0113	0.11–5.65 mmol/L
Urea nitrogen	10–20 mg/dL	0.3570	3.6–7.1 nmol/L
Uric acid	3.6–7.7 mg/dL	59.44	214–458 µmol/L
Urobilinogen	0–4.0 mg/dL	16.9	0.0–6.8 µmol/L
Vitamin A	90 µg/dL	0.03491	3.1 µmol/L
Vitamin B12	300–700 ng/L	0.738	221–516 pmol/L
Vitamin E	5.0–20.0 mg/L	2.32	11.6–46.4 µmol/L
D-xylose	30–40 mg/dL	0.06666	2.0–2.71 mmol/L
Zinc	75–120 µg/dL	0.1530	11.5–18.5 µmol/L

From Appendices. In: Bonagura JD, ed., Kirk's Current Veterinary Therapy XIII. Philadelphia: Saunders, 2000, p. 1214
(with permission).

APPENDIX II

ENDOCRINE TESTING

Table II-A

Endocrine function testing protocols	
ADRENAL GLAND DISORDERS	
ACTH STIMULATION TEST	
Dogs	
Administer 20 IU ACTH gel IM or 0.25 mg synthetic ACTH IV or IM (Cortrosyn, Organon Pharmaceuticals, West Orange, NJ). ACTH Gel	This pattern suggests that the animal does not have Cushing's disease. <i>Escape from Suppression</i> Cortisol value falls below 1 $\mu\text{g}/\text{dL}$ (30 nmol/L) at 4 hours and rises above 1 $\mu\text{g}/\text{dL}$ at 8 hours. This pattern is consistent with pituitary-dependent Cushing's disease. <i>High-Dose Dexamethasone Suppression Test (HDDST)</i> Administer 1 mg/kg dexamethasone (Azium) IV or IM. Obtain serum samples before and 4 and 8 hours after injection of dexamethasone for cortisol assay.
Synthetic ACTH	<i>Interpretation</i> Any cortisol determination that falls below 1.5 $\mu\text{g}/\text{dL}$ (45 nmol/L) at any point during the 8-hour testing period is considered suppression. Suppression after a high dose of dexamethasone is consistent with pituitary-dependent Cushing's disease. Lack of suppression (all cortisol values remain above 1.5 $\mu\text{g}/\text{dL}$) is diagnostic of a pituitary or adrenal tumor.
Cats	
Administer 0.125 mg synthetic ACTH IV. Serum samples should be obtained before and 1 hour after injection of ACTH for cortisol assay.	
Interpretation	
<i>Screening for Cushing's Disease</i>	
An exaggerated response to ACTH is consistent with Cushing's disease. High normal cut-off values differ slightly between laboratories.	
<i>Screening for Hypoadrenocorticism</i>	
Pre- and post-cortisol determinations <1 $\mu\text{g}/\text{dL}$ (30 nmol/L) are consistent with hypoadrenocorticism.	
Monitoring Mitotane or Ketoconazole.	
<i>Therapy for Cushing's Disease</i>	
Pre- and post-cortisol determinations should be within the normal basal cortisol range.	
LOW-DOSE DEXAMETHASONE SUPPRESSION TEST (LDDST)	
Dogs	
Administer 0.015 mg/kg dexamethasone (Azium, Schering-Plough, Union, NJ) IV or IM. Obtain serum samples before and 4 and 8 hours after injection of dexamethasone for cortisol assay.	
Cats	
Administer 0.1 mg/kg dexamethasone (Azium) IV or IM. Obtain serum sample before and 4 and 8 hours after injection of dexamethasone for cortisol assay.	
Interpretation	
Three basic patterns.	
<i>Lack of Suppression</i>	
All cortisol values remain above 1 $\mu\text{g}/\text{dL}$ (30 nmol/L). This pattern is consistent with Cushing's disease.	
<i>Suppression</i>	
Cortisol values fall below 1 $\mu\text{g}/\text{dL}$ (30 nmol/L) at 4 and 8 hours.	
INTERPRETATION	
Serum T_4 concentration after administration of $T_3 > 1.5 \mu\text{g}/\text{dL}$ (20 nmol/L) is consistent with hyperthyroidism.	
GASTRINOMA	
SECRETIN STIMULATION TEST	
Administer 2 units of secretin/kg IV. Take blood samples before administration of secretin and then 2, 5, 10, 15, and 30 minutes later. Assay the samples for gastrin.	
Interpretation	
Dogs with gastrinomas have a rise in gastrin levels after the injection of secretin. In three reported cases, two dogs had a rise in gastrin levels 2 times baseline 5 minutes after secretin injection, and one dog had a rise in gastrin levels 1.4 times baseline 5 minutes after secretin injection. Normal dogs have a decline in gastrin levels after administration of secretin.	
CALCIUM CHALLENGE TEST	
Administer 2 mg/kg of calcium gluconate IV over a 1-minute period or administer 5 mg/kg of calcium gluconate as an IV infusion over several hours.	
Obtain a blood sample before calcium administration and then 15, 30, 60, 90, and 120 minutes after calcium administration. Assay the samples for gastrin.	
Interpretation	
Two reported patients with gastrinoma had a doubling of the gastrin level 60 minutes after the calcium infusion.	
SEX HORMONE DISORDERS	
GNRH STIMULATION TEST	
Administer 0.5–1.0 μg of GnRH/kg IM. Obtain blood samples before GnRH administration and 1 hour later. Assay blood samples for testosterone.	
Interpretation	
Normal dogs have baseline testosterone levels between 0.5 and 5 ng/mL, and after administration of GnRH the testosterone levels rise above 5 ng/mL. Animals with hypoandrogenism have lower values.	
HCG STIMULATION TEST	
Administer 44 IU of hCG/kg IM. Obtain blood samples before hCG administration and 4 hours later. Assay blood samples for testosterone.	

(Continued)

ENDOCRINE TESTING (CONTINUED)

Table II-A

Endocrine function testing protocols (<i>continued</i>)	
Interpretation	
Normal dogs have baseline testosterone levels between 0.5 and 5 ng/mL, and after administration of hCG, the testosterone levels rise above 5 ng/mL. Animals with hypoandrogenism have lower values.	Day 1 130–165 mL/kg/day Day 2 100–125 mL/kg/day Day 3 65–70 mL/kg/day (normal maintenance requirement)
DIABETES INSIPIDUS	The morning of the fourth day, discontinue food and water. Start the test. Weigh the patient and empty the bladder. Weigh at 1- to 2-hour intervals. Monitor carefully for dehydration and depression. When 5% of body weight is lost or azotemia develops, empty the bladder and check urine specific gravity. Consider plasma vasopressin determination at this point.
MODIFIED WATER DEPRIVATION TEST	Interpretation If the urine specific gravity is > 1.025 (dogs) or > 1.030 (cats), stop the test. The patient does not have diabetes insipidus. If the urine specific gravity is not > 1.025 (dogs) or > 1.030 (cats), administer 0.55 U/kg aqueous vasopressin IM (maximum dose 5 U). Empty the bladder and check urine specific gravity at 30, 60, and 120 minutes post-administration. If urine specific gravity increases < 10%, nephrogenic diabetes insipidus is indicated; if it increases 10–50%, partial central diabetes insipidus is indicated; if it increases 50–800%, complete central diabetes insipidus is indicated.
Rule-out other causes of polyuria and polydipsia (especially hyperadrenocorticism). Begin water restriction 3 days before abrupt water deprivation.	

Table II-B

Tests of the endocrine system*			
Hormone	Unit	Dogs	Cats
Adrenocorticotropic hormone, basal (ACTH, plasma)	pmol/L	2–15	1–20
Aldosterone [†] (plasma)	pmol/L	14–957	194–388
Basal	pmol/L	197–2103	277–721
Post-ACTH	pmol/L		
Cortisol (serum or plasma, urine)	nmol/L	25–125	15–150
Basal	nmol/L	200–550	130–450
Post-ACTH	nmol/L	≤ 40	≤ 40
Post-low-dose dexamethasone (0.01 or 0.015 mg/kg)	nmol/L	≤ 40	≤ 40
Post-high-dose dexamethasone (0.1 or 1.0 mg/kg) [‡]	nmol/L	—	—
Urinary cortisol-creatinine ratio	× 10 ⁻⁶	8–24, [†] 10 [§]	35–200
Insulin, basal (serum)	pmol/L	35–200	0–4
Intact parathormone [†] (serum)	pmol/L	2–13	≤ 3.0 in anestrus, proestrus
Progesterone (serum or plasma, female)	mmol/L	50–220 in diestrus, pregnancy	50–220 in diestrus, pregnancy
Testosterone (serum or plasma, male)	nmol/L	1–20	1–20
Thyroxine (T ₄ , serum)	nmol/L	12–50	10–50
Basal	nmol/L	> 45	> 45
Post-thyroxine-stimulating hormone (TSH)	nmol/L	—	≤ 20
Triiodothyronine (T ₃) suppression*	nmol/L	0.7–2.3	0.5–2.0
Triiodothyronine, basal (T ₃ , serum)	nmol/L		

*Prepared with the assistance of ME Peterson, The Animal Medical Center, New York, NY. Unless indicated otherwise, values in this table are adapted from Kemppainen RJ, Zerbe CA. Common endocrine diagnostic tests: normal values and interpretations. In: Kirk RW, ed., Current Veterinary Therapy X. Philadelphia: Saunders, 1989, pp. 961–968. Hormone determinations are variable between laboratories. The laboratory performing the analysis should provide reference values. Before submitting samples for hormone determinations, consult the laboratory for sample specifications, use of anticoagulants, and sample preservation. General sampling conditions are discussed in Reimers TJ. Guidelines for collection, storage, and transport of samples for hormone assay. In: Kirk RW, ed., Current Veterinary Therapy X. Philadelphia: Saunders, 1989, pp. 968–973. Factors that affect serum thyroid and adrenocortical hormone concentrations in dogs are discussed in Reimers TJ, Lawler DF, Sutaria PM, et al. Effects of age, sex, and body size on serum concentrations of thyroid and adrenocortical hormones in dogs. Am J Vet Res 1990, 51:454.

[†]Provided by RF Nachreiner, Animal Health Diagnostic Laboratory, Endocrine Diagnostic Section, Michigan State University.

[‡]This test is used after adrenocortical hyperfunction has been confirmed. It is used to differentiate adrenal tumor (where no suppression is seen) from pituitary-dependent cases (where suppression occurs but is variable).

[§]From Stolp R, Rijnberk A, Meiher JC, Croughs RJM. Urinary corticoids in the diagnosis of canine hyperadrenocorticism. Res Vet Sci 1983, 34:141.

Rijnberk A, van Wees A, Mol JA. Assessment of two tests for the diagnosis of canine hyperadrenocorticism. Vet Record 1988, 122:178–180.

*From Peterson ME, Ferguson DC. Thyroid diseases. In: Ettinger SJ, ed., Textbook of Veterinary Internal Medicine: Diseases of the Dog and Cat, 3rd ed. Philadelphia: Saunders, 1989, pp. 1632–1675.

From Appendices. In: Bonagura JD, ed., Kirk's Current Veterinary Therapy XIII. Philadelphia: Saunders, 2000, p. 1223 (with permission).

ENDOCRINE TESTING (CONTINUED)

Table II-C

Conversion table for hormone assay units				
	<i>Unit</i>		<i>Conversion Factors</i>	
<i>Hormone</i>	<i>Traditional</i>	<i>SI</i>	<i>Traditional to SI</i>	<i>SI to Traditional</i>
Aldosterone	ng/dL	pmol/L	27.7	0.036
Corticotropin (ACTH)	pg/mL	pmol/L	0.22	4.51
Cortisol	μg/dL	mmol/L	27.59	0.36
β-endorphin	pg/mL	pmol/L	0.289	3.43
Epinephrine	pg/mL	pmol/L	5.46	0.183
Estrogen (estradiol)	pg/mL	pmol/L	3.67	0.273
Gastrin	pg/mL	ng/L	1.00	1.00
Glucagon	pg/mL	ng/L	1.00	1.00
Growth hormone (GH)	ng/mL	μg/L	1.00	1.00
Insulin	μU/mL	pmol/L	7.18	0.139
α-melanocyte-stimulating hormone (α-MSH)	pg/mL	pmol/L	0.601	1.66
Norepinephrine	pg/mL	nmol/L	0.006	169
Pancreatic polypeptide (PP)	mg/dL	mmol/L	0.239	4.18
Progesterone	ng/mL	mmol/L	3.18	0.315
Prolactin	ng/mL	μg/L	1.00	1.00
Renin	ng/mL/hr	ng/L/sec	0.278	3.60
Somatostatin	pg/mL	pmol/L	0.611	1.64
Testosterone	ng/mL	nmol/L	3.47	0.288
Thyroxine (T ₄)	μg/dL	nmol/L	12.87	0.078
Triiodothyronine (T ₃)	ng/dL	nmol/L	0.0154	64.9
Vasoactive intestinal polypeptide (VIP)	pg/mL	pmol/L	0.301	3.33

Contributed by ME Peterson, The Animal Medical Center, New York, NY.

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APPENDIX III

APPROXIMATE NORMAL RANGES FOR COMMON MEASUREMENTS IN DOGS AND CATS

	Dog	Cat
Heart rate (bpm)	60–180	140–220
Capillary refill time	< 2 sec	< 2 sec
Body temperature	99.5–102.5°F 37.5–39.2°C	100.5–102.5°F 38.1–39.2°C
Mean arterial pressure (mm Hg)	90–120	100–150
Blood volume (mL/kg)	75–90	47–66
Cardiac output (mL/kg/min) (L/M ² /min)	100–200 4.72 ± 1.09	167 ± 39
Systemic resistance (mm Hg/mL/kg/min) (dynes/sec/cm)	0.64 ± 0.16 2162 ± 458	
Mean pulmonary arterial pressure (mm Hg)	14 ± 3	
Central venous pressure (cm H ₂ O)	3 ± 4	
Pulmonary artery occlusion pressure (mm Hg)	5 ± 2	
Urine output	1–2 mL/kg/hr	1–2 mL/kg/hr
Breathing rate (breaths/min)	10–30	24–42
Minute ventilation (mL/kg/min)	170–350	200–350
Oxygen delivery (mL/kg/min) (mL/M ² /min)	29 ± 8 815 ± 234	
Oxygen consumption (mL/kg/min) (mL/M ² /min)	4–11 198 ± 53	3–8
Arterial Po ₂ (mm Hg)	85–105	100–115
Arterial So ₂	> 95	> 95
Arterial Pco ₂ (mm Hg)	30–44	28–35
Arterial pH	7.36–7.46	7.34–7.43
Bicarbonate (mEq/L)	20–25	17–21
Base deficit (mEq/L)	0 to –4	–1 to –8
Total plasma proteins (g/dL)	6.0–8.0	6.8–8.3
Albumin (g/dL)	2.5–3.5	1.9–3.9
Packed cell volume (%)	37–55	29–48
Hemoglobin (g/dL)	12–18	9–15.1
Sodium (mEq/L)	145–154	151–158
Potassium (mEq/L)	4.1–5.3	3.6–4.9
Chloride (mEq/L)	105–116	113–121
Total CO ₂ (mEq/L)	16–26	15–21

Modified from Aldrich J, Haskins SC. Monitoring the critically ill patient. In: Current Veterinary Therapy XII. Philadelphia: Saunders, 1995, pp. 98–105 (with permission).

APPENDIX IV**NORMAL VALUES FOR THE CANINE AND FELINE ELECTROCARDIOGRAM**

Rate		
Dog	60–140 beats/min for giant breeds 70–160 beats/min for adult dogs Up to 180 beats/min for toy breeds Up to 220 beats/min for puppies	
Cat	Range: 120–240 beats/min Mean: 197 beats/min	
Rhythm		
Dog	Normal sinus rhythm Sinus arrhythmia Wandering sinoatrial pacemaker	
Cat	Normal sinus rhythm Sinus tachycardia (physiologic reaction to excitement)	
<i>Measurements (lead II, 50 mm/sec, 1 cm = 1 mV)</i>		
Dog	P wave	Width: maximum, 0.04 second; 0.05 second in giant breeds Height: maximum, 0.4 mV
	PR interval	Width: 0.06–0.13 second
	QRS complex	Width: maximum, 0.05 second in small breeds maximum, 0.06 second in large breeds Height of R wave*: maximum, 3.0 mV in large breeds maximum, 2.5 mV in small breeds
	ST segment	No depression: not more than 0.2 mV No elevation: not more than 0.15 mV
	T wave	Can be positive, negative, or biphasic Not greater than one-fourth amplitude of R wave Amplitude range \pm 0.05–1.0 mV in any lead
	Q-T interval	Width: 0.15–0.25 second at normal heart rate; varies with heart rate (faster rates have shorter Q-T intervals and vice versa)
Cat	P wave	Width: maximum, 0.04 second Height: maximum, 0.2 mV
	PR interval	Width: 0.05–0.09 second
	QRS complex	Width: maximum, 0.04 second Height of R wave: maximum, 0.9 mV
	ST segment	No depression or elevation
	T wave	Can be positive, negative, or biphasic—most often positive Maximum amplitude: 0.3 mV
	Q-T interval	Width: 0.12–0.18 second at normal heart rate (range 0.07–0.20 second); varies with heart rate (faster rates have shorter Q-T intervals and vice versa)
<i>Mean Electrical Axis (frontal plane)</i>		
Dog	+40 to +100 degrees	
Cat	0 to + 160 degrees (not valid in many cats)	
<i>Precordial Chest Leads (values of special importance)</i>		
Dog	CV_5 RL (rV_2): T wave positive, R wave not greater than 3.0 mV CV_6 LL (V_2): S wave not greater than 0.8 mV, R wave not greater than 3.0 mV* CV_6 LU (V_4): S wave not greater than 0.7 mV, R wave not greater than 3.0 mV* V_{10} : negative QRS complex, T wave negative except in Chihuahuas	
Cat	CV_6 LL (V_2): R wave not greater than 1.0 mV CV_6 LU (V_4): R wave not greater than 1.0 mV $V10$: T wave negative, R/Q not greater than 1.0 mV	

*Not valid for thin, deep-chested dogs under 2 years of age.

Source: Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992, with permission.

APPENDIX V

ANTIDOTES AND USEFUL DRUGS: METHODS OF TREATMENT

Antidotes and Useful Drugs		
Drugs	Toxicant/Indication for Use	Dosage
Acepromazine	Amphetamine and other stimulant drugs with agitation and excitation; serotonin syndrome	Dogs and cats: 0.02–0.1 mg/kg IV, IM, SC. May cause hypotension.
Antivenin, crotalids	<i>Crotalus</i> and <i>Sistrurus</i> (rattlesnake); <i>Agkistrodon</i> (cottonmouth and copperhead) venom	Several products available. Follow the manufacturer's guidelines for dilution and administration. Dose varies from 1 to 5 vials IV depending on severity of symptoms. 95% of cases controlled with a single vial.
Antivenin, elapids	<i>Micruurus fulvius</i> , <i>Micruurus tenere</i> , <i>Micruroides euryxanthus</i> (coral snakes) venom	Extremely limited availability. The manufacturer's guidelines for dilution and administration should be followed closely.
Atipamezole	Medetomidine, dexmedetomidine reversal. Used off-label to reverse other alpha-2-adrenergic agonists, including amitraz, clonidine, and xylazine	Dogs: 50–100 µg/kg IM Cats: 25–50 µg/kg IM or IV (slow)
Atropine	Anticholinesterase pesticide muscarinic signs (OPs and carbamates); also cholinergic agents and clitocybe and inocybe (muscarinic) mushrooms	Dogs and cats: 0.2–2 mg/kg. One quarter of the dose should be given IV and the remainder IM or SQ. The dose will likely need to be repeated; heart rate and secretions should be used to guide redosing.
Barbiturates	Strychnine and other seizure-producing drugs	Dogs: Phenobarbital at 5–8 mg/kg IV q4–6h. Cats: Phenobarbital at 3 mg/kg IV, repeat every 20 minutes to maximum of 24 mg/kg/24 hours. 4–6 IU/kg, SQ q8–12h. Rarely used. Calcium gluconate 10% 0.54–1.61 mL/kg IV slowly; calcium chloride 10% 0.18–0.56 mL/kg IV slowly.
Calcitonin salmon	Hypercalcemia; vitamin D and analogs	
Calcium gluconate or chloride	Fluoride and hydrofluoric acid; oxalic acid and oxalates; beta and calcium channel antagonists; others	
Calcium disodium EDTA (CaEDTA or calcium disodium versenate)	Heavy metals, primarily lead and zinc. Also chelates cadmium, chromium, copper, cobalt, iron, manganese, nickel, plutonium, thorium, uranium, yttrium, and vanadium	Dilute product in 5% dextrose to a final concentration of 2–4 mg/mL prior to use. Give 25 mg/kg IV or SQ q6h. Maximum recommended daily dose of 2 g/day. Treat for 5 days; rest for 5–7 days; and repeat if needed. Do not use if metal still present in GIT.
Cyproheptadine	Drugs that cause serotonin syndrome (selective serotonin reuptake inhibitors, tricyclic antidepressants, 5-hydroxytryptophan)	Dogs: 1.1 mg/kg PO or rectally q4–8h PRN. Cats: 2–4 mg total dose PO or rectally q4–8h PRN.
D-penicillamine	Heavy metals, primarily lead; but also cadmium, copper, inorganic mercury, and zinc	
Dantrolene	Hops (<i>Humulus lupulus</i>) intoxication and black widow spider envenomation (<i>Latrodectus mactans</i>)	Dogs (home therapy after CaNa ₂ EDTA lead treatment): 110 mg/kg/day PO divided q6–8h for 1–2 weeks. Cats (home therapy after CaNa ₂ EDTA lead treatment and in the presence of elevated blood levels): 125 mg total dose, PO q12h for 5 days. Do not use if metal still present in GI tract.
Deferoxamine	Iron	Dogs: Black widow spider: 1 mg/kg IV followed by 1 mg/kg PO q4h as needed. Hops: 2–3 mg/kg IV or 3.5 mg/kg PO. Dogs and cats: 40 mg/kg IM q4–8h. In critical situations, an IV infusion of 15 mg/kg/hour can be used, but the cardiovascular system must be monitored closely during this time. The excreted complex turns the urine pink or salmon colored and is sometimes referred to as the "vin rose" of iron poisoning. Continue treatment until the urine is clear or serum iron levels are within normal limits.
Digoxin immune Fab fragments	Digoxin, <i>Rhinella</i> sp. (<i>Bufo</i>) toad toxins, and some cardiac glycoside-containing plants	If serum digoxin level is available: number of vials = serum digoxin level (ng/mL) × BW (kg)/100. If serum digoxin level is not available or if treating a <i>Rhinella</i> (<i>Bufo</i>) toad or cardiac glycoside-containing plant toxicosis, start therapy with 1–2 vials and reassess as needed.

ANTIDOTES AND USEFUL DRUGS: METHODS OF TREATMENT (CONTINUED)

<i>Antidotes and Useful Drugs</i>	<i>Toxicant/Indication for Use</i>	<i>Dosage</i>
Dimercaprol (BAL)	Heavy metals, primarily arsenic. Also used to chelated lead and mercury	Arsenic toxicosis: 5 mg/kg IM × one dose followed by 2.5 mg/kg IM q4h for 2 days, q8h for 1 day, and q12h until recovered. Lead toxicosis: 2.5–5 mg/kg IM as 10% solution q4h on days 1 and 2, then q6h on day 3. Preferred method: using 7% ethanol (70 mg/mL), load with 8.6 mL/kg (600 mg/kg) slow IV × 1 dose and follow with 1.43 mL/kg/hour (100 mg/kg/hour) IV CRI for 24–36 hours or until ethylene glycol (EG) test is negative.
Ethanol	Ethylene glycol	Dogs and cats: 0.01 mg/kg IV. Short half-life and may need to repeat in 1–3 hours. Doses 10–20× labeled dose have been used in some animals but there is currently no scientific data to support them.
Flumazenil	Benzodiazepine (clonazepam, diazepam, lorazepam, others); CNS depression or coma	Dogs: 20 mg/kg IV over 15–20 minutes as loading dose; 15 mg/kg IV at 12 and 24 hours; 5 mg/kg IV at 36 hours. Repeat EG test. If positive, continue 5 mg/kg IV every 12 hours until negative.
Fomepizole	Ethylene glycol	Cats: 125 mg/kg slow IV as a loading dose; 31.25 mg/kg IV at 12, 24, and 36 hours. 50 ng/kg IV bolus in 0.9% sodium chloride followed by 10–15 ng/kg/min CRI. May need to increase up to 40 ng/kg/min to maintain euglycemia.
Glucagon	Insulin and oral hypoglycemic agent-induced hypoglycemia; beta and calcium channel blockers and tricyclic antidepressants bradycardia, AV block, and hypotension.	75–150 mg/kg IV
Hydroxycobalamin (vitamin B12a; B12 precursor)	Cyanide	Standard protocol: 1.5 mL/kg IV bolus of 20% solution over 5–15 minutes, followed immediately with CRI of 0.25 mL/kg/min over 1–2 hours. May repeat dose in several hours if signs of toxicity return and serum is not lipemic. Suggested protocol: 1.5–4 mL/kg IV bolus of 20% over 1 minute, followed by CRI of 0.25 mL/kg/min over 30–60 min. Individual boluses may be repeated as needed up to 7 mL/kg.
Intravenous lipid emulsion (ILE); also referred to as intravenous fat emulsion (IFE)	Some lipophilic (fat-soluble) drugs including baclofen, barbiturates, ivermectin and moxidectin, propranolol, tricyclic antidepressants, verapamil, and others.	Dogs and cats: Methotrexate: Varies depending on methotrexate serum concentrations (25–200 mg/m ² IV, IM q6h for up to 8 doses). Pyrimethamine, trimethoprim: 0.1–0.3 mg/kg PO q24h. Dogs: 55–220 mg/kg slow IV. Labeled not to exceed 330 mg/kg/day but higher doses may be used in severe poisonings as long as the dog is monitored for CNS and respiratory depression. Cats: 44 mg/kg slow IV, up to 330 mg/kg/day. Labeled not to exceed 330 mg/kg/day but higher doses may be needed in severe poisonings. Monitor for CNS and respiratory depression when using high doses.
Leucovorin	Methotrexate; pyrimethamine trimethoprim, ormetoprim, others	Cats: Use with extreme caution or not at all. Dogs: 1–1.5 mg/kg as 1% solution IV over several minutes; may be repeated once in 30 min.
Methocarbamol	Metaldehyde, permethrin, strychnine, tremorgenic mycotoxins, other toxicants that cause tremors	Dogs and cats: 140 mg/kg IV or PO × 1 dose, then 70 mg/kg IV or PO q 6 hours for 7 doses. The product should be diluted to a 5% solution prior to use. IV administration preferred in cats due to low oral bioavailability (20%). A variety of other doses have been suggested; most based on extrapolation from human literature. Some recommend higher doses (280 mg/kg) and others additional doses (up to 17 doses) for massive ingestions. Emesis frequently occurs with oral dosing, especially after the initial dose, and an antiemetic may be required prior to starting NAC therapy.
Methylene blue	Aniline dyes, local anesthetics, naphthalene, nitrates and nitrites-induced methemoglobinemia	
N-acetylcysteine (NAC)	Acetaminophen; less often <i>Amanita phalloides</i> mushroom, sago palm, and xylitol intoxication	

ANTIDOTES AND USEFUL DRUGS: METHODS OF TREATMENT (CONTINUED)

<i>Antidotes and Useful Drugs</i>	<i>Toxicant/Indication for Use</i>	<i>Dosage</i>
Pamidronate	Cholecalciferol, calcipotriene, and calcitriol-induced hypercalcemia and hyperphosphatemia	Dogs and cats: 1.3–2 mg/kg diluted in 250–500 mL 0.9% NaCl, IV slowly over several hours. Monitor serum calcium levels q12–24h and adjust ancillary treatment as needed. If hypercalcemia is still present, a repeated dose of pamidronate may be necessary 5–7 days after the initial dose. Very large overdoses of cholecalciferol may require a second dose in 3–4 days.
Naloxone	Opioid and opiate-induced respiratory and CNS depression	Dogs and cat: 0.01–0.04 mg/kg, IV, IM, SQ; may need to use 0.04 mg/kg with larger overdoses. IM and SQ route result in slower onset of action (5 minutes). Short half-life and may need to repeat in 1–3 hours.
Phytanadione (vitamin K1)	Anticoagulant rodenticides, warfarin tablets	2–5 mg/kg PO q24h or divided twice a day.
Pralidoxime (2-PAM)	Organophosphates (nicotinic signs)	Dose (dogs and cats): 20 mg/kg IM or slow IV (over 30 min) for first dose. Repeat dose q8–12h, IM or SQ. Rapid IV administration has resulted in tachycardia, neuromuscular blockade, laryngospasm, muscle rigidity, and death.
Protamine sulfate	Heparin	Dogs and cats: 1 mg protamine sulfate IV per 100 units heparin to be inactivated. Give slowly, no faster than 50 mg per over 10 minutes. Decrease amount of protamine sulfate by 50% for every 30–60 minutes that has passed since heparin overdose given. 0.01–0.03 mg/kg/hour CRI. Longer half-life than other similar drugs.
Pyridostigmine	Anticholinergic plants (<i>Cestrum</i> spp., <i>Datura</i> spp., <i>Solanum</i> spp, etc.), atropine, avermectin and ivermectin, botulism, some elapid snake bites, and nondepolarizing neuromuscular blocking agents (curare, pancuronium, etc.)	
Pyridoxine	Isoniazid	71 mg/kg as 5–10% infusion over 30–60 minutes; if total amount of isoniazid consumed is known can give on a mg per mg (1:1) ratio.
Succimer (2-3 dimer-captosuccinic acid)	Lead	Dogs and cats: 10 mg/kg PO or rectal q8h × 10 days; retreat only if clinical signs are present. Monitor renal values closely in cats.
Trentine (TETA)	Copper hepatopathy in dogs	Dogs: 10–15 mg/kg PO 1–2 hours before meals. Useful in dogs unable tolerate vomiting associated with D-penicillamine.
Yohimbine	Xylazine and other alpha-2-adrenergic agonists (amitraz, clonidine, xylazine)	Dogs and cats: 0.11 mg/kg IV slowly. Shorter half-life than atipamezole.

Abbreviations: Standard**Comments:**

Specific antidotes are not free of side effects and should be used with knowledge and forethought. Many toxicants lack a true antidote, and symptomatic and supportive care, including many of the useful drugs found in this table, is imperative for survival of the poisoned patient. Other drugs may be needed and the reader is directed to the references below for further information.

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APPENDIX VI

GARY D. OSWEILER AND LYNN R. HOVDA

TOXIC HOME AND GARDEN HAZARDS FOR PETS

Table VI-A

Toxic plants and their clinical signs—antidotes and treatment		
Plant and Characteristics	Clinical Signs	Antidotes and/or Treatment
Air plant, Cathedral bells (<i>Kalanchoe</i> spp.) Bright red-orange to pink blooms; umbel flower pattern. Plant contains cardiotoxins similar to azalea and rhododendrons, concentrated mainly in flowers.	Cardiac glycoside causes acute signs 1–3 hours after ingestion. Signs include depression, salivation, diarrhea, bradycardia, heart block, tachypnea, ataxia, tremors, and paralysis.	Preventive emesis and/or activated charcoal early after ingestion. Treat as a cardiac glycoside. (See chapter, Cardiac Glycoside Plant Toxicosis.)
Aloe, Octopus plant, Candelabra plant (<i>Aloe</i> spp.) Succulent plant, used in folk and herbal medicine. Toxic fraction is anthraquinone glycoside; disrupts water and electrolyte balance in large intestine.	Anorexia, depression, vomiting, colic, diarrhea, tremors (uncommon), and change in urine color. Generally mild in nature.	Drugs for abdominal pain/diarrhea. Protect airway, treat locally for pharyngitis associated with oxalate crystals (rare).
Autumn crocus (<i>Colchicum autumnale</i>) Houseplant, garden plant. Typically blooms in fall, different from most other bulbs. Dosages above 6 g/kg BW considered lethal. Although the whole plant is toxic, the toxin (colchicine) is highest in bulbs.	Acute onset 2–12 hours post ingestion. Initial signs are nausea, salivation, vomiting, colic, diarrhea, incoordination, and weakness. Multiple organ systems (heart, lungs, and kidneys) also may be involved. Potential for coagulopathy and elevated serum enzymes.	Induce emesis if not vomiting. Activated charcoal if early. Evaluate CBC and serum chemistries, including prothrombin, LDH, CK, IV fluids, analgesics, anticonvulsants as needed.
Baneberry, Doll's eye, Cohosh (<i>Actaea</i> spp.) Toxic principal is protoanemonin glycoside, as well as irritant essential oils.	Clinical response ranges from dermatitis and blistering of skin to oral irritation, drooling, pawing at face or mouth, emesis, diarrhea, and hematuria. Neurologic and cardiovascular signs are occasionally reported. Nausea, vomiting, diarrhea, hypotension, depression. Oxalate crystals can cause direct pharyngeal irritation.	Cleanse mouth thoroughly with water; apply appropriate local demulcents; control emesis and diarrhea as necessary; monitor for organ dysfunction, especially renal damage.
Belladonna lily (<i>Amaryllis</i> spp.) Potted plant, bulbs are most toxic. Contains both lycorine alkaloid (systemic effects) and insoluble oxalates (local pharyngitis).	Gastric irritation, vomiting, diarrhea.	Gastric lavage, activated charcoal, fluids, and supportive treatment.
Bittersweet (<i>Celastrus</i> spp.) Weed, vine with red berries. Immature fruits are toxic. Toxins are sesquiterpene alkaloids (celaphanine, celastrine, paniculatine).		Fluids, supportive care as needed.
Bleeding heart (<i>Dicentra</i> spp.) Garden, woods, potted plant. Roots more toxic than leaves. Toxins are isoquinoline alkaloids (apomorphine, cularine, protoberberine).	Vomiting, diarrhea, muscle tremors, convulsions or paralysis.	Fluids and seizure control.
Castor bean (<i>Ricinus communis</i>) Garden shrub or ornamental grows to 2 meters. Seeds are 1 cm, dark and light mottled, and highly toxic; chewing the seed greatly increases toxicity. Toxin is ricin.	Severe, dangerous if seeds chewed before swallowing. Latent period 6–48 hours. Emesis, severe and hemorrhagic diarrhea, colic, muscle tremors, sudden collapse. Dehydration, hypotension, hemolysis and/or hemoglobinuria.	Emesis for recent exposure: sorbitol if diarrhea not present; charcoal, fluids, and electrolytes. Monitor electrolytes, liver, kidney, adrenal function up to 6 days; H ₂ blockers for GI signs; diazepam for seizures; Antibiotics, lactulose, SAM-e for liver damage.

(Continued)

TOXIC HOME AND GARDEN HAZARDS FOR PETS (CONTINUED)

Table VI-A

Toxic plants and their clinical signs—antidotes and treatment (continued)		
Plant and Characteristics	Clinical Signs	Antidotes and/or Treatment
Chinaberry tree (<i>Melia azedarach</i>) Other common names are Persian lilac, white cedar, Texas umbrella tree. Ornamental tree in temperate to subtropical areas: southern coastal states, Mexican border. Berry is most toxic. Toxins are meliatoxins.	Salivation, anorexia, vomiting, diarrhea. May be followed by weakness, ataxia, excitement or seizures. Fatalities have occurred, generally within two days post-ingestion.	Early emesis, GI lavage and charcoal are considered beneficial. Fluid and electrolyte replacement, anticonvulsants, and supportive care
Christmas rose (<i>Helleborus niger</i>) House and garden plant; entire plant is toxic, but fruits are most dangerous. Small amounts considered dangerous. Contains several toxins including ranunculin that is converted to protoanemonin when chewed, cardenolides, and bufadienolides.	Hypersalivation, vomiting, anorexia, diarrhea followed by cardiac arrhythmias, heart block with premature beats, premature beats, slow irregular pulse. Potent cardenolide action is greatest risk.	Gastric lavage or emesis; activated charcoal or saline cathartics to decontaminate the GI tract. Atropine may be helpful as for other cardenolide plants such as <i>Digitalis</i> spp.
Daphne (<i>Daphne mezereum</i>) Landscape shrub; evergreen or deciduous. Entire plant is toxic. Bitter or acid taste discourages consumption, may reduce toxic effects. Toxins are tricyclic daphnane and diterpenes.	Vesication and edema of the lips and oral cavity associated with ingestion. Signs progress to salivation, thirst, abdominal pain, emesis, hemorrhagic diarrhea.	Analgesics to control pain. General GI detoxification, medical treatment for vomiting and diarrhea. Fluid and electrolyte replacement as needed. Monitor body fluids and electrolytes.
Delphinium/Larkspur (<i>Delphinium</i> spp.) and Pheasant's eye, Yellow oxeye (<i>Adonis</i> spp.) Outdoor perennial, gardens, mountains; tall with blue, purple, or pinkish flowers. Seeds more toxic than leaves. Toxin is a diterpenoid alkaloid.	Small animal poisoning unlikely unless by access to seeds. Early signs are vomiting, colic and diarrhea. May progress to trembling, ataxia, weakness, lateral recumbency.	GI detoxification; demulcents and anti-diarrheal for GI signs; physostigmine to treat muscarinic signs.
English holly (<i>Ilex</i> spp.) Landscape plant; glossy green leaves with marginal spicules. Fruit (drupe) white, yellow, black, red, orange. Occurs in forested areas of eastern N. America; elsewhere as an ornamental. Fruit is most likely portion consumed. Fruit and leaves contain potentially toxic saponins.	Nausea, vomiting, diarrhea most common from consumption of berries. Some animals may be depressed. Clinical response most often mild/moderate and transient.	Relief of digestive distress, activated charcoal may be helpful. Fluid and electrolyte replacement as needed.
English ivy (<i>Hedera helix</i>), also known as Atlantic ivy, Irish ivy, Common ivy Houseplant, or in mild climates used as a ground cover. Occurs as a woody, climbing or creeping vine. Commonly grown throughout North America. Toxins are triterpenoid saponins.	Salivation, thirst, emesis, gastroenteritis, diarrhea, dermatitis. Relatively few reported cases, most are moderate GI irritation. Often moderate or mild.	Symptomatic relief of GI distress; supportive care for vomiting and diarrhea.
Golden angel's trumpet (<i>Brugmansia</i> spp.) Non-native ornamental, similar to Jimsonweed. Large pendulous flowers, similar to Angel's trumpet. Toxin similar to Jimsonweed (tropine alkaloid scopolamine) causes anticholinergic effects.	Typical anticholinergic effects are restlessness, dilated pupils, tachycardia, dyspnea, dry mouth, GI atony, rarely seizures. Rarely lethal.	Treat similar to <i>Datura</i> spp. (See Thorn apple below.)

TOXIC HOME AND GARDEN HAZARDS FOR PETS (CONTINUED)

Table VI-A

Toxic plants and their clinical signs—antidotes and treatment (continued)		
Plant and Characteristics	Clinical Signs	Antidotes and/or Treatment
Horse chestnut or Ohio buckeye (<i>Aesculus</i> spp.) Landscape or forest tree; palmate leaves. Native range is Midwest, east to Appalachian mountains, south into Texas. Planted as ornamental/landscape tree as well. Nuts and twigs most toxic; very early green foliage in spring. Horse chestnut highly toxic; Ohio buckeye very low toxicity. Contain several toxins including saponins, anthraquinones, and a coumarin glycoside.	Gastroenteritis, diarrhea, dehydration, electrolyte imbalance. Neurologic signs possible, including incoordination, hypermetria, staggering. Usually transient, rarely fatal. Recovery usual within 24–48 hours.	Fluid and electrolyte replacement, demulcents, and therapy for gastroenteritis. Confine animals during neurologic phase.
Iris or Blue or yellow flag (<i>Iris</i> spp.) Perennial garden flower, very commonly available. Rootstock (rhizome) most toxic; most risk at transplantation. Close to soil surface, may be dug up by dogs. Advise clients of potential risk. Rootstock contains purgative toxin known as irisin.	Hypersalivation, vomiting, colic, diarrhea which may be hemorrhagic. Occasionally irritation of the lips and muzzle.	GI decontamination early. Fluid and electrolyte therapy as needed.
Irish potato (<i>Solanum tuberosum</i>) Vegetable garden plant. Vines, green skin, and sprouts are toxic. Toxins vary but are solanine and other glycoalkaloids.	Vomiting, diarrhea, depression, rapid heart rate, mydriasis, muscle tremors. Signs may vary from atropine like to cholinesterase inhibition. Use antidotes accordingly and with caution.	GI decontamination. If atropine-like signs predominate: use physostigmine. If salivation and diarrhea are present: use atropine cautiously.
Jerusalem cherry, Winter cherry (<i>Solanum pseudocapsicum</i>) Common ornamental houseplant. Toxin is the glycoalkaloid solanine, similar to other plants of the nightshade (<i>Solanaceae</i>) family.	Severe GI irritation characterized by drooling, vomiting, diarrhea, ulceration, depression, and sometimes seizures.	GI decontamination if exposure is recent. If salivation and diarrhea are present and severe, use atropine cautiously. Provide fluid therapy based on condition of patient and results of laboratory tests.
Lantana (<i>Lantana camara</i>) Occurs wild and in gardens in mild temperate to tropical areas. Naturalized in southeastern coastal states of the USA. Bright orange, yellow, red, purple, or pink flowers. Foliage and immature berries are most toxic. Toxins are pentacyclic triterpenoid lantadenes A, B, and C.	Weakness, lethargy, vomiting, diarrhea, mydriasis, dyspnea. Continued ingestion can lead to chronic disease. Advanced signs: cholestasis, hyperbilirubinemia. Liver changes predispose to photosensitization.	GI decontamination, activated charcoal for acute exposures. Provide fluids and respiratory support. Protect from sunlight and treat for hepatic insufficiency.
Lily of the valley (<i>Convallaria majalis</i>) Ornamental garden plant. Prefers moist, shaded areas. Blossoms nodding/drooping on stem. Toxic principal (cardenolides) persists in dried plants; highest concentration in roots.	Multi-organ failure. Tremors, thirst, vomiting, diarrhea, cardiac arrhythmia/bradycardia, weakness, shock. Monitor for cardiac arrhythmias, shock and hyperkalemia.	Emesis or gastric lavage. Control dehydration, maintain electrolytes; control diarrhea; monitor ECG and serum potassium.

(Continued)

TOXIC HOME AND GARDEN HAZARDS FOR PETS (CONTINUED)

Table VI-A

Toxic plants and their clinical signs—antidotes and treatment (continued)		
Plant and Characteristics	Clinical Signs	Antidotes and/or Treatment
Lupine, Bluebonnet (<i>Lupinus</i> spp.) Common garden ornamental throughout USA; wild plants abundant in some regions, primarily western USA. Seeds more toxic than leaves, but plant, seeds, and pods are toxic. Toxin is lupine.	Signs begin 1–24 hours post exposure. Salivation, ataxia, mydriasis, depression or seizures, disorientation, dyspnea. Liver and kidney damage may develop from continued ingestion. Lupines are teratogenic in ruminants. Risk in small animals is not well known. Chewing on the plant releases oxalate spicules into mouth, tongue and lips.	GI decontamination with activated charcoal for acute exposure. Anticonvulsants may be needed if neurologic signs are severe.
Mexican breadfruit, Swiss cheese plant, Hurricane plant (<i>Monstera deliciosa</i>) Stems and leaves contain insoluble calcium oxalate spicules (raphides).	Response is immediate irritation, pain, salivation, and inflammation. Signs include pawing at face, drooling, and vomiting; potential interference with upper airway. Vomiting, GI pain, diarrhea; ataxia, hypotension, occasional seizures, cardiovascular failure.	Cleanse mouth thoroughly with water. Apply local and/or systemic anti-inflammatory agents based on clinical condition of patient.
Mistletoe (<i>Phoradendron</i> spp.) Access to pets in homes at holiday time. Oval evergreen leaves with white berries. Leaves, stems, and berries are moderately toxic, contain toxic amines and proteins.	Vomiting, GI pain, diarrhea; ataxia, hypotension, occasional seizures, cardiovascular failure. Principal risk may be from use during holiday season.	Fluid and electrolyte replacement; demulcents for gastroenteritis.
Monkshood (<i>Aconitum</i> spp.) Perennial garden ornamental. Entire plant is toxic, contains diterpene alkaloids that are primarily neurotoxic.	Interferes with inactivation of Na^+ channels in nerves. Salivation, vomiting, diarrhea. Muscle tremors, weakness, cardiac arrhythmia and/or heart failure; respiratory depression.	GI decontamination, fluid and electrolyte replacement. Manage similar to digitalis glycoside overdose, with caution for potassium administration.
Morning glory (<i>Ipomoea purpurea</i> and <i>Ipomoea tricolor</i>) Garden annual, potted plant. Seeds most toxic. Increased risk when seeds are pre-soaked, consumed by dogs. Indole alkaloid toxin similar to ergot alkaloids; abused as hallucinogen.	Nausea, mydriasis, ataxia, muscle tremors, hallucinations, decreased reflexes, diarrhea, hypotension.	Dark, quiet surroundings; tranquilization as needed. GI decontamination is not routinely recommended.
Mountain laurel (<i>Kalmia</i> spp.) Native of eastern and southeastern woods, mountains. Both leaves and flowers are toxic. Honey from nectar also toxic. Toxins are diterpenoids, in particular grayanotoxins I and II.	Oral irritation, salivation, projectile vomiting, diarrhea, weakness, impaired vision, bradycardia, hypotension, AV block.	Activated charcoal, fluid replacement, and respiratory support as needed.
Narcissus, Daffodil, Jonquil (<i>Narcissus</i> spp.) Garden ornamental bulb. Bulb is most toxic. Contains lycorine alkaloid.	Nausea, vomiting, salivation, hypotension, diarrhea. Prolonged signs may cause dehydration.	Gastric lavage, activated charcoal, fluid replacement, supportive treatment for gastroenteritis.
Nettle (<i>Urtica</i> spp.) Garden or waste area weed. Hairs on leaves contain toxin that enters skin on contact. Most common in hunting or outdoor free-roaming dogs. Toxins are biogenic amines (acetylcholine, histamine, etc.).	Oral irritation and pain, hypersalivation, swelling and edema of nose and periocular areas or other areas of skin contact	Antihistamines and analgesics. Local or systemic anti-inflammatory supportive therapy to treat affected contact areas.

TOXIC HOME AND GARDEN HAZARDS FOR PETS (CONTINUED)

Table VI-A

Toxic plants and their clinical signs—antidotes and treatment (continued)		
Plant and Characteristics	Clinical Signs	Antidotes and/or Treatment
Persian violet, Sowbread (<i>Cyclamen persicum</i>) Popular florists' plant; widely available. Irritant saponins in all parts of the plant, especially tubers or roots.	Chewing plant parts causes oral irritation with drooling, vomiting and diarrhea. Occasional hemoglobinuria may color urine red-brown. Large amounts may cause cardiac arrhythmias, seizures and rarely mortality.	Control vomiting and diarrhea if severe; administer fluids as needed. Monitor urine for color and/or hemoglobin. Control seizures and cardiac arrhythmias as needed.
Philodendron spp. Very common indoor ornamental vine. Toxic principal is insoluble oxalate.	Chewing on the plant releases oxalate spicules into mouth, tongue and lips. Response is immediate irritation, pain, salivation, and inflammation. Signs include pawing at face, drooling, and vomiting; also potential interference with upper airway. Irritation of mouth: may cause vomiting, diarrhea, and dermatitis. Usually transient and not life-threatening.	Cleanse mouth thoroughly with water. Apply local and/or systemic anti-inflammatory agents based on clinical condition of patient.
Poinsettia (<i>Euphorbia pulcherrima</i>) Garden or potted plant, especially during Holiday season. Sap of stem and leaves mild irritant. Contains a variety of diterpenoid euphorbol esters.		Demulcents for local lesions; fluids to prevent dehydration.
Rosary pea, Precatory bean (<i>Abrus precatorius</i>) Native of Caribbean islands. Seeds (when broken or chewed) are highly toxic. Seeds used in ornamental jewelry in some countries. Illegal to import into USA. Toxin is abrin.	Signs may be delayed up to 2 days after ingestion. Early signs are nausea, vomiting, diarrhea (often hemorrhagic) followed by weakness, tachycardia, possible renal failure, coma, death.	Emesis or lavage followed by activated charcoal, demulcents, fluids, and electrolytes. Early and thorough detoxication is important for survival.
Thorn apple, Jimsonweed (<i>Datura stramonium</i>) Annual weed, some species are ornamental (<i>Datura metel</i>). Entire plant is toxic, but seeds are most toxic and available. Toxins are tropane alkaloids (hyoscyamine and scopolamine) with effects similar to atropine.	Thirst, disturbances of vision, delirium, mydriasis, tachycardia, hyperthermia, GI atony/constipation. Commonly described as "Hot as a pistol, blind as a bat, red as a beet, mad as a hatter."	GI decontamination if early after ingestion. Parasympathomimetic drug (e.g., physostigmine).
Tulip (<i>Tulipa spp.</i>) and Hyacinth (<i>Hyacinthus spp.</i>) Poisoning usually occurs when dogs consume available bulbs or dig up freshly planted bulbs. Toxic principal includes allergenic lactones and similar alkaloids.	Signs reflect direct irritation and include drooling, nausea, vomiting, diarrhea, dyspnea, tachycardia, and hyperpnea.	GI decontamination if early after ingestion. Apply local and/or systemic anti-inflammatory agents based on clinical condition of patient. Monitor and control gastrointestinal effects; medicate as needed for tachycardia and dyspnea.
Tobacco (<i>Nicotiana tabacum</i>) Garden plant, weed, cigarettes. Entire plant toxic. Nicotine alkaloid is toxic principal.	Rapid onset of salivation, nausea, emesis, tremors, incoordination, ataxia, collapse and respiratory failure.	Assist ventilation, provide vascular support. Gastric lavage with activated charcoal.

(Continued)

TOXIC HOME AND GARDEN HAZARDS FOR PETS (CONTINUED)

Table VI-A

Toxic plants and their clinical signs—antidotes and treatment (continued)		
Plant and Characteristics	Clinical Signs	Antidotes and/or Treatment
Wisteria (<i>Wisteria</i> spp.) Woody vine or shrub with bluish purple to white legume flowers. Entire plant is toxic. Toxin is a glycoprotein lectin.	Nausea, abdominal pain, prolonged vomiting; diarrhea. Signs may persist 2–3 days.	Antiemetics and fluid replacement therapy.
Yellow Jessamine (<i>Gelsemium sempervirens</i>) Mild temperate to subtropical climates; mainly SE United States. Yellow trumpet-shaped flowers grow on evergreen vines. Neurotoxic alkaloids and sempervirine, an indole, are toxins.	Weakness, ataxia, clonic/tonic seizures, paralysis, respiratory failure.	GI decontamination early in course of toxicosis. Symptomatic and supportive therapy for respiration. Fluid replacement therapy as needed.

Supplemental Resources

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APPENDIX VI

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TOXIC HOME AND GARDEN HAZARDS FOR PETS (CONTINUED)

Table VI-B

Herbal toxicities						
Class	Toxic Principle	Genus Species	Common Names	Clinical Signs	Treatment Overview	Popular Usage
Sympathomimetics	Ephedrine, pseudoephedrine, synephrine	<i>Ephedra sinica</i> , <i>Sida cordifolia</i> , <i>Citrus aurantium</i>	Ma huang, Indian common mallow, bitter orange	Hyperthermia, hypertension, tachycardia, tremors, seizures, hallucinations, agitation, serotonin syndrome	Decontamination, monitor CV, CNS. Acepromazine for agitation, Cyproheptadine for serotonin syndrome. Beta blockers for tachycardia.	Weight loss, Weight lifting, Herbal “ecstasy,” decongestants
Methylxanthines	Caffeine, theobromine	<i>Camellia sinensis</i> , <i>Paullinia cupana</i> , <i>Cola acuminata</i> , <i>Theobroma cacao</i>	Epigallocatechin gallate or ECGC (green tea), guarana, cocoa, cola, kola nut, chocolate	Agitation, hyperactivity, polyuria, polydipsia, cardiac arrhythmias, tremors, seizures	Decontamination, fluid diuresis, monitor CV and CNS, manage arrhythmias, tremors, seizures, symptomatic supportive care.	Weight loss, herbal “NoDoz”
Hypoglyemics	Alpha lipoic acid, cinnamon, xylitol	Alpha lipoic acid (ALA), <i>Cinnamomum cassia</i>	Thioctic acid, cinnamon, xylitol	Hypersalivation, vomiting, hypoglycemia, increased liver or renal enzymes, death (ALA)	Monitor blood glucose, manage hypoglycemia, monitor liver enzymes.	Diabetic treatment, sugar substitute, amanita mushroom poisoning (ALA)
Serotonin syndrome	5-hydroxytryptophan (5-HTP)	<i>Griffonia simplicifolia</i>	5-HTP	Vomiting, diarrhea, tremors, seizures, ataxia, hyperesthesia, depression	Decontamination, Methocarbamol for tremors. Phenobarbital or propofol for seizures. Avoid benzodiazepines.	Depression, headaches, insomnia, obesity
Allergenic	Arabinogalactan	<i>Echinacea purpurea</i>	Purple coneflower	Vomiting, diarrhea	Cyproheptadine is a specific antagonist.	
Anticoagulant	Hydroxycoumarin, bisabolol	<i>Matricaria recutita</i> , <i>Chamaemelum nobile</i>	Chamomile	Vomiting, diarrhea, lethargy, rarely epistaxis, hematoma (cats)	Symptomatic/supportive care. Monitor coagulation, symptomatic and supportive care, very rarely blood transfusion.	Cold and flu support, immune stimulant Sedative, gastrointestinal ulcers
MAO inhibitor	Hypericin	<i>Hypericum perforatum</i>	St. John's wort	Depression, vomiting, diarrhea, rarely tremors, seizures	Decontamination, symptomatic and supportive care, cyproheptadine for serotonin syndrome.	Antidepressant, insomnia

(Continued)

TOXIC HOME AND GARDEN HAZARDS FOR PETS (CONTINUED)

Table VI-B

Herbal toxicities (continued)						
Class	Toxic Principle	Genus Species	Common Names	Clinical Signs	Treatment Overview	Popular Usage
Sedative	Valpotriates	<i>Valeriana officianalis</i>	Valerian	Lethargy, sedation	Generally home care, prevent injury.	Sedative, sleep aid
Essential oil	Melaleuca oil, pulegone, menthofuran	<i>Melaleuca alternifolia</i> , <i>Mentha pulegium</i>	Tea tree oil, pennyroyal oil	Orally: vomiting, diarrhea, CNS depression, hepatotoxicity, aspiration pneumonia. Dermally (as a spot-on): transient paresis	Dermal—bath. Oral—fluids, N-acetylcysteine, monitor liver enzymes for pennroyal ingestions. Pain control, thermoregulation as needed.	Germicidal, fungal infections, antiseptic, flea control
Polysulfated glycosaminoglycan (PSGAG)	PSGAG	Glucosamine, chondroitin sulfate	Adequan and many other brands	Oral: vomiting, diarrhea, polydipsia, hepatopathy. IM: transient	Manage vomiting and diarrhea, baseline liver enzymes if large ingestion.	Arthritis, chondroprotective
Cationic detergents	Quaternary ammonium compounds	<i>Citrus X paradisi</i>	Grapefruit seed extract (GSE)	dose-dependent prolongation of PT, aPTT, reduced platelet aggregation, diathesis	Coagulopathies only expected with injectable overdoses, monitor clotting parameters.	Disinfectant, antifungal
Alpha 2-adrenergic blocking agent	Alpha 2-adrenergic blocking agent	<i>Pausinystalia yohimbine</i>	Yohimbine	Drooling, vomiting ± blood, weakness, anorexia, hyperthermia,	Dilution, carafate slurries, H2 blocker, fluids, nutritional support, broad-spectrum antibiotic, pain control.	
Salicylates	Methyl salicylate	<i>Gaultheria procumbens</i>	Wintergreen extract	oral/esophageal ulceration or irritation, dermal erythema, pain, ulceration	Hyperactivity, agitation, tremors, seizures, vomiting, diarrhea, abdominal pain, hypotension	Monitor glucose, blood pressure, control agitation, tremors, seizures. Fluids and dextrose PRN.
					GI upset, GI ulcers, hyperthermia, hepatotoxicity, coagulopathies, coma	Hypertension, angina, "herbal Viagra"

Suggested Reading:

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APPENDIX VI

LYNN R. HOVDA

TOXIC HOME AND GARDEN HAZARDS FOR PETS (CONTINUED)

Table VI-C

Household cleaners, disinfectants, and solvents—products, clinical signs and treatment		
Products	Toxicity and Clinical Signs	Treatment
SOAPs, DETERGENTS, AND CLEANING AGENTS		
Soaps (fatty acid salts)—includes commercial bar soaps, some liquid hand soaps, laundry bar soaps, homemade soaps, some baby and infant products.	Low order toxicity	Generally dilution with water and observation is all that is required. Fluids and electrolytes should be used to replace fluid loss from excessive vomiting and diarrhea. If vomiting has not yet occurred, emesis should be induced in noncorrosive bar soap ingestions > 20 g soap/kg body weight (BW). Eyes should be irrigated with tepid water or isotonic saline for 10–15 minutes and observed for signs of irritation. Any exposed skin and hair coat should be washed well to prevent re exposure.
Anionic Detergents (sulfonated or phosphorylated straight chain hydrocarbons)—includes most laundry detergents, some automatic dishwashing detergents, and some shampoos. Common detergents include alkyl sodium sulfate, alkyl sodium sulfonate, dioctyl sodium sulfosuccinate, sodium lauryl sulfate, others. Hard water "boosters" or "builders" such as sodium carbonate, sodium phosphate, and sodium silicate are often added.	Generally slight to moderate toxicity with high alkaline and potentially corrosive automatic dishwashing detergents, including pods or complete packs, the exception. Irritation to the gastrointestinal tract (GIT) with discomfort, vomiting, and diarrhea the most common signs. Absorption occurs through the GIT and irritated skin; IV hemolysis has been reported. Repeated dermal exposure may result in irritation. Ocular exposure may cause conjunctivitis and irritation; ocular exposure to automatic dishwashing detergents may result in corneal erosion and opacity. Laundry pods or complete packs have caused more serious problems than expected based on the ingredients. The reason is unknown but may be related to increased amounts ingested due to a concentrated product packaged in a small, colorful pod.	Depends on specific product and amount ingested. With most products, dilution with water or milk and replacement of fluid and electrolyte losses secondary to vomiting and diarrhea are all that are required. Serum should be monitored for hemolysis. Skin and hair coat should be washed well with tepid water to prevent exposure, especially those animals that are known to self-groom. Eyes should be irrigated well for 10–15 minutes with tepid water or isotonic saline and monitored closely for irritation. Animals exposed in any manner to automatic dishwashing detergents or laundry pods should be examined and monitored for corrosive type injuries.
Cationic Detergents (quaternary ammonium compounds with aryl or alkyl substituent groups, often a very long hydrophobic carbon chain with a halogen such as chloride or iodide is attached)—includes fabric softeners, sanitizers, germicides. Compounds such as benzethonium chloride, benzalkonium chloride, and cetyl pyridinium chloride are used as cationic detergents. Liquid potpourris, covered elsewhere, are also in this group.	Highly toxic compounds. Effects are concentration dependent with 1% concentrations causing irritation and damage to mucous membranes and 7.5% concentrations resulting in corrosive burns to the mouth, tongue, pharynx, and esophagus. Salivation is profuse and vomiting ± blood may occur. Other signs include shock at any stage of exposure, muscle weakness, fever, CNS and respiratory depression, seizures, collapse and coma. Dermal effects are concentration dependent. Hair loss and skin ulceration are frequently seen in cats and inflammatory lesions on the paws in dogs. Ocular signs after exposure are concentration dependent and range from irritation and discomfort to corneal damage and ulceration.	Depends on the concentration of the product and route of exposure. Animals ingesting the product should be given water or another diluent such as milk. Vomiting should not be induced, especially when the concentration is greater than 7.5%. Activated charcoal may be administered in asymptomatic animals but the use is controversial. The mouth and oropharynx should be examined for lesions and those animals with continued profuse salivation, stridor, or dysphagia should undergo endoscopic examination for analysis of mucosal damage. Supportive care includes IV fluids as needed, attention to respiratory effort, adequate caloric intake, seizure medication as needed, and close monitoring for shock. Exposed skin and hair coat should be washed with tepid water and mild soap for 10–25 minutes and monitored for irritation and ulceration. The eyes should be thoroughly evaluated and irrigated with isotonic saline for 20 minutes followed by a slit lamp examination. Further treatment depends on the examination results.

(Continued)

TOXIC HOME AND GARDEN HAZARDS FOR PETS (CONTINUED)

Table VI-C

Household cleaners, disinfectants, and solvents—products, clinical signs and treatment (continued)		
Products	Toxicity and Clinical Signs	Treatment
Nonionic Detergents (uncharged aqueous solutions)—includes hand dishwashing detergents, shampoos, few laundry detergents. Alkyl ethoxylate, alkylphenoxy polyethoxy ethanol (alcohol ethoxylates), and polyethylene glycol stearate are examples.	Primarily of low toxicity after ingestion. Ocular exposure may result in irritation.	Dilution with water and observation normally all that is required. IV fluids and electrolytes may be used to replace fluid losses from excessive vomiting and diarrhea. Eyes should be irrigated with tepid water or isotonic saline for 10–15 minutes and observed for signs of continued irritation. Any exposed skin and hair coat should be washed well to prevent re-exposure.
CORROSIVES Acids (pH < 7; strong acids pH < 2.5–3)—includes rust removers, drain and toilet bowl cleaners, gun barrel cleaning fluids and other metal cleaners, swimming pool cleaning agents. Hydrochloric acid (muriatic acid), sulfuric acid, nitric acid, oxalic acid, phosphoric acid, and sodium bisulfite (sodium acid sulfate) are all acid corrosives. Hydrofluoric acid, a rust remover product, carries a special warning.	<p>Signs are concentration and time dependent although in general these are highly toxic substances. Acids typically have a localized necrotic effect and rarely cause full-thickness mucous membrane lesions. Exposure in animals results in immediate, intense pain which typically limits further exposure.</p> <p>Corrosive mucous membranes burns are initially gray to milky white, turning black as an eschar forms. Stricture formation may follow in several weeks. The animal may vocalize or become lethargic; excessive panting may indicate pain and inability to swallow may be noted. Other effects are hematemesis, abdominal pain, polydipsia, epiglottal edema with secondary respiratory distress, and shock. Secondary pneumonitis results from aspiration or exposure to acid vapors.</p> <p>Serious burns result from ocular or dermal exposure. Pain is severe. Acids tend to penetrate the eye more slowly than bases and may result in a delayed corneal damage including corneal and conjunctiva necrosis.</p> <p><i>Hydrofluoric acid (HF)</i> penetrates tissues and poisoning can occur through ingestion, inhalation, or skin or eye exposure. Signs are often delayed and pain may not be immediately evident. Once systemic, HF binds with calcium ions producing insoluble calcium fluoride. Severe pain and swelling as well as hypocalcemia result. In severe exposures death from cardiac arrest may occur.</p>	<p>All exposures should be diluted immediately with water or milk. Attempts to neutralize the burn with other chemicals are contraindicated as is emesis or gastric lavage. Activated charcoal is ineffective in binding acid corrosives and should not be administered. Supportive care including IV fluids is indicated. Therapy for shock may be required as uncorrected circulatory collapse can lead to renal failure, ischemic lesions in vital organs, and acute death. The presence of severe pharyngeal edema indicates the need for an endotracheal or tracheostomy tube. Esophageal complications are less common with acid exposures than alkali ingestions. If necessary, endoscopy should be carefully performed 12–24 hours after exposure to determine the extent of injury. The procedure should be stopped at the first sign of mucosal damage. Radiographic examination is another alternative.</p> <p>Affected skin and hair coat should be irrigated for 15–20 minutes with copious amounts of tepid water and monitored for lesions.</p> <p>Affected eyes should be irrigated for 20–30 minutes with isotonic saline followed by an examination with a slit lamp. Further treatment depends on the result of the examination.</p> <p>Any deterioration in the animal's signs necessitates a second examination.</p> <p><i>Hydrofluoric acid</i> exposures require immediate attention even though they may not show any signs. Caretakers should take precautions to protect themselves when bathing or applying medications. Exposed areas should be washed well with cool water and ice packs applied to slow diffusion of the fluoride ion. Calcium gluconate gel applied liberally to the affected area will help bind fluoride. If calcium gluconate gel is not readily available the area can be soaked in any magnesium hydroxide containing antacid product until the gel is located.</p>

TOXIC HOME AND GARDEN HAZARDS FOR PETS (CONTINUED)

Table VI-C

Household cleaners, disinfectants, and solvents—products, clinical signs and treatment (<i>continued</i>)		
Products	Toxicity and Clinical Signs	Treatment
Bases (pH >7; strong base pH >11.5–12; some references state >10)—includes drain and oven cleaners, cleaning agents, toilet bowl cleaners, washing products. Lye (sodium or potassium hydroxide or caustic soda), sodium carbonate (washing soda or soda ash), sodium metasilicate, and ammonium hydroxide are alkaline ingredients present in many of these products.	Rapid liquefaction necrosis on contact with deep, penetrating ulcers. Ingestion may result in full thickness esophageal burns with secondary stricture formation. Little pain on contact so animals are not repelled and significant exposure may occur. The remaining signs are similar to those found under corrosive acids.	All exposures should be diluted immediately with water or milk. Attempts to neutralize with other chemicals are contraindicated as is emesis or gastric lavage. Activated charcoal is ineffective in binding and should not be administered. Supportive care includes IV fluids, analgesics, and adequate nutrition. Corticosteroids have been recommended to decrease stricture formation but their use is controversial. Antibiotics should be used in animals with known perforations or infections. Therapy for shock may be required as uncorrected circulatory collapse can lead to renal failure, ischemic lesions in vital organs, and acute death. The presence of severe pharyngeal edema indicates the need for an endotracheal or tracheostomy tube. Endoscopy should be carefully performed 12–24 hours after exposure to determine the extent of injury. The procedure should be stopped at the first sign of mucosal damage. Radiographic examination is another alternative. Affected skin and hair coat should be flushed for 15–20 minutes with copious amounts of tepid water and monitored for lesions.
DISINFECTANTS		Affected eyes should be irrigated for 20–30 minutes with isotonic saline followed by an examination with a slit lamp. Further treatment depends on the results of the examination.
Bleaches —includes common household bleach (3 to 6% sodium hypochlorite); industrial or swimming pool bleach (up to 50% sodium hypochlorite); powdered bleach (calcium hypochlorite, sodium dichloroisocyanurate), non-chlorine or colorfast bleach (sodium carbonate peroxide, hydrogen peroxide, sodium perborate).	The toxicity of chlorine bleach depends on the pH and concentration of the hypochlorite ion. Exposed animals may smell like chlorine and their exposed hair coat bleached. Household chlorine bleach products are mild to moderate irritants and generally not associated with significant tissue destruction. Common clinical signs secondary to ingestion include oral irritation, salivation, abdominal pain, and vomiting. Inhalation of fumes may result in coughing, gagging and retching. Systemic reactions are rare. Oral, pharyngeal, esophageal, and gastric burns have been reported from household chlorine bleach ingestions but are rare. The more concentrated hypochlorite solutions and bleach powders can produce corrosive effects. Non-chlorine bleach products are of low order toxicity with gastric irritation and vomiting the most commonly reported signs. Borate containing products decompose to peroxide and borate resulting in a more alkaline and potentially irritating product.	Any deterioration in the animal's signs necessitates a second examination. All oral exposures should be diluted with water or another appropriate diluent. Exposed skin and hair coat should be washed with a mild soap and copious amounts of water; eyes should be irrigated with isotonic saline for 10–15 minutes. Animals inhaling chlorine bleach fumes should be moved to fresh air. The incidence of esophageal damage is low so endoscopy is not routinely recommended. Animals with dysphagia, dyspnea, or severe oropharyngeal burns should undergo careful endoscopic examination and treated as needed for corrosive injuries.

(Continued)

TOXIC HOME AND GARDEN HAZARDS FOR PETS (CONTINUED)

Table VI-C

Products	Toxicity and Clinical Signs	Treatment
Phenols (coal tar derived aromatic alcohols)—chlorophenols, phenylphenols in a variety of concentrations and products; some concentrated commercial products contain up to 50% pure phenol.	<p>Considered highly toxic and a medical emergency due to rapid absorption by inhalation, ingestion, or dermal exposure. Cats are more sensitive than dogs. The oral LD₅₀ in dogs is 0.5g/kg BW. Concentrations >1% have caused dermal burns and >5% oral burns.</p> <p>Oral exposure causes burns to the mouth, oropharynx, and esophagus. Hypersalivation, panting, agitation, and vomiting progress to tremors, cardiac arrhythmias, shock, and coma. Methemoglobinemia, respiratory alkalosis, and renal and hepatic damage may develop.</p> <p>Dermal and ocular exposure results in a short period of intense pain followed by local anesthesia. Necrotic skin areas are white followed in a few days by a dry, grey black eschar. Ocular exposure results in severe corneal burns and erosions.</p>	<p>Dilution with water is considered controversial as it may increase systemic absorption; milk is preferred and small amounts should be administered at home prior to obtaining veterinary care. Emesis is contraindicated. The mouth and oropharynx should be examined carefully for evidence of mucosal damage prior to gastric lavage. If present gastric lavage is contraindicated. If there is no mucosal damage, activated charcoal with a cathartic may be administered. Further care is supportive and includes monitoring of renal and hepatic function, acid-base status, and respiratory effort. Shock and respiratory depression are complicating factors. N-acetylcysteine (NAC) may be used to limit hepatic and renal toxicity.</p> <p>Individuals treating dermal exposures should protect themselves prior to animal treatment. Polyethylene glycol (PEG) or glycerol is recommended for the initial dilution and removal of phenolic compounds followed by washing with a mild soap and water. Oil based creams and ointments should be avoided as they may increase phenol absorption.</p>
Pine Oils (terpene alcohols) and Turpentine (mixture of terpenes derived from pine oil)—Concentration of pine oil in disinfectants varies from 0.3% to 60%. Turpentine is used to thin oil-based paints.	<p>The oral LD₅₀ of pine oil varies from 1 to 2.7 mL/kg BW but much lower doses may result in severe toxicosis. Cats are more susceptible than dogs. Pine oil products are direct irritants to mucous membranes resulting in erythema in contact areas (mouth, oropharynx, skin).</p> <p>Ingestion results in profuse salivation, abdominal pain, and vomiting ± blood. Systemic effects include respiratory depression, CNS depression, weakness, ataxia, and hypotension. Aspiration during ingestion or emesis or chemical pneumonitis secondary to systemic absorption results in pulmonary toxicity. Myoglobinuria and acute renal may develop with massive ingestions.</p> <p>Dermal exposure causes redness and irritation. Ocular signs include photosensitivity, blepharospasm, epiphora, and conjunctival and scleral erythema.</p>	<p>Affected eyes should be irrigated for 20–30 minutes with isotonic saline and a slit lamp examination performed. Medications and further therapy depend on exam results.</p> <p>All oral exposures should be diluted with water or milk. Induction of emesis is contraindicated and gastric lavage carries a risk. Activated charcoal with a cathartic should be administered after dilution. Further treatment is symptomatic and includes close monitoring of renal perfusion, electrolytes, and acid base status.</p> <p>Affected skin should be washed well with a mild soap and copious amounts of water.</p> <p>Ocular exposures should be irrigated for 10–15 minutes with isotonic saline and monitored for further signs.</p>

TOXIC HOME AND GARDEN HAZARDS FOR PETS (CONTINUED)

Table VI-C

<i>Products</i>	<i>Toxicity and Clinical Signs</i>	<i>Treatment</i>
SOLVENTS AND ALCOHOLS		
Acetone —found in nail polish remover, glues and rubber cement, paint thinner, varnish.	The oral LD ₅₀ in dogs is 8 mL/kg BW but doses as low as 2–3 mL/kg BW may be toxic. The odor of acetone and presence of elevated urinary ketones indicate exposure. Clinical signs associated with a mild exposure include CNS depression, ataxia, and vomiting; stupor and coma occur with larger amounts. Hyperglycemia and ketonemia may be present.	Emesis followed by activated charcoal with a cathartic has been suggested but is controversial due to rapid absorption of acetone and poor binding of activated charcoal. It may be useful if performed within 15–30 minutes of ingestion. Further therapy is symptomatic and supportive and may need to be continued for several days due to the long plasma half-life.
Isopropanol —found in perfume, cologne, hand sanitizers, fuel additives.	The toxic dose of 70% isopropanol is 1 mL/kg BW but doses as low as 0.5 mL/kg BW may be toxic. Signs occur rapidly, generally within 30–60 minutes, and include vomiting ± blood, stupor, and ataxia which may progress to CNS and respiratory depression, severe hypotension, and coma. Mild acidosis may occur.	The rapid onset of signs prevents most forms of decontamination. Emesis may be induced in asymptomatic animals if the ingestion occurred with 15–30 minutes. Activated charcoal is not recommended as it does not readily bind alcohols. Further treatment includes IV fluids and monitoring of acid-base and electrolyte status. Hemodialysis may be useful in animals with severe hypotension and coma.
Methanol (methyl or wood alcohol, "denatured alcohol")—found in windshield wiper solutions, antifreeze products for door locks.	The lethal dose of oral methanol in dogs is 4–8 mL/kg BW. Clinical signs include CNS and respiratory depression, ataxia, hypothermia, and coma. Blindness and severe acidosis do NOT occur in dogs and cats.	Treatment is similar to isopropanol toxicosis.

Acknowledgment: Anita Kore, Sharon Gwaltney-Brant.

APPENDIX VII

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PAIN MANAGEMENT

Table VII-A

Recommended parenteral opioid dosages and indications			
Opioid	Dose/Route/Duration	Indications	Comments
Butorphanol (injectable)	Dog: 0.2–0.4 mg/kg IM, IV, or SC Cat: 0.2–0.4 mg/kg IM, IV, or SC Duration: 1–3 h	Mild to moderate pain	Mild or no sedation; mild ventilatory depression.
Buprenorphine (injectable)	Dog: 0.005–0.03 mg/kg IM, IV Cat: 0.005–0.03 mg/kg IM, IV or transmucosal Duration: 3–8 h Cat: 0.24 mg/kg SC once daily for up to 3 days for post-operative pain (SIMBADOL) Duration: 24 h	Mild to moderate pain	May be difficult to antagonize, onset of effect 15–30 minutes.
Morphine (injectable)	Dog: 0.2–1.0 mg/kg IM or SC; 0.05–0.5 mg/kg IV Cat: 0.05–0.2 mg/kg IM or SC Duration: 3–6 h	Moderate to severe pain	Sedation; respiratory depression; bradycardia; nausea; hypothermia; dysphoria in cats without pain or with large dosage; rapid IV injection may cause histamine release.
Methadone (injectable)	Dog: 0.25–0.5 mg/kg IV, IM or SC Cat: 0.1–0.25 mg/kg IV, IM or SC Duration 3–4 h	Moderate to severe pain	Sedation; dysphoria, vomiting, and constipation are reportedly less than with morphine.
Hydromorphone (injectable)	Dog: 0.05–0.2 mg/kg IM, IV, or SC Cat: 0.05–0.2 mg/kg IM, IV, or SC Duration: 3–6 h	Moderate to severe pain	Similar side effects as those observed with morphine, but less vomiting and minimal histamine release. May be associated with hyperthermia in cats.
Fentanyl (injectable)	Dog: 0.002–0.01 mg/kg IV or IM Cat: 0.001–0.005 mg/kg IV or IM Duration: 0.5–2 h	Moderate to severe pain; CRI necessary for long-term analgesia	Sedation; respiratory depression; bradycardia; nausea; inadequate duration of analgesia from single IV bolus or IM injection.
Fentanyl (topical)	Dog: 1.3–2.7 mg/kg applied topically to the dorsal scapular area 2–4 h prior to surgery (RECUVYRA) Duration: 4 days	Severe pain	Sedation, decreased food and water intake: RECUVYRA Risk Minimization Action Plan (RiskMAP) training required to minimize risk of human exposure.

CRI = constant rate infusion.

Table VII-B

Recommended dispensable opioid dosages and indications			
Opioid	Dose/Route/Duration	Indications	Comments
Codeine (tablets)	Dog: 1.0–2.0 mg/kg PO Cat: 0.1–1.0 mg/kg PO Duration: 4–8 h	Mild to moderate pain	Minimal side effects; when dosed with acetaminophen, avoid in dogs with liver disease or Heinz body anemia; do not use in combination with acetaminophen in cats.
Butorphanol (tablets)	Dog: 0.5–1.0 mg/kg PO Cat: 0.5–1.0 mg/kg PO Duration: 2–4 h	Mild to moderate pain	Mild or no sedation; mild ventilatory depression.
Tramadol (immediate-release tablets)	Dog: 2–5 mg/kg PO q8–12h Cat: 2–5 mg/kg PO q8–12h	Mild to moderate pain	Sedation, anxiety, urinary retention.

PAIN MANAGEMENT (CONTINUED)

Table VII–C

Recommended parenteral NSAID dosages and indications			
NSAID	Dose/Route/Duration	Indications	Comments
Carprofen (injectable)	Dog: 2–4 mg/kg IV, SC q24h Cat: 1.0 mg/kg SC only once	Mild to moderate pain	Primarily used perioperatively before switching to oral formulation; GI irritation and altered renal function.
Meloxicam (injectable)	Dog: 0.2 mg/kg initially IM, IV, or SC; 0.1 mg/kg thereafter SC Cat: 0.1–0.2 mg/kg initially IM, SC (single dose only per label) Duration: 24 h	Mild to moderate pain	Can be mixed with food; GI irritation and altered renal function.
Ketoprofen (injectable)	Dog: 1.0–2.0 mg/kg initially IM, IV, or SC; 0.5–1.0 mg/kg thereafter SC Cat: 1.0–2.0 mg/kg initially IM, IV, or SC; 0.5–1.0 mg/kg thereafter SC Duration: 24 h	Mild to moderate pain; approved in Canada for dogs and cats and in the United States for horses	GI irritation and altered renal function. Dosing should not exceed 5 days for dogs and 3 days for cats.
Robenacoxib (injectable)	Dog: 2.0 mg/kg SC once prior to surgery; PO administration as per Table VII–D thereafter		

GI = gastrointestinal; NSAID = nonsteroidal anti-inflammatory drug.

Table VII–D

Recommended dispensable NSAID dosages and indications			
NSAID	Dosage/Route/Duration	Indications	Comments
Carprofen (tablets and chewables)	Dog: 4.4 mg/kg PO q24h or divided q12h Cat: 1.0 mg/kg PO (1 dose only) Duration: 12–24 h	Mild to moderate pain; approved for use in dogs with osteoarthritis or perioperative pain	Toxicity associated with chronic use in cats due to variable half-life; may cause GI irritation and altered renal function in some patients.
Deracoxib (chewable tablets)	Dog (post-operative pain): 3.0–4.0 mg/kg PO q24 h as needed for 7 days Dog (osteoarthritis): 1–2 mg/kg PO q24 h for long-term treatment over 7 days Duration: 24 h	Pain and inflammation associated with osteoarthritis. Post-operative pain and inflammation associated with orthopedic surgery in dogs with osteoarthritis.	GI irritation and altered renal function.
Firocoxib (chewable tablets)	Dog: 5 mg/kg PO q24 h	Pain and inflammation associated with osteoarthritis and perioperative pain	GI irritation and altered renal function.
Etodolac (tablets)	Dog: 10–15 mg/kg PO Cat: not used Duration: 24 h	Mild to moderate pain	Hypoproteinemia; GI irritation and altered renal function. Associated with KCS in a small number of dogs.
Aspirin (tablets)	Dog: 10–25 mg/kg PO Cat: 10–15 mg/kg PO Duration: 8–12 h for dogs, 24–72 h for cats	Mild to moderate pain and inflammation	GI irritation and altered renal function; more likely at higher doses.

(Continued)

PAIN MANAGEMENT (CONTINUED)

Table VII-D

Recommended dispensable NSAID dosages and indications (continued)			
NSAID	Dosage/Route/Duration	Indications	Comments
Meloxicam (oral liquid suspension, tablets)	Dog: 0.2 mg/kg initially PO; 0.1 mg/kg thereafter PO Cat: 0.1–0.2 mg/kg initially PO; 0.05–0.1 mg/kg thereafter PO (reduce to minimum effective dose) Duration: 24 h	Mild to moderate pain	GI irritation and altered renal function; can be mixed with food. Cats should not be given meloxicam for > 5 days.
Robenacoxib (oral tablets)	Dog: 1 mg/kg PO q24h for up to 12 days Cat: 1 mg/kg PO q24h for up to 3 days Duration: 24 h	Mild to moderate pain; not approved for dogs in US	GI irritation and altered renal function.
Ketoprofen (tablets)	Dog: 1.0–2.0 mg/kg initially PO; 0.5–1.0 mg/kg thereafter PO Cat: 1.0–2.0 mg/kg initially PO; 0.5–1.0 mg/kg thereafter PO Duration: 24 h	Mild to moderate pain; approved in Canada for dogs and cats and in the United States for horses	GI irritation and altered renal functions. Limit administration to 5 days for both dogs and cats.
Acetaminophen (tablets and oral liquid suspension)	Dog: 10–15 mg/kg PO Cat: contraindicated Duration (in dogs): 8–12 h	Mild to moderate pain; low anti-inflammatory action	Toxic to cats; often given in combination with codeine to dogs (see oral analgesic preparations).

GI = gastrointestinal; NSAID = nonsteroidal anti-inflammatory drug; KCS = keratoconjunctivitis sicca.

Table VII-E

Dosages and indications for selected drugs used to treat neuropathic pain			
Drug	Dosage/Route	Duration (PO)	Comments
Ketamine (NMDA antagonist)	Dog: 0.1–1.0 mg/kg IM, SC, or PO Cat: 0.1–1.0 mg/kg IM or SC	4–6 h 4–6 h	Low doses potentiate postoperative analgesics. Do not use with intracranial hypertension.
Amantadine (NMDA antagonist)	Dog: 3.0–5.0 mg/kg PO Cat: 3.0–5.0 mg/kg PO	24 h 24 h	Used to potentiate or prolong analgesia. Efficacious when combined with an NSAID for management of osteoarthritis-associated pain in dogs.
Amitriptyline (tricyclic antidepressant)	Dog: 1.0 mg/kg PO Cat: 2.5–10.0 mg/cat PO	12–24 h 24 h	Used to potentiate or prolong analgesia.
Gabapentin (antiepileptic)	Dog: 2–10 mg/kg PO q8–12h; dose can be titrated up to 20 mg/kg q8–12h if necessary Cat: 1–8 mg/kg PO q8–12h	24 h 24 h	Usually associated with few side effects other than sedation, and, occasional ataxia in cats. Has shown good results in human and animal studies.

To select and administer an adjuvant analgesic properly, the veterinarian should be aware of the drug's clinical pharmacology. The following information about the drug is necessary: (1) approved indication, (2) unapproved indication (e.g., as an analgesic) widely accepted in veterinary medical practice, (3) common side effects and potentially serious adverse effects, (4) pharmacokinetic features, and (5) specific dosing guidelines for pain.

NMDA = *N*-methyl-D-aspartate.

APPENDIX VIII

CHRISTOPHER L. MARIANI

GLOSSARY OF TERMINOLOGY FOR SEIZURES AND EPILEPTIC DISORDERS

GLOSSARY OF TERMINOLOGY FOR SEIZURES AND EPILEPTIC DISORDERS

There is no formally approved classification system for seizures or epilepsy in veterinary medicine and authors proposing such systems in the past have largely adapted human classification schemes (1–5). This proposed glossary is no different and is based mainly on publications sanctioned by the International League Against Epilepsy (ILAE) (6–11). Terms have been added, changed or eliminated to better reflect the seizure types seen in veterinary patients and the challenges inherent with the interpretation of such events in animals. This glossary is adapted from a more detailed proposal of terminology for veterinary patients (12), and interested readers are referred to this work for more details on seizure description and semiology, background on ILAE classification and adaptations for animals, and rationale for the currently proposed terms.

GENERAL TERMS AND DEFINITIONS

Seizure: a discrete episode suspected to be epileptic in origin. Synonym: ictus.

Epileptic seizure: manifestation(s) of excessive and/or hypersynchronous activity of neurons in the brain; usually self-limiting.

Epilepsy: a chronic neurologic condition characterized by recurrent seizures; has an intracranial origin.

Focal seizure: a seizure whose initial signs indicate, or are consistent with, initial activation of only part of one cerebral hemisphere. Synonym: partial.

Generalized seizure: a seizure whose initial signs indicate, or are consistent with, more than minimal involvement of both cerebral hemispheres.

CLASSIFICATION OF EPILEPTIC SEIZURES

1. Motor Seizures: involving somatic musculature in any form. May consist of an increase (positive) or decrease (negative) in muscle contraction to produce a movement.

1A. Elementary Motor: a single type of contraction of a muscle or group of muscles that is usually stereotyped.

• **Tonic:** a sustained increase in muscle contraction lasting a few seconds to minutes.

• **Myoclonic:** sudden, brief (< 100 ms), involuntary single or multiple contractions of muscles or muscle groups of variable topography (axial, proximal limb, distal limb, facial).

◦ **Clonic:** myoclonus that is regularly repetitive, involves the same muscle groups,

at a frequency of approximately 2–3 per second, and is prolonged.

• **Tonic-clonic:** a sequence consisting of a tonic followed by a clonic phase.

◦ **Generalized tonic-clonic seizure:** bilateral symmetric tonic contraction and then bilateral clonic contractions of somatic muscles, usually associated with autonomic phenomena and loss of consciousness. Synonyms: grand mal seizure, bilateral tonic-clonic seizure, major motor seizure.

• **Atonic:** sudden loss or diminution of muscle tone without an apparent preceding myoclonic or tonic event lasting greater than 1–2 seconds and involving the head, trunk, jaw or limb musculature.

• **Astatic:** loss of erect posture that results from an atonic, myoclonic or tonic mechanism. Synonym: drop attack.

1B. Automatism: a more or less coordinated, repetitive, motor activity usually occurring when cognition is impaired. Often resembles a voluntary movement. Examples might include chewing, licking, aimless running, or vocal utterances (e.g., barking, meowing, whining or growling).

2. Non-motor Seizures

Aura: an ictal phenomenon that may precede an observable seizure or if occurring alone, constitutes a sensory seizure.

Sensory seizure: a perceptual experience not caused by appropriate stimuli in the external world.

Note: Although sensory seizures almost certainly occur in animals, documenting their existence is obviously very difficult without the ability of the patient to describe sensory phenomena. Therefore, we are left to observe the behavior that the suspected sensory seizure produces. Some potential sensory phenomena include visual events (e.g., flashing or flickering lights, or other objects or patterns; the animal may bite or snap in response (“fly biting”)), somatosensory events (tingling, numbness or electric-shock sensations; the animal may bite or lick itself or run frantically during episode), auditory, olfactory, gustatory and affective events (e.g., fear, depression, joy or anger; the animal may become aggressive towards people or other animals).

Dyscognitive seizure: events in which disturbance of cognition is the predominant or most apparent feature.

Note: In the ILAE glossary, cognition is composed of perception, attention, emotion, memory and executive function (which includes decision making and initiation of motor activity) (8). In animals,

without a description from the patient it may again be difficult to prove that certain dyscognitive seizure types exist or differentiate them from sensory seizures. However, certain examples (e.g., events where animals suddenly stop what they are doing and stare into space, often with a lack of appropriate responsiveness to external stimuli (“behavioral arrest”)) might be best classified here.

3. Autonomic Seizures: an objectively documented and distinct alteration of autonomic nervous system function involving cardiovascular, pupillary, gastrointestinal, sudomotor, vasomotor, and thermoregulatory functions.

MODIFIERS AND DESCRIPTORS OF SEIZURE TIMING

Duration: time between the beginning of initial seizure manifestations and the cessation of observed seizure activity. Does not include prodrome or postictal states but might include aura.

Cluster seizures: two or more seizures within a 24-hour period. Synonyms: acute repetitive seizures, serial seizures

Status epilepticus: 1) a seizure that persists for greater than 5 minutes or 2) recurrent seizures without interictal resumption of baseline central nervous system function.

Prodrome: a pre-ictal phenomenon. A subjective or objective clinical alteration (e.g., agitation, attention-seeking) that heralds the onset of an epileptic seizure but does not form part of it.

Note: It may be quite challenging or impossible to differentiate a prodrome (pre-ictal period) from an aura (start of ictus) in many veterinary patients although videotaping of the episodes, close observation and/or ictal electroencephalography may be helpful in this regard.

Postictal phenomenon: a transient clinical abnormality of central nervous system function that appears or becomes accentuated when clinical signs of the ictus have ended. May manifest as impaired mentation, altered behavior or motor or sensory deficits.

Provocative factor: transient and sporadic endogenous or exogenous element capable of augmenting seizure incidence in animals with chronic epilepsy or evoking seizures in susceptible individuals without epilepsy.

• **Reactive:** occurring in association with transient systemic perturbation or illness such as some metabolic conditions (e.g., hypoglycemia, electrolyte disorders) or intoxications.

• **Reflex:** objectively and consistently demonstrated to be evoked by a specific

(Continued)

afferent stimulus or by activity of the patient. Examples include stimuli such as light flashes, certain noises or startling and activities such as specific motor movements or more complex behaviors.

CLASSIFICATION OF EPILEPSY

Epilepsy is defined here as a chronic neurologic disorder that causes recurrent seizure activity, and that has an intracranial etiology. As stated by the ILAE Classification Core Group in 2006, “the diagnosis of epilepsy implies a persistent epileptogenic abnormality of the brain that is able to spontaneously generate paroxysmal activity. This is in contrast to a brain that has an acute seizure as a natural response to a transient insult or loss of homeostasis” (10). Thus, seizures caused by extracranial disorders such as metabolic conditions (e.g., hypoglycemia, electrolyte abnormalities) or toxins are not considered to be epilepsy, even when repetitive seizures occur over time (e.g., with hypoglycemia secondary to an insulinoma). These seizures are termed reactive seizures (see definition under “provocative factor” above).

Note however that such a disorder might secondarily cause structural damage to a previously normal brain (e.g., through necrosis or excitotoxicity) and result in true epilepsy. An explanation of the term “idiopathic epilepsy” is also warranted here, as veterinarians use the word “idiopathic” in various ways. Some use this term to imply epilepsy of genetic or heritable origin (as it was originally intended for use in humans), while others use “idiopathic” to mean “cause unknown.” The following classification is proposed to replace those previously used in veterinary medicine and has been adapted from a 2010 ILAE report (11).

Genetic epilepsy: Epilepsy as a direct result of a known or strongly suspected genetic defect or defects in which seizures are the core

sign of the disorder. Generally, genetic epilepsies have no identifiable structural brain lesion or other neurologic signs, and have an age-dependent onset. Synonyms: Primary, inherited, idiopathic (for some).

Structural epilepsy: Epilepsy as a result of one or more identifiable structural lesions of the brain. Synonyms: Symptomatic, secondary. Structural epilepsies include disorders such as brain tumors, encephalitis, and cerebrovascular accidents. Note that some disorders that may have a genetic cause or that are strongly heritable may still be best classified here; these include anomalous disorders such as hydrocephalus, lissencephaly, degenerative disorders such as ceroid lipofuscinosis, and others.

Unknown epilepsy: The underlying cause of the epilepsy is unknown. This may be the result of a subtle structural lesion that is undetectable with currently available diagnostic technologies or an as yet unrecognized genetic disorder. Synonyms: Cryptogenic, probably symptomatic, idiopathic (for some).

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APPENDIX IX

MARK G. PAPICH

Blackwell's Five-Minute Consult Drug Formulary

<i>Drug Name (Trade or Other Names)</i>	<i>Pharmacology and Indications</i>	<i>Adverse Effects and Precautions</i>	<i>Dosing Information and Comments</i>	<i>Formulations</i>	<i>Dosage (Unless Otherwise Indicated, Dose is the Same for Dogs and Cats)</i>
Acepromazine (PromAce and many generic brands)	Phenothiazine tranquilizer. Inhibits action of dopamine as neurotransmitter. Used for sedation and preanesthetic purposes.	Phenothiazines can cause sedation as a common side effect. May cause α -adrenergic blockade. Produces extrapyramidal side effects in some individuals.	Usually used as preanesthetic in combination with other drugs. When used as preanesthetic, dose is ordinarily 0.02–0.2 mg/kg IM, SC, IV.	5, 10, 25 mg tablet and 10 mg/mL injection	Dog: Sedation 0.5–2.2 mg/kg PO q6–8h, or 0.02–0.1 mg/kg IV, IM, SC in a single dose. Do not exceed 3 mg total dose in dogs Cat: Sedation 1.13–2.25 mg/kg PO q6–8h, or 0.02–0.1 mg/kg IM, SC, IV in a single dose
Acetaminophen (Tylenol and many generic brands)	Analgesic agent. Exact mechanism of action is not known. <i>Not a prostaglandin synthesis inhibitor.</i>	Well tolerated in dogs at doses listed. High doses have caused liver toxicity. <i>Do not administer to cats.</i>	Many OTC formulations available. Acetaminophen with codeine may have synergistic analgesic efficacy in some animals.	120, 160, 325, 500 mg tablets	Dog: 15 mg/kg PO q8h Cat: not recommended
Acetaminophen with codeine (Tylenol with codeine and many generic brands)	Same as above, except the opiate codeine is added to enhance analgesia	See Codeine and Acetaminophen.	See Codeine and Acetaminophen.	Oral solution and tablets. Many forms, for example: 300 mg acetaminophen plus either 15, 30, or 60 mg codeine	Dog: Follow dosing recommendations for codeine Cat: Contraindicated
Acetazolamide (Diamox)	Glaucoma, Ca inhibitor	Can potentially produce hypokalemia in some patients. Significant bicarbonate loss can occur with repeated administration. In dogs, possible respiratory acidosis.	In combination with other agents, is usually used to decrease intraocular pressure in treatment of glaucoma. Has been used to produce alkaline urine to prevent formation of some urinary calculi.	125, 250 mg tablets	5–10 mg/kg PO q8–12h (glaucoma); 4–8 mg/kg PO q8–12h (other diuretic uses)
Acetylcysteine (Mucomyst)	Decreases viscosity of secretions. Used as mucolytic agent in eyes and in bronchial nebulizing solutions. However, as a donator of sulphydryl group, used as antidote for intoxications (e.g., acetaminophen toxicosis in cats).	May cause sensitization with prolonged topical administration. May react with certain materials in nebulizing equipment.	Available as agent for decreasing viscosity of respiratory secretions, but most common use is as a treatment for intoxications	20% solution	Antidote: 140 mg/kg (loading dose), then 70 mg/kg q4h IV or PO for 5 doses Eye: 2% solution topically q2h
Acetylsalicylic acid	See Aspirin.				

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ACTH	See Corticotropin.				
Activated charcoal	See Charcoal, activated.				
Adequan	See Polysulfated glycosaminoglycan (PSGAG).				
Albendazole (Valbazen)	Benzimidazole antiparasitic drug. Inhibits glucose uptake in parasites.	At approved doses, there is a wide margin of safety. Adverse effects can include anorexia, lethargy, and bone marrow toxicity. At high doses, has been associated with bone marrow toxicity. Adverse effects are possible when administered for longer than 5 days.	Used primarily as antihelmintic, but also has demonstrated efficacy for giardiasis	113.6 mg/mL suspension and 300 mg/mL paste	25–50 mg/kg q12h PO × 3 days For <i>Giardia</i> , use 25 mg/kg q12h × 2 days For respiratory parasites, use 50 mg/kg q24h PO × 10–14 days
Albuterol (Proventil, Ventolin)	β_2 -adrenergic agonist. Bronchodilator. Stimulates β_2 receptors to relax bronchial smooth muscle. May also inhibit release of inflammatory mediators, especially from mast cells.	Causes excessive β -adrenergic stimulation at high doses (tachycardia, tremors). Arrhythmias occur at toxic doses. Avoid use in pregnant animals.	Doses are primarily derived from extrapolation of human dose. Well-controlled efficacy studies in veterinary medicine are not available. Onset of action is 15–30 min; duration of action may be as long as 8 h.	2, 4, 5 mg tablets; 2 mg/5 mL syrup	20–50 μ g/kg q6–8h; or up maximum of 100 μ g/kg q6h
Allopurinol (Lopurin, Zylorprim)	Decreases production of uric acid by inhibiting enzymes responsible for uric acid synthesis. Also used for leishmaniasis	May cause skin reactions (hypersensitivity)	Used in people primarily for treating gout. In animals, used to decrease formation of uric acid uroliths.	100, 300 mg tablets	For urate urolith, 10 mg/kg q8h, then reduce to 10 mg/kg q24h, PO For leishmaniasis, use 10 mg/kg q12h PO for at least 4 months
Alprazolam (Xanax)	Tranquilizer Benzodiazepine	Excess sedation; paradoxical excitement	Often combined with other sedatives and anesthetics	0.25, 0.5, 1, and 2 mg tablets	Dog: 0.025–0.1 mg/kg q8h, PO Cat: 0.125 mg per cat, PO q8h
Alumunium carbonate gel (Basaljel)	Antacid (neutralizes stomach acid), and phosphate binder in intestine	Generally safe. May interact with other drugs administered orally.	Antacid doses are designed to neutralize stomach acid, but duration of acid suppression is short.	Capsules (equivalent to 500 mg aluminum hydroxide)	10–30 mg/kg PO q8h (with meals)
Aluminium hydroxide gel (Amphojel)	Antacid (neutralizes stomach acid), and phosphate binder in intestine	Generally safe. May interact with other drugs administered orally.	Antacid doses are designed to neutralize stomach acid, but duration of acid suppression is short.	64 mg/mL oral suspension; 600 mg tablet	10–30 mg/kg PO q8h (with meals)

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Amikacin (Amiglyde-V [veterinary] and Amikin [human])	Aminoglycoside antibacterial drug (inhibits protein synthesis). Mechanism is similar to other aminoglycosides (see Gentamicin sulfate), but may be more active than gentamicin.	May cause nephrotoxicosis with high doses or prolonged therapy. May also cause ototoxicity and vestibulotoxicity.	Once-daily doses are designed to maximize peak minimum inhibitory concentration (MIC) ratio.	50, 250 mg/mL injection	Dog: 15–30 mg/kg q24h IV, IM, SC Cat: 10–14 mg/kg q24h IV, IM, SC
Aminopentamide (Centrine)	Antidiarrheal drug. Anticholinergic (blocks acetylcholine at parasympathetic synapse).	Use cautiously in animals with GI stasis or when anticholinergic drugs are contraindicated (e.g., glaucoma).	Dosing guidelines based on manufacturer's recommendation	0.2 mg tablets; 0.5 mg/mL injection	Dog: 0.01–0.03 mg/kg q8–12h IM, SC, PO Cat: 0.1 mg/cat q8–12h IM, SC, PO
6-Aminosalicylic acid	See Mesalamine, Olsalazine.				
Amiodarone (Cordarone)	Class III antiarrhythmic agent with potassium-channel blocking properties; indicated for severe refractory atrial and ventricular arrhythmias	Most common effect in dogs is decreased appetite. Prolonged QT interval is a concern. Other adverse effects include: bradycardia, chronic heart failure (CHF), hypotension, atrioventricular (AV) block, thyroid dysfunction, pulmonary fibrosis, and hepatotoxicity. Acute cardiac toxicity has been observed in dogs.	Use for recurrent hemodynamically unstable ventricular tachycardia; takes weeks to achieve therapeutic levels. Typically, loading doses are administered, followed by maintenance dose. Safe doses for injection have not been established.	100, 200, 300, 400 mg tablets; 50 mg/mL injection	Dog: start with 10–15 mg/kg q12h PO for 1 week, then 5–7 mg/kg q12h for 2 weeks Maintenance doses are 7.5 mg/kg q24h, PO Cat: no safe dose established
Amitraz (Mitaban)	Antiparasitic drug for ectoparasites. Used for treatment of mites, including <i>Demodex</i> . Inhibits monoamine oxidase in mites.	Causes sedation in dogs (α 2-agonist), which may be reversed by yohimbine or atipamezole. When high doses are used, other side effects reported include pruritus, polyuria and polydipsia (PU/PD), bradycardia, hypothermia, hyperglycemia, and (rarely) seizures.	Manufacturer's dose should be used initially. But, for refractory cases, this dose has been exceeded to produce increased efficacy.	10.6 mL concentrated dip (19.9%)	10.6 mL per 7.5 L water (0.025% solution). Apply 3–6 topical treatments q14d. For refractory cases, this dose has been exceeded to produce increased efficacy. Doses that have been used include: 0.025, 0.05, and 0.1% concentration applied 1–2× per week In extreme cases 0.125% solution applied to one-half of the body alternating side the next day, every day for 4 weeks to 5 months

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Amitriptyline hydrochloride (Elavil)	Tricyclic antidepressant drug. Action is via inhibition of uptake of serotonin and other transmitters at presynaptic nerve terminals. Used in animals to treat variety of behavioral disorders, such as anxiety. Used in cats for chronic idiopathic cystitis.	Multiple side effects are associated with tricyclic antidepressants, such as antimuscarinic effects (dry mouth, rapid heart rate) and antihistamine effects (sedation). High doses can produce life-threatening cardiotoxicity. In cats, reduced grooming, weight gain, and sedation are possible.	Doses are primarily based on empiricism. There are no controlled efficacy trials available for animals. There is evidence for success treating idiopathic cystitis in cats. Clomipramine is preferred for behavior problems.	10, 25, 50, 75, 100, 150 mg tablets	Dog: 1–2 mg/kg PO q12–24h Cat: 2–4 mg per cat/day PO (0.5–1.0 mg/kg PO/day. May be divided into 12h intervals.); cystitis: 2 mg/kg/day PO (2.5–7.5 mg/cat/day)
Amlodipine besylate (Norvasc)	Calcium channel-blocking drug of the dihydropyridine class. Decreases calcium influx in cardiac and vascular smooth muscle. Its greatest effect is as a vasodilator. In cats and dogs, it is used to treat hypertension.	Can cause hypotension and bradycardia. Use cautiously with other vasodilators.	In cats, efficacy has been established at 0.625 mg/cat once daily. If cats are large size (> 4.5 kg) or refractory, increase to higher dose (J Vet Int Med 12:157–162, 1998).	2.5, 5, and 10 mg tablets	Dog: 2.5 mg/dog, or 0.1 mg/kg once daily PO Cat: 0.625 mg/cat initially, PO once daily, and increase if needed to 1.25 mg/cat (average is 0.18 mg/kg, once daily for hypertension)
Ammonium chloride (generic)	Urine acidifier	Do not use in patients with systemic acidemia. May be unpalatable when added to some animals' food.	Doses are designed to maximize urine acidifying effect.	Available as crystals	Dog: 100 mg/kg q12h PO Cat: 800 mg/cat (approximately 1/3 to 1/4 tsp) mixed with food daily
Amoxicillin (Amoxi-Tabs, Biomox, and other brands. [Omnipen, Principen, Totacillin are human forms])	β -lactam antibiotic. Inhibits bacterial: cell wall synthesis. Generally broad-spectrum activity. Used for a variety of infections in all species.	Usually well tolerated. Allergic reactions are possible. Diarrhea is possible with oral doses.	Dose recommendations vary depending on the susceptibility of bacteria and location of infection.	50, 100, 150, 200, 400 mg tablets; 250 and 500 mg capsules; 50 mg/mL oral suspension (human forms)	6.6–20 mg/kg q8–12h PO
Amoxicillin + clavulanate potassium (Clavamox)	β -lactam antibiotic + β -lactamase inhibitor (clavulanate/clavulanic acid)	Same as for amoxicillin	Same as for amoxicillin	62.5, 125, 250, 375 mg tablets and 62.5 mg/mL suspension	Dog: 12.5–25 mg/kg q12h PO Cat: 62.5 mg/cat q12h PO.

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Amphotericin B (Fungizone)	Antifungal drug. Fungicidal for systemic fungi, by damaging fungal membranes.	Produces a dose-related nephrotoxicosis. Also produces fever, phlebitis, and tremors.	Administer IV via slow infusion diluted in fluids, and monitor renal function closely. When preparing IV solution, do not mix with electrolyte solutions (use D-5-W, for example); administer NaCl fluid loading before therapy.	50 mg injectable vial	Dog: 0.5 mg/kg IV (slow infusion) q48h to a cumulative dose of 4–8 mg/kg Cat: 0.25 mg/kg IV (slow infusion) q48h
Amphotericin B, liposomal formulation (ABLC, Abelcet)	Same indications as for conventional amphotericin B. Liposomal formulations may be used at higher doses, and safety margin is increased. Expense is much higher than for conventional formulations.	Renal toxicity is the most dose-limiting effect.	Higher doses can be used compared to conventional formulation of amphotericin B. Dilute in 5% dextrose in water to 1 mg/mL, and administer IV over 1–2 hours.	100 mg/20 mL in lipid formulation	Dog: 2–3 mg/kg IV 3 times/week for 9–12 treatments to a cumulative dose of 24–27 mg/kg Cat: 1 mg/kg IV 3 times/week for up to 12 treatments
Ampicillin (Omnipen, Principen, others [human forms])	β -lactam antibiotic. Inhibits bacterial cell wall synthesis.	Use cautiously in animals allergic to penicillin-like drugs.	Dose requirements vary depending on susceptibility of bacteria. Absorbed approximately 50% less, compared with amoxicillin, when administered orally.	250, 500 mg capsules; 125, 250, 500 mg vials of ampicillin sodium. Ampicillin trihydrate: 10 and 25 g vials for injection	Ampicillin sodium: 10–20 mg/kg q6–8h IV, IM, SC or 20–40 mg/kg q8h PO Ampicillin trihydrate: Dog: 10–50 mg/kg q12–24h IM, SC Cat: 10–20 mg/kg q12–24h IM, SC
Ampicillin + sulbactam (Unasyn)	Ampicillin plus a β -lactamase inhibitor (sulbactam). Sulbactam has similar activity as clavulanate.	Same as for ampicillin	Same as for amoxicillin + clavulanate.	2:1 combination for injection. 1.5 and 3 g vials	10–20 mg/kg IV, IM q8h
Ampicillin trihydrate (Polyflex)	β -lactam antibiotic. Inhibits bacterial cell wall synthesis.	Use cautiously in animals allergic to penicillin-like drugs.	Absorption is slow and may not be sufficient for acute serious infection.	10, 25 mg vials for injection	Dog: 10–50 mg/kg q12–24h IM, SC Cat: 10–20 mg/kg q12–24h IM, SC
Amprolium (Corid)	Enteric coccidiostat	Toxicity observed only at high doses. CNS signs are caused by thiamin deficiency, which may be reversed by adding thiamin to the diet.	Used to control and treat coccidiosis in puppies. It is administered orally, often mixed with food.	9.6% (9.6 g/dL) oral solution; soluble powder	1.25 g of 20% amprolium powder to daily feed, or 30 mL of 9.6% amprolium solution to 3.8 L of drinking water for 7 days

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Antacid drugs	See Aluminum hydroxide, Magnesium hydroxide, Calcium carbonate.				
Apomorphine hydrochloride (generic)	Emetic drug. Causes emesis via dopamine release or direct effects on chemoreceptor trigger zone	Produces emesis before serious adverse effects occur. Use cautiously in cats that may be sensitive to opiates.	Consult local poison center or pharmacist for availability. Not as effective in cats as dogs.	6 mg tablets 10 mg/mL ampule or 3 mL preloaded syringes	0.03–0.05 mg/kg IV IM, 0.1 mg/kg SC, or instill 0.25 mg in conjunctiva of eye (dissolve 6 mg tablet in 1–2 mL of saline)
Ascorbic acid (Vitamin C)	Vitamin. Used as acidifier.	Toxicity only at very high doses	Primarily used as nutritional supplement, but high doses have been used for treatment of certain diseases.	Various forms, including 250 mg/ml sodium ascorbate	100–500 mg/animal/day (diet supplement), or 100 mg/animal q8h (urine acidification)
L-Asparaginase (Elspar)	Anticancer agent. Purified enzyme from <i>E. coli</i> . Used in lymphoma protocols. Depletes cancer cells of asparagine and interferes with protein synthesis.	Hypersensitivity, allergic reactions	Usually used in combination with other drugs in cancer chemotherapy protocols	10,000 U per vial for injection	Dog: 400 U/kg IM weekly or 10,000 U/m ² weekly × 3 weeks Cat: 400 U/kg SC weekly
Aspirin (many generic and brand names [Bufferin, Ascriptin])	Nonsteroidal anti-inflammatory drug (NSAID). Anti-inflammatory action is generally considered to be caused by inhibition of prostaglandins. Used as analgesic, anti-inflammatory, and antiplatelet drug.	Narrow therapeutic index. High doses frequently cause vomiting. Other GI effects can include ulceration and bleeding. Cats susceptible to salicylate intoxication because of slow clearance. Use cautiously in patients with coagulopathies because of platelet inhibition.	Analgesic and anti-inflammatory doses have primarily been derived from empiricism. Antiplatelet doses are lower because of prolonged effect of aspirin on platelets.	81, 325 mg tablets	Mild analgesia: (dog) 10 mg/kg q12h PO Anti-inflammatory: Dog: 20–25 mg/kg q12h PO Cat: 10–20 mg/kg q48h PO Antiplatelet: Dog: 5–10 mg/kg q24–48h PO Cat: 81 mg/cat q48–72h PO
Atenolol (Tenormin)	β-adrenergic blocker. Relatively selective for β ₁ -receptor. Used primarily as an antiarrhythmic or for other cardiovascular conditions to slow sinus rate.	Bradycardia and heart block are possible. May produce bronchospasm in sensitive patients.	Dosing precautions are similar to other β-blocking drugs. Atenolol is reported to be less affected by changes in hepatic metabolism than other β-blockers.	25, 50, 100 mg tablets	Dog: 6.25–12.5 mg/dog q12–24h (or 0.25–1.0 mg/kg q12–24h), PO Cat: 6.25–12.5 mg per cat q12h PO

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Atipamezole (Antisedan)	α_2 -antagonist. Used to reverse α_2 -agonists, such as dexmedetomidine and xylazine.	Can cause some initial excitement in some animals shortly after reversal.	When used to reverse dexmedetomidine, inject same volume as used for dexmedetomidine.	5 mg/mL injection	Inject same volume as used for dexmedetomidine. Range of doses = 0.32 mg/kg for small animals to 0.14 mg/kg for large dogs
Atovaquone (Mepron)	In animals, it has been used, often in combination with azithromycin, to treat refractory protozoan diseases and bloodborne pathogens. In dogs, it has been used to treat Babesia gibsoni.	Adverse effects have not been reported in animals. In people, adverse reactions consist of skin rash, cough, and diarrhea.	There has been only limited experience for treatment of infections in animals. A few clinical trials have shown efficacy when combined with azithromycin for treatment of protozoa infections.	750 mg/5 mL liquid oral suspension (150 mg/mL)	Dog: 13.3 mg/kg q8h, PO for 10 days, usually in combination with azithromycin (10 mg/kg q24h, PO) Cat: 15 mg/kg q8h, PO, in combination with azithromycin (10 mg/kg q24h)
Atracurium (Tracrium)	Neuromuscular blocking agent (nondepolarizing). Competes with acetylcholine at neuromuscular end plate. Used primarily during anesthesia or other conditions in which it is necessary to inhibit muscle contractions.	Produces respiratory depression and paralysis. Neuromuscular blocking drugs have no effect on analgesia.	Administer only in situations in which careful control of respiration is possible. Doses may need to be individualized for optimum effect. Do not mix with alkalinizing solutions or lactated Ringer's solution.	10 mg/mL injection	0.2 mg/kg IV initially, then 0.15 mg/kg every 30 min (or IV infusion at 4–9 μ g/kg/min)
Atropine (many generic brands)	Anticholinergic agent (blocks acetylcholine effect at muscarinic receptor), parasympatholytic. Used primarily as adjunct to anesthesia or other procedures to increase heart rate and decrease respiratory and gastrointestinal secretion. Also used as antidote for organophosphate intoxication.	Potent anticholinergic agent. Do not use in patients with glaucoma, intestinal ileus, gastroparesis, or tachycardia. Side effects of therapy include xerostomia, ileus, constipation, tachycardia, urine retention.	Used ordinarily as adjunct with anesthesia or other procedures. Do not mix with alkaline solutions.	400, 500, 540 μ g/mL injection; 15 mg/mL injection	0.02–0.04 mg/kg q6–8h IV, IM, SC; 0.2–0.5 mg/kg IV, IM (as needed) for organophosphate and carbamate toxicosis

<i>Drug Name (Trade or Other Names)</i>	<i>Pharmacology and Indications</i>	<i>Adverse Effects and Precautions</i>	<i>Dosing Information and Comments</i>	<i>Formulations</i>	<i>Dosage (Unless Otherwise Indicated, Dose is the Same for Dogs and Cats)</i>
Azathioprine (Imuran)	Thiopurine immunosuppressive drug. Acts to inhibit T cell lymphocyte function. This drug is metabolized to 6-mercaptopurine, which may account for immunosuppressive effects. Used to treat various immune-mediated disease.	Bone marrow suppression is most serious concern. Cats particularly are susceptible. There has been some association with development of pancreatitis when administered with corticosteroids.	Usually used in combination with other immunosuppressive drugs (such as corticosteroids) to treat immune-mediated disease. Doses of 2.2 mg/kg in cats have produced toxicity.	25, 50, 75, and 100 mg tablets; 10 mg/mL for injection	Dog: 2 mg/kg q24h PO initially then 0.5–1 mg/kg q48h Cat (use cautiously): 0.3 mg/kg q24h PO initially, then q48h, with careful monitoring (will require compounding)
Azithromycin (Zithromax)	Azalide antibiotic. Similar mechanism of action as macrolides (erythromycin), which is to inhibit bacteria protein synthesis via inhibition of ribosome. Spectrum is primarily gram-positive.	Vomiting is likely with high doses. Diarrhea may occur in some patients.	Azithromycin may be better tolerated than erythromycin. Primary difference from other antibiotics is the high intracellular concentrations achieved.	250 mg capsules, 250 and 600 mg tablets, 100 or 200 mg/5 mL oral suspension, and 500 mg vials for injection	Dog: 5–10 mg/kg PO once daily for 5–7 days then tapering to q48h Cat: 5–10 mg/kg PO once daily for 7 days, then tapering to q48h; upper respiratory infection: 15 mg/kg q72h PO
AZT (Azidothymidine)	See Zidovudine.				
BAL (British antilewisite)	See Dimercaprol.				
Benazepril (Lotensin)	Angiotensin-converting enzyme (ACE) inhibitor. Used for hypertension and heart failure. Action is similar to enalapril and captopril	Similar to those for captopril and enalapril	Dose is based on approved use in dogs in Europe and Canada. Monitor renal function and electrolytes 3–7 days after initiating therapy and periodically thereafter.	5, 10, 20, 40 mg tablets	Dog: 0.25–0.5 mg/kg q24h PO, may be increased to 1 mg/kg in dogs that are not responsive. Cat (systemic hypertension and renal disease): 0.5–1 mg/kg q24h PO, or 2.5 mg/cat per day up to maximum of 5 mg/cat per day PO
Bethanechol chloride (Urecholine)	Muscarinic, cholinergic agonist. Parasympathomimetic. Stimulates gastric and intestinal motility, but primarily used to increase contraction of urinary bladder.	High doses of cholinergic agonists will increase motility of GI tract and cause abdominal discomfort and diarrhea. Can cause circulatory depression in sensitive animals.	Administer injection SC only, <i>not</i> IV. Doses are derived from extrapolation of human doses or via empiricism. There are no well-controlled efficacy studies available for veterinary species.	No longer commercially available. However, available through compounding pharmacies	Dog: 5–15 mg/dog q8h PO Cat: 1.25–5 mg/cat q8h PO

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Bisacodyl (Dulcolax)	Laxative/cathartic. Acts via local stimulation of GI motility, most likely by irritation of bowel. Used primarily as laxative or for procedures in which bowel evacuation is necessary.	Avoid use in patients with renal disease. Avoid overuse.	Available as OTC tablet. Doses are derived from extrapolation of human doses or via empiricism. There are no well-controlled efficacy studies available for veterinary species. Onset of action is approx. 1 h.	5 mg tablets	Dog: 5 mg/animal q8–24h PO Cat: 5 mg/cat q24h PO
Bismuth subsalicylate (Pepto-Bismol)	Antidiarrhea agent and GI protectant. Anti-prostaglandin action of salicylate component may be beneficial for enteritis. Bismuth component is efficacious or treating infections caused by spirochete bacteria (<i>Helicobacter gastritis</i>).	Adverse effects are uncommon; however, salicylate component is absorbed systemically, and overuse should be avoided in animals that cannot tolerate salicylates (such as cats and animals allergic to aspirin). Owners should be warned that bismuth will discolor stools.	Available as OTC product. Doses are derived from extrapolation of human doses or via empiricism. There are no well-controlled efficacy studies available for veterinary species.	Oral suspension: 262 mg/15 mL, or 525 mg/mL in extra strength formulation; 262 mg tablets	1–3 mL/kg/day (in divided doses) PO
Bleomycin (Blenoxane)	Anticancer, antibiotic agent. Used for treatment of various sarcomas and carcinomas. Exact mechanism of action is unknown, but may bind to DNA and prevent synthesis.	Causes local reaction at site of injection. Causes pulmonary toxicity in people as well as fever and chills, but side effects are not well documented in veterinary species.	Injectable solution usually used in combination with other anticancer agents. Consult anticancer protocols for details regarding use.	15 U vials for injection	Dog: 10 U/m ² IV or SC q24h for 3 days, then 10 U/m ² weekly (maximum cumulative dose 200 U/m ²)
Budesonide (Entocort)	Corticosteroid. Budesonide is a locally-acting corticosteroid. It is designed to release locally – in the intestine – after oral administration. Only a small fraction is absorbed systemically. Budesonide is used to treat inflammatory bowel disease.	No serious adverse effects are reported. However, some systemic absorption may cause glucocorticoid effects in animals (such as adrenal suppression).	The capsules are designed for human use. When administering to animals, do not disrupt the coating on the drug or the intestinal release may be compromised.	1, 3 mg capsule	0.125 mg/kg q6–8h, PO. Dose interval may be increased to every 12 hours when condition improves

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Bunamidine hydrochloride (Scolaban)	Used as anticestodal agent. Primarily to treat tapeworm infections in dogs and cats. Mechanism of action is to damage integrity of protective integument on parasite.	Vomiting and diarrhea have occurred after use. Avoid use in young animals.	Do not break tablets. Administer tablets on empty stomach. Do not feed for 3 h after administration.	100, 200, 400 mg tablets	20–50 mg/kg once PO
Bupivacaine hydrochloride (Marcaine, and generics)	Local anesthetic. Inhibits nerve conduction via sodium channel blockade. Longer-acting and more potent than lidocaine or other local anesthetics.	Adverse effects rare with local infiltration. High doses absorbed systemically can cause nervous system signs (tremors and convulsions). After epidural administration, respiratory paralysis is possible with high doses.	Used for local infiltration or infusion into epidural space. One may admix 0.1 mEq sodium bicarbonate per 10 mL solution to increase pH, decrease pain from injection, and increase onset. Use immediately after mixing with bicarbonate.	2.5 and 5 mg/mL solution injection	1 mL of 0.5% solution per 10 cm for an epidural
Buprenorphine hydrochloride (Buprenex [Vetergesic in the UK]) Simbadol	Opioid analgesic. Partial μ -receptor agonist, κ -receptor antagonist. 25–50 \times more potent than morphine. Buprenorphine may cause less respiratory depression than other opiates.	Adverse effects are similar to other opiate agonists, except there may be less respiratory depression. Dependency from chronic use may be less than with pure agonists.	Used for analgesia, often in combination with other analgesics or in conjunction with general anesthesia. Longer acting than morphine. Only partially reversed by naloxone	0.324 mg/mL solution, 1.8 mg/mL solution for SC administration in cats. For people, transdermal patches and buccal tablets also are available.	Dog: 0.02 mg/kg IV, IM, SC q4–8h Cat: 0.01–0.02 mg/kg IV, IM, q4–8h Buccal administration in cat: 0.02–0.04 mg/kg q8h, SC administration to cats using Symbadol 1.8 mg/mL solution: 0.24 mg/kg q24h, SC.
Buspirone (BuSpar)	Antianxiety agent. Acts by binding to serotonin receptors. In veterinary medicine, has been primarily used for treatment of urine spraying in cats.	Some cats show increased aggression; some cats show increased affection to owners.	Some efficacy trials suggest effectiveness for treating urine spraying in cats. There may be a lower relapse rate compared to other drugs.	5, 10, 15, and 30 mg tablets	Dog: 2.5–10 mg/dog q12–24h PO or 1 mg/kg q12h PO Cat: 2.5–5 mg/cat q12–24h PO (may be increased to 5–7.5 mg per cat twice daily for some cats)
Busulfan (Myleran)	Anticancer agent. Bifunctional alkylating agent and acts to disrupt DNA of tumor cells. Used primarily for lymphoreticular neoplasia.	Leukopenia is most severe side effect.	Usually used in combination with other anticancer agents. Consult specific protocol for details.	2 mg tablets	3–4 mg/m ² q24h PO

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Butorphanol tartrate (Torbutrol, Torbugesic)	Opioid analgesic. κ -receptor agonist and weak μ -receptor antagonist. Butorphanol is used for perioperative analgesia, chronic pain, and as an antitussive agent.	Adverse effects are similar to other opioid analgesic drugs. Sedation is common at analgesic doses. Respiratory depression can occur with high doses. Dysphoric effects have been observed with some agonist/antagonist drugs.	Often used in combination with anesthetic agents or in conjunction with other analgesic drugs.	1, 5, 10 mg tablets; 0.5 or 10 mg/mL injection	Dog: (antitussive) 0.055 mg/kg q6–12h SC or 0.55–1 mg/kg q6–12h PO; (preanesthetic) 0.2–0.4 mg/kg IV, IM, SC (with acepromazine); (analgesic) 0.2–0.4 mg/kg q2–4h IV, IM, SC Cat (analgesic): 0.2–0.4 mg/kg q2–6h, IV, SC or 1.5 mg/kg PO q4–8h
Calcitriol (Rocaltrol, Calcijex)	Used to treat calcium deficiency and diseases such as hypocalcemia associated with hypoparathyroidism. Also used to lower parathyroid levels in patients with renal secondary hyperparathyroidism. Not indicated as vitamin D supplement. Action is to increase calcium absorption in intestine.	Overdose can result in hypercalcemia.	Doses should be adjusted in each patient according to response and monitoring of calcium plasma concentration, (hypoparathyroidism) or parathyroid levels (renal secondary hyperparathyroidism).	Available as injection (Calcijex) and capsules (Rocaltrol); 0.25, 0.5 μ g capsules, 1 or 2 μ g/mL injection, and 1 μ g/mL oral solution (Rocaltrol)	Dog: 2.5–3.5 ng/kg PO q24h Cat: 0.25 μ g/cat q48h PO Renal secondary hyperparathyroidism: 2.5–3.5 ng/kg PO q24h
Calcium carbonate (many brands available: Titrалac, Tums, generic)	Used as oral calcium supplement for hypocalcemia. Used as antacid to treat gastric hyperacidity and GI ulcers. Neutralizes stomach acid. Also used as intestinal phosphate binder for hyperphosphatemia.	Few side effects. Increased calcium concentrations are possible. <i>Drug interactions:</i> Avoid use with oral fluoroquinolones (e.g., ciprofloxacin, enrofloxacin) as it may decrease their absorption.	Doses are primarily derived from extrapolation of human doses. When used as calcium supplement, doses should be adjusted according to serum calcium concentrations.	Many tablets or oral suspension, e.g., 650 mg tablets (contain 260 mg calcium ion)	Phosphate binder: 60–100 mg/kg/day in divided doses PO with food Calcium supplementation: 70–180 mg/kg/day with food
Calcium chloride (generic)	Calcium supplement. Used in acute situations to supplement as electrolyte replacement or as a cardiotonic.	Overdose with calcium is possible. Do not administer IV solution SC or IM because it may cause tissue necrosis.	Injection is 27.2 mg of calcium ion (1.36 mEq) per mL. Usually used in emergency situations. Intracardiac administration has been performed, but avoid injections into the myocardium.	10% (100 mg/mL) solution	0.1–0.3 mL/kg IV (slowly)

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Calcium citrate (Citracal [OTC])	Calcium supplement. Used in treatment of hypocalcemia, such as with hypoparathyroidism.	Hypercalcemia possible with oversupplementation.	Doses should be adjusted according to serum calcium concentration.	950 mg tablets (contain 200 mg calcium ion)	Dog: 20 mg/kg/day PO (with meals) Cat: 10–30 mg/kg q8h PO (with meals)
Calcium disodium EDTA	See Eddetate calcium disodium.				
Calcium gluconate (Kalcinate and generic)	Calcium supplement. Used in treatment of hypocalcemia, such as with hypoparathyroidism. Used in electrolyte deficiency.	Hypercalcemia possible with over supplementation.	Injection is 97 mg (9.5 mg of calcium ion [0.47 mEq]) per mL. 500 mg tablets contain 45 mg of calcium ion. Avoid administration of IV solution IM or SC because it will cause tissue necrosis.	10% (100 mg/mL) injection	50–200 mg/kg IV (slowly)
Calcium lactate (generic)	Calcium supplement	Hypercalcemia possible with over supplementation.	Calcium lactate contains 130 mg of calcium ion per gram.	325 mg, 650 mg OTC tablets	Dog: 0.5 g/dog/day PO (in divided doses) Cat: 0.2–0.5 g/cat/day PO (in divided doses)
Captopril (Capoten)	ACE inhibitor. Inhibits conversion of angiotensin I to angiotensin II. Generally used to treat hypertension and congestive heart failure.	Hypotension possible with excessive doses. May cause azotemia in some patients, especially when administered with potent diuretics (furosemide). <i>Drug interactions:</i> Use cautiously with diuretics, potassium supplements. NSAIDs may diminish antihypertensive effect.	Monitor patients carefully to avoid hypotension. With all ACE inhibitors, monitor electrolytes and renal function 3–7 days after initiating therapy and periodically thereafter. Use of captopril has been replaced by enalapril and benazepril in dogs and cats.	25 mg tablet	Dog: 0.5–2 mg/kg q8–12h PO Cat: 3.12–6.25 mg/cat q8h PO
Carbimazole (Neomercazole)	Antithyroid drug converted to methimazole for activity.	Similar to methimazole, with perhaps fewer GI effects.	Used in Europe. Clinical experience in US is limited.	Available in Europe, but not US	Cat: 5 mg/cat q8h PO (induction), followed by 5 mg/cat q12h PO
Carboplatin (Paraplatin)	Anticancer agent. Used for treating various carcinomas. Interrupts replication of DNA in tumor cells by cross-linking. Used for squamous cell carcinoma and other carcinomas, melanoma, osteosarcomas, and other sarcomas. Action is similar to cisplatin.	Dose-limiting toxicosis is myelosuppression. May cause anemia, leukopenia, or thrombocytopenia. Carboplatin may induce renal toxicity. Compared to cisplatin, carboplatin is less emetogenic and less nephrotoxic. In cats, causes a dose-limiting neutropenia and thrombocytopenia with a nadir at 17 days.	Available for reconstitution for injection. Do not use with administration sets containing aluminum, because of incompatibility. Usually administered in specific anticancer protocols.	50 and 150 mg vial for injection	Dog: 300 mg/m ² every 3–4 weeks IV Cat: 200–227 mg/m ² every 4 weeks IV × 4 treatments

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Carprofen (Rimadyl; Zenecarp in the UK) Novox (generic)	NSAID. Used for treatment of pain and inflammation, particularly pain and inflammation associated with osteoarthritis. Shown to be safe and effective for perioperative use for surgical pain either by injection or PO. Carprofen's action may be via cyclooxygenase inhibition but is relatively COX-1 sparing.	Most common adverse effects in clinical patients have been GI (vomiting, nausea, diarrhea). Other adverse effects are more rare and include idiosyncratic hepatotoxicosis. If they occur, signs of hepatotoxicosis appear 2–3 weeks after beginning therapy. Perioperative use has not adversely affected renal function or bleeding times. Avoid use with other NSAIDs or with corticosteroids.	Doses are based on manufacturer's field trials and US registration data. Clinical trials conducted with canine patients with osteoarthritis and surgical patients. Injectable carprofen administered for surgery may be given 2 hours prior to the procedure.	25, 75, 100 mg tablets (regular and chewable); 50 mg/mL injectable solution	Dog: 4.4 mg/kg/day PO, administered either once a day or divided into 2.2 mg/kg q12h; 4.4 mg/kg/day SC, administered once daily or 2.2 mg/kg q12h Cat: 4 mg/kg one-time injection
Carvedilol (Coreg)	Nonselective β -blocker with α -blocking and antioxidant properties; indicated for systemic hypertension and upregulation of β -receptors in animals with myocardial failure.	Bradycardia, CHF due to initial myocardial depression. Adverse effects from nonselective β -blockade are possible, including weakness and bronchospasm.	Typical starting dose is 0.2 mg/kg q12h, then gradually titrate the dose upward to 0.4 mg/kg. If signs of heart failure worsen at higher doses, lower to the previously well-tolerated dose. Oral absorption highly variable in dogs.	3.125, 6.25, 12.5, 25 mg tablets	Dog: 0.2–0.4 mg/kg q12h PO. If not in heart failure, the dose could cautiously be titrated to 1.5 mg/kg q12h PO based on pharmacokinetic studies. Cat: no dose established
Cascara sagrada (many brands [e.g., Nature's Remedy])	Stimulant cathartic. Action is believed to be by local stimulation of bowel motility. Used as laxative to treat constipation or evacuate bowel for procedures.	Overuse can cause electrolyte losses.	Available in various OTC products.	100 and 325 mg tablets and oral liquid	Dog: 1–5 mg/kg/day PO Cat: 1–2 mg/cat/day PO
Castor oil (generic)	Stimulant cathartic. Action is believed to be by local stimulation of bowel motility. Used as laxative to treat constipation or evacuate bowel for procedures.	Overuse can cause electrolyte losses. Castor oil has been known to stimulate premature labor in pregnancy.	Available as OTC product	Oral liquid (100%)	Dog: 8–30 mL/day PO Cat: 4–10 mL/day PO

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Cefadroxil (Cefa-Tabs, Cefa-Drops)	Cefadroxil is a 1st-generation cephalosporin antibiotic.	Cefadroxil has been known to cause vomiting after oral administration in dogs.	Spectrum of cefadroxil is similar to other 1st-generation cephalosporins. For susceptibility test, use cephalothin as test drug.	50 mg/mL oral suspension; 50, 100, 200, 1000 mg tablet. Availability of some oral formulations is inconsistent.	Dog: 22 mg/kg q12h, up to 30 mg/kg q12h PO Cat: 22 mg/kg q24h PO
Cefazolin sodium (Ancef, Kefzol, and generic)	Cefazolin is a 1st-generation cephalosporin antibiotic.	Adverse effects uncommon.	Commonly used 1st-generation cephalosporin as injectable drug for prophylaxis for surgery as well as for acute therapy for serious infections.	50 and 100 mg/50 mL for injection	20–35 mg/kg q8h IV, IM. For perisurgical use: 22 mg/kg q2h IV during surgery.
Cefepime (Maxipime)	4th-generation cephalosporin with broader spectrum than other classes.	Similar adverse effects as other cephalosporins.	Dosing regimens are based on pharmacokinetic studies in dogs.	500 mg; 2 g vials for injection	Dog: 40 mg/kg q6h IM or IV
Cefotaxime sodium (Claforan)	Cefotaxime is a 3rd-generation cephalosporin. Cefotaxime is used when resistance is encountered to other antibiotics or when infection is in central nervous system.	Similar to those of other cephalosporins.	3rd-generation cephalosporin used when resistance encountered to 1st- and 2nd-generation cephalosporins.	500 mg; 1, 2, and 10 g vials for injection	Dog: 50 mg/kg IV, IM, SC q12h Cat: 20–80 mg/kg q6h IV, IM
Cefovecin (Convenia)	3rd-generation cephalosporin for injection in dogs and cats. Very long half-life compared to other cephalosporins.	Adverse effects may include transient GI problems.	Dose intervals are usually q14d in dogs and cats, or a single injection.	80 mg/mL vial for injection	Dog and Cat: 8 mg/kg SC every 14 days, injections may be repeated
Cefoxitin sodium (Mefoxin)	Cefoxitin is a 2nd-generation cephalosporin. May have increased activity against anaerobic bacteria.	Similar to those of other cephalosporins.	2nd-generation cephalosporin, which is often used when activity against anaerobic bacteria is desired.	1, 2, and 10 g vials for injection (20 or 40 mg/mL)	30 mg/kg q6–8h IV, IM, presurgical use: 22 mg/kg IV
Cefpodoxime proxetil (Simplicef)	Oral 3rd-generation cephalosporin. Activity includes gram-negative bacilli and staphylococcus.	Vomiting and diarrhea are the most common adverse effects.	Approved for skin and soft-tissue infections in dogs.	100, 200 mg tablets	Dog: 5–10 mg/kg PO q24h Cat: dose not established
Ceftazidime (Fortaz, Ceptaz, Tazicef)	3rd-generation cephalosporin. Ceftazidime has more activity than other cephalosporins against <i>Pseudomonas aeruginosa</i> .	Similar to those of other cephalosporins.	3rd-generation cephalosporin. May be reconstituted with 1% lidocaine for IM injection.	Vials (0.5, 1, 2, 6 g) reconstituted to 280 mg/mL	Dog and Cat: 30 mg/kg q6h IV, IM Dog: 30 mg/kg q4–6h SC

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Ceftiofur (Naxcel [ceftiofur sodium]; Excenel [ceftiofur HCl]).	Ceftiofur spectrum resembles many of the 3rd-generation cephalosporins.	Similar to those of other cephalosporins. Do not substitute the crystalline free acid (Excede) for Naxcel.	Available as powder for reconstitution prior to injection. After reconstitution, stable for 7 days when refrigerated or 12 h at room temperature, or frozen for 8 weeks.	50 mg/mL injection	2.2–4.4 mg/kg SC q24h (for urinary tract infections)
Cephalexin (Keflex and generic forms)	Cephalexin is a 1st-generation cephalosporin.	Similar to those of other cephalosporins.	Veterinary approved chewable formulations and human generic formulations are both used in veterinary medicine.	250, 500 mg capsules; 250, 500 mg tablets; 100 mg/mL oral suspension, and 125, 250 mg/5 mL oral suspension	Dog: 22–25 mg/kg q12h, PO Cat: 15–20 mg/kg q12h PO
Cetirizine (Zyrtec)	Antihistamine (H-1 blocker). It acts by blocking the histamine type-1 receptor (H1) and suppressing inflammatory reactions caused by histamine. The H1-blockers have been used to control pruritus and skin inflammation, rhinorrhea, and airway inflammation. Cetirizine is considered a 2nd-generation antihistamine, which may be associated with less sedation than older drugs.	No adverse effects have been reported in dogs or cats.	There are no studies published that demonstrate clinical efficacy in dogs and cats. Clinical use is based on experimental animals.	1 mg/mL oral syrup; 5 and 10 mg tablets	Dog: 2 mg/kg, q12h, PO Cat: 1 mg/kg per day, PO
Charcoal, activated (Acta-Char, Charcodote, Toxiban, generic)	Adsorbent. Used primarily to adsorb drugs and toxins in intestine to prevent their absorption	Not absorbed systemically. Safe for administration	Available in variety of forms; usually used as treatment of poisoning. Many commercial preparations contain sorbitol, which acts as flavoring agent and promotes intestinal catharsis.	Oral suspension and granules	1–4 g/kg PO (granules); 6–12 mL/kg (suspension)
Chlorambucil (Leukeran)	Cytotoxic agent. Acts in similar manner as cyclophosphamide as alkylating agent. Used for treatment of various tumors and immunosuppressive therapy.	Myelosuppression is possible.	Consult anticancer drug protocol for specific regimens.	2 mg tablets	Dog: 2–6 mg/m ² q24h initially, then q48h PO Cat: 0.1–0.2 mg/kg q24h initially, then q48h PO

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Chloramphenicol and chloramphenicol palmitate (Chloromycetin, generic forms)	Antibacterial drug. Mechanism of action is inhibition of protein synthesis via binding to ribosome. Broad spectrum of activity.	Bone marrow suppression is possible with high doses or prolonged treatment (especially in cats). Avoid use in pregnant or neonatal animals. Drug interactions with other drugs (e.g., barbiturates) possible because chloramphenicol will inhibit hepatic microsomal enzymes.	Chloramphenicol palmitate requires active enzymes and should not be administered to fasted (or anorectic) animals. Note: Some forms of chloramphenicol are no longer available in the US.	30 mg/mL oral suspension (palmitate), 250 mg capsules, and 100, 250, and 500 mg tablets	Dog: 50 mg/kg q8h PO Cat: 50 mg/cat q12h PO or 12.5–20 mg/kg q12h PO
Chlorothiazide (Diuril)	Thiazide diuretic. Inhibits sodium reabsorption in distal renal tubules. Used as diuretic and antihypertensive. Since it decreases renal excretion of calcium, it also has been used to treat calcium-containing uroliths.	Do not use in patient with elevated calcium. May cause electrolyte imbalance, such as hypokalemia	Not as effective as high-ceiling diuretics (such as furosemide).	250 and 500 mg tablets, 50 mg/mL oral suspension, and injection vials of 500 mg	20–40 mg/kg q12h PO
Chlorpheniramine maleate (Chlor-Trimeton, Phenetron, and others)	Antihistamine (H ₁ -blocker). Blocks action of histamine on receptors. Also may have direct anti-inflammatory action. Used most often to prevent allergic reactions. Used for pruritus therapy in dogs and cats.	Sedation is most common side effect. Antimuscarinic effects (atropine-like effects) also are common.	Chlorpheniramine is included as ingredient in many OTC cough/cold and allergy medications.	4, 8 mg tablets, 2 mg/5 mL syrup, and 2 mg chewable tablets	Dog: 4–8 mg/dog q12h PO (up to a maximum of 0.5 mg/kg q12h) Cat: 2 mg/cat q12h PO
Chlorpromazine (Thorazine)	Phenothiazine tranquilizer/antiemetic. Inhibits action of dopamine as neurotransmitter. Most often used as central antiemetic. Also used for sedation and preanesthetic purposes.	Causes sedation. May cause α-adrenergic blockade. Produces extrapyramidal side effects in some individuals.	Used for vomiting caused by toxins, drugs, or GI disease. Higher doses than listed in dose section have been used with cancer chemotherapy (2 mg/kg q3h SC).	25 mg/mL injection solution	Dog: 0.5 mg/kg q6–8h IM, SC Cat: 0.2–0.4 mg/kg q6–8h IM, SC
Chorionic gonadotropin	See Gonadotropin, chorionic.				

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Cimetidine (Tagamet [OTC and prescription])	Histamine-2 antagonist (H ₂ -blocker). Blocks histamine stimulation of gastric parietal cells to decrease gastric acid secretion. Used to treat ulcers and gastritis.	Adverse effects usually seen only with decreased renal clearance. In people, CNS signs may occur with high doses. <i>Drug interactions:</i> May increase concentrations of other drugs used concurrently (e.g., theophylline) because of inhibition of hepatic enzymes.	Precise doses needed to treat ulcers have not been established.	100, 200, 300, 400, 800 mg tablets; 60 mg/mL oral solution; 6 mg/mL injection	10 mg/kg q6–8h IV, IM, PO
Ciprofloxacin (Cipro) and generic	Fluoroquinolone antibacterial. Acts to inhibit DNA gyrase and inhibit cell DNA and RNA synthesis. Bactericidal. Broad antimicrobial activity	Avoid use in dogs 4 weeks to 7 months of age. High concentrations may cause CNS toxicity, especially in animals with renal failure. Causes occasional vomiting. IV solution should be given slowly.	Efficacy studies have not been performed in dogs or cats. Ciprofloxacin is not absorbed orally as well as enrofloxacin.	250, 500, 750 mg tablets; 2 mg/mL injection	Dog: 20–25 mg/kg, PO, q24h 10–15 mg/kg IV, q24h Cat: 20 mg/kg, PO, q24h 10 mg/kg, IV, q24h
Cisapride	Prokinetic agent. Stimulates gastric and intestinal motility by either acetylcholine action, activity on serotonin receptors, or direct effect on smooth muscle. Used for gastric reflux, gastroparesis, ileus, constipation.	Contraindicated in patients with GI obstruction	Doses are based on extrapolation from human doses, experimental studies, and anecdotal evidence. Efficacy studies have not been performed in dogs or cats.	No longer commercially available. However, available through compounding pharmacies.	Dog: 0.1–0.5 mg/kg q8–12h PO (as high as 0.5–1.0 mg/kg q8h) Cat: 2.5–5 mg/cat q8–12h PO (as high as 1 mg/kg q8h)
Cisplatin (Platinol)	Anticancer agent. Used for treating various solid tumors, including osteosarcoma. Action is believed to be similar to bifunctional alkylating agents and interrupts replication of DNA in tumor cells.	Nephrotoxicity is the most limiting factor to cisplatin therapy. In cats, causes a dose-related, species-specific, primary pulmonary toxicosis. Vomiting may occur in dogs with administration. Transient thrombocytopenia may occur in dogs.	To avoid toxicity, fluid loading before administration using sodium chloride should be performed. Antiemetic agents are often administered before therapy to decrease vomiting.	1 mg/mL injection	Dog: 60–70 mg/m ² every 3–4 weeks IV (administer fluid for diuresis with therapy) Cat: Do not administer to cats

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Clarithromycin (Biaxin)	Macrolide antibiotic with bacteriostatic activity. Spectrum includes primarily gram-positive bacteria. Resistance is expected for most gram-negative bacteria. Efficacy is not established for animals. Most common use in people is for treatment of <i>Helicobacter</i> gastritis, and respiratory infections.	Well tolerated in animals. Most common side effects are vomiting, nausea, and diarrhea.	Doses are not established for animals due to lack of clinical trials. Dose recommendations are extrapolated from human or empirical use.	250, 500 mg tablets; 25 and 50 mg/mL oral suspension	7.5 mg/kg q12h PO
Clavamox	See Amoxicillin/clavulanate potassium.				
Clemastine (Tavist, Contac 12 Hour Allergy, and generic)	Antihistamine (H_1 -blocker). Blocks action of histamine on tissues. Used primarily for treatment of allergy. Some evidence suggests that clemastine is more effective than other antihistamines for pruritus in dogs.	Sedation is most common side effect.	Used for short-term treatment of pruritus in dogs. May be more efficacious when combined with other anti-inflammatory drugs. Tavist syrup contains 5.5% alcohol.	1.34 mg tablets (OTC), 2.64 mg tablets (Rx), and 0.134 mg/mL syrup	Dog: 0.05–0.1 mg/kg q12h PO
Clindamycin (Antirobe [veterinary], Cleocin [human])	Antibacterial drug of the lincosamide class (similar in action to macrolides). Inhibits bacterial protein synthesis via inhibition of bacterial ribosome. Primarily bacteriostatic, with spectrum of activity primarily against gram-positive bacteria and anaerobes.	Generally well tolerated in dogs and cats. Oral liquid product may be unpalatable to cats. Lincomycin and clindamycin may alter bacterial population in intestine and cause diarrhea; for this reason, do not administer to rodents or rabbits.	Most doses are based on manufacturer's drug approval data and efficacy trials. See dosing column for specific guidelines for different infections.	Oral liquid 25 mg/mL; 25, 75, 150, and 300 mg capsules, and 150 mg/mL injection (Cleocin)	Dog: 11–33 mg/kg q12h PO; for periodontal and soft tissue infection, 5.5–33 mg/kg q12h PO Cat: 11–33 mg/kg q24h PO; for skin and anaerobic infections, 11 mg/kg q12h PO; for toxoplasmosis, 12.5–25 mg/kg PO q12h
Clofazimine (Lamprene)	Antimicrobial agent used to treat feline leprosy. Slow bactericidal effect on <i>Mycobacterium leprae</i> .	Adverse effects have not been reported in cats. In people, the most serious adverse effects are GI.	Doses based on empiricism or extrapolation of human studies	50 and 100 mg capsules	Cat: 1 mg/kg up to a maximum 4 mg/kg/day PO

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Clomipramine (Clomicalm [veterinary]; Anafranil [human])	Tricyclic antidepressant (TCA) drug. Used in people to treat anxiety and depression. Used in animals to treat variety of behavioral disorders, including obsessive-compulsive disorders and separation anxiety. Action is via inhibition of uptake of serotonin at presynaptic nerve terminals.	Reported adverse effects include sedation, reduced appetite. Other side effects associated with TCAs are antimuscarinic effects (dry mouth, rapid heart rate) and antihistamine effects (sedation). Overdoses can produce life-threatening cardiotoxicity.	When adjusting doses, one may initiate therapy with low dose and increase gradually. There may be a 2–4 week delay after initiation of therapy before beneficial effects are seen.	5, 20, 80 mg tablets (veterinary); 10, 25, 50 mg tablets (human)	Dog: 1–2 mg/kg q12h PO Cat: 1–5 mg per cat q12–24h PO
Clonazepam (Klonopin)	Benzodiazepine. Action is to enhance inhibitory effects of γ -aminobutyric acid (GABA) in CNS. Used for antiseizure action, sedation, and treatment of some behavioral disorders.	Side effects include sedation and polyphagia. Some animals may experience paradoxical excitement.	Doses are based primarily on reports from human medicine, empiricism, or experimental studies. No clinical efficacy studies have been performed in dogs or cats.	0.5, 1, and 2 mg tablets	Dog: 0.5 mg/kg q8–12h PO Cat: 0.1–0.2 mg/kg q12–24h PO
Clopidogrel (Plavix)	Clopidogrel is used to inhibit platelets in patients that are prone to forming blood clots. In cats, clopidogrel has been recommended to prevent cardiogenic arterial thromboembolism associated with heart disease and atrial enlargement.	Bleeding complications can occur.	Administer with or without aspirin in patients prone to thrombi and emboli. The dose of 19 mg is approximately 1/4 of a human tablet.	75 mg tablets	Dog: 0.5–1 mg/kg q24h PO Oral loading dose of 2–4 mg/kg may be followed with 1 mg/kg q24h. Cat: 19 mg per cat (1/4 tablet), q24h PO
Clorazepate dipotassium (Tranxene)	Benzodiazepine. Action is to enhance inhibitory effects of GABA in CNS. Used for antiseizure action, sedation, and treatment of some behavioral disorders.	Side effects include sedation and polyphagia. Some animals may experience paradoxical excitement.	Doses are based primarily on reports from human medicine, empiricism, or experimental studies. No clinical efficacy studies have been performed in dogs or cats. Clorazepate tablets degrade quickly in presence of light, heat, or moisture. Keep in original packaging or in tightly sealed container.	3.75, 7.5, 11.25, 15 mg tablets	Dog: 0.5–2 mg/kg q8–12h, PO, but as frequently as q4h Cat: 0.2–0.4 mg/kg q12–24h PO (up to 0.5–2 mg/kg) q12h PO

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Codeine (generic)	Opiate agonist. Mechanism is similar to morphine, except with approximately 1/10 potency of morphine. Poorly absorbed in dogs.	Primary adverse effect is sedation.	Available as codeine phosphate and codeine sulfate oral tablets. Doses listed for analgesia are considered initial doses; individual patients may need higher doses, depending on degree of tolerance or pain threshold.	15, 30, 60 mg tablets, 5 mg/mL syrup, 3 mg/mL oral solution	Dog: (analgesia) 0.5–1 mg/kg q4–6h PO; (antitussive) 0.1–0.3 mg/kg q4–6h PO Cat: (analgesia) 0.5 mg/kg q6h PO; (antitussive) 0.1 mg/kg q6h PO
Colchicine (generic)	Anti-inflammatory agent. Used primarily to treat gout. In animals, used to decrease fibrosis and development of hepatic failure (possibly by inhibiting formation of collagen)	Do not administer to pregnant animals. Adverse effects are not well documented in animals. Colchicine may cause dermatitis in people.	Doses based on empiricism. There are no well controlled efficacy studies in veterinary species.	600 µg tablets	0.01–0.03 mg/kg q24h PO
Colony-stimulating factor: Sargramostim (Leukine) and Filgrastim (Neupogen)	Stimulates granulocyte development in bone marrow. Used primarily to regenerate blood cells to recover from cancer chemotherapy or other therapy.	Pain from injection	Doses based on limited experimental information performed in dogs. Leukine: reconstitute with 1 mL sterile water to make solution of 250 or 500 µg/mL. Gently swirl, do not shake; then further dilute with sterile 0.9% saline to concentration less than 10 µg/mL for IV infusion.	300 µg/mL (Neupogen) and 250–500 µg/mL (Leukine)	Leukine: 0.25 mg/m ² q12h SC or IV infusion over 2h Neupogen: 0.005 mg/kg q24h SC × 2 weeks
Corticotropin (ACTH) (Acthar)	Used for diagnostic purposes to evaluate adrenal gland function. Stimulates normal synthesis of cortisol from adrenal gland.	Adverse effects unlikely when used as single injection for diagnostic purposes.	Doses established by measuring normal adrenal response in animals.	80 U/mL gel	Response test: Collect pre-ACTH sample and inject 2.2 IU/kg IM. Collect post-ACTH sample at 2 h in dogs and at 1 and 2 h in cats.

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Cosyntropin (Cortrosyn)	Cosyntropin is a synthetic form of corticotropin (ACTH) used for diagnostic purposes only. In humans, it is preferred over corticotropin because it is less allergenic.	Same as for corticotropin	Use for diagnostic purposes only; not intended for treatment of hypoadrenocorticism. Maximum dosage for dog should be 250 µg. Frozen preparations can be stored for up to 6 months.	250 µg per vial	ACTH response test: collect pre-ACTH sample and inject 5 µg/kg IV or IM (dog) or 125 µg (0.125 mg) IM (cat) Cat: collect sample at 60 and 90 min after IV administration or 30 and 60 min after IM administration Dog: Collect post sample at 30 and 60 min
Cyanocobalamin (Vitamin B ₁₂) (many) and Cobalamin	Vitamin B ₁₂ analogue	Adverse effects rare except in high overdoses.	Adjust dose by monitoring. See Vitamin B ₁₂ for more information.	1000 µg/mL (= 1 mg/mL) injection; 25–100 µg tablets	Dog: 100–200 µg/day PO Cat: 50–100 µg/day PO, or 250 µg IM or SC weekly
Cyclophosphamide (Cytoxan, Neosar)	Cytotoxic agent. Bifunctional alkylating agent. Disrupts base-pairing and inhibits DNA and RNA synthesis. Cytotoxic for tumor cells and other rapidly dividing cells. Used primarily as adjunct for cancer chemotherapy and as immunosuppressive therapy	Bone marrow suppression is most common adverse effect. Can produce severe neutropenia (that usually is reversible). Vomiting and diarrhea may occur in some patients. Dogs are susceptible to bladder toxicity (sterile hemorrhagic cystitis). May cause hair loss when used in some chemotherapeutic protocols	Cyclophosphamide is usually administered with other drugs (other cancer drugs in cancer protocols or corticosteroids) when used for immunosuppressive therapy. Consult specific anticancer protocols for specific regimens.	25 mg/mL injection; 25, 50 mg tablet	Dog: Anticancer: 50 mg/m ² once daily 4 days/week PO, or 150–300 mg/m ² IV, and repeat in 21 days Immunosuppressive therapy: 50 mg/m ² (approx. 2.2 mg/kg) q48h PO, or 2.2 mg/kg once daily for 4 days/week Cat: 6.25–12.5 mg/cat once daily 4 days/week
Cyclosporine (Neoral [human], Atopica [veterinary], Optimmune [ophthalmic]. Other name for cyclosporine is cyclosporin A).	Immunosuppressive drug. Suppresses induction of T cell lymphocytes. Used for atopic dermatitis and treatment of immune-mediated diseases.	Can cause vomiting, diarrhea, anorexia. In comparison to other immunosuppressive drugs, does not cause myelosuppression. <i>Drug interactions:</i> erythromycin, or ketoconazole may increase cyclosporine concentrations when used concurrently.	Neoral oral products are the same formulation as Atopica. Topical cyclosporine has been used successfully as treatment for keratoconjunctivitis sicca.	10, 25, 50, and 100 mg capsules, 100 mg/mL oral solution	Dog: 5 mg/kg PO, once daily. Higher doses may be needed for some immune-mediated diseases. Cat: 7.5 mg/kg, PO, once daily.

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Cyproheptadine hydrochloride (Periactin)	Phenothiazine with antihistamine and antiserotonin properties. Used as appetite stimulant (probably by altering serotonin activity in appetite center)	May cause increased appetite and weight gain	Clinical studies have not been performed in veterinary medicine. Use is based primarily on empiricism and extrapolation from human results. Syrup contains 5% alcohol.	4 mg tablet; 2 mg/5 mL syrup	Antihistamine: 0.5–1.1 mg/kg q8–12h PO Appetite stimulant: 2 mg/cat PO Feline asthma: 1–2 mg/cat q12h PO
Cytarabine (cytosine arabinoside) (Cytosar)	Anticancer agent. Exact mechanism is not known. Probably inhibits DNA synthesis. Used for lymphoma and leukemia protocols. Also used for meningoencephalitis.	Bone marrow suppression. Causes vomiting and nausea	Consult anticancer protocols for precise dosing regimens.	100 mg vial	Dog (lymphoma): 100–150 mg/m ² once daily, or 50 mg/m ² twice daily for 4 days IV, SC, or 600 mg/m ² IV, SC single dose Dog (meningoencephalitis): 50 mg/m ² twice daily for 2 days and repeated every 3 weeks SC Continuous rate intravenous (CRI) administration at 25 mg/m ² for 8 hours Cat: 100 mg/m ² once daily for 2 days
Dacarbazine (DTIC)	Anticancer agent. Monofunctional alkylating agent. Used for melanoma.	Leukopenia, nausea, vomiting, diarrhea. Do not use in cats.	Consult anticancer protocol for specific regimens.	200 mg vial for injection	Dog: 200 mg/m ² for 5 days every 3 weeks IV; or 800–1000 mg/m ² every 3 weeks IV
Dalteparin sodium (Fragmin)	Low molecular weight heparin (LMWH); anticoagulant; indicated for prevention of thromboembolism in at-risk patients. Anti-Xa: anti-IIa ratio: 2.7:1	May increase risk of bleeding.	No need to monitor clotting times as with conventional (unfractionated) heparin when dalteparin is used at recommended dosages. Dosages extrapolated from humans may not apply to dogs and cats.	16 mg (2500 U)/0.2 mL; 32 mg (5000 U)/0.2 mL prefilled syringes for injection; 64 mg (10,000 U) mL multidose vials for injection	Dogs: 150–175 U/kg, q8h, SC Cats: 150 U/kg, q4h, to 180 U/kg q6h, SC
Danazol (Danocrine)	Gonadotropin inhibitor. Suppresses luteinizing hormone (LH) and follicle-stimulating hormone (FSH) and estrogen synthesis. In humans, used for endometriosis. May reduce destruction of platelets or RBC in immune-mediated disease.	May cause signs similar to other androgenic drugs. Adverse effects have not been reported in animals.	When used to treat autoimmune disease, usually used in conjunction with other drugs (e.g., corticosteroids). Efficacy has not been evaluated.	50, 100, 200 mg capsules	5–10 mg/kg q12h PO

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Dantrolene sodium (Dantrium)	Muscle relaxant. Inhibits calcium leakage from sarcoplasmic reticulum. In addition to muscle relaxation, it has been used for malignant hyperthermia. Also has been used to relax urethral muscle in cats.	Muscle relaxants can cause weakness in some animals.	Doses have been primarily extrapolated from experimental studies or extrapolation of human studies. No clinical trials available in veterinary medicine. Studies in which dantrolene relaxed urethra in cats used 1 mg/kg IV.	100 mg capsule and 0.33 mg/mL injection	For prevention of malignant hyperthermia: 2–3 mg/kg IV For muscle relaxation: Dog: 1–5 mg/kg q8h PO Cat: 0.5–2 mg/kg q12h PO
Dapsone (generic)	Antimicrobial drug used primarily for treatment of mycobacterium. May have some immunosuppressive properties or inhibit function of inflammatory cells. Used primarily for dermatologic diseases in dogs and cats.	Hepatitis and blood dyscrasias may occur. Toxic dermatologic reactions have been seen in people. <i>Drug interactions:</i> Do not administer with trimethoprim (may increase blood concentrations). Do not administer to cats.	Doses are derived from extrapolation of human doses or empiricism. No well-controlled clinical studies have been performed in veterinary medicine.	25 and 100 mg tablets	Dog: 1.1 mg/kg q8–12h PO Cat: do not use
Deferoxamine mesylate (Desferal)	Chelating agent with strong affinity for trivalent cations. Used to treat acute iron toxicosis. Indicated in cases of severe poisoning. Deferoxamine also has been used to chelate aluminum and facilitate removal.	Adverse effects have not been reported in animals. Allergic reactions and hearing problems have occurred in people.	100 mg of deferoxamine binds 8.5 mg of ferric iron. Monitor serum iron concentrations to determine severity of intoxication and success of therapy. Contact local poison control center for guidance. Successful therapy is indicated by monitoring urine color (orange-rose color change to urine indicates chelated iron is being eliminated).	500 mg vial for injection	10 mg/kg IV, IM q2h for 2 doses, then 10 mg/kg q8h for 24 h
Deprenyl (L-deprenyl)	See Selegiline.				

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Deracoxib (Deramaxx)	NSAID of the coxib class; high COX-1: COX-2 in vitro inhibitory ratio. Indicated for the control of postoperative pain and inflammation associated with orthopedic surgery and pain and inflammation associated with osteoarthritis.	Most common adverse effect from clinical trials has been GI (vomiting and diarrhea).	Recommended doses are for dogs weighing > 1.8 kg (4 lb). Safety has not been established for dogs under 4 months of age, dogs used for breeding, pregnant or lactating dogs, or for cats.	25, 100 mg tablets; chewable tablets	Dog (postoperative pain): 3.0–4.0 mg/kg q24h PO as needed for 7 days Dog (osteoarthritis): 1–2 mg/kg PO q24h for long-term treatment over 7 days Cat: 1 mg/kg PO, single dose
DES	See Diethylstilbestrol.				
Desmopressin acetate (DDAVP)	Synthetic peptide similar to antidiuretic hormone (ADH). Used as replacement therapy for patients with diabetes insipidus. Desmopressin also has been used for treatment of patients with mild to moderate von Willebrand disease prior to surgery or other procedure that may cause bleeding.	No side effects reported. In people, it rarely has caused thrombotic events.	Desmopressin is used only for central diabetes insipidus. Duration of effect is variable (8–20 h). It is ineffective for treatment of nephrogenic diabetes insipidus or polyuria from other causes. Intranasal product has been administered as eye drops in dogs. Onset of effect is within 1 h.	4 µg/mL injection and desmopressin acetate nasal solution 100 µg/mL (0.01%) metered spray. Tablets 0.1 and 0.2 mg.	Diabetes insipidus: 2–4 drops (2 µg) q12–24h intranasally or in eye. 0.05–0.1 mg q12h PO as needed. von Willebrand disease treatment: 1 µg/kg (0.01 mL/kg) SC, IV, diluted in 20 mL of saline administered over 10 min
Desoxycorticosterone pivalate (Percorten-V, DOCP, or DOCA pivalate)	Mineralocorticoid. Used for adrenocortico-insufficiency (hypoadrenocorticism). No glucocorticoid activity.	Excessive mineralocorticoid effects with high doses.	Initial dose based on studies performed in clinical patients. Individual doses may be based on monitoring electrolytes in patients. Actual interval between doses may range from 14–35 days.	25 mg/mL Injection	1.5–2.2 mg/kg every 25 days IM
Dexamethasone (Dexamethasone solution and dexamethasone sodium phosphate) (Azium, Decaject SP, Dexavet, and Dexasone. Tablets include Decadron and generic)	Corticosteroid. Dexamethasone has approximately 30× potency of cortisol. Multiple anti-inflammatory effects.	Corticosteroids produce multiple systemic side effects and adverse effects from chronic therapy.	Doses based on severity of underlying disease. Dexamethasone is used for testing hyperadrenocorticism. Low-dose dexamethasone suppression test: dogs 0.01 mg/kg IV, cats 0.1 mg/kg IV, and collect sample at 0, 4, and 8 hours. For high-dose dexamethasone suppression test: dogs 0.1 mg/kg IV, cats 1.0 mg/kg IV.	Azium solution, 2 mg/mL. Sodium phosphate forms are 3.33 mg/mL. 0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6 mg tablets, 0.1 and 1 mg/mL oral solution	Anti-inflammatory: 0.07–0.15 mg/kg q12–24h IV, IM, PO Dexamethasone 21-isonicotinate 0.03–0.05 mg/kg IM

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Dexmedetomidine (Dexdomitor)	Alpha-2 agonist; similar to medetomidine, except it is more specific because it is the active isomer. Used for sedation, analgesia, and anesthesia; may be used with other anesthetics and sedatives.	Vomiting may occur. Use cautiously in animals with heart disease.	Doses may vary depending on degree of sedation desired. Reverse with equal volume of atipamezole (Antisedan).	0.5 mg/mL injection, and a lower concentration of 0.1 mg/mL in sterile vials	Dog: 125 µg/m ² IM (3–9 µg/kg) 375 µg/m ² IV or 500 µg/m ² IM for deeper anesthesia. Cat: 40 µg/kg IM, lower doses of 10 µg/kg for short-term sedation.
Dextran (Dextran 70, Gentrant 70)	Synthetic colloid used for volume expansion. High molecular weight fluid replacement. Primarily used for acute hypovolemia and shock.	Only limited use in veterinary medicine, and adverse effects have not been reported. In people, coagulopathies are possible because of decreased platelet function. Anaphylactic shock also has occurred.	Used primarily in critical care situations. Delivered via constant rate infusion slowly. Monitor patient's cardiopulmonary status carefully during administration.	Injectable solution 250, 500, 1000 mL	Dog: 10–20 mL/kg IV over 30–60 min Cat: 5–10 mL/kg IV over 30–60 min
Dextrose solution 5% (D-5-W)	Sugar added to fluid solutions. Isotonic	High doses produce pulmonary edema.	Commonly used fluid solution administered via constant rate infusion. <i>Not a maintenance solution</i>	Fluid solution for IV administration	40–50 mL/kg q24h IV
Diazepam (Valium and generic)	Benzodiazepine. Central-acting CNS depressant. Mechanism of action appears to be via potentiation of GABA-receptor mediated effects in CNS. Used for sedation, anesthetic adjunct, anticonvulsant, and behavioral disorders. Diazepam metabolized to desmethyldiazepam (nordiazepam) and oxazepam.	Sedation is most common side effect. May cause paradoxical excitement in dogs. Causes polyphagia. In cats, idiopathic fatal hepatic necrosis has been reported.	Clearance in dogs is many times faster than in people (half-life in dogs less than 1 h); requires frequent administration. For treatment of status epilepticus, may be administered IV intranasal, or rectally. Avoid administration IM.	2, 5, 10 mg tablets; 5 mg/mL solution for injection	Preanesthetic: 0.5 mg/kg IV Status epilepticus: 0.5 mg/kg IV, 1 mg/kg rectal; repeat if necessary Appetite stimulant (cat): 0.2 mg/kg IV For behavior treatment in cats: 1–4 mg/cat q12–24h PO
Dichlorvos (Task)	Antiparasitic drug, used primarily to treat hookworms, roundworms, whipworms. Kills parasites by anticholinesterase action.	Do not use in heartworm-positive patients. Overdoses can cause organophosphate intoxication. (Treat with 2-PAM, atropine.)	Doses based on manufacturer's recommendations	10, 25 mg tablets	Dog: 26.4–33 mg/kg PO Cat: 11 mg/kg PO

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Diethylstilbestrol (DES)	Synthetic estrogen compound. Used for estrogen replacement in animals. DES is most commonly used to treat estrogen-responsive incontinence in dogs. Also has been used to induce abortion in dogs	Side effects may occur that are caused by excess estrogen. Estrogen therapy may increase risk of pyometra and estrogen-sensitive tumors.	Doses listed are for treating urinary incontinence and vary depending on response. Titrate dose to individual patients. Although used to induce abortion, it was <i>not</i> efficacious in one study that administered 75 µg/kg.	1, 5 mg tablets; 50 mg/mL injection (no longer manufactured in US, but available from compounding pharmacist)	Dog: 0.1–1.0 mg/dog q24h PO. After initial response, reduce frequency to 2–3× per week. Cat: 0.05–0.1 mg/cat q24h PO
Digoxin (Lanoxin, Cardoxin)	Cardiac ionotropic agent. Increases cardiac contractility and decreases heart rate. Mechanism is via inactivation of cardiac muscle sodium-potassium ATPase. Beneficial effects for heart failure may occur via neuroendocrine effects (alters sensitivity of baroreceptors). Used in heart failure for ionotropic effect and to decrease heart rate. Used in supraventricular arrhythmias to decrease ventricular response to atrial stimulation.	Digitalis glycosides have narrow therapeutic index. May cause variety of arrhythmias in patients (e.g., heart block, ventricular tachycardia). Causes vomiting, anorexia, diarrhea. Adverse effects potentiated by hypokalemia, reduced by hyperkalemia. Some breeds of dogs (Doberman pinschers) and cats are more sensitive to adverse effects.	Monitor patients carefully. Optimum plasma concentration is 1–2 ng/mL. Adverse effects common at concentration above 3.5 ng/mL. When dosing, calculate dose on lean body weight. Doses should be 10% less for elixir because of increased absorption.	0.0625, 0.125, 0.25 mg tablets; 0.05 and 0.15 mg/mL elixir	Dog: 0.0025–0.005 mg/kg q12h PO Cat: 0.008–0.01 mg/kg q48h PO (approximately 1/4 of a 0.125 mg tablet/cat)
Dihydrotachysterol (Vitamin D, Hytakerol)	Treatment of hypocalcemia, especially hypoparathyroidism associated with thyroidectomy. The most common use is for replacement in cats that have had thyroidectomy for treatment of hyperthyroidism.	Overdose may cause hypercalcemia.	Doses for individual patients should be adjusted by monitoring serum calcium concentrations.	No formulations are currently available in the US. It can only be obtained from some compounding pharmacies.	0.01 mg/kg/day PO. Acute treatment: 0.02 mg/kg initially, then 0.01–0.02 mg/kg q24–48h PO thereafter. The dose should be adjusted on the basis of measuring calcium concentrations. Effective doses can range from 0.1 to 0.3 mg/kg.

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Diltiazem (Cardizem, Dilacor)	Calcium channel-blocking drug. Blocks calcium entry into cells via blockade of slow channel. Produces vasodilation, negative chronotropic effects. Used for supraventricular arrhythmias in dogs; hypertrophic cardiomyopathy in cats	Hypotension, cardiac depression, bradycardia, AV block. May cause anorexia in some patients	Higher doses of 5 mg/kg PO q8h has been used in some dogs for atrial fibrillation.	30, 60, 90, 120 mg tablets. 5 mg/mL injection. Extended release capsules are 60, 90, 120, 180, 240, 300 mg.	Dog: 0.5–1.5 mg/kg q8h PO, 0.25 mg/kg over 2 min IV (repeat if necessary) Cat: 1.75–2.4 mg/kg q8h PO. For Dilacor XR or Cardizem CD, dose is 10 mg/kg once daily PO. In cats use either Dilacor XR 30 or Dilacor XR 60 per cat.
Dimenhydrinate (Dramamine, [Gravol in Canada])	Antihistamine drug. Converted to active diphenhydramine. Used for antiemetic treatment.	Primary side effect is sedation.	There have been no clinical studies on the use of dimenhydrinate. It is primarily used empirically for treatment of vomiting.	50 mg tablets and 50 mg/mL injection	Dog: 4–8 mg/kg q8h PO, IM, IV Cat: 12.5 mg/cat q8h IV, IM, PO
Dimercaprol (BAL) (BAL in Oil)	Chelating agent, used to treat lead, gold, arsenic toxicity.	Adverse effects not reported in veterinary medicine. In people, sterile abscesses occur at injection site. High doses have caused seizures, drowsiness, and vomiting.	Use as soon as possible after intoxicant exposure. Alkalization of urine will increase toxin removal. For lead intoxication, may be used with edetate calcium.	Injection, usually prepared by compounding	4 mg/kg q4h IM
Dinoprost tromethamine	See Prostaglandin F2α.				
Diocetyl calcium sulfosuccinate	See Docusate calcium.				
Diocetyl sodium sulfosuccinate	See Docusate sodium.				
Diphenhydramine hydrochloride (Benadryl)	Antihistamine used for allergy treatment and antiemetic	Primary side effect is sedation.	Antihistamine used primarily for allergic disease in animals.	Available OTC; 2.5 mg/mL elixir; 25, 50 mg capsules and tablets; 50 mg/mL injection	Dog: 2.2 mg/kg q8–12h PO, IM, SC Cat: 2–4 mg/kg q6–8h PO, or 1 mg/kg q6–8h IM, IV
Diphenoxylate (Lomotil)	Opiate agonist. Stimulates smooth muscle segmentation in intestine, as well as electrolyte absorption. Used for acute treatment of nonspecific diarrhea.	Adverse effects have not been reported in veterinary medicine. Diphenoxylate is poorly absorbed systemically and produces few systemic side effects. Excessive use can cause constipation.	Doses are based primarily on empiricism or extrapolation of human dose. Clinical studies have not been performed in animals. Contains atropine, but dose is not high enough for significant systemic effects.	2.5 mg tablets	Dog: 0.1–0.2 mg/kg q8–12h PO Cat: 0.05–0.1 mg/kg q12h PO
Diphenylhydantoin	See Phenytoin.				
Diphosphonate disodium etidronate	See Etidronate disodium.				

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Dipyridamole (Persantine)	Platelet inhibitor. Mechanism of action is attributed to increased levels of cyclic adenosine monophosphate (cAMP) in platelet, which decreases platelet activation. Indicated to prevent thromboembolism	Adverse effects have not been reported in animals.	Used primarily in people to prevent thromboembolism. Use in animals has not been reported. When used in people, it is combined with other antithrombotic agents (e.g., warfarin).	25, 50, 75 mg tablets; 5 mg/mL injection	4–10 mg/kg q24h PO
Dirlotapide (Slentrol)	Dirlotapide is one of the microsomal triglyceride transfer protein (MTP) inhibitors used to treat obesity in dogs. The MTP inhibitors block the processing of lipid molecules in the enterocytes of the intestine. Release of lipids from enterocytes is blocked, causing decreased appetite in dogs.	It will decrease appetite in all dogs in which it is effective (the mechanism for producing weight loss). Anorexia and vomiting will be observed in some animals. Diarrhea also is possible. Liver enzymes may become elevated in some dogs.	The dosing regimen must be followed closely and a program of regular evaluation (weighing the dog) and dose adjustment with each visit is necessary for successful therapy.	Oral oil-based solution 5 mg/mL	Dog: Start with 0.01 mL/kg/day PO. Adjust by doubling the dose in two weeks. monthly adjustments to dose should be done on the basis of animal's weight loss. Do not exceed 0.2 mL/kg/day Cat: do not administer to cats
Disopyramide (Norpace [Rythmodan in Canada])	Antiarrhythmic agent of Class 1. Depresses myocardial electrophysiologic conduction rate	Adverse effects have not been reported in animals. High doses may cause cardiac arrhythmias.	Not commonly used in veterinary medicine. Other antiarrhythmic drugs are preferred.	100, 150 mg capsules (10 mg/mL injection in Canada only)	Dog: 6–15 mg/kg q8h PO
Dithiazanine iodide (generic)	Microfilaricidal drug for dogs. Also effective for hookworms, roundworms, and whipworms	Adverse effects are rare. Causes vomiting in some dogs. Causes discoloration of feces	Before ivermectin and similar drugs, this was the only microfilaricidal agent for dogs. Not commonly used and may not be commercially available anymore	10, 50, 100, 200 mg tablets	Dog: (heartworm) 6.6–11 mg/kg q24h PO for 7–10 days; (other parasites) 22 mg/kg PO Cat: no dose established
Dobutamine hydrochloride (Dobutrex)	Adrenergic agonist. Action is primarily to stimulate myocardium via action on cardiac β_1 -receptors. Increases heart contraction without increase in heart rate. Some action may occur via α -receptors. Primarily used for acute treatment of heart failure	May cause tachycardia and ventricular arrhythmias at high doses or in sensitive individuals.	Dobutamine has a rapid elimination half-life (minutes) and therefore must be administered via carefully monitored constant rate infusion. When mixing, avoid alkalinizing solutions. Usually dilute in 5% dextrose solution (e.g., 250 mg in 1 L 5% dextrose).	250 mg/20 mL vial for injection (12.5 mg/mL)	Dog: 5–20 μ g/kg/min IV infusion Cat: 2 μ g/kg/min IV infusion

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Docusate calcium (Surfak, Doxidan)	Stool softener (surfactant). Acts to decrease surface tension to allow more water to accumulate in the stool	No adverse effects reported in animals. In people, high doses have caused abdominal discomfort.	Doses are based on extrapolations from humans or empiricism. No clinical studies reported for animals. Docusate calcium products may contain stimulant cathartic phenolphthalein, which should be used cautiously in cats.	60 mg tablets (and many others)	Dog: 50–100 mg/dog q12–24h PO Cat: 50 mg/cat q12–24h PO
Docusate sodium (Colace, Doxan, Doss; many OTC brands)	See Docusate calcium.	See Docusate calcium.	See Docusate calcium.	50, 100 mg capsules; 10 mg/mL liquid	Dog: 50–200 mg/dog q8–12h PO Cat: 50 mg/cat q12–24h PO
Dolasetron mesylate (Anzemet)	Antiemetic drug. Acts by inhibiting serotonin (5-HT, type 3) receptors. Used for antiemetic therapy, especially from vomiting induced by chemotherapy.	No adverse effects have been reported in animals.	The use of serotonin antagonists is based primarily on experience from human medicine. There have been no efficacy trials in veterinary medicine. It is more effective if used to prevent vomiting, rather than inhibiting on-going vomiting.	50, 100 mg tablets; 20 mg/mL injection	Prevention of nausea and vomiting: 0.6 mg/kg IV or PO q12–24h. Treating vomiting and nausea: 1.0 mg/kg PO or IV q24h
Dopamine hydrochloride (Intropin)	Adrenergic agonist. Action is primarily to stimulate myocardium via action on cardiac β_1 -receptors. There is no evidence to support the use for acute kidney injury.	May cause tachycardia and ventricular arrhythmias at high doses or in sensitive individuals. High doses cause vasoconstriction via α -receptor action.	Dopamine has a very rapid elimination half-life (minutes) and therefore must be administered via carefully monitored constant rate infusion. When mixing, avoid alkalinizing solutions. Administer in 5% dextrose solution or lactated Ringer's solution. Mix 200–400 mg in 250 to 500 mL of fluid.	40, 80, or 160 mg/mL for IV injection	2–10 μ g/kg/min IV infusion
Doxapram hydrochloride (Dopram, Respiram)	Respiratory stimulant via action on carotid chemoreceptors and subsequent stimulation of respiratory center. Used to treat respiratory depression or to stimulate respiration post anesthesia. May also increase cardiac output.	Adverse effects not reported in animals. Cardiovascular effects and convulsions have occurred with high doses in people. Contains benzyl alcohol as a vehicle.	Used for short-term treatment only. No longer available from manufacturer.	20 mg/mL injection	5–10 mg/kg IV; neonate: 1–5 mg SC, sublingual, or via umbilical vein

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Doxorubicin (Adriamycin)	Anticancer agent. Acts to intercalate between bases on DNA, disrupting DNA and RNA synthesis in tumor cell. Doxorubicin also may affect tumor cell membranes. Used for treatment of various neoplasias, including lymphoma	Most common acute effects are anorexia, vomiting, and diarrhea. Dose-related toxicity also includes bone marrow suppression, hair loss (in certain breeds), and cardiotoxicity. Cardiotoxicity limits the total dose administered (usually not to exceed 200 mg/m ²).	Regimen listed may differ for various tumors. Consult specific anticancer protocol for guidelines. Dose must be infused IV (over 20–30 min). Animals may require antiemetic and antihistamine (diphenhydramine) prior to therapy. Monitor ECG during therapy. Dose according to body weight may be more effective for small dogs.	2 mg/mL injection	Dog: 30 mg/m ² IV every 21 days, or: > 20 kg, use 30 mg/m ² and < 20 kg, use 1 mg/kg Cat: 20 mg/m ² (or approximately 1–1.25 mg/kg) every 3 weeks IV
Doxycycline (Vibramycin and generic forms)	Tetracycline antibiotic. Mechanism of action of tetracyclines is to bind to 30S ribosomal subunit and inhibit protein synthesis. Usually bacteriostatic. Broad spectrum of activity including bacteria, some protozoa, <i>Rickettsia</i> , <i>Ehrlichia</i> . Also used as adjunctive treatment for heartworm disease	Severe adverse reactions not reported with doxycycline. Tetracyclines in general may cause renal tubular necrosis at high doses. Tetracyclines can affect bone and teeth formation in young animals, but this is less likely with doxycycline.	Many pharmacokinetic and experimental studies have been conducted in small animals, but no clinical studies. Ordinarily considered the drug of choice for <i>Rickettsia</i> and <i>Ehrlichia</i> infections in dogs. Doxycycline IV infusion is stable for only 12 h at room temperature and 72 h if refrigerated.	10 mg/mL oral suspension; 100 mg injection vial doxycycline hydiate 50, 100 mg tablets or capsules. Doxycycline monohydrate 50 or 100 mg tablets or capsules	5 mg/kg q12h, or 10 mg/kg once daily For <i>Rickettsia</i> or <i>Ehrlichia</i> in dogs: 5 mg/kg q12h. Heartworm treatment: 10 mg/kg PO per day, intermittently at 4–6 week intervals; used with ivermectin or ivermectin + melarsomine.
Edetate calcium disodium (CaNa ₂ EDTA, Calcium Disodium Versenate)	Chelating agent. Indicated for treatment of acute and chronic lead poisoning. Sometimes used in combination with dimercaprol	No adverse effects reported in animals. In people, allergic reactions (release of histamine) occur after IV administration	May be used with dimercaprol. Equally effective when administered IV or IM, but IM injection may be painful. Ensure adequate urine flow before the first dose.	20 mg/mL injection	25 mg/kg q6h SC, IM, IV for 2–5 days
Edrophonium (Tensilon and others)	Cholinesterase inhibitor. Causes cholinergic effects by inhibiting metabolism of acetylcholine. Very short acting and ordinarily is only used for diagnostic purposes (e.g., for myasthenia gravis). Also has been used to reverse neuromuscular blockade of nondepolarizing agents (pancuronium)	Short acting, so side effects are minimal. Excessive muscarinic/cholinergic effects may occur with high doses (counteract with atropine).	Usually used only for determination of diagnosis of myasthenia gravis in patients.	10 mg/mL injection	Dog: 0.11–0.22 mg/kg IV Cat: 0.25–0.5 mg per cat IV

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Enalapril maleate (Enacard, Vasotec)	ACE inhibitor vasodilator via inhibition of angiotensin II synthesis. Used for vasodilation and treatment of heart failure. Primarily used in dogs, but may benefit some cats in heart failure.	May cause azotemia in some patients; carefully monitor patients receiving high doses of diuretics. <i>Drug interactions:</i> Use cautiously with other hypotensive drugs and diuretics. NSAIDs may decrease vasodilating effects.	Doses are based on clinical trials conducted in dogs by manufacturer. For dogs, start with once-daily administration and increase to q12h if needed. Other drugs used for treatment of heart failure may be used concurrently. Monitor electrolytes and renal function 3–7 days after initiating therapy and periodically thereafter.	2.5, 5, 10, 20 mg tablets	Dog: 0.5 mg/kg q12–24h PO Cat: 0.25–0.5 mg/kg q12–24h PO, or 1.0–1.25 mg/cat/day
Enilconazole (Imaverol, Clinafarm EC)	Azole antifungal agent for topical use only. Like other azoles, inhibits membrane synthesis (ergosterol) in fungus. Highly effective for dermatophytes	Administered topically. Adverse effects have not been reported.	Imaverol is available only in Canada as 10% emulsion. In the US, Clinafarm EC is available for use in poultry units as 13.8% solution. Dilute solution to at least 50:1, and apply topically every 3–4 days for 2–3 weeks. Enilconazole also has been instilled as 1:1 dilution into nasal sinus for nasal aspergillosis.	10% or 13.8% emulsion	Nasal aspergillosis: 10 mg/kg q12h instilled into nasal sinus for 14 days (10% solution diluted 50/50 with water) Dermatophytes: dilute 10% solution to 0.2%, and wash lesion with solution 4 times at 3–4 day intervals
Enoxaparin (Lovenox)	LMWH; anticoagulant; indicated for prevention of thromboembolism in at-risk patients. It has been used in cats with severe left atrial enlargement secondary to cardiomyopathy prior to and following embolism. Anti-Xa: anti-IIa ratio: 3.8:1	Bleeding may be a problem.	No need to monitor clotting times as with conventional (unfractionated) heparin when enoxaparin is used at recommended dosages. More consistent absorption and clearance than unfractionated (conventional) heparin.	30 mg/0.3 mL, 40 mg/0.4 mL, 60 mg/0.6 mL, 80 mg/0.8 mL, and 100 mg/1 mL prefilled syringes for injection	Dog: 0.8 mg/kg SQ q6h Cats: 1 mg/kg SQ, q12h, up to 1.25 mg/kg SQ, q6h

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Enrofloxacin (Baytril)	Fluoroquinolone antibacterial drug. Acts via inhibition of DNA gyrase in bacteria to inhibit DNA and RNA synthesis. Bactericidal. Broad spectrum of activity	Adverse effects include seizures in epileptic animals, arthropathy in dogs 4–28 weeks of age, vomiting in dogs and cats at high doses. Blindness in cats has been reported. Drug interactions: May increase concentrations of theophylline if used concurrently. Coadministration with di- and trivalent cations (e.g., sucralfate) may decrease absorption.	Solution is not approved for IV use but has been administered via this route safely if given slowly. Do not mix IV solutions with cation-containing fluids (e.g., Mg ⁺⁺ , Ca ⁺⁺).	22.7 and 68 mg tablets. Taste Tabs are 22.7, 68 and 136 mg. 22.7 mg/mL injection	Dog: 5–20 mg/kg/q24h PO, IV, IM Cat: 5 mg/kg q24h PO, IM. Do not administer to cats at doses higher than 5 mg/kg and do not administer to cats IV.
Ephedrine (many, generic)	Adrenergic agonist. Agonist on α - and β_1 -adrenergic receptors but not β_2 -receptors. Used as vasopressor, e.g., administered during anesthesia. CNS stimulant	Adverse effects related to excessive adrenergic activity (e.g., peripheral vasoconstriction and tachycardia)	Used primarily in acute situations to increase blood pressure	25, 50 mg/mL injection	Vasopressor: 0.75 mg/kg IM, SC, repeat as needed
Epinephrine hydrochloride (Adrenalin chloride and generic forms)	Adrenergic agonist. Nonselectively stimulates α -, β_1 and β_2 -adrenergic receptors. Used primarily for emergency situations to treat cardiopulmonary arrest and anaphylactic shock	Overdose will cause excessive vasoconstriction and hypertension. High doses can cause ventricular arrhythmias. When high doses are used for cardiopulmonary arrest, an electrical defibrillator should be available.	Doses are based on experimental studies, primarily in dogs. IV doses are ordinarily used, but endotracheal administration is acceptable when IV access is not available. Intraosseous route also has been used, and doses are equivalent to IV. When endotracheal route is used, the dose is higher and duration of effect may be longer than with IV administration. Avoid intracardiac injection.	1 mg/mL (1:1000) injection solution	Cardiac arrest: 10–20 μ g/kg IV or 100–200 μ g/kg endotracheal (may be diluted in saline before administration) The low dose (0.01 mg/kg) of epinephrine is recommended because high-dose therapy has not been associated with increased survival. A shortcut to calculate low-dose epinephrine volume for administration is 0.1 mL/10kg. The dose may be repeated at 3 to 5-minute intervals. Anaphylactic shock: 2.5–5 μ g/kg IV or 50 μ g/kg endotracheal (may be diluted in saline)

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Epoetin alfa (Erythropoietin) (Epogen, [r-HuEPO])	Human recombinant erythropoietin. Hematopoietic growth factor that stimulates erythropoiesis. Used to treat nonregenerative anemia.	Since this product is a human recombinant product, it may induce local and systemic allergic reactions in animals. Injection site pain and headache have occurred in people. Seizures also have occurred. Delayed anemia may occur because of crossreacting antibodies against animal erythropoietin (reversible when drug is withdrawn).	Use has been based on clinical reports in dogs and cats. The only form currently available is a human recombinant product.	2000 U/mL injection	Dog: Doses range from 35 or 50 U/kg 3 times/week to 400 U/kg/week SC (adjust dose to hematocrit of 30%–34%). Cat: start with 100 U/kg three times weekly SC. Adjust dose based on hematocrit.
Epsiprantel (Cestex)	Anticestodal agent	Anorexia and transient diarrhea. Vomiting at high doses.		12.5, 25, 50, or 100 mg tablets	Dog: 5.5 mg/kg PO Cat: 2.75 mg/kg PO
Ergocalciferol (vitamin D ₂) (Calciferol, Drisdol)	Vitamin D analogue. Used for vitamin D deficiency and as treatment of hypocalcemia, especially that associated with hypothyroidism. Vitamin D promotes absorption and utilization of calcium.	Overdose may cause hypercalcemia. Avoid use in pregnant animals because it may cause fetal abnormalities. Use cautiously with high doses of calcium-containing preparations.	Should not be used for renal hypoparathyroidism because of inability to convert to active compound. Available as oral solution, tablets, capsules, and injection. Doses for individual patients should be adjusted by monitoring serum calcium concentrations.	400 U tablets (OTC); 50,000 U tablets (1.25 mg); 500,000 U/mL (12.5 mg/mL) injection	500–2000 U/kg/day PO
Ertapenem (Invanz)	Carbapenem antibiotic of the β-lactam group. Like meropenem and imipenem, highly active against a broad spectrum of bacteria, including those resistant to other drugs. Ertapenem is not as active against <i>Pseudomonas</i> as meropenem or imipenem.	Well tolerated in animals. CNS toxicity may be possible with high doses. Allergy to β-lactam antibiotics is possible.	Dosing information is extrapolated from human medicine or limited empirical use in veterinary medicine. As with other carbapenems, use only when organisms are resistant to other drugs.	1 g vial for injection	30 mg/kg q8h IV or SC

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Erythromycin (many brands and generic)	Macrolide antibiotic. Inhibits bacteria by binding to 50S ribosome and inhibiting protein synthesis. Spectrum of activity limited primarily to gram-positive aerobic bacteria. Used for skin and respiratory infections.	Most common side effect is vomiting (probably caused by cholinergic-like effect or motilin-induced motility). May cause diarrhea in some animals. Do not administer PO to rodents or rabbits.	There are several forms of erythromycin, including the ethylsuccinate and estolate esters, and stearate salt for oral administration. There is no convincing data to suggest that one form is absorbed better than another, and one dose is included for all.	250 or 500 mg capsules or tablets	10–20 mg/kg q8–12h PO; GI motility effects at 0.5–1.0 mg/kg q8–12h PO or IV
Esmolol hydrochloride (Brevibloc)	β -blocker. Selective for β_1 -receptor. The difference between esmolol and other β -blockers is the short duration of action. Indicated for short-term control of heart rate and arrhythmias	Same as other precautions for β -blockers	Indicated for short-term IV therapy only. Doses are based primarily on empiricism or extrapolation of human dose. No clinical studies have been reported in animals.	10 mg/mL injection	50–100 μ g/kg IV bolus every 5 min (up to 500 μ g/kg max) 25–200 μ g/kg/min CRI
Estradiol cypionate (ECP, Depo-Estradiol Cypionate, generic)	Semisynthetic estrogen compound. Used primarily to induce abortion in animals	High risk of endometrial hyperplasia and pyometra. High doses can produce leukopenia, thrombocytopenia, and fatal aplastic anemia.	Ordinarily, 22 μ g/kg is administered once IM during days 3–5 of estrus or within 3 days of mating. However, in one study, a dose of 44 μ g/kg was more efficacious than 22 μ g/kg when given during estrus or diestrus.	2 mg/mL injection	Dog: 22–44 μ g/kg IM (total dose not to exceed 1.0 mg) Cat: 250 μ g/cat IM between 40 h and 5 days of mating
Estriol (Incurin)	Estrogen drug used to treat urinary incontinence in dogs.	May be better tolerated than other estrogens.	May be combined with phenylpropanolamine.	1 mg tablet	Dog: Starting dose – 2 mg/dog q24h PO. After 1 week reduce dose to 1.5 mg/dog/day for 1 week, then 1 mg/dog/day for 1 week, and gradually taper the dose and increase the interval (every other day, every third day, etc.) until a goal of 0.5 mg/dog, once per week is achieved.

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Etidronate disodium (Didronel)	Bisphosphonate drug. Used to treat osteoporosis and hypercalcemia. Decreases bone turnover, inhibits osteoclast activity, retards bone resorption, and decreases rate of osteoporosis	Adverse effects not reported for animals. In people, GI problems are common.	At high doses, may inhibit mineralization of bone.	200, 400 mg tablets; 50 mg/mL injection	Dog: 5 mg/kg q24h PO Cat: 10 mg/kg q24h PO
Etodolac (EtoGesic, veterinary; Iodine, human)	An NSAID of the pyranocarboxylic acid group. Inhibits inflammatory prostaglandins.	NSAIDs may cause GI ulceration. Other adverse effects caused by NSAIDs include decreased platelet function and renal injury. Keratoconjunctivitis sicca has been reported in dogs. In clinical trials with etodolac, some dogs at recommended doses showed weight loss, loose stools, or diarrhea. At high doses, etodolac caused GI ulceration in dogs.	Studies in dogs showed etodolac to be more efficacious than placebo for treatment of arthritis.	150 and 300 mg tablets	Dog: 10–15 mg/kg q24h PO Cat: Dose not established
Famciclovir (Famvir)	Antiviral drug. Famciclovir is a synthetic purine analogue (acyclic nucleoside analogue). It is converted to the antiviral drug penciclovir via deacetylation and oxidation and is used to treat feline herpesvirus infections.	Possible adverse effects: mild anemia, mild increase in WBC.	It may produce improvement in some cats, but response can be variable.	125, 250, and 500-mg tablets.	Cat: Treatment of feline herpes: 62.5 mg/cat q8h PO, for 3 weeks. However, a higher dose of 125 mg/cat q8h may be more effective. Lower doses should be used in kittens (30–50 mg/kg oral, q12h).
Famotidine (Pepcid)	Histamine H ₂ -receptor antagonist. Used to suppress acid secretion for treatment and prevention of ulcers.	None reported for animals.	Clinical studies for famotidine have not been performed, therefore optimal dose for ulcer prevention and healing is not known.	10 mg tablet; 10 mg/mL injection; 8 mg/mL oral suspension	Dog: 0.1–0.2 mg/kg PO, IV, SC, IM q12h Cat: 0.2–0.25 mg/kg IM, IV, SC, PO q12–24h

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Felbamate (Felbatol)	Anticonvulsant. Usually used when dogs are refractory to other anticonvulsants. Mechanism may be via antagonism at the N-methyl-D-aspartate (NMDA) receptor and block effects of excitatory amino acids.	Not documented with use in dogs. In people, the most severe reactions have been hepatotoxicity and aplastic anemia. It may increase phenobarbital concentrations.	Dosing has been empirical.	120 mg/mL oral liquid; 400 and 600 mg tablets	Dog: Start with 15–20 mg/kg q8h PO. Or 200 mg/dog q8h for small dogs and 400 mg/dog q8h for larger dogs. Increase dose gradually by 200 mg increments until seizure control. Maximum dose for small dogs is 600 mg/dog q8h and for large dogs is 1200 mg/dog q8h Cat: No dose reported
Fenbendazole (Panacur, Safe-Guard)	Benzimidazole antiparasite drugs. Effective for treatment of <i>Giardia</i>	Good safety margin, but vomiting and diarrhea have been reported. No known contraindications.	Dose recommendations based on clinical studies by manufacturer. Granules may be mixed with food. In studies for treatment of <i>Giardia</i> , it was safer than other treatments.	Panacur granules 22.2% (222 mg/g); 100 mg/mL oral suspension	50 mg/kg/day × 3 days PO
Fentanyl citrate (Sublimaze, generic)	Synthetic opiate analgesic. Approximately 80–100 times more potent than morphine.	Adverse effects similar to morphine.	Doses are based on empiricism and experimental studies. No clinical studies have been reported. In addition to fentanyl injection, transdermal fentanyl is available (see below).	250 µg/5 mL injection	Anesthetic use: 0.02–0.04 mg/kg IV q2h IM, SC or 0.01 mg/kg IV, IM, SC (with acetylpromazine or diazepam) Analgesia: 0.005–0.01 mg/kg, q2h IV, IM, SC CRI: 0.003 mg/kg loading dose, followed by 0.005 mg/kg/h IV in dogs or 0.002 mg/kg/h in cats
Fentanyl transdermal (Recuvyra)	Synthetic opioid analgesic.	Same properties and adverse effects as other fentanyl products.	Approved for use in dogs to treat pain. After transdermal absorption, analgesia is maintained for 4 days.	10 mL amber-colored glass vials (50 mg fentanyl/mL).	Dog: 2.7 mg/kg (1.2 mg/pound) applied topically to the dorsal scapular area 2 to 4 hours prior to surgery. Cat: No dose established.

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Fentanyl, transdermal (Duragesic)	Same as for fentanyl. Transdermal fentanyl incorporates fentanyl into adhesive patches applied to skin of dogs and cats. Studies have determined that patches release sustained levels of fentanyl for 72–108 hours in dogs and cats. One 100 µg/h patch is equivalent to 10 mg/kg of morphine q4h IM.	Adverse effects have not been reported. However, if adverse effects are observed (e.g., respiratory depression, excess sedation, excitement in cats), remove patch and, if necessary, administer naloxone.	Patches available in sizes of 25, 50, 75, and 100 µg/h. Patch size is related to release rate of fentanyl. Studies have determined that 25 µg/h patches are appropriate for cats; 50 µg/h patches are appropriate for dogs 10–20 kg. Follow manufacturer's recommendations carefully when applying patches.	25, 50, 75, and 100 µg/h patch	Dog: 10–20 kg, 50 µg/h patch q72h Cat: 25 µg patch q120h
Ferrous sulfate (many OTC brands)	Iron supplement	High doses cause stomach ulceration.	Recommendations based on dose needed to increase hematocrit	Many	Dog: 100–300 mg/dog q24h PO Cat: 50–100 mg/cat q24h PO
Finasteride (Proscar)	Inhibits conversion of testosterone to dihydrotestosterone (DHT). Since DHT stimulates prostate growth, this drug has been used for benign prostatic hypertrophy.	No adverse effects reported in dogs. Contraindicated in pregnancy	Doses based on study in dogs in which decrease in prostate size was reported.	5 mg tablets	Dog: 0.1 mg/kg PO q24h (or 5 mg tablet q24h in 10–50 kg dogs)
Firocoxib (Previcox)	Firocoxib is a Nonsteroidal Anti-inflammatory Drug (NSAID). Like other drugs in this class, firocoxib produces analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. Firocoxib is highly selective for COX-2.	GI problems are the most common adverse effects associated with NSAIDs and can include vomiting, diarrhea, nausea, ulcers, and erosions of the GI tract.	Dose for cats has only been reported from one study. Not registered for cats.	Tablets 57 or 277 mg	Dog: 5 mg/kg PO, q24h Cat: 1.5 mg/kg, once. Long-term safety in cats has not been determined
Florfenicol (Nuflor)	Chloramphenicol derivative with same mechanism of action as chloramphenicol (inhibition of protein synthesis) and broad antibacterial spectrum. Use in small animals has been infrequent.	Use in dogs and cats has been limited, therefore adverse effects have not been reported. Chloramphenicol has been linked to dose-dependent bone marrow depression, and similar reactions may be possible with florfenicol. However, there does not appear to be a risk of aplastic anemia, as for chloramphenicol.	Dose form is only approved for use in cattle, and these doses have not been evaluated in small animals. Doses listed are derived from pharmacokinetic studies.	300 mg/mL injectable solution	Dog: 20 mg/kg q6h PO, IM Cat: 22 mg/kg q8h IM, PO

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Fluconazole (Diflucan)	Azole antifungal drug. Similar mechanism as other azole antifungal agents. Inhibits ergosterol synthesis in fungal cell membrane. Fungistatic. Active against dermatophytes and variety of systemic fungi, but not <i>Aspergillus</i> sp.	Adverse effects have not been reported from fluconazole administration. Compared to ketoconazole, has less effect on endocrine function. However, increased liver enzyme plasma concentrations and hepatopathy are possible. Compared to other oral azole antifungals, fluconazole is absorbed more predictably and completely, even on an empty stomach.	Doses for fluconazole are primarily based on studies performed in cats for treatment of cryptococcosis. Efficacy for other infections has not been reported. The primary difference between fluconazole and other azoles is that fluconazole attains higher concentrations in the CNS.	50, 100, 150, or 200 mg tablets; 10 or 40 mg/mL oral suspension; 2 mg/mL IV injection	Dog: 10–12 mg/kg q24h PO. For <i>Malassezia</i> , 5 mg/kg q12h PO has been used. Cat: 50 mg/cat q24h, PO
Flucytosine (Ancobon)	Antifungal drug. Used in combination with other antifungal drugs for treatment of cryptococcosis. Action is to penetrate fungal cells and is converted to fluorouracil, which acts as antimetabolite.	Anemia and thrombocytopenia are possible.	Flucytosine is used primarily to treat cryptococcosis in animals. Efficacy is based on flucytosine's ability to attain high concentrations in cerebrospinal fluid (CSF). Flucytosine may be synergistic with amphotericin B.	250 mg capsule; 75 mg/mL oral suspension	25–50 mg/kg q6–8h PO (up to a maximum dose of 100 mg/kg q12h PO)
Fludrocortisone Acetate (Florinef)	Mineralocorticoid. Used as replacement therapy in animals with adrenal atrophy/adrenocortical insufficiency. Has high potency of mineralocorticoid activity compared to glucocorticoid activity	Adverse effects are primarily related to glucocorticoid effects with high doses. Long-term treatment for hypoadrenocorticism may result in glucocorticoid side effects.	Dose should be adjusted by monitoring patient response (i.e., monitoring electrolyte concentrations). In some patients, it is administered with a glucocorticoid and sodium supplementation.	100 µg (0.1 mg) tablets	Dog: 15–30 µg/kg per day PO Cat: 0.1–0.2 mg per cat q24h PO; to test for primary aldosteronism 0.05 mg/kg q12h × 4 days
Flumazenil (Romazicon)	Benzodiazepine receptor antagonist. Used as reversal agent after benzodiazepine administration in people (not commonly used in veterinary medicine)	No adverse effects reported in animals	Used primarily to reverse effects of benzodiazepine drugs. May be used to treat toxicity caused by high doses of benzodiazepines (e.g., diazepam). Although used experimentally for hepatic encephalopathy, it is not recommended for this use.	100 µg/mL (0.1 mg/mL) injection	0.02 mg/kg (20 µg/kg) IV

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Flumethasone (Flucort)	Potent glucocorticoid anti-inflammatory drug. Potency is approximately 15× that of cortisol. Used to treat inflammatory disorders when a potent drug is needed.	Corticosteroids produce multiple systemic side effects. Adverse effects are common with chronic therapy.	Doses are based on severity of underlying disease.	0.5 mg/mL injection	Anti-inflammatory uses: 0.15–0.3 mg/kg q12–24h IV, IM, SC
Flunixin meglumine (Banamine)	NSAID. Acts to inhibit cyclooxygenase (COX) enzyme, which synthesizes prostaglandins. Other anti-inflammatory effects may occur (such as effects on leukocytes), but have not been well characterized. Used primarily for shortterm treatment of moderate pain and inflammation	Most severe adverse effects related to GI system. Causes gastritis, GI ulceration with high doses or prolonged use. Renal ischemia has also been documented. Therapy in dogs should be limited to 4 consecutive days. Avoid use in pregnant animals near term. <i>Drug interactions:</i> Ulcerogenic effects are potentiated when administered with corticosteroids.	Not approved for small animals, but has been shown in experimental studies to be an effective prostaglandin synthesis inhibitor. Usually other NSAIDs are preferred for dogs and cats.	250 mg packet granules; 10, 50 mg/mL injection	1.1 mg/kg once IV, IM, SC or 1.1 mg/kg/day 3 day/week PO Ophthalmic: 0.5 mg/kg once IV
5-Fluorouracil (Fluorouracil)	Anticancer agent. Antimetabolite. Action is via inhibition with nucleic acid synthesis.	Causes mild leukopenia, thrombocytopenia. CNS toxicity. Do not use in cats.	Used in anticancer protocols. Consult anticancer treatment protocol for precise dosage and regimen.	50 mg/mL vial	Dog: 150 mg/m ² once/week IV Cat: do not use
Fluoxetine (Reconcile [veterinary] Prozac [human])	Antidepressant drug. Used to treat behavioral disorders, such as obsessive-compulsive disorders and dominance aggression. Mechanism of action via selective inhibition of serotonin reuptake and down-regulation of 5-HT1 receptors.	Most common adverse effects during field trials were lethargy, reduced appetite, shaking, diarrhea, restlessness, aggression, and vocalization. In cats, nervousness and increased anxiousness have been observed.	Because of long half-life, accumulation in plasma may take several days to weeks.	Human formulations: 10 and 20 mg capsules; 4 mg/mL oral solution Veterinary formulations: 8, 16, 32, 64 mg chewable tablets (Veterinary formulation may no longer be available and human forms should be used instead.)	Dog: 1–2 mg/kg per day, PO Cat: 0.5–1.0 mg/kg per day, PO

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Fluticasone Propionate (Flovent)	Used as an inhaled (topical) corticosteroid for treatment of airway disease. Most of the use has been established for cats. Most common use is for inflammatory airway diseases such as asthma, bronchitis, or bronchospasm.	Although systemic absorption is low, some systemic exposure will occur in animals. Side effects can occur but are not expected to be as severe as with systemic corticosteroids.	It is delivered via a metered-dose inhaler. These inhalers can be used in animals if special adaptations, such as a spacer device, which are available for use in pediatrics or for cats and horses, are used.	Metered-dose inhaler at 44, 110, or 220 µg per puff	Dog: Start with 220 µg per dose, q12h Cat: Start with 44 µg per dose (one puff from a 44 µg inhaler), twice daily. Increase the dose as needed, to 110 µg, then to 220 µg
Follicle-stimulating hormone (FSH)	See Urofollitropin.				
Furosemide (Lasix, generic)	Loop diuretic. Inhibits sodium and water transport in ascending loop of Henle, which produces diuresis. Also may have vasodilating properties, increasing renal perfusion, and decreasing preload	Adverse effects primarily related to diuretic effect (loss of fluid and electrolytes). Administer conservatively in animals receiving ACE inhibitors to decrease risk of azotemia.	Furosemide may be used with other cardiovascular drugs, including pimobendan.	12.5, 20, 50 mg tablets; 10 mg/mL oral solution; 50 mg/mL injection	Dog: 2–6 mg/kg q8–12h (or as needed) IV, IM, SC, PO Cat: 1–4 mg/kg q8–24h IV, IM, SC, PO
Gabapentin (Neurontin)	Anticonvulsant and analgesic. Gabapentin is an analogue of the inhibitory neurotransmitter GABA. The mechanism of anticonvulsant action and analgesic effects are not known.	Warning: oral solution contains xylitol, which may be toxic to dogs.	Gabapentin has been used for treating refractory epilepsy and as adjunct for analgesia (with other drugs). It has not been effective for acute pain in dogs or cats.	100, 300, 400 mg capsules; 100, 300, 400, 600, 800 mg scored tablets; 50 mg/mL oral solution	Anticonvulsant dose: Dog: 2.5–10 mg/kg q8–12h, PO Cat: 5–10 mg q12h PO For analgesia: Dog: 10–15 mg/kg q8h, PO Cat: 8 mg/kg q12h, PO
Gemfibrozil (Lopid)	Cholesterol-lowering agent	Adverse effects have not been reported in animals.	Used primarily in people to treat hyperlipidemia. Clinical studies have not been performed in animals.	300 mg capsules; 600 mg tablets	7.5 mg/kg q12h PO
Gentamicin sulfate (Gentocin)	Aminoglycoside antibiotic. Action is to inhibit bacteria protein synthesis via binding to 30S ribosome. Bactericidal. Broad spectrum of activity except streptococci and anaerobic bacteria	Nephrotoxicity is the most dose-limiting toxicity. Ensure that patients have adequate fluid and electrolyte balance during therapy. Ototoxicity, vestibulotoxicity also are possible. Do not mix in vial or syringe with other antibiotics.	Dosing regimens are based on sensitivity of organisms. Some studies have suggested that once-daily therapy (combining multiple doses into a single daily dose) is as efficacious as multiple treatments.	50 and 100 mg/mL solution for injection	Dog: 9–14 mg/kg q24h IV, IM, SC Cat: 5–8 mg/kg q24h IV, IM, SC
Glibenclamide	British name for glyburide				

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Glipizide (Glucotrol)	Sulfonylurea oral hypoglycemic agent. Used as oral treatment in the management of diabetes mellitus, particularly in cats. Response rate is approximately 50%. This drug acts to increase secretion of insulin from pancreas, probably by interacting with sulfonylurea receptors on β cells. These drugs also may increase sensitivity of existing insulin receptors.	It may cause dose-related vomiting, anorexia, increased bilirubin, and elevated liver enzymes in some cats. Causes hypoglycemia, but less so than insulin. <i>Drug interactions:</i> Many drug interactions have been reported in people. It is not known if these occur in animals. Use cautiously with β -blockers, antifungal drugs, anticoagulants, fluoroquinolones, sulfonamides, and others (consult package insert).	Oral hypoglycemic agents are successful in people only for non-insulin-dependent diabetes. Since response to oral hypoglycemic agents in cats is unpredictable, it is recommended to use a trial first of at least 4 weeks. If the cat responds, the drug can be continued; otherwise, insulin may be indicated. Feed cats a high-fiber diet when using oral hypoglycemic agents. Efficacy in cats is unpredictable.	5, 10 mg tablets	Cat: 2.5–7.5 mg/cat q12h PO. Start with 2.5 mg per cat and increase to 5 mg/cat, q12h Dog: not recommended
Glucosamine and Chondroitin sulfate (Cosequin)	Cosequin is brand name for combination of glucosamine HCl and chondroitin sulfate. According to manufacturer, these compounds stimulate synthesis of synovial fluid and inhibit degradation and improve healing of articular cartilage. Used primarily for degenerative joint disease.	Adverse effects have not been reported, although hypersensitivity is possible.	Doses are based primarily on empiricism and manufacturer's recommendations. May be used with NSAIDs for arthritis in dogs.	Regular (RS) and double strength (DS) capsules	Dog: 1–2 RS capsules per day (2–4 capsules of DS for large dogs) Cat: 1 RS capsule daily
Glyburide (DiaBeta, Micronase, Glynase)	Sulfonylurea hypoglycemic agent. See Glipizide.	Dose-related anorexia and vomiting and elevated liver enzymes	Response is unpredictable. Glipizide is usually preferred in cats.	1.25, 2.5, 5 mg tablets	Cat: 0.2 mg/kg daily PO or 0.625 mg (1/2 tab) per cat/day
Glycerin (generic)	Used to treat acute glaucoma	No adverse effects reported		Oral solution, 40 mg/mL emulsion	1–2 mL/kg, q8h PO
Glycopyrrrolate (Robinul-V)	Anticholinergic drug, Glycopyrrrolate may have less effect on CNS compared to atropine because of lower CSF levels. May have longer duration of action than atropine.	Adverse effects attributed to antimuscarinic (anticholinergic) effects.	Glycopyrrrolate is often used in combination with other agents, particularly anesthetic drugs.	0.2 mg/mL injection	0.005–0.01 mg/kg IV, IM, SC

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GoLYTELY	Oral solution for producing catharsis	See Polyethylene glycol electrolyte solution.			
Gonadorelin (GnRH, LHRH) (Factrel)	Stimulates synthesis and release of luteinizing hormone (LH) and, to a lesser degree, follicle-stimulating hormone (FSH). Used to induce luteinization.	Adverse effects have not been reported in animals.	Gonadorelin has been used to manage various reproductive disorders. Consult specific reference on reproductive problems in animals to guide therapy.	50 µg/mL injection	Dog: 50–100 µg/dog q24–48h IM Cat: 25 µg/cat once IM
Gonadotropin, chorionic (HCG) (Profasi, Pregnyl, generic, A.P.L.)	Action of HCG is identical to that of leutinizing hormone (LH). Used to induce luteinization in animals.	Adverse effects have not been reported in animals.	Consult specific reference on reproductive problems in animals to guide therapy.	Injection sizes of 5000, 10,000, and 20,000 U vials	Dog: 22 U/kg q24–48h IM, or 44 U once IM Cat: 250 U/cat once IM
Gonadotropinreleasing hormone	See Gonadorelin.				
Granisetron (Kytril)	Antiemetic drug that acts by inhibiting serotonin (5-HT) receptors. Used primarily for antiemetic during chemotherapy	None reported in dogs or cats.	Doses extrapolated from human uses.	1 mg tablets and 1 mg/mL injection	0.01 mg/kg IV (in people, dose is 1 mg/person PO)
Griseofulvin (microsize) (Fulvicin U/F) or (ultra-microsize) (Fulvicin P/G, Gris-PEG)	Antifungal drug. Incorporates into skin layers and inhibits mitosis of fungi. Antifungal activity is limited to dermatophytes.	Adverse effects in animals include teratogenicity in cats; anemia and leukopenia in cats; anorexia, depression, vomiting, and diarrhea. Do not administer to pregnant cats.	A wide range of doses has been reported. Doses listed here represent the current consensus. Griseofulvin should be administered with food to enhance absorption. Ultra-microsize is absorbed to a greater extent, and doses should be less than microsize.	125, 250, 500 mg tablets; 25 mg/mL oral suspension; 125 mg/mL oral syrup or ultramicrosize 100, 125, 165, 250, 330 mg tablets	50 mg/kg q24h PO (up to a maximum dose of 110–132 mg/kg/day in divided treatments) Ultramicrosize: 30 mg/kg/day in divided treatments PO
Growth hormone (hGH, somatrem, somatropin) (Protropin, Humatrop, Nutropin)	Growth hormone, also known as human growth hormone. Used to treat growth hormone deficiencies	Growth hormone is diabetogenic in all animals. Excess growth hormone causes acromegaly.	There is only limited clinical experience in animals. Dose form must be reconstituted with sterile diluent before use. Prepared solution is stable for 14 days, if refrigerated.	5 and 10 mg per vial	0.1 U/kg 3 times/week for 4–6 weeks, SC IM (usual human pediatric dose is 0.18–0.3 mg/kg/week)
Guaifenesin (glyceryl guaiacolate, Guaiphenesin, Mucinex)	Expectorant and muscle relaxant. The mechanism for expectorant effects is not known, but may increase respiratory secretions.	A vagal effect (e.g., stimulation of secretions) may occur when the drug is used as an expectorant.	Guaifenesin oral use is primarily for respiratory problems. Intravenous solutions have been used as adjunct for anesthesia, but primarily in horses.	Tablets: 100, 200 mg; Extended release tablets: 600 mg; Oral solution: 20 mg/mL or 40 mg/mL	Dog: Expectorant: 3–5 mg/kg q8h PO Anesthetic adjunct: 2.2 mL/kg/h of a 5% solution IV Cat: Expectorant: 3–5 mg/kg q8h PO

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Halothane (Fluothane)	Inhalent anesthetic	Adverse effects related to anesthetic effects (e.g., cardiovascular and respiratory depression). Hepatotoxicosis has been reported in people.	Use of inhalent anesthetics requires careful monitoring. Dose is determined by depth of anesthesia.	250 mL bottle	Induction: 3% Maintenance: 0.5%–1.5%
Heparin sodium (Liquaemin ([US]; Hepalean [Canada])	Anticoagulant. Potentiates anticoagulant effects of antithrombin III. Used primarily for prevention of thrombosis	Adverse effects caused by excessive inhibition of coagulation: bleeding	Dose adjustments should be performed by monitoring clotting times. For example, dose is adjusted to maintain activated partial thromboplastin time (APTT) to 1.5 to 2× normal.	1000 and 10,000 U/mL injection	Low-dose prophylaxis (dog and cat): 70 U/kg q8–12h SC. Dog: 100–200 U/kg IV loading dose, then 100–300 U/kg q6–8h SC Cat: 300 U/kg, q8h; then up to 500 U/kg, if necessary
Hycodan	See Hydrocodone bitartrate.				
Hydralazine (Apresoline)	Vasodilator. Antihypertensive. Used to dilate arterioles and decrease afterload. Primarily used for treatment of CHF and other cardiovascular disorders characterized by high peripheral vascular resistance.	Adverse effects attributed to excess vasodilation. Monitor patients for hypotension. May dangerously decrease cardiac output. Allergic reactions (lupus-like syndrome) have been reported in people and are related to acetylator status, but have not been reported in animals.	Use in heart failure may accompany other drugs, such as digoxin and diuretics. It is advised to monitor patient for hypotension to adjust dosage.	10 mg tablets; 20 mg/mL injection	Dog: 0.5 mg/kg (initial dose), titrate to 0.5–2 mg/kg q12h PO Cat: 2.5 mg/cat q12–24h PO
Hydrochlorothiazide (HydroDIURIL, generic)	Thiazide diuretic. Inhibits sodium reabsorption in distal renal tubules. Used as diuretic and antihypertensive. Since it decreases renal excretion of calcium, it also has been used to treat calcium containing uroliths.	Do not use in patient with elevated calcium. May cause electrolyte imbalance, such as hypokalemia	Not as potent as loop diuretics (such as furosemide). Clinical efficacy has not been established in veterinary patients.	10, 100 mg/mL oral solution and 25, 50, and 100 mg tablets	2–4 mg/kg q12h PO

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Hydrocodone bitartrate (Hycodan)	Opiate agonist. Used primarily for antitussive action. Hycodan contains homatropine, but other combinations may contain guaifenesin or acetaminophen.	Oral opiate. May cause systemic opiate effects.	Hydrocodone is combined with atropine in the product Hycodan.	5 mg tablets and 1 mg/mL syrup	Dog: antitussive: 0.5 mg/kg, q8h PO; analgesic: 0.5 mg/kg, q8–12h, PO Cat: no dose available
Hydrocortisone (Cortef and generic)	Glucocorticoid anti-inflammatory drug. Hydrocortisone has weaker anti-inflammatory effects and greater mineralocorticoid effects compared with prednisolone or dexamethasone. Also used for replacement therapy	Adverse effects are attributed to excessive glucocorticoid effects.	Dose requirements are related to severity of disease.	5, 10, 20 mg tablets	Replacement therapy: 1–2 mg/kg q12h PO Anti-inflammatory: 2.5–5 mg/kg q12h PO
Hydrocortisone sodium succinate (Solu-Cortef)	Same as hydrocortisone, except that this is a rapid-acting, injectable product	Same as for hydrocortisone	Same as for hydrocortisone. Prepare vials according to manufacturer's recommendations.	Various size vials for injection	Shock: 50–150 mg/kg IV q8h for 2 days Anti-inflammatory: 5 mg/kg q12h IV
Hydromorphone (Dilaudid, Hydrostat, and generic)	Opiate analgesic. Like other opiates, it binds to mu-opiate and kappa-opiate receptors. Hydromorphone is 6 or 7 times more potent than morphine.	Hydromorphone is an opiate agonist, with effects similar to morphine. However it is more potent than morphine and should be used at lower doses.	Hydromorphone may be used interchangeably with morphine, provided that doses are adjusted for potency differences.	Injection: 1, 2, 4, 10 mg/mL; 1 mg/mL oral solution; and 1, 2, 3, 4, 8 mg tablets	Dog: 0.22 mg/kg IM or repeat q4–6h, or as needed for pain treatment. A dose of 0.1 mg/kg may be used with acepromazine Cat: 0.1–0.2 mg/kg, SC or IM or 0.05–0.1 mg/kg IV q2–6h
Hydroxyethyl starch	Synthetic colloid volume expander. Used primarily to treat acute hypovolemia and shock	Kidney injury is possible, but not reported widely in veterinary medicine. Most of the serious adverse effects reported, such as kidney injury and coagulation abnormalities have been observed in human studies, and have not been documented with the clinical use in veterinary medicine.	Used in critical care situations. Infused via constant rate infusion.	6%- to 10% injectable solution	Dogs: Small volume resuscitation: 5 mL/kg IV Large volume resuscitation: 5–15 mL/kg, IV CRI: 10–20 mL/kg/day IV (0.4–0.8 mL/kg/hr). Maximum dose is 33–50 mL/kg/day. Cats: Resuscitation: 2–5 mL/kg IV CRI: 5–10 mL/kg/day IV (0.2–0.4 mL/kg/hr).

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Hydroxyurea (Hydrea)	Antineoplastic agent. Used in combination with other anticancer modalities for treatment of certain tumors. Has been used to treat polycythemia vera	Only limited use in veterinary medicine. No adverse effects have been reported. In people, hydroxyurea causes leukopenia, anemia, thrombocytopenia.	Limited use in veterinary medicine	200, 300, 400, and 500 mg capsules	Dog: 50 mg/kg PO q24h, 3 days/week Cat: 25 mg/kg PO q24h, 3 days/week
Hydroxyzine (Atarax)	Antihistamine of the piperazine class. Used primarily to treat pruritus in animals	Side effects of therapy are related primarily to antihistamine effects. Sedation occurs in some animals.	Clinical studies have shown hydroxyzine to be somewhat effective for treatment of pruritus in dogs. Clinical effects of hydroxyzine are attributed to conversion to cetirizine.	10, 25, 50 mg tablets; 2 mg/mL oral solution	Dog: 2 mg/kg, q8–12h, IM or PO Cat: Effective dose not established
Ibuprofen (Motrin, Advil, Nuprin)	NSAID. Produces anti-inflammatory action via inhibition of prostaglandins.	Safe doses have not been established for dogs and cats. Vomiting and severe GI ulceration and hemorrhage have been reported in dogs.	Avoid use, especially in dogs.	200, 400, 600, 800 mg tablets	Safe dose not established
Imipenem (Primaxin)	β -lactam antibiotic with broad-spectrum activity. Action is similar to other β -lactams except that imipenem is the most active of all β -lactams. Used primarily for serious, multiple-resistant infections	Allergic reactions may occur with β -lactam antibiotics. With rapid infusion or in patients with renal insufficiency, neurotoxicity may occur (seizures). Vomiting and nausea are possible. IM or SC injections may cause pain in dogs.	Reserve the use of this drug for only resistant, refractory infections. Observe manufacturer's instructions carefully for proper administration. For IV administration, add to IV fluids. For IM administration, add 2 mL lidocaine (1%); suspension is stable for only 1 hour.	250 or 500 mg vials for injection	3–10 mg/kg q6–8h IV, SC or IM; usually 5 mg/kg q6–8h IV, IM, or SC
Imipramine (Tofranil)	Tricyclic antidepressant drug (TCA). Used in people to treat anxiety and depression. Used in animals to treat variety of behavioral disorders, including obsessive-compulsive disorders. Action is via inhibition of uptake of serotonin at presynaptic nerve terminals.	Multiple side effects are associated with TCAs, such as antimuscarinic effects (dry mouth, rapid heart rate) and antihistamine effects (sedation). Overdoses can produce life-threatening cardiotoxicity.	Doses are primarily based on empiricism. There are no controlled efficacy trials available for animals. There may be a 2–4 week delay after initiation of therapy before beneficial effects are seen.	10, 25, 50 mg tablets	Dog: 2–4 mg/kg q12–24h PO Cat: 0.5–1.0 mg/kg q12–24h, PO

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Insulin	Insulin has multiple effects associated with utilization of glucose. Used to treat diabetes mellitus in dogs and cats	Adverse effects primarily related to overdoses (hypoglycemia)	Doses should be carefully adjusted in each patient, depending on response. Monitor plasma/serum glucose concentrations.	100 U/mL injection or 40 U/mL injection	Insulin doses are specific for each species and formulation available. Consult specific information on each product to derive starting dose.
Interferon (interferon- α , HuIFN- α) (Roferon)	Human interferon. Used to stimulate the immune system in patients.	Adverse effects have not been reported in animals.	Doses and indications for animals have primarily been based on extrapolation of human recommendations or limited experimental studies. To prepare, add 3 million U to 1 L sterile saline and divide into aliquots and freeze. Thaw as needed for 30 U/mL solution.	5 and 10 million U/vial	Dog: 2.5 million U/kg IV once daily for 3 days Cat: 1 million U/kg IV once daily for 5 consecutive days on days 0, 14, and 60
Iodide	See Potassium iodide.				
Ipecac syrup (Ipecac)	Emetic drug. For emergency treatment of poisoning. Active ingredient is thought to be emetine.	No adverse effects with acute therapy for poisoning. Chronic administration can lead to myocardial toxicity.	Available as non-prescription drug. Onset of vomiting may require 20–30 min.	Oral solution; 30 mL bottle	Dog: 3–6 mL per dog PO Cat: 2–6 mL per cat PO
Ipodate or lopanoic acid.	Cholecystographic agent. Used as treatment for hyperthyroidism in cats. Used as alternative to methimazole, radiation therapy, or surgery.	No adverse effects reported	Use of ipodate has been experimental, and precise doses have not been evaluated. In one study, 2/3 of treated cats responded.	Formulated into 50 mg capsules (these may have to be formulated for cats)	Ipodate: Cat: 15 mg/kg q12h PO. Most common dose has been 50 mg/cat q12h lopanoic acid: 50 mg per cat q12h, PO
Iron	See Ferrous sulfate.				
Isoflurane (AErrane)	Inhalent anesthetic.			100 mL bottle	Induction: 5% Maintenance: 1.5%–2.5%
Isoniazid (INH)	Antibacterial agent that interferes with nucleic acid synthesis. Used for mycobacterium	Do not use in animals with hepatic disease.		100, 300, and 500 mg tablets or 10 mg/mL syrup	5 mg/kg/day, PO, IM, IV; 15 mg/kg 2–3 times/wk

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Isoproterenol (Isuprel)	Adrenergic agonist. Stimulates both β_1 - and β_2 -adrenergic receptors. Used to stimulate heart (inotropic and chronotropic). Also used to relax bronchial smooth muscle for acute treatment of bronchoconstriction.	Adverse effects are related to excessive adrenergic stimulation and are seen primarily as tachycardia and tachyarrhythmias.	Short half-life. Must be infused via constant rate infusion or repeated if administered IM or SC. Recommended for short-term use only.	Ampules for injection, 0.2 mg/mL	10 $\mu\text{g}/\text{kg}$ q6h IM, SC; or dilute 1 mg in 500 mL of 5% dextrose or Ringer's solution and infuse IV 0.5–1 mL/min (1–2 $\mu\text{g}/\text{min}$), or to effect
Isosorbide dinitrate (Isordil, Isorbid, Sorbitrate)	Nitrate vasodilator. Causes vasodilation via generation of nitric oxide. Relaxes vascular smooth muscle, especially venous. Reduces preload in patients with CHF.	Adverse effects are primarily related to overdoses that produce excess vasodilation and hypotension. Tolerance may develop with repeated doses.	Generally, doses are titrated to individual, depending on response.	2.5, 5, 10, 20, 30, 40 mg tablets; 40 mg capsules	2.5–5 mg/animal q12h PO (or 0.22–1.1 mg/kg q12h PO)
Isosorbide mononitrate (Monoket)	Same comments as for isosorbide dinitrate, except that this is a biologically active form of isosorbide dinitrate. Compared to isosorbide dinitrate, it does not undergo first-pass metabolism and is completely absorbed orally.	Same as for isosorbide dinitrate and nitroglycerin	Generally absorbed better than isosorbide dinitrate	10, 20 mg tablets	5 mg/dog two doses per day 7 hours apart PO
Isotretinoin (Accutane)	Keratinization stabilizing drug. Isotretinoin reduces sebaceous gland size, inhibits sebaceous gland activity, and decreases sebum secretion. In people, it is primarily used to treat acne. In animals, it has been used to treat sebaceous adenitis.	Absolutely contraindicated in pregnant animals. Adverse effects not reported for animals, although experimental studies have demonstrated that it can cause focal calcification (such as in myocardium and vessels)	Use in veterinary medicine is confined to limited clinical experience and extrapolation from human reports.	10, 20, 40 mg capsules	Dog: 1–3 mg/kg/day (up to a maximum recommended dose of 3–4 mg/kg/day PO) Cat: no dose established

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Itraconazole (Sporanox)	Azole (triazole) antifungal drug. Active against dermatophytes and systemic fungi, such as <i>Blastomyces</i> , <i>Histoplasma</i> , and <i>Coccidioides</i> . Also used for <i>Malassezia</i> dermatitis.	Itraconazole is better tolerated than ketoconazole. However, vomiting and hepatotoxicosis are possible, especially at high doses. High doses in cats may cause vomiting and anorexia.	Doses are based on studies in animals in which itraconazole has been used to treat blastomycosis in dogs. In cats, lower doses have been effective for dermatophytes (see dosage section). Other uses or doses are based on empiricism or extrapolation from human literature.	100 mg capsules and 10 mg/mL oral liquid. Compounded formulations are not be absorbed as well as proprietary formulations.	Dog: 2.5 mg/kg q12h, or 5 mg/kg q24h PO For <i>Malassezia</i> dermatitis: 5 mg/kg q24h PO for 2 days, repeated each week for 3 weeks Dermatophytes: 3 mg/kg/day PO for 15 days Cat: 5 mg/kg q12h PO For Dermatophytes: 1.5–3.0 mg/kg (up to 5 mg/kg) q24h PO for 15 days
Ivermectin (Heartgard, Ivermectin, Eqvalan liquid)	Antiparasitic drug. Neurotoxic to parasites by potentiating glutamate-gated chloride channels; used for anti-parasitic treatment and heartworm prevention.	Toxicity may occur at high doses, and in breeds in which ivermectin crosses blood–brain barrier. Sensitive breeds include collies, Australian shepherds, shelties, and Old English sheepdogs. Toxicity is neurotoxic, and signs include depression, ataxia, difficulty with vision, coma, and death. Ivermectin appears to be safe for pregnant animals. Do not administer to animals under 6 weeks of age. Animals with high microfilaremia may show adverse reactions to high doses.	Doses vary, depending on use. Heartworm prevention is lowest dose, other parasites require higher doses. Heartgard is only form approved for small animals; for other indications, large animal injectable products are often administered PO, IM, or SC to small animals.	1% (10 mg/mL) injectable solution; 10 mg/mL oral solution; 18.7 mg/mL oral paste; 68, 136, and 272 µg tablets; and 55 and 165 mg feline tablets	Heartworm preventative: 6 µg/kg every 30 days PO in dogs and 24 µg/kg every 30 days PO in cats Microfilaricide: 50 µg/kg PO 2 wks after adulticide therapy Ectoparasite therapy (dogs and cats): 200–300 µg/kg IM, SC, PO Endoparasites (dogs and cats): 200–400 µg/kg weekly SC, PO <i>Demodex</i> therapy: start with 100 µg/kg/day and increase dose by 100 µg/kg/day to 600 µg/kg/day for 60–120 days PO Heartworm prevention in cats: 25 µg/kg every 30 days, PO
Kanamycin (Kantrim)	Aminoglycoside antibiotic with broad-spectrum activity	Shares same properties with other aminoglycosides (see Amikacin, Gentamicin)	See Gentamicin.	200, 500 mg/mL injection	10 mg/kg q12h or 20 mg/kg q24h IV IM, SC

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Ketamine (Ketalar, Ketavet, Vetalar)	Anesthetic agent. NMDA receptor antagonist. Exact mechanism of action is not known, but appears to act as dissociative agent. Rapidly metabolized and eliminated in most animals.	Causes pain with IM injection. Tremors, spasticity, and convulsive seizures have been reported. Increases cardiac output compared to other anesthetic agents. Do not use in animals with head injury because it may elevate CSF pressure.	Often used in combination with other anesthetics and anesthetic adjuncts, such as alpha-2 agonists, acepromazine, or diazepam. IV doses generally less than IM doses.	100 mg/mL injection solution	Dog: 5.5–22 mg/kg IV, IM (recommend adjunctive sedative or tranquilizer treatment). Cat: 2–25 mg/kg IV, IM (recommend adjunctive sedative or tranquilizer treatment). Dog and cat: Dose for constant rate infusion: 0.3–0.5 mg/kg IV followed by 0.3–0.6 mg/kg/h. May be used in combination with other analgesics
Ketoconazole (Nizoral)	Azole (imidazole) antifungal drug. Similar mechanism of action as other azole antifungal agents. Inhibits ergosterol synthesis in fungal cell membrane. Fungistatic. Efficacious against dermatophytes and variety of systemic fungi, such as <i>Histoplasma</i> , <i>Blastomyces</i> , and <i>Coccidioides</i> . Also active against <i>Malassezia</i> .	Adverse effects in animals include dose-related vomiting, diarrhea, and hepatic injury. Enzyme elevations are common. Do not administer to pregnant animals. Ketoconazole causes endocrine abnormalities, especially, inhibition of cortisol synthesis. <i>Drug interactions:</i> Ketoconazole will inhibit metabolism of other drugs (anticonvulsants, cyclosporine, cisapride).	Oral absorption depends on acidity in stomach. Do not administer with antisecretory drugs or antacids. Because of endocrine effects, ketoconazole has been used for short-term treatment of hyperadrenocorticism.	200 mg tablets; 100 mg/mL oral suspension (only available in Canada)	Dog: 10–15 mg/kg q8–12h PO. For <i>Malassezia canis</i> infection: 5 mg/kg q24h PO. For hyperadrenocorticism: start with 5 mg/kg q12h for 7 days, then 12–15 mg/kg q12h PO. Cat: 5–10 mg/kg q8–12h PO
Ketoprofen (Orudis KT [human OTC tablet]; Ketofen [veterinary injection])	NSAID. Anti-inflammatory agent. Used to treat arthritis and other inflammatory disorders.	All NSAIDs share similar adverse effect of GI toxicity. Ketoprofen has been administered for 5 consecutive days in dogs, without serious adverse effects. Most common side effect is vomiting. GI ulceration is possible in some animals.	Although not approved in the US, ketoprofen is approved for small animals in other countries. Doses listed are based on approved use in those countries. It is available as OTC drug for humans in the US.	12.5 mg tablet OTC; 25, 50, 75 mg Rx' human form; 100 mg/mL injection for horses	1 mg/kg q24h PO for up to 5 days. Initial dose can be given via injection at up to 2 mg/kg SC, IM, IV

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Ketorolac tromethamine (Toradol)	NSAID. Used for short-term relief of pain and inflammation. Acts by inhibiting cyclooxygenase enzyme (COX). Use of ketorolac has been evaluated clinically in dogs but not cats.	NSAIDs may cause GI ulceration. Ketorolac may cause gastrointestinal lesions if administered more frequently than q8h. Do not administer more than 2 doses.	Available as 10 mg tablet and injection for IV or IM use. Dosing q12h is recommended to avoid GI problems.	10 mg tablets; 15 and 30 mg/mL injection in 10% alcohol	Dog: 0.5 mg/kg q8–12h PO, IM, IV Cat: safe dose not established
Lactated Ringer's solution (many)	Fluid solution for replacement. IV administration.	Administer IV fluids only in carefully monitored patients.	Fluid requirements vary depending on animal's needs (replacement vs maintenance). Consult fluid therapy reference for optimum rate. Rate listed here is for maintenance and shock.	250, 500, 1000 mL bags	Maintenance: 55–65 mL/kg/day IV Severe dehydration: 50 mL/kg/h, IV Shock: 90 mL/kg IV (dogs) and 60–70 mL/kg IV (cats)
Lactulose (Chronulac, generic)	Laxative. Produces laxative effect by osmotic effect in colon. Lactulose also has been used for treatment of hyperammonemia (hepatic encephalopathy) because it decreases blood ammonia concentrations via lowering pH of colon, thus ammonia in colon is not as readily absorbed.	Excessive use may cause fluid and electrolyte loss.	In veterinary medicine, clinical studies to establish efficacy are not available. In addition to doses cited, 20–30 mL/kg of 30% solution retention enema has been used in cats.	10 g/15 mL	Constipation: 1 mL/4.5 kg q8h (to effect) PO Hepatic encephalopathy—Dog: 0.5 mL/kg q8h PO Cat: 2.5–5 mL/cat q8h PO
L-Dopa	See Levodopa.				
Leflunomide (Arava)	Immunosuppressive agent. Used to suppress T- and β -cell proliferation. Used to treat immune-mediated disease in dogs.	No adverse effects reported in dogs, but may decrease appetite or cause diarrhea.	Usually used as alternative to other immunosuppressive agents.	5, 10, 20 mg tablets	Dogs: 4 mg/kg per day, usually in divided doses of 2 mg/kg q12h, tapered to 2 mg/kg q24h, PO Cats: 2 mg/kg per day, for 2 days, PO, then 2 mg/kg, q48h, PO

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Leucovorin calcium (folinic acid) (Wellcovorin and generic)	Leucovorin is a reduced form of folic acid, which is converted to active folic acid derivatives for purine and thymidine synthesis. It is used as antidote for folic acid antagonists.	Allergic reactions have been reported in people.	Used primarily as rescue for overdoses of folic acid antagonists (methotrexate). Clinical studies have not been reported in veterinary medicine. It is not established whether leucovorin will prevent toxicity from trimethoprim-sulfonamide administration.	5, 10, 15, 25 mg tablets; 3 or 5 mg/mL injection	With methotrexate administration: 3 mg/m ² IV, IM, PO As antidote for pyrimethamine toxicosis: 1 mg/kg q24h PO
Levamisole hydrochloride (Levasole, Tramisol, Ergamisol)	Antiparasitic drug of the imidazothiazole class. Mechanism of action due to neuromuscular toxicity to parasites. Levamisole has been used for endoparasites in dogs and as microfilaricide.	May produce cholinergic toxicity. May cause vomiting in some dogs.	In heartworm-positive dogs, it may sterilize female adult heartworms.	0.184 g bolus; 11.7 g per 13 g packet; 50 mg tablet (Ergamisol)	Dog: hookworms, 5–8 mg/kg once PO (up to 10 mg/kg PO for 2 days); microfilaricide, 10 mg/kg q24h PO for 6–10 days; immunostimulant, 0.5–2 mg/kg 3 times/week PO. Cat: endoparasites, 4.4 mg/kg once PO; lungworms, 20–40 mg/kg q48h for 5 treatments PO
Levetiracetam (Keppra)	Anticonvulsant. Used for treating epilepsy when other treatments have been ineffective. It inhibits burst firing of neurons without affecting normal neuronal excitement.	Weakness, lethargy, dizziness have been reported in people. No adverse effects have been reported in animals.	May be used with other anticonvulsants, such as KBR and phenobarbital.	250-, 500-, 750-, and 1,000-mg tablets. Extended-release formulation (XR) available in 500-, 750-, and 1,000 mg-tablets. Oral solution 100 mg/mL, and 100 and 500 mg/mL solution for injection	Dog: start with 20 mg/kg q8h PO and increase gradually as necessary. Oral extended-release tablets: 30 mg/kg q12h, PO Cat: 20 mg/kg q8h PO
Levodopa (L-dopa) (Larodopa)	Converted to dopamine after crossing blood-brain barrier. Stimulates CNS dopamine receptors. In people, used for treating Parkinson disease. In animals, has been used for treating hepatic encephalopathy.	Adverse effects in animals have not been reported. In people, dizziness, mental changes, difficult urination, and hypotension are among the reported adverse effects.	Clinical studies have not been reported in veterinary medicine. Titrate dose for each patient.	100, 250, 500 mg tablets or capsules	Hepatic encephalopathy: 6.8 mg/kg initially, then 1.4 mg/kg q6h PO

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Levothyroxine sodium (Soxoloxine, Thyo-Tabs, Synthroid Leventa)	Replacement therapy for treating patients with hypothyroidism. Levothyroxine is T4, which is converted in most patients to the active T3.	High doses may produce thyrotoxicosis, which is uncommon (compared to people). Drug interactions: Patients receiving corticosteroids may have decreased ability to convert T4 to T3.	Thyroid supplementation should be guided by testing to confirm diagnosis and postmedication monitoring to adjust dose.	0.1–0.8 mg tablets (in 0.1 mg increments), 1 mg/mL oral solution	Dog: (tablets) 18–22 µg/kg q12h PO (adjust dose via monitoring) Dog (oral solution): 20 µg/kg q24h PO Cat: 10–20 µg/kg/day PO (adjust dose via monitoring)
Lidocaine (Xylocaine and generic brands)	Local anesthetic and Class I antiarrhythmic. Lidocaine is also used commonly for acute treatment of cardiac arrhythmias.	High doses cause CNS effects (tremors, twitches, and seizures). Lidocaine can produce cardiac arrhythmias, but has greater effect on abnormal cardiac tissue than normal tissue. Cats are more susceptible to adverse effects, and lower doses should be used.	When used for local infiltration, many formulations contain epinephrine to prolong activity at injection site. Avoid epinephrine in patients with cardiac arrhythmias. Note that human formulations may contain epinephrine, but no veterinary formulations contain epinephrine. To increase pH, increase onset of action, and decrease pain from injection, one may add 1 mEq sodium bicarbonate to 10 mL lidocaine (use immediately after mixing).	5, 10, 15, 20 mg/mL injection	Dog (antiarrhythmic): 2–4 mg/kg IV (to a maximum dose of 8 mg/kg over 10-min period); 25–75 µg/kg/min IV infusion; 6 mg/kg q1.5h IM Cat (antiarrhythmic): start with 0.1–0.4 mg/kg, then increase to 0.25–0.75 mg/kg IV slowly, or 10–20 µg/kg/min infusion. For epidural (dog and cat): 4.4 mg/kg of 2% solution
Lincomycin (Lincocin)	Lincosamide antibiotic, similar in mechanism to clindamycin and erythromycin. Spectrum includes primarily grampositive bacteria. Used for pyoderma and other soft tissue infections.	Adverse effects uncommon. Lincomycin has caused vomiting and diarrhea in animals. Do not administer orally to rodents and rabbits.	Action of lincomycin and clindamycin are similar enough that clindamycin can be substituted for lincomycin.	100, 200, 500 mg tablets	15–25 mg/kg q12h PO. For pyoderma, doses as low as 10 mg/kg q12h have been used.
Linezolid (Zyvox)	Oxazolidinone antibiotic. Gram-positive spectrum that includes drug resistant strains of <i>Enterococcus</i> and <i>Staphylococcus</i> . High expense limits routine use.	Adverse effects include diarrhea and nausea. Rarely in people anemia and leukopenia have been observed. Use cautiously with monoamine oxidase inhibitors and serotonergic drugs.	Use in animals is reserved for only drug resistant infections (e.g., methicillin-resistant <i>Staphylococcus</i> spp.) for which other drugs are ineffective.	400 and 600 mg tablets. 20 mg/mL oral suspension. 2 mg/ML injection	10 mg/kg, q8–12h PO or IV

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Liothyronine (Cytomel)	Thyroid supplement. Liothyronine is equivalent to T ₃ . Usually levothyroxine is preferred.	Adverse effects have not been reported (see Levothyroxine sodium).	Doses of liothyronine should be adjusted on the basis of monitoring T ₃ concentrations in patients.	5, 25, 50, and 60 µg tablets	4.4 µg/kg q8h PO. For T ₃ suppression test in cats: collect presample for T ₄ and T ₃ , administer 25 µg q8h for 7 doses, then collect postsamples for T ₃ and T ₄ after last dose.
Lisinopril (Prinivil, Zestril)	ACE inhibitor. Used for treatment of CHF and hypertension. Inhibits synthesis of angiotensin II, producing vasodilation and decreased aldosterone.	Lisinopril has not been used extensively in animals to document adverse effects.	Clinical studies using lisinopril in animals have not been reported. With all ACE inhibitors, monitor electrolytes and renal function 3–7 days after initiating therapy and periodically thereafter.	2.5, 5, 10, 20, 40 mg tablets	Dog: 0.5 mg/kg q24h PO Cat: 0.25 mg/kg q24h PO
Lithium carbonate (Lithotabs, Lithane)	Stimulates granulopoiesis and elevates neutrophil pool in animals. In people, it is used for treatment of depression. CNS effect is related to decreased concentrations of neurotransmitters.	Adverse effects have not been reported in animals. In people, cardiovascular problems, drowsiness, and diarrhea are among the adverse effects.	Use in animals is not common. It has been used experimentally to increase neutrophils following cancer therapy.	150, 300, 600 mg capsules; 300 mg tablets; 300 mg/5 mL syrup	Dog: 10 mg/kg q12h PO Cat: not recommended
Lomustine (CCNU) (CeeNU)	Anticancer drug—alkylating agent in the nitrosourea class. Highly lipid-soluble and crosses blood-brain barrier. Used for lymphoma and brain tumors	Myelosuppression, hepatotoxicosis, vomiting	Administering on empty stomach decreases nausea. Monitor hemogram for evidence of myelosuppression.	10, 40, 100 mg capsules	Dog: 70–90 mg/m ² every 4 weeks PO. For brain tumors: 60–80 mg/m ² q6–8 week PO Cat: 50–60 mg/m ² PO every 3–6 weeks or 10–20 mg per cat PO every 3–6 weeks
Loperamide (Imodium and generic)	Opiate agonist. Stimulates smooth muscle segmentation in intestine, as well as electrolyte absorption. Used for acute treatment of nonspecific diarrhea	Loperamide does not produce systemic opiate adverse effects. Its systemic effects are low and it does not cross the blood-brain barrier. However, some breeds (e.g., collies, Australian shepherds, and collie-mixed breeds) may be susceptible to adverse effects because of a deletion of the P-gp. In any animal, excessive use can cause constipation.	Doses are based primarily on empiricism or extrapolation of human dose. Clinical studies have not been performed in animals.	2 mg tablet; 0.2 mg/mL oral liquid	Dog: 0.1 mg/kg q8–12h PO Cat: 0.08–0.16 mg/kg q12h PO

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Lorazepam (Ativan)	Is a benzodiazepine, may be considered for anxiety disorders in animals, but it has not been used as commonly as other drugs such as diazepam.	Sedation is the most common side effect. Lorazepam causes polyphagia. Some animals may experience paradoxical excitement. Chronic administration may lead to dependence and a withdrawal syndrome if discontinued.	There have been no clinical trials in veterinary medicine, although it is expected to produce effects similar to other benzodiazepines.	0.5, 1, and 2 mg tablets and 2 and 4 mg/mL injection	Dog: 0.05 mg/kg q12h PO Seizures: 0.2 mg/kg IV. Repeat every 3–4 hours for seizure control, if necessary Cat: 0.05 mg/kg q12–24h PO.
Lufenuron (Program)	Antiparasitic. Used for controlling fleas in animals. Inhibits development in hatching fleas. May be used for dermatophytes in dogs and cats, although efficacy has been questioned by some experts	Adverse effects have not been reported. Appears to be relatively safe during pregnancy and in young animals	Lufenuron may control flea development with administration once every 30 days in animals.	45, 90, 135, 204.9, 409.8 mg tablets; 135 and 270 mg suspension per unit pack	Flea control: Dog: 10 mg/kg PO every 30 days Cat: 30 mg/kg PO every 30 days Cat injection: 10 mg/kg SC every 6 months Antifungal dose: Dog: 80 mg/kg Cat: 100 mg/kg. In endemic areas (e.g., catteries) treat cats once a month
Lufenuron + milbemycin oxime (Sentinel tablets and Flavor Tabs)	Combination of two antiparasitic drugs. See Lufenuron or Milbemycin oxime. Used to protect against fleas, heartworms, roundworms, hookworms, and whipworms	See Lufenuron or Milbemycin oxime.	See Lufenuron or Milbemycin oxime.	Milbemycin oxime/lufenuron ratio is as follows: 2.3/46 mg tablets; 5.75/115, 11.5/230, and 23/460 mg Flavor Tabs	Dog: Administer one tablet every 30 days. Each tablet formulated for size of dog. Cat: This product is not registered for cats.
Luteinizing hormone	See Gonadorelin.				
L-Lysine (Enisyl-F)	Amino acid for treatment of herpes infections. Oral supplementation for cats with feline herpesvirus-1 (FHV-1) infection. In clinical trials, efficacy for FHV has not been demonstrated for controlling upper respiratory or ocular infections.	Well tolerated in cats	Powder can be mixed with food. Paste can be given directly.	250 mg/mL paste	Cat: 400 mg PO/day Paste formulation: 1–2 mL PO to adult cats and 1 mL to kittens

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Magnesium citrate (Citroma, Citro-Nesia [Citro-Mag in Canada])	Saline cathartic. Acts to draw water into small intestine via osmotic effect. Fluid accumulation produces distention, which promotes bowel evacuation. Used for constipation and bowel evacuation prior to certain procedures	Adverse effects have not been reported in animals. However, fluid and electrolyte loss can occur with overuse. Magnesium accumulation may occur in patients with renal impairment. <i>Drug interactions:</i> Magnesium-containing cathartics decrease oral absorption of ciprofloxacin and other fluoroquinolones.	Commonly used to evacuate bowel prior to surgery or diagnostic procedures. Onset of action is rapid.	Oral 6% suspension	2–4 mL/kg/day PO
Magnesium hydroxide (Milk of Magnesia)	Same as for magnesium citrate. Magnesium hydroxide also is used as oral antacid to neutralize stomach acid.	Magnesium accumulation in patients with renal failure is possible.	Same as Magnesium citrate.	Oral liquid 400 mg/5 mL	Antacid: 5–10 mL/kg q4–6h PO Cathartic (dog): 15–50 mL/kg q24h PO Cathartic (cat): 2–6 mL/cat q24h PO
Magnesium sulfate (Epsom salts)	Magnesium sulfate (Epsom salts) is used as cathartic when administered orally. It also has been used as a source of magnesium for treating refractory arrhythmias.	Same as Magnesium citrate.	See Magnesium citrate.	Crystals. Many generic preparations	Dog: 8–25 g/dog q24h PO For treating arrhythmias: 0.15–0.3 mEq/kg slowly IV over 5–15 minutes followed by 0.75–1.0 mEq/kg per day When supplementing fluid solutions: 0.75–1.0 mEq/kg/day Cat: 2–5 g/cat q24h PO
Mannitol (Osmotrol)	Hyperosmotic diuretic. Increases plasma osmolality, which draws fluid from tissues to plasma. Antiglaucoma agent. Used for treatment of edema and reducing intraocular pressure. Mannitol also has been used to promote urinary excretion of certain toxins.	Causes fluid and electrolyte imbalance. Do not use in dehydrated patients. Use cautiously when intracranial bleeding is suspected because it may increase bleeding. Administration that is too rapid may expand the extracellular volume excessively.	Use only in patients in which fluid and electrolyte balance can be monitored. Once solutions are prepared, discard unused portions.	5%–25% solution for injection	Diuretic: 1 g/kg of 5%–25% solution IV to maintain urine flow. Glaucoma or CNS edema: 0.25–2 g/kg of 15%–25% solution over 30–60 min IV (repeat in 6 h, if necessary). Fluid expansion: Dog: 0.5–2 g/kg IV Cat: 0.5–0.8 g/kg IV over 5 min followed by CRI of 1 mg/kg/min

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Marbofloxacin (Zeniquin)	Fluoroquinolone antimicrobial. Spectrum includes staphylococci, gram-negative bacilli, and some <i>Pseudomonas</i> .	May cause some nausea and vomiting at high doses. Avoid use in young animals. Safe for cats (ocular safety) at recommended dose.	Use susceptibility testing to guide therapy.	25, 50, 100, and 200 mg tablets	2.75–5.55 mg/kg q24h PO
Maropitant (Cerenia)	Antiemetic. Neurokinin (NK) type-1 inhibitor. Maropitant acts to prevent vomiting caused by chemotherapy and motion sickness. It is also effective for inhibiting vomiting from both central and peripheral stimulation.	In clinical trials, there were few adverse effects in dogs or cats. Salivation and muscle tremors occurred in some animals.	Studies have shown NK-1 inhibitors to be effective antiemetics for a variety of stimuli in both dogs and cats. Keep refrigerated to avoid pain from injection.	10 mg/mL injection; 16, 24, 60, or 160 mg tablets	Dog: 1 mg/kg SC q24h for up to 5 days; 2 mg/kg PO q24h for up to 5 days; for motion sickness, 8 mg/kg PO q24h for up to 2 days. Cat: 1 mg/kg, once per day SC or PO
MCT oil (medium chain triglyceride oil [many sources])	Medium chain triglycerides. Used to treat hepatic encephalopathy	Adverse effects not reported in veterinary medicine. May cause diarrhea in some patients.	Results of clinical trials using MCT oil have not been reported. Many enteral feeding formulas contain MCT oil (many polymeric formulations).	Oral liquid	1–2 mL/kg q24h in food
Meclizine (Antivert, generic)	Antiemetic and antihistamine. Used for treatment of motion sickness. Action may be caused by central anticholinergic actions. Also may suppress chemoreceptor trigger zone (CRTZ)	Adverse effects have not been reported in animals. Anticholinergic (atropine-like) effects may cause side effects.	Results of clinical studies in animals have not been reported. Use in animals is based on experience in people or anecdotal experiences in animals.	12.5, 25, 50 mg tablets	Dog: 25 mg q24h PO (for motion sickness, administer 1 h prior to traveling) Cat: 12.5 mg q24h PO, (1 h prior to traveling)
Meclofenamate sodium (Arquel, Meclofen)	NSAID. Used for treatment of arthritis and other inflammatory disorders. Use has diminished because of availability of other NSAIDs.	Adverse effects have not been reported in animals, but adverse effects common to other NSAIDs are possible.	Results of clinical studies in animals have not been reported. Use in animals is based on experience in people or anecdotal experiences in animals. Administer with food.	50, 100 mg capsules Formulations for dogs are rarely available any longer.	Dog: 1 mg/kg PO q24h for up to 5 days Cat: not recommended
Medetomidine (Domitor)	α_2 -adrenergic agonist. Used primarily as sedative, anesthetic adjunct, and analgesia. Use has diminished because of availability of dexmedetomidine (Dexdomitor), which is more specific.	α_2 -agonists decrease sympathetic output. Cardiovascular depression may occur. Medetomidine will cause an initial bradycardia and hypertension.	May be used for sedation, analgesia, and minor surgical procedures. Should be reversed with equal volume of atipamezole	1.0 mg/mL injection	750 μ g/m ² IV or 1000 μ g/m ² IM Lower doses may be used for short-term sedation and analgesia

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Medium chain triglycerides	See MCT oil.				
Medroxy-progesterone acetate (Depo-Provera [injection]; Provera [tablets])	Progesterin hormone. Derivative of acetoxyprogesterone. In animals, used as progesterone hormone treatment to control estrous cycle. Also used for management of some behavioral and dermatologic disorders (such as urine spraying in cats and alopecia)	Adverse effects include polyphagia, polydipsa, adrenal suppression (cats), increased risk of diabetes, pyometra, diarrhea, and increased risk of neoplasia.	Clinical studies in animals have studied primarily the reproductive use and effects on behavioral use. Medroxyprogesterone acetate may have fewer side effects than megestrol acetate.	150, 400 mg/mL suspension injection; 2.5, 5, 10 mg tablets	1.1–2.2 mg/kg q7d IM. For behavioral use, 10–20 mg/kg is injected SC. For prostatic disease in dogs, use 3–5 mg/kg IM, SC
Megestrol acetate (Ovaban)	Progesterin hormone	Long-term use may produce adverse effects including increased risk of neoplasia and diabetes.	Avoid chronic use. Use for controlling behavior problems or dermatologic therapy is discouraged.	5 mg tablets	Dog—proestrus: 2 mg/kg q24h PO for 8 days; anestrus: 0.5 mg/kg q24h PO for 30 days; behavior: 2–4 mg/kg q24h for 8 days (reduce dose for maintenance). Cat—dermatologic therapy or urine spraying: 2.5–5 mg/cat q24h PO for one week, then reduce to 5 mg once or twice/week; suppress estrus: 5 mg/cat/day for 3 days, then 2.5–5 mg once/week for 10 weeks
Melarsomine (Immiticide)	Organic arsenical compound used for heartworm therapy. Heartworm adulticide. Arsenicals alter glucose uptake and metabolism in heartworms.	Adverse effects: pulmonary thromboembolism (7–20 days after therapy), anorexia (13% incidence), injection site reaction (myositis) (32% incidence), lethargy or depression (15% incidence). Causes elevations of hepatic enzymes. High doses (3×) can cause pulmonary inflammation and death. If high doses are administered, dimercaprol (3 mg/kg IM) may be used as antidote.	Avoid human exposure. (Wash hands after handling, or wear gloves.) Do not freeze solutions after they are prepared.	25 mg/mL injection. After reconstitution, retains potency for 24 h	Dog: Administer via deep IM injection. 2.5 mg/kg q24h for two consecutive days. Three dose protocol includes 2.5 mg/kg once, then in 1 month, two additional doses 24 h apart. Doxycycline may be administered to improve efficacy and reduce pulmonary reaction.

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Meloxicam (Mobic [human drug], Metacam [veterinary drug])	NSAID of the oxicam class. Meloxicam is relatively COX-1-sparing and has high COX-1: COX-2 ratio. It has been used in dogs and cats for pain and osteoarthritis.	Adverse effects are GI and include vomiting, diarrhea, and ulceration.	Oral suspension is in a palatable flavor, which may be added to pet's food. Use reduced dose in cats. OroCAM is a transmucosal spray applied to the oral mucosa of dogs (0.1 mg/kg).	0.5 mg/mL (0.02 mg per drop) oral suspension, 1.5 mg/mL (0.05 mg per drop) oral suspension, 0.5% (5 mg/mL) injection, and 7.5- and 15-mg tablets (human preparation). An oral transmucosal is available as a spray. The spray is available in 3 sizes: 0.25 mg, 0.5 mg, and 1.075 mg per spray	Dog: 0.2 mg/kg initial loading dose, then 0.1 mg/kg q24h PO. Injection: 0.2 mg/kg IV or SC. Cat: single antipyretic dose, 0.15–0.3 mg/kg single dose SC. Long-term dose, 0.05 mg/kg once daily, or extend interval to q48–72h PO
Melphalan (Alkeran)	Anticancer agent. Alkylating agent, similar in action to cyclophosphamide	Adverse effects related to its action as an anticancer agent. Causes myelosuppression.	Used to treat multiple myeloma and certain carcinomas.	2 mg tablets, 50 mg vials for injection	1.5 mg/m ² (or 0.1–0.2 mg/kg) q24h PO for 7–10 days (repeat every 3 weeks)
Meperidine (Demerol)	Synthetic opioid agonist with activity primarily at the μ -opiate receptor. Similar in action to morphine, except with approximately 1/7 of the potency. 75 mg meperidine IM or 300 mg PO has similar potency as 10 mg morphine.	Side effects similar to other opiates.	Although comparative clinical studies have not been conducted in animals, meperidine is considered an effective analgesic in dogs and cats, but with short duration.	50, 100 mg tablets; 10 mg/mL syrup; 25, 50, 75, 100 mg/mL injection	Dog: 5–10 mg/kg IV, IM as often as q2–3h (or as needed) Cat: 3–5 mg/kg IV, IM q2–4h (or as needed)
Mepivacaine (Carbocaine-V)	Local anesthetic of the amide class. Medium potency and duration of action, compared to bupivacaine. Compared to lidocaine, longer-acting, but equal potency	Mepivacaine may cause less irritation to tissues than lidocaine.	For epidural use, do not exceed 8 mg/kg total dose. Duration of epidural is 2.5–3 h.	2% (20 mg/mL) injection	Variable dose for local infiltration. For epidural, 0.5 mL of 2% solution every 30 sec until reflexes are absent
6-Mercaptopurine (Purinethol)	Anticancer agent. Antimetabolite agent that inhibits synthesis of purines in cancer cells.	Many side effects are possible that are common to anticancer therapy (many of which are unavoidable), including bone marrow suppression and anemia. Do not use in cats.	Used for various forms of cancer, including leukemia and lymphoma. Consult specific anticancer protocol for specific regimen.	50 mg tablets	Dog: 50 mg/m ² q24h PO Cat: do not use

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Meropenem (Merrem IV)	Broad-spectrum carbapenem antibiotic; indicated primarily for resistant infections caused by bacteria resistant to other drugs. Bactericidal. More active than imipenem and ertapenem.	Risks similar to those of other β -lactam antibiotics. Meropenem does not cause seizures as frequently as imipenem. SC injections may cause slight hair loss at injection site.	Dosage guidelines have been extrapolated from pharmacokinetic studies in animals and not tested for efficacy in animals. Meropenem is more soluble than imipenem and can be injected via bolus rather than administered in fluid solutions.	500 mg/20 mL or 1g/30 mL vial for injection	Dogs: 8.5 mg/kg q12h SC up to 12 mg/kg q8h SC or 24 mg/kg IV q12h For <i>Pseudomonas</i> : 12 mg/kg q8h, SC or 25 mg/kg q8h IV Cats: 10 mg/kg IV, or SC. q12h.
Mesalamine (Asacol, Mesalal, Pentasa)	5-Aminosalicylic acid. Used as treatment for colitis. Action is not precisely known, but suppresses inflammation in colon. Component of sulfasalazine.	Mesalamine alone has not been associated with side effects in animals.	Mesalamine use has not been reported in animals from clinical trials; however, it has been used as a substitute for sulfasalazine in animals that cannot tolerate sulfonamides.	400 mg tablets; 250 mg capsules	Veterinary dose has not been established. The usual human dose is 400–500 mg PO q6–8h which has been used to extrapolate animal dose of 5–10 mg/kg q8h PO (also see Sulfasalazine, Olsalazine)
Metaproterenol (Alupent, Metaprel)	β -adrenergic agonist. β_2 -specific. Used primarily for bronchodilation.	Adverse effects related to excessive β -adrenergic stimulation.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. β_2 -agonists also have been used in people to delay labor (inhibit uterine contractions).	10, 20 mg tablets; 5 mg/mL syrup; and inhalers	0.325–0.65 mg/kg q4–6h PO
Methadone (Methadose, and generic)	Opiate analgesic. Methadone has analgesic properties via binding to opiate receptors, and may also produce some NMDA-receptor antagonism. Methadone is used as an adjunct to anesthesia protocols and for analgesia.	Adverse effects in dogs include sedation and vomiting (rarely). However, other opiate adverse effects in dogs have not been reported.	Oral doses that are available for humans have not been absorbed in dogs.	2 mg/mL oral solution; 10 and 20 mg/mL solution for injection; 5, 10, and 40 mg tablets.	Dog: 0.1–0.5 IV, or 0.5–2.2 mg/kg SC or IM q3–4h Cat: 0.05–0.1 mg/kg IV or 0.2–0.5 mg/kg SC or IM q3–4h
Methazolamide (Neptazane)	Carbonic anhydrase inhibitor. Produces less diuresis than others (See Dichlorphenamide and Acetazolamide).	Use cautiously in patients sensitive to sulfonamides. (See Acetazolamide, Dichlorphenamide.)	Used to treat glaucoma in patients. May be used with other glaucoma agents. (See Acetazolamide, Dichlorphenamide.)	25, 50 mg tablets	2–3 mg/kg q8h PO

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Methenamine hippurate (Hiprex, Urex) (Mandelamine and generic)	Urinary antiseptic. Converted to formaldehyde in acidic urine to produce antibacterial/antifungal effect. Active against a wide range of bacteria. Resistance does not develop. Less effective against <i>Proteus</i> , which produces an alkaline urine pH. Not effective for systemic infections	Although formaldehyde formation in bladder may be irritating, in people, high doses were required (> 8 gm/day). In animals, no adverse effects have been reported.	Results of clinical studies in animals have not been reported. Use in animals is based on experience in people, or anecdotal experience in animals. Urine must be acidic for methenamine to convert to formaldehyde (monitor pH periodically). pH below 5.5 is optimal. Supplement with ascorbic acid or ammonium chloride to lower pH.	Methenamine hippurate: 0.6 and 1 g tablets. Methenamine mandelate is no longer available.	Methenamine hippurate: Dog: 500 mg/dog q12h PO Cat: 250 mg/cat q12h PO
Methimazole (Tapazole, Felimazole)	Antithyroid drug. Used for treating hyperthyroidism, primarily in cats. Action is to serve as substrate for thyroid peroxidase and decrease incorporation of iodide into tyrosine molecules.	In people, it has caused agranulocytosis and leukopenia. In cats, lupus-like reactions are possible, such as vasculitis and bone marrow changes. Well tolerated in dogs.	Use in cats is based on experimental studies in hyperthyroid cats. Methimazole has, for the most part, replaced propylthiouracil for use in cats. Transdermal formulations (compounded) have been used. They may be effective in some cats, but results are inconsistent. Cats should be monitored for response by measuring T4 levels periodically.	5 and 10 mg tablets (human form) and 2.5 and 5 mg tablets (veterinary form)	Cat: 2.5 mg per cat q12h PO × 7–14 days, then 5–10 mg per cat PO q12h, and monitor T ₄ concentrations
DL-Methionine	See Racemethionine.				
Methocarbamol (Robaxin-V)	Skeletal muscle relaxant. Depresses polysynaptic reflexes. Used for treatment of skeletal muscle spasms.	Causes some depression and sedation of the CNS.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.	500, 750 mg tablets; 100 mg/mL injection	44 mg/kg q8h PO, IV on the first day, then 22–44 mg/kg q8h PO. Up to 130 mg/kg for severe conditions
Methohexitol (Brevital)	Barbiturate anesthetic. Methohexitol is about 2–3 × more potent than pentothal, but with shorter duration.	Similar to other barbiturates such as thiopental.	Monitor respiratory and cardiovascular function.	0.5, 2.5, and 5 g vials for injection	3–6 mg/kg IV (give slowly to effect)

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Methotrexate (MTX, Mexate, Folex, Rheumatrex, and generic)	Anticancer agent. Used for various carcinomas, leukemia, and lymphomas. Action is via antimetabolite action. Analogue of folic acid that binds dihydrofolate reductase. Inhibits DNA, RNA, and protein synthesis. In people, methotrexate is also commonly used for autoimmune diseases, such as rheumatoid arthritis.	Anticancer drugs cause predictable (and sometimes unavoidable) side effects that include bone marrow suppression, leukopenia, and immunosuppression. Hepatotoxicity has been reported in people from methotrexate therapy. <i>Drug interactions:</i> Concurrent use with NSAIDs may cause severe methotrexate toxicity. Do not administer with pyrimethamine, trimethoprim, or sulfonamides.	Use in animals has been based on experimental studies. There is only limited clinical information available. Consult specific anticancer protocols for precise dosage and regimen.	2.5 mg tablets; 2.5 or 25 mg/mL injection	2.5–5 mg/m ² q48h PO (dose depends on specific protocol) Dog: 0.3–0.5 mg/kg once/week IV Cat: 0.8 mg/kg IV every 2–3 weeks
Methoxamine (Vasoxyl)	Adrenergic agonist. Sympathomimetic. α_1 -adrenergic agonist. Specific for α_1 -receptors used as a vasopressor.	Adverse effects related to excessive stimulation of α_1 -receptor (prolonged peripheral vasoconstriction). Reflex bradycardia may occur.	Used primarily in critical care patients or during anesthesia to increase peripheral resistance and increase blood pressure. Short onset and duration of action	20 mg/mL injection is no longer available in the US. Some solutions have been compounded.	200–250 μ g/kg IM, or 40–80 μ g/kg IV; repeat dose as needed
Methylene blue 0.1% (generic, also called new methylene blue)	Antidote for intoxication. Used to treat methemoglobinemia. Methylene blue acts as reducing agent to reduce methemoglobin to hemoglobin.	Methylene blue can cause Heinz body anemia in cats, but is safe when used at therapeutic doses listed here.	Comparison of effects for intoxication has only been performed in experimental studies.	1% solution (10 mg/mL)	1.5 mg/kg IV, slowly, once
Methylprednisolone (Medrol)	Glucocorticoid anti-inflammatory drug. Compared to prednisolone, methylprednisolone is 1.25× more potent.	Same as for other glucocorticoids. Manufacturer suggests that methylprednisolone causes less PU/PD than prednisolone.	Use of methylprednisolone is similar to that of other corticosteroids. Dose adjustment should be made to account for difference in potency. (See dose section.)	1, 2, 4, 8, 18, 32 mg tablets	0.22–0.44 mg/kg q12–24h PO

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Methylprednisolone acetate (Depo-Medrol)	Depot form of methylprednisolone. Slowly absorbed from IM injection site, producing glucocorticoid effects for 3–4 weeks in some animals. Used for intralesional therapy, intra-articular therapy, and inflammatory conditions	Many adverse effects are possible from use of corticosteroids. Cardiovascular problems (congestive heart failure) have been associated with use in cats. Chronic use of methylprednisolone acetate may cause long-term adverse effects.	Use of methylprednisolone acetate should be evaluated carefully because one injection will cause glucocorticoid effects that persist for several days to weeks.	20 or 40 mg/mL suspension for injection	Dog: 1 mg/kg (or 20–40 mg/dog) IM every 1–3 weeks Cat: 10–20 mg/cat IM every 1–3 weeks
Methylprednisolone sodium succinate (Solu-Medrol)	Same as methylprednisolone, except that this is a water-soluble formulation intended for acute therapy when high IV doses are needed for rapid effect. Used for treatment of shock and CNS trauma.	Adverse effects are not expected from single administration; however, with repeated use, other side effects are possible.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.	1 and 2 g and 125 and 500 mg vials for injection	For emergency use: 30 mg/kg IV and repeat at 15 mg/kg in 2–6 h, IV
Methyltestosterone (Android, generic)	Anabolic androgenic agent. Used for anabolic actions or testosterone hormone replacement therapy (androgenic deficiency). Testosterone has been used to stimulate erythropoiesis.	Adverse effects caused by excessive androgenic action of testosterone. Prostatic hyperplasia is possible in male dogs. Masculinization can occur in female dogs. Hepatopathy is more common with oral methylated testosterone formulations.	See also Testosterone cypionate, Testosterone propionate. Use of testosterone androgens has not been evaluated in clinical studies in veterinary medicine. Use is based primarily on experimental evidence or experiences in people.	10, 25 mg tablets	Dog: 5–25 mg/dog q24–48h PO Cat: 2.5–5 mg/cat q24–48h PO
Metoclopramide (Reglan, Maxolon)	Prokinetic drug. Centrally acting antiemetic. Stimulates motility of upper GI tract. Action is to inhibit dopamine receptors and enhance action of acetylcholine in GI tract. Used primarily for gastroparesis and treatment of vomiting. It is not effective for dogs with gastric dilation.	Adverse effects are primarily related to blockade of central dopaminergic receptors. Adverse effects similar to phenothiazines (e.g., acepromazine) have been reported, in addition to behavioral changes. Do not use in epileptic patients or with diseases caused by GI obstruction.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. Most use is for general antiemetic purposes, but doses as high as 2 mg/kg have been used to prevent vomiting during cancer chemotherapy.	5, 10 mg tablet; 1 mg/mL oral solution; 5 mg/mL injection	0.2–0.5 mg/kg q6–8h IV, IM, PO CRI: loading dose of 0.4 mg/kg IV, followed by 0.3 mg/kg/h IV. In refractory patients, rates up to 1.0 mg/kg/h have been used Antiemetic treatment with cancer chemotherapy: up to 2 mg/kg/24h

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Metoprolol tartrate (Lopressor)	Adrenergic-blocking agent, β_1 -adrenergic blocker. Similar properties to propranolol, except that metoprolol is specific for β_1 -receptor. Used to control tachyarrhythmias and slow heart rate.	Adverse effects are primarily caused by excessive cardiovascular depression (decreased inotropic effects). May cause heart block. Use cautiously in animals prone to bronchoconstriction.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.	50, 100 mg tablets; 1 mg/mL injection	Dog: 5–50 mg/dog (0.5–1.0 mg/kg) q8h PO Cat: 2–15 mg/cat q8h PO
Metronidazole (Flagyl and generic) and Metronidazole benzoate	Antibacterial and antiprotozoal drug. Disrupts DNA in organism via reaction with intracellular metabolite. Action is specific for anaerobic bacteria and protozoa, such as <i>Giardia</i> .	Most severe adverse effect is caused by toxicity to CNS. High doses have caused lethargy, CNS depression, ataxia, vomiting, and weakness. Metronidazole may be mutagenic. Fetal abnormalities have not been demonstrated in animals with recommended doses, but use cautiously during pregnancy.	Metronidazole is one of the most commonly used drugs for anaerobic infections and for giardiasis. Maximum dose that should be administered is 50–65 mg/kg/day in any species. Although tablets have been broken or crushed for oral administration to cats, they find these unpalatable. When palatability is a problem in cats, consider metronidazole benzoate.	250, 500 mg tablet; 50 mg/mL suspension; 5 mg/mL injection; the benzoate form is not available commercially and must be obtained from compounding pharmacies. 20 mg of metronidazole benzoate = 12.4 mg metronidazole.	For anaerobes—Dog: 15 mg/kg q12h, or 12 mg/kg q8h PO Cat: 10–25 mg/kg q24h PO For <i>Giardia</i> —Dog: 12–15 mg/kg q12h for 8 days PO Cat: 17 mg/kg (1/3 tablet per cat) q24h for 8 days
Mexiletine (Mexitil)	Antiarrhythmic drug. Used for ventricular arrhythmias. Mechanism of action is to block fast sodium channel. Class IB antiarrhythmic agent. An additional use of mexiletine is its use for treating chronic pain. It is used to treat pain caused by diabetic neuropathy and nerve injury and lower doses than the antiarrhythmic dose.	May produce arrhythmias. Use cautiously in animals with liver disease. Do not use in cats.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.	150, 200, 250 mg capsules	Dog: 6–10 mg/kg q8–12h PO Chronic pain caused by nerve injury: 4–10 mg/kg PO, q8h. Not recommended for cats

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Midazolam hydrochloride (Versed)	Benzodiazepine. Action is similar to other benzodiazepines. Used as anesthetic adjunct. Absorbed better from IM injection than other benzodiazepines	Use very cautiously IV, especially with opiates. IV midazolam may cause cardiorespiratory depression.	Clinical experience is based on anecdotal reports and experimental studies. Compared to other benzodiazepines, midazolam can be administered IM.	5 mg/mL injection	Dog: 0.1–0.25 mg/kg IV, IM or 0.1–0.3 mg/kg/h IV infusion Cat: (sedation) 0.05 mg/kg IV; (induction) 0.3–0.6 mg/kg IV; combined with 3 mg/kg ketamine
Milbemycin oxime (Interceptor, Interceptor Flavor Tabs, and SafeHeart)	Antiparasitic drug of the macrocyclic lactone group. Mechanism of action is similar to ivermectin. Used as heartworm preventative, miticide, and microfilaricide. Used to control infections of hookworm, roundworms, and whipworms. At high doses, it has been used to treat Demodex infections in dogs.	In susceptible dogs (collie breeds), milbemycin may cross the blood–brain barrier and produce CNS toxicosis (depression, lethargy, coma). At doses used for heartworm prevention, this effect is less likely.	Doses vary, depending on parasite treated. Consult dose column. Treatment of Demodex requires high dose administered daily. See also Lufenuron + milbemycin oxime.	2.3, 5.75, 11.5, and 23 mg tablet	Dog: microfilaricide: 0.5 mg/kg q30 days PO; Demodex: 2 mg/kg q24h PO for 60–120 days; heartworm prevention and control of endoparasites: 0.5 mg/kg every 30 days PO. Cat: for heartworm and endoparasite control, 2.0 mg/kg every 30 days PO
Mineral oil (generic)	Lubricant laxative. Increases water content of stool. Used to increase passage of feces for treatment of impaction and constipation.	Adverse effects have not been reported. Chronic use may decrease absorption of fat-soluble vitamins.	Use is empirical. No clinical results reported.	Oral liquid	Dog: 10–50 mL/dog q12h PO Cat: 10–25 mL/cat q12h PO
Minocycline hydrochloride (Minocin, Solodyn)	Tetracycline antibiotic. Similar to doxycycline.	Minocycline may cause vomiting and gastrointestinal disturbances, especially at high doses.	Clinical use has not been reported, but properties are similar to doxycycline. Used in dogs and cats as a substitute for minocycline. It has similar activity and clinical indications as for doxycycline.	50, 75 and 100 mg tablets; or capsules 10 mg/mL oral suspension	Dog: 5 mg/kg q12h PO Cat: 8.8 mg/kg (or 50 mg per cat) q24h PO

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Mirtazapine (Remeron)	Used as an antiemetic and appetite stimulant. Action is via blockade of serotonin receptors and antagonism of alpha-2 receptors.	In cats, twitching and changes in behavior have been observed.	Doses and recommendations in animals are based primarily on studies performed in cats. Use in dogs is based primarily on anecdotal experience.	15 and 30 mg tablets	Dogs: 0.5 mg/kg q24h, PO. Generally in the range of 3.75–7.5 mg per dog, daily, PO Cats: 1.9 mg per cat, PO. Doses have ranged from 3.75 to 7.5 mg per cat, per day, PO (one fourth to one half of a 15-mg tablet). In healthy cats it can be administered once daily. In cats with chronic kidney disease, increase interval to q48h
Misoprostol (Cytotec)	Prostaglandin E ₂ analogue. Prostaglandins provide a cytoprotective role in the GI mucosa. Misoprostol is used to prevent gastritis and ulcers associated with NSAID therapy. Misoprostol also has been effective for atopic dermatitis in dogs.	Adverse effects are caused by effects of prostaglandins. Most common side effects are GI discomfort, vomiting, and diarrhea. Do not administer to pregnant animals; may cause abortion.	Doses and recommendations are based on clinical trials in which misoprostol was administered to prevent GI mucosal injury caused by aspirin.	0.1 mg (100 µg), 0.2 mg (200 µg) tablets	Dog: 2–5 µg/kg q12h PO Atopic dermatitis: 5 µg/kg q8h, PO Cat: dose not established
Mithramycin	Older name for plicamycin				
Mitotane (<i>o,p'</i> -DDD) (Lysodren)	Adrenocortical cytotoxic agent. Causes suppression of adrenal cortex. Used to treat adrenal tumors and pituitary-dependent-hyperadrenocorticism (PDH).	Adverse effects, especially during induction period, include lethargy, anorexia, ataxia, depression, vomiting. Corticosteroid supplementation (e.g., hydrocortisone or prednisolone) may be administered to minimize side effects.	Dose and frequency often are based on patient response. Adverse effects are common during initial therapy. Administration with food increases oral absorption. Maintenance dose should be adjusted on the basis of periodic cortisol measurements and ACTH stimulation tests. Cats usually have not responded to mitotane treatment.	500 mg tablets	Dog—for PDH: 50 mg/kg/day (in divided doses) PO for 5–10 days, then 50–70 mg/kg/week PO; for adrenal tumor: 50–75 mg/kg/day for 10 days, then 75–100 mg/kg/week PO

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Mitoxantrone hydrochloride (Novantrone)	Anticancer antibiotic. Similar to doxorubicin in action. Used for leukemia, lymphoma, and carcinomas.	As with all anticancer agents, certain adverse effects are predictable, unavoidable, and related to drug's action. Mitoxantrone produces myelosuppression, vomiting, anorexia, and GI upset, but may be less cardiotoxic than doxorubicin.	Proper use of mitoxantrone usually follows a specific anticancer protocol. Consult specific protocol for dosing regimen.	2 mg/mL injection	Dog: 5–5.5 mg/m ² IV every 21 days Cat: 6.0–6.5 mg/m ² IV every 21 days
Morphine sulfate (generic)	Opioid agonist, analgesic. Prototype for other opioid agonists. Action of morphine is to bind to μ - and κ -opiate receptors on nerves and inhibit release of neurotransmitters involved with transmission of pain stimuli (such as substance P). Morphine also may inhibit release of some inflammatory mediators. Central sedative and euphoric effects are related to μ -receptor effects in brain.	Like all opiates, side effects from morphine are predictable and unavoidable. Side effects from morphine administration include sedation, constipation, and bradycardia. Respiratory depression occurs with high doses. Tolerance and dependence occur with chronic administration. Cats are more sensitive to excitement than other species.	Effects from morphine administration are dose dependent. Low doses (0.1–0.25 mg/kg) produce mild analgesia. Higher doses (up to 1 mg/kg) produce greater analgesic effects and sedation. Usually morphine is administered IM, IV, or SC. Oral absorption is inconsistent and unreliable. Epidural administration has been used for surgical procedures.	1 and 15 mg/mL injection; 30, 60 mg delayed-release tablets	Dog: 0.1–1 mg/kg IV, IM, SC (dose is escalated as needed for pain relief) q4–6h. 0.5 mg/kg q2h has been used to provide consistent analgesia CRI: 0.2 mg/kg followed by 0.1 mg/kg/h, IV Epidural: 0.1 mg/kg Cat: 0.1 mg/kg IM, SC q3–6h (or as needed)
Moxidectin (canine form: ProHeart; equine oral gel: Quest; cattle pour-on: Cydectin)	Antiparasitic drug. Neurotoxic to parasites by potentiating glutamate-gated chloride ion channels in parasites. Used for endo- and ectoparasites, as well as heartworm prevention.	Toxicity may occur at high doses and in species in which ivermectin crosses blood–brain barrier (collie breeds). Toxicity is neurotoxic, and signs include depression, ataxia, difficulty with vision, coma, and death.	Similar use as ivermectin. Extreme caution is recommended if equine formulation is considered for use in small animals. Toxic overdoses are likely because the equine formulation is highly concentrated.	30, 68, 136 μ g tablets for dogs; 20 mg/mL equine oral gel; and 5 mg/mL cattle pour-on	Dog—heartworm prevention: 3 μ g/kg q30d PO Endoparasites: 25–300 μ g/kg Demodex: 400 μ g/kg/day PO and up to 500 μ g/kg/day for 21–22 weeks Long-acting: Proheart-6: 0.17 mg/kg SC as a single dose
Moxifloxacin (Avelox)	Fluoroquinolone antibiotic. Similar to other fluoroquinolones, except with greater activity against gram-positive and anaerobic bacteria.	Similar to those of other fluoroquinolones. Because of the increased spectrum of action on anaerobic bacteria, greater GI disturbance is possible from oral dose.	Doses and recommendations based primarily on limited clinical experience and extrapolation from human studies	400 mg tablet	10 mg/kg q24h PO

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Mycophenolate (Cell Cept)	Mycophenolate is metabolized to mycophenolic acid. It is used to suppress immunity for transplantation and for treatment of immune-mediated diseases.	In dogs, gastrointestinal problems (diarrhea, vomiting) have been the most common effects reported.	Mycophenolate is used in some patients that cannot tolerate other immunosuppressive drugs such as azathioprine or cyclophosphamide.	250 and 500 mg capsule	Dog: 10 mg/kg q8h PO, or 20 mg/kg q12h PO Cats: 10 mg/kg q12h, PO
Naloxone (Narcan)	Opiate antagonist. Used to reverse effects from opiate agonists (such as morphine). Naloxone may be used to reverse sedation, anesthesia, and adverse effects caused from opiates.	Adverse effects are not reported. Tachycardia and hypertension have been reported in people.	Administration may have to be individualized based on response in each patient. Naloxone's duration of action is short in animals (60 min) and may have to be repeated.	20 or 400 µg/mL or 1 mg/mL injection	0.01–0.04 mg/kg IV, IM, SC, as needed, to reverse opiate
Naltrexone (Trexan)	Opiate antagonist. Similar to naloxone, except that it is longer acting and administered orally. Used in people for treatment of opiate dependence. In animals, it has been used for treatment of some obsessive-compulsive behavioral disorders.	Adverse effects have not been reported in animals.	Treatment for obsessive-compulsive disorders in animals has been reported with naltrexone. Relapse rates may be high.	50 mg tablets	Dog: For behavior problems: 2.2 mg/kg q12h PO
Nandrolone decanoate (Deca-Durabolin)	Anabolic steroid. Derivative of testosterone. Anabolic agents are designed to maximize anabolic effects while minimizing androgenic action. Anabolic agents have been used for reversing catabolic conditions, increasing weight gain, increasing muscling in animals, and stimulating erythropoiesis.	Adverse effects from anabolic steroids can be attributed to the pharmacologic action of these steroids. Increased masculine effects are common. Increased incidence of some tumors has been reported in people.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.	50, 100, 200 mg/mL injection	Dog: 1–1.5 mg/kg/week IM Cat: 1 mg/kg/week IM

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Naproxen (Naprosyn, Naxen, Aleve [naproxen sodium])	NSAID. Action is via inhibition of prostaglandins. Used for treatment of inflammatory disorders (e.g., arthritis). Use in animals has declined because of availability of other NSAIDs.	Naproxen is a potent NSAID. Adverse effects attributed to GI toxicity are common to all NSAIDs. Naproxen has produced serious ulceration in dogs because elimination in dogs is much slower than in people or horses.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on pharmacokinetic studies in experimental animals. Use caution when using the OTC formulation designed for people because the tablet size is much larger than safe dose for dogs. 220 mg naproxen sodium is equivalent to 200 mg naproxen.	220 mg tablet (OTC); 25 mg/mL oral suspension; 250, 375, 500 mg tablets (Rx)	Dog: 5 mg initially, then 2 mg/kg q48h PO Cat: not recommended
Neomycin (Biosol)	Aminoglycoside antibiotic. Neomycin differs from other aminoglycosides because it is only administered topically or orally. Systemic absorption is minimal from oral absorption.	Although oral absorption is so small that systemic adverse effects are unlikely, some oral absorption has been demonstrated in young animals (calves). Alterations in intestinal bacterial flora from therapy may cause diarrhea.	Neomycin is primarily used for oral treatment of diarrhea. Efficacy for this indication (especially for nonspecific diarrhea) is questionable. Used also for treatment of hepatic encephalopathy.	500 mg bolus; 50 and 200 mg/mL oral liquid; 325 mg soluble powder	10–20 mg/kg q6–12h PO
Neostigmine bromide and Neostigmine methylsulfate (Prostigmin; Stiglyn)	Anticholinesterase drug. Cholinesterase inhibitor. Inhibits breakdown of acetylcholine at synapse. Antimyasthenic drug. Used primarily for treatment of myasthenia gravis or as an antidote for neuromuscular blockade caused by neuromuscular blocking drugs.	Adverse effects are related to drug's pharmacologic effects: excessive cholinergic stimulation (muscarinic effects), which include diarrhea, salivation, respiratory problems, vomiting, CNS effects, muscle twitching, or used to treat overdose.	Compared to other drugs in this class (e.g., pyridostigmine) produces more severe muscarinic effects. When injected for diagnosis or treatment of myasthenia, it is recommended to use atropine to counteract side effects.	15 mg tablet (neostigmine bromide); 0.25, 0.5 mg/mL injection (neostigmine methylsulfate)	2 mg/kg/day PO (in divided doses, to effect). Injection—antimyasthenic: 10 µg/kg IM, SC, as needed; antidote for neuromuscular block: 40 µg/kg IM or SC; diagnostic aid for myasthenia gravis: 40 µg/kg IM or 20 µg/kg IV

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Nifedipine (Adalat, Procardia)	Calcium channel-blocking drug of the dihydropyridine class. Action is similar to other calcium channel-blocking drugs, except nifedipine is more specific for vascular smooth muscle than cardiac tissue. Used for smooth muscle relaxation, vasodilation.	Adverse effects have not been reported in veterinary medicine. Most common side effect is hypotension.	Use of nifedipine is limited in veterinary medicine. Other calcium channel blockers, such as diltiazem, are used to control heart rhythm.	10, 20 mg capsules; and 30, 60, 90 extended release capsules	Animal dose not established. In people, the dose is 10 mg/person three times a day and increased in 10 mg increments to effect.
Nitenpyram (Capstar)	Antiparasitic drugs. It rapidly kills adult fleas.	No adverse reactions are reported. It was safe in studies in dogs and cats in which up to 10× dose was administered. Transient pruritus may be observed shortly after administration which coincides with rapid flea death.	Do not use in dogs or cats less than 1 kg (2 pounds) in weight. Do not use in cats or dogs less than 4 weeks of age.	Tablet: 11.4 or 57 mg	1 mg/kg, PO, daily as needed to kill fleas
Nitrofurantoin (Macrodantin, Furalan, Furatoxin, Furadantin, and generic)	Antibacterial drug. Urinary antiseptic. Action is via reactive metabolites that damage DNA. Therapeutic concentrations are reached only in the urine. Not to be used for systemic infections. May be active against some bacteria that are resistant to other antimicrobials.	Adverse effects include nausea, vomiting, and diarrhea. Turns urine color rust-yellow brown. Do not administer during pregnancy.	Two dosing forms exist. Microcrystalline is rapidly and completely absorbed. Macrocystalline (Macrodantin) is more slowly absorbed and causes less GI irritation. Urine should be at acidic pH for maximum effect. Administer with food to increase absorption.	Macrodantin and generic: 25, 50, 100 mg capsules; Furalan, Furatoxin, and generic: 50, 100 mg tablets; Furadantin: 5 mg/mL oral suspension	10 mg/kg/day divided into four daily treatments, for 10–14 days, then 1 mg/kg at night PO Macrocrystalline formulation: 2–3 mg/kg q8h PO, followed by 1–2 mg/kg once at night
Nitroglycerin ointment (Nitrol, Nitro-Bid, Nitrostat)	Nitrate. Nitrovasodilator. Relaxes vascular smooth muscle (especially venous) via generation of nitric oxide. Used primarily in heart failure to reduce preload or decrease pulmonary hypertension. In people, used to treat angina pectoris.	Most significant adverse effect is hypotension. Methemoglobinemia can occur with accumulation of nitrates, but is a rare problem.	Tolerance can develop with repeated, chronic use. Use should be intermittent for optimum effect. Nitroglycerin has high presystemic metabolism, and oral availability is poor. When using ointment, 1 inch of ointment is approximately 15 mg.	0.5, 0.8, 1, 5, 10 mg/mL injection; 2% ointment; transdermal systems (0.2 mg/h patch)	Dog: 4–12 mg (up to 15 mg) topically q12h Cat: 2–4 mg topically q12h (or 1/4 inch of ointment per cat)

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Nitroprusside (Sodium nitroprusside) (Nitropress)	Nitrate vasodilator. See Nitroglycerin ointment. Nitroprusside is used only as an IV infusion, and patients should be monitored carefully during administration.	Severe hypotension is possible during therapy. Monitor patients carefully during administration. Cyanide is generated via metabolism during nitroprusside treatment, especially at high infusion rates. Sodium thiosulfate has been used in people to prevent cyanide toxicity. Methemoglobinemia is possible, and if necessary, treated with methylene blue.	Nitroprusside is administered via IV infusion. IV solution should be delivered in 5% dextrose solution (e.g., add 50 mg to 250 mL of 5% dextrose). Protect from light. Discard solution if color change is observed. Titrate dose carefully in each patient.	50 mg vial for injection	1–5 µg/kg/min up to a maximum of 10 µg/kg/min IV infusion. Start with 2 µg/kg/min and increase gradually until desired blood pressure is achieved.
Nizatidine (Axit)	Histamine H ₂ blocking drug. Same as cimetidine, except up to 10× more potent. Inhibits acid secretion in stomach. Used for ulcers and gastritis.	Side effects from nizatidine have not been reported in animals.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. Nizatidine and ranitidine have been shown to stimulate gastric emptying and colonic motility via anticholinesterase activity.	150, 300 mg capsules	Dog: 2.5–5 mg/kg q24h PO
Norfloxacin (Noroxin)	Fluoroquinolone antibacterial drug. Same action as ciprofloxacin, except spectrum of activity is not as broad as with enrofloxacin or ciprofloxacin.	Adverse effects have not been reported in animals. Some effects are expected to be similar to enrofloxacin and other veterinary fluoroquinolones.	Use in animals (and doses) is based on pharmacokinetic studies in experimental animals, experience in people, or anecdotal experience in animals.	400 mg tablets	22 mg/kg q12h PO
Oclacitinib (Apoquel)	A Janus kinase inhibitor used for control of pruritus in dogs associated with allergic dermatitis and atopic dermatitis.	Adverse effects are rare if the recommended dosing schedule is followed.	Oclacitinib has a rapid onset of effect to control pruritus in dogs.	3.6, 5.4 and 16 mg tablets.	Dog: 0.5 mg/kg (0.4–0.6 mg/kg, with or without food) PO q12h for 14 days, then decrease frequency to q24h. Cat: Dose not established.

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Olsalazine sodium (Dipentum)	Anti-inflammatory drug for treating colitis. Two molecules of mesalamine joined by an azo bond.	No adverse effects reported in dogs.	Olsalazine is used in patients that cannot tolerate sulfasalazine.	500 mg tablets	Dose not established, but 5–10 mg/kg q8h PO has been used. (The usual human dose is 500 mg twice daily.)
Omeprazole (Prilosec)	Proton pump inhibitor. Omeprazole inhibits gastric acid secretion by inhibiting the K ⁺ /H ⁺ pump. Omeprazole is more potent and longer acting than most available antisecretory drugs. Used for treatment and prevention of GI ulcers.	Side effects have not been reported in animals. Drug interactions: Do not administer with drugs that depend on stomach acid for absorption (e.g., itraconazole or ketoconazole).	Due to omeprazole's potency and accumulation in gastric cells, once-daily administration is possible. Equine paste has been diluted to 40 mg/mL in oil and administered to dogs at a dose of 1 mg/kg PO.	20 or 40 mg capsules and equine paste (370 mg/g)	Dog: 20 mg/dog q24h PO (or 1–2 mg/kg q24h PO) Cat: 1 mg/kg q24h PO
Ondansetron (Zofran)	Antiemetic drug. Ondansetron's action is to inhibit action of serotonin (blocks 5-HT ₃ receptors). It is administered to treat or prevent vomiting caused by chemotherapy or GI disease.	Adverse effects have not been reported in animals.	Granisetron has similar action.	4, 8 mg tablets; 2 mg/mL injection; 4 mg/5 mL syrup and 2-mg/mL injection	0.5 to 1.0 mg/kg IV or PO 30 min prior to administration of cancer drugs. To control vomiting due to other causes, doses as low as 0.1–0.2 mg/kg IV q6–12h may be considered.
o,p'-DDD	See Mitotane				
Orbifloxacin (Orbax)	Fluoroquinolone antimicrobial. Same mechanism as enrofloxacin and ciprofloxacin. Spectrum includes staphylococci, gram-negative bacilli, and some Pseudomonas.	May cause some nausea and vomiting at high doses. Avoid use in young animals. Blindness in cats has not been reported with doses ≤ 15 mg/kg/day.	Dose range is wide to account for susceptibility of bacteria. Dosing should be guided by susceptibility tests.	5.7, 22.7, and 68 mg tablets and oral suspension 30 mg/mL	Tablets (dog and cat): 2.5 to 7.5 mg/kg q24h PO Oral suspension in cats: 7.5 mg/kg q24h PO
Ormetoprim + sulfadimethoxine	Trimethoprim-like drug used in combination with sulfadimethoxine. (See Primor.)				
Oxazepam (Serax)	Benzodiazepine. Central-acting CNS depressant. Mechanism of action appears to be via potentiation of GABA–receptor mediated effects in CNS. Used for sedation and to stimulate appetite.	Sedation is most common side effect. Causes polyphagia. In cats, fatal hepatic necrosis has been reported from diazepam.	Doses based on empiricism. There have been no clinical trials in veterinary medicine.	15, 30 mg tablets; 10, 15, 30 mg capsules	Dog: 0.2–1.0 mg/kg q12h PO but may be increased to q6h Cat: appetite stimulant, 2.5 mg/cat PO Cat: behavior treatment, 0.2–0.5 mg/kg q12–24h PO

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Oxtriphylline (Choledyl-SA)	Choline theophyllinate. Methylxanthine bronchodilator, similar in mechanism to theophylline.	Same adverse effects as theophylline	Adverse effects similar to theophylline. Some formulations (Theocon) contain oxtriphylline and guaifenesin. When administering slow-release tablet, do not crush tablet.	400, 600 mg tablets (oral solutions and syrup available in Canada, but not US)	Dog: 47 mg/kg (equivalent to 30 mg/kg theophylline) q12h PO
Oxybutynin chloride (Ditropan)	Anticholinergic agent. Inhibits smooth muscle spasms via blocking action of acetylcholine. Used primarily to increase bladder capacity and to decrease spasms of urinary tract.	Adverse effects are related to anticholinergic effects but are less frequent compared to other anticholinergic drugs. Administer physostigmine for overdose.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.	5 mg tablets; 1 mg/mL oral syrup	Dog: 5 mg/dog q6–8h PO, or 0.2 mg/kg q12h PO
Oxymetholone (Anadrol)	Anabolic steroid. Derivative of testosterone. Used to stimulate androgenic activity, increase weight gain, and stimulate erythropoiesis.	Produces androgenic side effects. Liver injury is possible.	Use is based primarily or anecdotal experience.	50 mg tablets	1–5 mg/kg q24h PO
Oxymorphone hydrochloride (Numorphan)	Opioid agonist. Action is similar to morphine, except that oxymorphone is more lipophilic than morphine and 10–15× more potent than morphine.	Same adverse effects and precautions as morphine.	There is some evidence that oxymorphone may have fewer cardiovascular effects compared to morphine. Since oxymorphone is more lipophilic, it is readily absorbed from epidural injection.	1.5 and 1 mg/mL injection	Analgesia: 0.1–0.2 mg/kg IV, SC, IM (as needed), redose with 0.05–0.1 mg/kg q1–2h Preanesthetic: 0.025–0.05 mg/kg IM or SC Sedation: 0.05–0.2 mg/kg (with or without acepromazine) IM, SC
Oxytetracycline (Terramycin)	Tetracycline antibiotic. Same mechanism and spectrum as tetracycline. Oxytetracycline may be absorbed to higher extent.	Generally safe. Use cautiously in young animals.	Oral dose forms are from large-animal use. Use of injectable long-acting forms has not been studied in small animals. For most indications, doxycycline or minocycline can be used as substitute.	250 mg tablets; 100, 200 mg/mL Injection; 500 mg bolus	7.5–10 mg/kg IV q12h; 20 mg/kg q12h PO

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Oxytocin (Pitocin, Syntocinon [nasal solution] and generic)	Stimulates uterine muscle contraction via action on specific oxytoxin receptors. Used to induce or maintain normal labor and delivery in pregnant animals. Does not increase milk production but will stimulate contraction leading to milk ejection.	Adverse effects are uncommon if used carefully. Fetal stress and progression of normal labor should be monitored closely.	Used to induce labor. In people, oxytocin is administered via injection, constant IV infusion, and intranasal solution. Repeat up to 3x every 30–60 min. (maximum dose is 3 U/cat).	10, 20 U/mL injection; 40 U/mL nasal solution	Dog: 5–20 U/dog IM or SC (repeat every 30 min for primary inertia) Cat: 2.5–3 U/cat IM or IV, repeat up to 3 times, every 30–60 min
2-PAM	See Pralidoxime chloride.				
Pamidronate (Aredia)	Bisphosphonate drug; it slows the formation and dissolution of hydroxyapatite crystals. Is used in animals to decrease calcium in conditions that cause hypercalcemia, such as cancer and vitamin D toxicosis.	No serious adverse effects have been identified; however, use in animals has been uncommon.	Bisphosphonates may be effective in animals for treatment of hypercalcemia of cancer and vitamin D toxicosis. For IV infusion, dilute in fluid solution and administer over several hours (dilute 30 mg pamidronate in 250 mL of fluids).	Available as 30, 60, and 90 mg vials for injection; 1 mg/mL single use vial for injection.	Dog: Treatment of cholecalciferol toxicosis: 1.3–2 mg/kg IV or SC × 2 treatments after toxin exposure Treatment of hypercalcemia: 1–2 mg/kg IV, SC Treatment of malignancy: 1–2 mg/kg IV every 28 days (2 h infusion) Cat: 1–2 mg/kg IV
Pancrelipase (Viokase)	Pancreatic enzyme. Used to treat pancreatic exocrine insufficiency. Provides lipase, amylase, and protease.	Adverse effects not reported.	Mix with food when administering, approximately 20 minutes prior to feeding.	16,800 U of lipase, 70,000 U of protease, and 70,000 U of amylase per 0.7 g Also capsules and tablets	Dog: Mix 2 tsp powder with food per 20 kg body weight, or 1–3 tsp/0.45 kg of food Cat: 1/2 tsp per cat with food
Pancuronium bromide (Pavulon)	Nondepolarizing neuromuscular blocker (see Atracurium)	Similar precautions as atracurium.	Similar to atracurium.	1, 2 mg/mL injection	0.1 mg/kg IV, or start with 0.01 mg/kg and add 0.01 mg/kg doses every 30 min
Pantoprazole sodium (Protonix, Protonix IV)	Ulcer treatment. Proton pump inhibitor; indicated for treatment of gastroduodenal ulcer disease and gastroesophageal reflux. Pantoprazole is the first proton pump inhibitor for IV use. Antisecretory effects persist for > 24 h.	Side effects have not been reported in animals. However, in humans, there is concern about hypergastrinemia with chronic use.	Give IV dose over 15 minutes, and do not mix with other drugs that may interfere with stability.	20 and 40 mg delayed-release tablets; 4 mg/mL vials for IV injection	0.5 mg/kg q24h PO. IV use: 0.5–1 mg/kg IV infusion over 24 h, which may be delivered in 2 or 15 min, depending on dilution.

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Paregoric (corrective mixture)	Paregoric (opium tincture) is an outdated product used to treat diarrhea. Paregoric contains 2 mg of morphine in every 5 mL of paregoric.	Same as other opiates.	Use of paregoric has been replaced by more specific products, such as loperamide or diphenoxylate.	2 mg morphine per 5 mL of paregoric	0.05–0.06 mg/kg q12h PO
Paroxetine (Paxil)	Selective serotonin reuptake inhibitor (SSRI) much like fluoxetine (Prozac) in action. Used for obsessive-compulsive disorders, anxiety disorders, aggression, and other behavioral problems.	Some effects similar to fluoxetine, but in some animals, paroxetine is better tolerated.	Dosing recommendations are empirical.	10, 20, 30, 40 mg tablets; 2 mg/mL oral suspension	Dog: 0.5–1 mg/kg q24h PO. Cat: 1/8 to 1/4 of a 10 mg tablet q24h PO
Penicillamine (Cuprimine, Depen)	Chelating agent for lead, copper, iron, and mercury. Used primarily in animals for treatment of copper toxicity and hepatitis associated with accumulation of copper. It also has been used to treat cystine calculi. Penicillamine has been used in people to treat rheumatoid arthritis.	Do not use in pregnant animals. In people, allergic reactions have been reported, as well as agranulocytosis and anemia.	Administer on an empty stomach (2 h before meals).	125, 250 mg capsules and 250 mg tablets	10–15 mg/kg q12h PO
Penicillin G potassium; Penicillin G sodium (many brands)	β -lactam antibiotic. Action is similar to other penicillins. Spectrum of penicillin G is limited to gram-positive bacteria and anaerobes.	Injections may induce allergic reactions.	Penicillin G does not have good activity against most small animal pathogens.	5–20 million U vials	20,000–40,000 U/kg q6–8h IV or IM
Penicillin G procaine (generic)	Same as other forms of penicillin G, except procaine penicillin is absorbed slowly, producing concentrations for 12–24 h after injection.	IM and SC injection can produce reactions at injection site.	Avoid SC injection with procaine penicillin G.	300,000 U/mL suspension	20,000–40,000 U/kg q12–24h IM
Penicillin V	Oral penicillin is not highly absorbed and is narrow spectrum in comparison with other penicillin derivatives.		Same as for other penicillins (amoxicillin). Penicillin V should be administered on an empty stomach for maximum absorption (250 mg = 400,000 U).	250, 500 mg tablets	10 mg/kg q8h PO

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Pentobarbital (Nembutal and sodium generic)	Short-acting barbiturate anesthetic. Action is via nonselective CNS depression. Pentobarbital usually is used as IV anesthetic. Used to control severe seizures in animals. Duration of action may be 3–4 h.	Cardiac and respiratory depression is common.	Pentobarbital has narrow therapeutic index. When administering IV, inject first half of dose initially, then remainder of calculated dose gradually, until anesthetic effect is achieved.	50 mg/mL	25–30 mg/kg IV, to effect CRI: 2–15 mg/kg IV to effect, followed by 0.2–1.0 mg/kg/h Status epilepticus: 2–6 mg/kg IV
Pentoxifylline (Trental)	Methylxanthine. Pentoxifylline is used primarily as a rheological agent in people (increases blood flow through narrow vessels). It may have anti-inflammatory action via inhibition of cytokine synthesis. Used in dogs for some dermatoses (dermatomyositis) and vasculitis.	May cause signs similar to those of other methylxanthines. Nausea and vomiting have been reported in people. When broken tablet is administered to cats, the taste is unpleasant.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.	400 mg tablets; IV solution 50 mg/mL	Dog—10 mg/kg q12h and up to 15 mg/kg q8h PO or 400 mg/dog for most animals. Use 25 mg/kg q12h PO for dermatologic conditions. Cat: 1/4 of a 400 mg tablet (100 mg) q8–12h PO
Pepto-Bismol	See Bismuth subsalicylate.				
Phenobarbital (Luminal and generic)	Long-acting barbiturate. Phenobarbital's major use is as an anticonvulsant, in which it potentiates inhibitory actions of GABA.	Adverse effects are dose-related. Phenobarbital causes polyphagia, sedation, ataxia, and lethargy. Some tolerance develops to side effects after initial therapy. Hepatotoxicity has been reported in some dogs receiving high doses.	Phenobarbital doses should be carefully adjusted via monitoring serum/plasma concentrations. Optimum range for therapeutic effect is 15–40 µg/mL	15, 30, 60, 100 mg tablets; 30, 60, 65, and 130 mg/mL injection; 4 mg/mL oral elixir solution	Dog: 2–8 mg/kg q12h PO Status epilepticus: administer in increments of 10–20 mg/kg IV (to effect) Cat: 2–4 mg/kg q12h PO
Phenoxybenzamine hydrochloride (Dibenzyline)	α1-adrenergic antagonist. Binds α1-receptor on smooth muscle, causing relaxation. Potent vasodilator. Used primarily to treat peripheral vasoconstriction. In some animals, has been used to relax urethral smooth muscle.	Causes prolonged hypotension in animals. Use carefully in animals with cardiovascular compromise.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or limited experimental experience in animals.	10 mg capsules	Dog: 0.25 mg/kg q8–12h PO, or 0.5 mg/kg q24h. Cat: 2.5 mg/cat q8–12h, or 0.5 mg/kg q12h PO. (In cats, doses as high as 0.5 mg/kg IV have been used to relax urethral smooth muscle.)

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Phentolamine mesylate (Regitine, [Rogitine in Canada])	Nonselective α -adrenergic blocker. Vasodilator. Blocks stimulation of α -receptors on vascular smooth muscle. Primarily used to treat hypertension.	May cause excess hypotension with high doses or in animals that are dehydrated. May cause tachycardia.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. Titrate dose for each patient to produce desired vasodilation.	5 mg vials for injection	0.02–0.1 mg/kg IV
Phenylbutazone (Butazolidin and generic)	NSAID. Inhibits prostaglandin synthesis. Phenylbutazone is used primarily for arthritis and various forms of musculoskeletal pain and inflammation.	Phenylbutazone is generally well-tolerated in dogs, but there is no data for cats. Adverse effects possible are GI toxicity. Do not administer injectable formulation IM. Phenylbutazone causes bone marrow depression in people, which also is possible in dogs.	Doses are based primarily on manufacturer's recommendations and clinical experience. Use has declined in small animals because of availability of other NSAIDs.	100, 200, 400 mg and 1g tablets; 200 mg/mL injection	Dog: 15–22 mg/kg q8–12h (44 mg/kg/day) PO or IV (800 mg/dog maximum) Cat: 6–8 mg/kg q12h IV or PO
Phenylephrine hydrochloride (Neo-Synephrine)	Specific adrenergic agonist; specific for α_1 -receptor	Vasoconstriction and increased blood pressure	Phenylephrine also is used as topical vasoconstrictor (as in nasal decongestants).	10 mg/mL injection; 1% nasal solution	0.01 mg/kg every 15 min IV; 0.1 mg/kg every 15 min IM or SC
Phenylpropanolamine (PPA) (Proin PPA, Propalin syrup)	Adrenergic agonist. Used as decongestant, mild bronchodilator, and to increase tone of urinary sphincter.	Adverse effects are attributed to excess stimulation of adrenergic (α and β) receptors. Side effects: tachycardia, cardiac effects, CNS excitement, restlessness, and appetite suppression.	Phenylpropanolamine has been removed from human decongestant formulations. Only veterinary compounded formulations are available.	25, 50, 75 mg flavored tablet and 25 mg/mL vanilla flavored oral solution	Dog: 1 mg/kg, q8h, PO. Increase to 1.5–2.0 mg/kg as needed, q8h PO, or decrease to q12–24h in some animals.
Phenytoin (Dilantin)	Anticonvulsant. Depresses nerve conduction via blockade of sodium channels. Also classified as Class I antiarrhythmic. Commonly used as anticonvulsant in people, but not effective in dogs and not used in cats.	Adverse effects: sedation, gingival hyperplasia, skin reactions, CNS toxicity. Do not administer to pregnant animals.	Because of short half-life and poor efficacy in dogs and questionable safety in cats, other anticonvulsants are used as first choice before phenytoin.	30, 100 mg capsules; 50 mg/mL injection, 25 mg/mL oral suspension, and 50 mg chewable tablets	Dog: Antiepileptic: 20–35 mg/kg q8h. Antiarrhythmic: 30 mg/kg q8h PO or 10 mg/kg IV over 5 min Cat: do not use

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Physostigmine (Antilirium)	Cholinesterase inhibitor. Antidote for anticholinergic intoxication, especially intoxication that exhibits CNS signs. Major difference between physostigmine and neostigmine or pyridostigmine is that physostigmine crosses blood–brain barrier and the others do not.	Adverse effects attributed to excessive cholinergic effects (treat overdoses with atropine)	Physostigmine is indicated primarily only for treatment of intoxication. For routine systemic use of anticholinesterase drug, neostigmine and pyridostigmine have fewer side effects. When used, frequency of dose may be increased, based on observation of effects.	1 mg/mL injection	0.02 mg/kg q12h IV
Phytomenadione	See Vitamin K1.				
Phytonadione	See Vitamin K1.				
Pimobendan (Vetmedin)	Phosphodiesterase 3 inhibitor and a calcium sensitizer that acts as an inotropic vasodilator (inodilator). Licensed for treating CHF due to dilated cardiomyopathy and valvular insufficiency.	Safe in most dogs. Contraindicated with aortic stenosis and hypertrophic cardiomyopathy	May be used with furosemide and ACE inhibitors	Chewable tablets: 1.25 mg, 2.5 mg and 5 mg (US) Capsules: 2.5 mg and 5 mg (Canada, Europe, and Australia)	Dog: 0.25–0.3 mg/kg q12h PO Cat: 1.25 mg per cat q12h PO (0.1–0.3 mg/kg)
Piperacillin (Pipracil) and Zosyn (with tazobactam)	β-lactam antibiotic of the acylureidopenicillin class. Similar to other penicillins, except with high activity against <i>Pseudomonas aeruginosa</i> . Also good activity against streptococci.	Same precautions as for other injectable penicillins.	Reconstituted solution should be used within 24 hours (or 7 days if refrigerated). Piperacillin is combined with tazobactam (β-lactamase inhibitor) in Zosyn. Piperacillin and tazobactam has a broader spectrum of activity and is preferred when a beta-lactam and beta-lactamase inhibitor are needed.	2, 3, 4, 40 g vials for injection	50 mg/kg IV or IM q6h, or CRI using 2.4 mg/kg loading dose, followed by 3.2 mg/kg per hour infusion
Piperazine (many)	Antiparasitic compound. Produces neuromuscular blockade in parasite through inhibition of neurotransmitter, which causes paralysis of worms. Used primarily for treatment of helminth (ascaris) infections.	Remarkably safe in all species	Used to treat all species for roundworms	860 mg powder; 140 mg capsules; 120, 160, 170, 340, and 800 mg/mL oral solution; and 50, 250 mg tablets	44–66 mg/kg PO, administered once

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Piroxicam (Feldene and generic)	NSAID of the oxicam class. Prostaglandin synthesis inhibitor. Clinical effects are similar to other NSAIDs. Piroxicam has been used for treatment of transitional cell carcinoma in dogs.	Elimination of piroxicam is slow; use cautiously in dogs. Adverse effects are primarily GI toxicity (ulcers); see Flunixin meglumine.	Piroxicam is primarily used to treat arthritis and other musculoskeletal conditions, but there are reports of its activity for treating certain tumors (e.g., transitional cell carcinoma of bladder).	10 mg capsules	Dog: 0.3 mg/kg q48h PO; Cancer Tx: 0.3 mg/kg q24h PO Cat: 0.3 mg/kg q24h PO
Pitressin (ADH)	See Vasopressin and Desmopressin acetate.				
Plicamycin (old name is mithramycin) (Mithracin)	Anticancer agent. Action is to combine with DNA in presence of divalent cations and inhibit DNA and RNA synthesis. Lowers serum calcium. May have direct action on osteoclasts to decrease serum calcium. Used for carcinomas and treatment of hypercalcemia.	Adverse effects have not been reported in animals. In people, hypocalcemia and GI toxicity have been reported. May cause bleeding problems. <i>Drug interactions:</i> Do not use with drugs that may increase the risk of bleeding (e.g., NSAIDs, heparin, or anticoagulants).	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.	2.5 mg injection	Antihypercalcemic (dogs or cats): 25 µg/kg q24h IV (slow infusion) over 4 h Antineoplastic (dogs): 25–30 µg/kg q24h IV (slow infusion) for 8–10 days
Polyethylene glycol electrolyte solution (GoLYTELY)	Saline cathartic. Nonabsorbable compounds that increase water secretion into bowel via osmotic effect. Used for bowel evacuation prior to surgical or diagnostic procedure.	Water and electrolyte loss with high doses or prolonged use.	Used primarily to evacuate bowel as preparation for procedures	Oral solution	25 mL/kg, repeat in 2–4 h PO
Polymyxin B sulfate	Antibiotic peptide; disrupts bacterial cell membrane. Active against a broad spectrum of bacteria	Renal injury is possible. IM injection is painful.	Use is primarily topical, but systemic use may be indicated for resistant infections.	Vials of 500,000 U per vial; 1 mg is equivalent to 10,000 U	Dog and Cat: 15,000–25,000 U/kg IV q12h
Polysulfated glycosaminoglycan (PSGAG) (Adequan Canine)	Large molecular weight compounds similar to normal constituents of healthy joints. Chondroprotective. Inhibits enzymes that may degrade articular cartilage. Used primarily to treat or prevent degenerative joint disease.	Adverse effects are rare. Allergic reactions are possible. PSGAG has heparin-like effects and may potentiate bleeding problems in some animals.	Doses are derived from empirical evidence, experimental studies, and clinical studies in dogs. Although effective for acute arthritis, may not be as effective for chronic arthropathy.	100 mg/mL injection in 5 mL vial	4.4 mg/kg IM, twice weekly for up to 4 weeks

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Potassium bromide (KBr)	Anticonvulsant. Anticonvulsant action is to stabilize neuronal cell membranes. Bromide ordinarily is used in patients refractory to phenobarbital, or added to phenobarbital treatment.	Adverse effects are related to high levels of bromide. Signs of toxicosis are CNS depression, weakness, ataxia. Consider using sodium bromide in patients with hypoadrenocorticism. Adverse effects in cats are more common than in dogs. Respiratory side effects similar to asthma have been reported in some cats.	Bromide usually is administered in combination with phenobarbital. Monitor serum bromide concentrations to adjust dose. Effective plasma concentrations should be 1–2 mg/mL, but if used alone (without phenobarbital), higher concentrations of 2–4 mg/mL may be needed. Diets high in chloride will cause shorter half-life and need for higher dose. Sodium bromide can be substituted for potassium bromide. Note that 30 mg/kg potassium bromide is equal to 20 mg/kg of elemental bromide.	Usually prepared as oral solution. (No commercial formulation, but can be formulated by a pharmacist)	Standard starting dose: 30–40 mg/kg q24h PO. If administered without phenobarbital, higher doses of up to 40–50 mg/kg may be needed by monitoring plasma concentrations. Rapid IV loading dose: 800 mg/kg (sodium bromide) given over 8 hours slowly IV. Rapid oral loading dose: 600 mg/kg PO divided over 3–5 days. Slow (60 day) oral loading dose: 60 mg/kg/day (30 mg/kg q12h), then monitor blood level. Cats: Not recommended for use in cats.
Potassium chloride (generic)	Potassium supplement. Used for treatment of hypokalemia. Usually added to fluid solutions.	Toxicity from high potassium concentrations can be dangerous. Hyperkalemia can lead to cardiovascular toxicity (bradycardia and arrest) and muscular weakness. Oral potassium supplements can cause nausea and stomach irritation.	1 g of potassium chloride provides 13.41 mEq of potassium. When potassium is supplemented in fluids, do not administer at a rate faster than 0.5 mEq/kg/h.	Various concentrations for injection (usually 2 mEq/mL). Oral suspension and oral solution.	0.5 mEq potassium/kg/day, or supplement 10–40 mEq/500 mL of fluids, depending on serum potassium
Potassium citrate (generic, Urocit-K)	Potassium supplement. Alkalizes urine and may increase urine citric acid. Used for calcium oxalate urolithiasis. Also used for renal tubular acidosis.	Same as potassium chloride.	1 g of potassium citrate provides 9.26 mEq of potassium.	5 mEq and 10 mEq tablets. Some forms are in combination with potassium chloride. 1,000 mg potassium citrate = 9.26 mEq potassium	0.5 mEq/kg/day PO
Potassium gluconate (Kaon, Tumil-K, generic)	Potassium supplement. Used for renal tubular acidosis.	Same as for potassium chloride	1 g of potassium gluconate provides 4.27 mEq of potassium.	2 mEq tablets; 500 mg tablets; Kaon is 20 mg/15 mL elixir.	Dog: 0.5 mEq/kg q12–24h PO Cat: 2–8 mEq/day divided twice daily, PO

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Potassium iodide	Iodine supplement, with some additional antimicrobial properties. It has been used to treat some fungal infections. It also may be used to protect the thyroid from radiation injury.	High doses produce iodism, which includes lacrimation, skin irritation, swelling of eye lids, cough, and poor hair coat.	Doses are purely empirical.	10% solution and 145 mg tablets	Dog and Cat: Start with 5 mg/kg q8h PO, and increase to 25 mg/kg q8h PO Radiation exposure: 2 mg/kg, per day, PO
Potassium phosphate	Phosphorus supplement. Used for severe hypophosphatemia associated with diabetic ketoacidosis.	May cause hypocalcemia		500 mg tablets contain 3.7 mmol (114 mg) phosphorus Injection contains 3 mmol (93 mg) phosphorus per mL	4 mg/kg phosphorus PO, up to 4x per day. 0.03–0.12 mmol/kg/h IV for acute treatment
Pradofloxacin (Vevafox)	Fluoroquinolone antimicrobial for dogs and cats. Increased activity against some Gram-positive and anaerobic bacteria compared to other fluoroquinolones	Use cautiously in young dogs. Oral treatment may cause vomiting and diarrhea.	New fluoroquinolone approved in Europe, but not yet available in US. Pradofloxacin is a 3rd generation fluoroquinolone with greater antimicrobial activity than other fluoroquinolones. It is approved in the U.S. for cats only, but in both dogs and cats in Europe.	Formulations contain pradofloxacin in a 2.5% oral suspension in the U.S. and Europe and 15, 60, and 120 mg tablets in Europe	Dog: 3–5 mg/kg q24h PO Cats: Tablets: 3–5 mg/kg q24h, PO Oral suspension: 5–7.5 mg/kg q24h, PO
Pralidoxime chloride (2-PAM) (Protopam)	Used for treatment of organophosphate toxicosis	Adverse effects have not been reported.	When treating intoxication, consult poison control center for precise guidelines. May be used with atropine (0.1 mg/kg).	50 mg/mL injection	20 mg/kg up to 50 mg/kg q8–12h; initial dose IV slow, or IM
Praziquantel (Droncit), and combined with pyrantel in Drontal	Antiparasitic drug. Action on parasites related to neuromuscular toxicity and paralysis via altered permeability to calcium. Used primarily to treat infections caused by tapeworms.	Vomiting occurs at high doses. Anorexia and transient diarrhea have been reported. Safe in pregnant animals.	Dose recommendations based on label dose supplied by manufacturer.	23, 34 mg tablet; 56.8 mg/mL injection. Also combined with pyrantel in tablets of 13.6/54.3, 18.2/72.6, and 27.2/108.6 of praziquantel/pyrantel.	Dog (oral dose): < 6.8 kg: 7.5 mg/kg PO, once; > 6.8 kg: 5 mg/kg PO, once. Dog (injection): ≤ 2.3 kg: 7.5 mg/kg IM or SC, once; 2.7–4.5 kg: 6.3 mg/kg IM or SC, once; ≤ 5 kg: 5 mg/kg IM or SC, once. Cat (oral dosage): < 1.8 kg: 6.3 mg/kg PO, once; > 1.8 kg: 5 mg/kg PO, once. For <i>Paragonimus</i> infection use 25 mg/kg q8h PO for 2–3 days. Cat (injection): 5 mg/kg IM or SC.

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Prazosin (Minipress)	α_1 -adrenergic blocker. Relaxes smooth muscle, especially of vasculature. Prazocin is used as vasodilator and to relax smooth muscle (occasionally urethral muscle).	High doses cause vasodilation and hypotension.	Titrate dose to needs of individual patient. Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.	1, 2, 5 mg capsules	0.5–2 mg/animal (1 mg/15 kg) q8–12h PO
Prednisolone (Delta-Cortef and many others)	Glucocorticoid anti-inflammatory drug. Potency is approximately 4× cortisol.	All glucocorticoids produce expected (and sometimes unavoidable) side effects. Chronic therapy may lead to several adverse effects.	Doses for prednisolone are based on severity of underlying condition.	5 and 20 mg tablets; 3 mg/mL syrup; 25 mg/mL acetate suspension injection	Dog (cats often require 2× dog dose)—anti-inflammatory: 0.5–1 mg/kg q12–24h IV, IM, PO initially, then taper to q48h; immunosuppressive: 2.2–6.6 mg/kg/day IV, IM, PO initially, then taper to 2–4 mg/kg q48h; replacement therapy: 0.2–0.3 mg/kg/day PO
Prednisolone sodium succinate (Solu-Delta-Cortef)	Same as for prednisolone, except that this is a water-soluble formulation intended for acute therapy when high IV doses are needed for rapid effect. Used for treatment of shock and CNS trauma	Adverse effects are not expected from single administration; however, with repeated use, other side effects are possible.	Although shock doses are listed, efficacy for treatment of shock is questionable.	100, 500 mg vials for injection (10 and 50 mg/mL)	Shock: 15–30 mg/kg IV (repeat in 4–6 h) CNS trauma: 15–30 mg/kg IV, taper to 1–2 mg/kg q12h Anti-inflammatory: 1 mg/kg/day IV Replacement therapy: 0.25–0.5 mg/kg/day IV
Prednisone (Deltasone and generic; Meticorten for injection)	Same as for prednisolone, except that, after administration, prednisone is converted to prednisolone	Adverse effects are same as for prednisolone.	Same as for prednisolone. In cats use prednisolone.	1, 2.5, 5, 10, 20, 25, and 50 mg tablets; 1 mg/mL syrup (Liquid Pred in 5% alcohol) and 1 mg/mL oral solution (in 5% alcohol)	Dogs convert prednisone to prednisolone, and doses are similar; in cats there is inadequate conversion of prednisone to prednisolone.
Pregabalin (Lyrica)	Analgesic and anticonvulsant, similar to gabapentin. Action is via stabilization of excitable neurons. Used to treat seizure disorders, and as adjunct for pain management.	Sedation is most common adverse effect, especially at high doses.	Clinical use is based primarily on anecdotal experience and extrapolation from human medicine.	25, 50, 75, 100, 150, 200, 225, and 300 mg capsules. Oral solution 20 mg/mL	Dog (anticonvulsant dose): 2 mg/kg q8h PO; (analgesic dose): 4 mg/kg q12h, PO maximum dose) Cat: 2 mg/kg q12h, PO and increase to 4 mg/kg if necessary

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Primidone (Mylepsin, Neurosyn [Mysoline in Canada])	Anticonvulsant. Primidone is converted to phenylethylmalonamide and phenobarbital, both of which have anticonvulsant activity, but most of activity (85%) is probably due to phenobarbital. See Phenobarbital for more details.	Adverse effects are same as for phenobarbital. Primidone has been associated with idiosyncratic hepatotoxicity in dogs. Although some labels caution its use in cats, one study in experimental cats determined that it is safe if used at recommended doses.	When monitoring therapy with primidone, phenobarbital plasma concentrations should be measured to estimate anticonvulsant effect.	50 and 250 mg tablets	8–10 mg/kg q8–12h as initial dose PO, then adjust via monitoring to 10–15 mg/kg q8h.
Primor (ormetoprim + sulfadimethoxine) (Primor)	Antibacterial drug. Ormetoprim inhibits bacterial dihydrofolate reductase; sulfonamide competes with <i>p</i> -aminobenzoic acid (PABA) for synthesis of nucleic acids. Bactericidal/bacteriostatic. Broad antibacterial spectrum and active against some coccidia.	Several adverse effects have been reported from sulfonamides. Ormetoprim has been associated with CNS adverse effects.	Doses listed are based on manufacturer's recommendations. Controlled trials have demonstrated efficacy for treatment of pyoderma on once-daily schedule.	Combination tablet (ormetoprim + sulfadimethoxine) 120, 240, 600 and 1200 mg tablets in 1:5 ratio	Dog: 55 mg/kg on first day, PO, followed by 27.5 mg/kg q24h PO. Daily doses can be divided into twice-daily.
Procainamide (Pronestyl, Procanbid, generic)	Antiarrhythmic drug. Class 1 antiarrhythmic used primarily for treatment of ventricular arrhythmias. Action is to inhibit sodium influx into cardiac cell via sodium channel blockade.	Adverse effects include cardiac arrhythmias, cardiac depression, tachycardia, and hypotension. In people, procainamide produces hypersensitivity effects (lupus-like reactions), but these have not been reported in animals. <i>Drug interactions:</i> Cimetidine may increase plasma concentrations.	Since dogs do not produce active metabolite (N-acetyl-procainamide), dose may be higher to control some arrhythmias compared to dose for people. Monitor plasma concentrations during chronic therapy (effective plasma concentration in experimental dogs is 20 µg/mL). In animals, slow-release oral formulations do not produce longer duration of sustained blood concentrations.	250, 375, 500 mg tablet or capsule; 100, 500 mg/mL injection, some oral formulations may be unavailable.	Dog: 10–30 mg/kg q6h PO to a maximum dose of 40 mg/kg; 8–20 mg/kg IV, IM; 25–50 µg/kg/min IV infusion. Cat: 3–8 mg/kg IM, PO q6–8h or CRI 1–2 mg/kg IV then 10–20 µg/kg/min IV.

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Prochlorperazine + isopropamide (Darbazine)	Combination product. Chlorpromazine is a central-acting dopamine antagonist (antiemetic); isopropamide is an anticholinergic drug (atropine-like effects). Used primarily to control vomiting in animals.	Side effects are attributed to each component. Prochlorperazine produces phenothiazine-like effects. Isopropamide produces antimuscarinic effects. Use of antimuscarinic drugs is contraindicated in animals with gastroparesis and should be used cautiously in animals with diarrhea.	Doses are based on manufacturer's recommendations	No. 1, 2, and 3 capsules	Dog and Cat: 0.14–0.2 mL/kg q12h SC Dog 2–7 kg: 1–#1 capsule q12h PO Dog 7–14 kg: 1–#2 capsule q12h PO Dog > 14 kg: 1–#3 capsule q12h PO
Promethazine (Phenergan)	Phenothiazine with strong antihistamine effects. Used for treatment of allergy and as antiemetic (motion sickness).	Adverse effects include sedation and antimuscarinic (atropine-like) effects. Both phenothiazine effects and anticholinergic effects are possible in some patients.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.	6.25 and 25 mg/5 mL syrup; 12.5, 25, 50 mg tablets; 25, 50 mg/mL injection	0.2–0.4 mg/kg q6–8h IV, IM, PO (up to a maximum dose of 1 mg/kg)
Propantheline bromide (Pro-Banthine)	Anticholinergic (antimuscarinic) drug. Blocks acetylcholine receptor to produce parasympatholytic effects (atropine-like effects). Used to decrease smooth muscle contraction and secretion of GI tract. Used to treat vagal-mediated cardiovascular effects.	Side effects are attributed to excess anticholinergic (antimuscarinic) effects. Treat overdoses with physostigmine. Use cautiously for treating gastrointestinal disease.	Propantheline has not been evaluated in clinical trials in animals, but propantheline is often the drug of choice for oral therapy in cases in which an anticholinergic effect is desired.	7.5, 15 mg tablet	0.25–0.5 mg/kg q8–12h PO
Propiopromazine Hydrochloride (Tranvet)	Phenothiazine sedative. Also has antiemetic, antihistaminic actions.	Adverse effects and precautions are similar to other phenothiazines such as acepromazine.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. Do not confuse this drug with propiomazine (Largon), which is a discontinued human drug.	5–10 mg/mL injection, or 20 mg chewable tablet	1.1–4.4 mg/kg q12–24h PO 0.1–1.1 mg/kg IV, IM (Range of dose depends on degree of sedation needed.)

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Propofol (Rapinovet, Propoflo, [veterinary]; Diprivan [human])	Anesthetic. Used for induction or producing short-term general anesthesia. Mechanism of action is not well-defined, but may be barbiturate-like. Propofol may be used as induction agent, followed by inhalation with halothane or isoflurane.	Apnea and respiratory depression are most common adverse effects. Adverse effects attributed to general anesthetic properties.	Propofol is primarily used for general anesthesia, or adjunct for general anesthesia. Propofol's advantage over other agents is smooth, rapid recovery. Use strict aseptic technique for administration. Propofol may be diluted in 5% dextrose, lactated Ringer's solution, or 0.9% saline, but not to less than 2 mg/mL concentration.	1% (10 mg/mL) injection in 20 mL ampules	Dog: 6.6 mg/kg IV slowly over 60 sec. Constant rate IV CRI: 5 mg/kg slow IV followed by 100–400 µg/kg/min Cat: Anesthesia induction: 7 mg/kg IV slowly CRI: 6 mg/kg slow IV, then 200–300 µg/kg/min IV Short-term surgery: 10 mg/kg IV
Propranolol hydrochloride (Inderal)	β-adrenergic blocker. Nonselective for β ₁ - and β ₂ -adrenergic receptors. Class II antiarrhythmic. Used primarily to decrease heart rate, cardiac conduction, tachyarrhythmias, and blood pressure.	Adverse effects related to β ₁ -blocking effects on heart. Causes cardiac depression, decreases cardiac output. β ₂ -blocking effects can cause bronchoconstriction. Decreases insulin secretion.	Usually, dose is titrated according to patient's response. Start with low dose and increase gradually to desired effect. Clearance relies on hepatic blood flow; use cautiously in animals with impaired hepatic perfusion.	10, 20, 40, 60, 80, and 90 mg tablets; 1 mg/mL injection; 4 and 8 mg/mL oral solution	Dog: 20–60 µg/kg over 5–10 min IV; 0.2–1 mg/kg PO q8h (titrate dose to effect) Cat: 0.4–1.2 mg/kg (2.5–5 mg/cat) PO q8h
Propylthiouracil (PTU) (generic, Propyl-Thyracl)	Antithyroid drug. Compared to methimazole, PTU inhibits conversion of T ₄ to T ₃ .	Adverse effects in cats include hemolytic anemia, thrombocytopenia, and other signs of immune-mediated disease.	Use of PTU in most cats has been replaced with methimazole.	50 and 100 mg tablets	11 mg/kg q12h PO
Prostaglandin F _{2α} (dinoprost) (Lutalyse)	Prostaglandin induces luteolysis. Has been used to treat open pyometra in animals. Use for inducing abortion has been questioned.	Side effects include vomiting, diarrhea, and abdominal discomfort.	Use in treating pyometra should be monitored carefully.	5 mg/mL solution for injection	Pyometra (dog): 0.1–0.2 mg/kg, once daily for 5 days SC; (cat): 0.1–0.25 mg/kg, once daily for 5 days SC. Termination of pregnancy (dog): 0.025–0.05 mg (25–50 µg)/kg q12h IM; (cat): 0.5–1 mg/kg IM for 2 injections.

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Pseudoephedrine hydrochloride (Sudafed, and many others [some formulations have other ingredients])	Adrenergic agonist. Similar to ephedrine, phenylpropanolamine in action. Used to increase peripheral resistance, as a decongestant, and in animals to treat urinary incontinence.	Side effects attributed to adrenergic effects (excitement, rapid heart rate, arrhythmias)	Although clinical trials have not been conducted for comparison, it is believed that pseudoephedrine's action and efficacy are similar to ephedrine and phenyl-propanolamine.	30, 60 mg tablets; 120 mg capsules; 6 mg/mL syrup. Most formulations have been removed from human market, because of risk of diversion to manufacture methamphetamine.	Dog: 0.2–0.4 mg/kg (or 15–60 mg/dog) q8–12h PO
Psyllium (Metamucil and others)	Bulk-forming laxative. Use for treatment of constipation and bowel evacuation. Action is to absorb water and expand to provide increased bulk and moisture content to the stool, which encourages normal peristalsis and bowel motility.	Adverse effects have not been reported in animals. Intestinal impaction can occur with overuse, or in patients with inadequate fluid intake.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.	Available as powder 3.4 g per teaspoon	1 tsp/5–10 kg (added to each meal)
Pyrantel pamoate (Nemex, Strongid)	Antiparasitic drug. Acts to block ganglionic neurotransmission via cholinergic action.	No adverse effects reported	Dose recommendations based on manufacturer's recommendations	171, 180, 226 mg/mL paste; 50 mg/mL suspension 22.7, 113.5 mg tablets	Dog: 5 mg/kg once PO and repeat in 7–10 days Cat: 20 mg/kg once PO
Pyridostigmine bromide (Mestinon, Regonol)	Anticholinesterase. Same as for neostigmine, except that pyridostigmine has longer duration of action. Use to treat anticholinergic toxicity and treatment of myasthenia gravis.	Adverse effects caused by excessive anticholinesterase activity. Signs are attributed to acetylcholine. <i>Drug interactions:</i> Since this product contains bromide, use cautiously in patients already receiving bromide (e.g., potassium bromide for epilepsy).	Same as for neostigmine, except that adverse effects may persist longer.	12 mg/mL oral syrup; 60 mg tablets; 5 mg/mL injection	Antimyasthenic: 0.02–0.04 mg/kg q2h IV, or 0.5–3 mg/kg q8–12h PO Antidote for muscle blockade: 0.15–0.3 mg/kg IM, IV
Pyridoxine	Vitamin B ₆				

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Pyrimethamine (Daraprim)	Antibacterial, antiprotozoal drug. Blocks dihydrofolate reductase enzyme, which inhibits synthesis of reduced folate and nucleic acids. Activity of pyrimethamine is more specific against protozoa than bacteria.	When administered with trimethoprim-sulfonamide combinations, anemia has been observed. Folic or folinic acid has been supplemented to prevent anemia, but benefit of this treatment is unclear.	Used either alone or in combination with sulfonamides	25 mg tablets	Dog: 1 mg/kg q24h PO for 14–21 days (5 days for <i>Neosporum caninum</i>) Cat: 0.5–1 mg/kg q24h PO for 14–28 days
Quinidine gluconate (Quinaglute, Duraquin) Quinidine sulfate (Cin-Quin, Quinora) Quinidine polygalacturonate (Cardioquin)	Antiarrhythmic drug. Class I antiarrhythmic. Action is to inhibit sodium influx via blockade of sodium channels. Used to treat ventricular arrhythmias and occasionally atrial fibrillation. Mexilitine is often used as a Class I antiarrhythmic instead.	Side effects with quinidine are more common than procainamide and include nausea and vomiting. Adverse effects: hypotension, tachycardia (due to antivagal effect). <i>Drug interactions:</i> Coadministration with digoxin may increase digoxin concentrations.	Quinidine is not used as commonly as other Class I antiarrhythmic drugs. Doses calculated according to amount of quinidine base in each product. 324 mg quinidine gluconate = 202 mg quinidine base. 300 mg quinidine sulfate = 250 mg quinidine base. 275 mg quinidine polygalacturonate = 167 mg quinidine base	Many human formulations are no longer available due to diminished use. Quinidine gluconate 324 mg tablets; 80 mg/mL injection Quinidine polygalacturonate 275 mg tablets Quinidine sulfate 100, 200, 300 mg tablets; 200, 300 mg capsules; 200 mg/mL injection	Dog: 6–20 mg/kg q6h IM; 6–20 mg/kg q6–8h PO (of base)
Racemethionine (DL-methionine) (Uroeze, Methio-Form, and generic. Human forms include Pedameth, Uracid, and generic.)	Urinary acidifier. Lowers urinary pH. Also has been used to protect against acetaminophen overdose in people by restoring hepatic concentrations of glutathione. In people, it also is used to treat dermatitis caused by urinary incontinence (reduces urine ammonia).	Adverse effects have not been reported. Do not use in patients with metabolic acidosis or hepatic function impairment. Do not use in young cats.	Used for urinary acidification. Use for acetaminophen toxicity has been replaced by acetylcysteine.	500 mg tablets, powders added to animal's food; 75 mg/5 mL pediatric oral solution; 200 mg capsules	Dog: 150–300 mg/kg q24h PO Cat: 1–1.5g/cat PO (added to food each day)
Ranitidine hydrochloride (Zantac)	Histamine H ₂ -antagonist. Same as cimetidine except 4–10× more potent and longer acting.	Ranitidine may have fewer effects on endocrine function and drug interactions, compared to cimetidine.	Pharmacokinetic information in dogs suggests that ranitidine may be administered less often than cimetidine to achieve continuous suppression of stomach acid secretion. Ranitidine may stimulate stomach emptying and colon motility via anticholinesterase action.	75, 150, 300 mg tablets; 150, 300 mg capsules; 25 mg/mL injection	Dog: 2 mg/kg q8h IV, PO Cat: 2.5 mg/kg q12h IV; 3.5 mg/kg q12h PO

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Retinoids	See Isotretinoin and Vitamin A.				
Retinol	See Vitamin A.				
Riboflavin (Vitamin B ₂)	See Vitamin B ₂ .				
Rifampin (Rifadin)	Antibacterial. Action is to inhibit bacterial RNA synthesis. Spectrum of action includes staphylococci and mycobacteria. Other susceptible bacteria include streptococci. Used in dogs treat staphylococcosis, including methicillin-resistant strains.	Adverse effects in dogs include gastrointestinal disturbance, increased liver enzymes, and hepatic injury. <i>Drug interactions:</i> Multiple drug interactions are possible. Induces cytochrome P-450 enzymes. Drugs affected include barbiturates, chloramphenicol, and corticosteroids.	Clinical trials in dogs indicate that rifampin is effective for treating Staphylococcal infections, including methicillin-resistant strains, even when used as monotherapy.	150, 300 mg capsules; injection solution: 600 mg Rifadin IV	5 mg/kg q12h PO, or 10 mg/kg per day PO
Ringer's solution, lactated (generic)	IV solution for replacement	Monitor pulmonary pressure when infusing high doses.	When administering IV fluid solution, monitor rate and electrolyte concentrations carefully.	250, 500, 1000 mL bags for infusion	55–65 mL/kg/day IV, SC 50 mL/kg/h IV for severe dehydration
Ronidazole	Antiprotozoal drug. Ronidazole has mechanism of action similar to other nitroimidazoles, such as metronidazole. Ronidazole has been used to treat tritrichomonas intestinal infections in cats.	Neurotoxicity is the most serious adverse effect, which is more likely at high doses.	Do not exceed 60 mg/kg per day in cats to avoid neurotoxicity. Doses are based only on experimental studies.	There are no commercial formulations; however, compounding pharmacies have prepared formulations for cats.	Dog: No established dose Cat: 30 mg/kg q24h PO for 2 weeks.
Salicylate	See Aspirin.				
Selamectin (Revolution)	Topical parasiticide and heartworm prevention	Transient localized alopecia with or without inflammation at or near the site of application was observed in approximately 1% of 691 treated cats. Other signs observed rarely included GI signs, anorexia, lethargy, salivation, tachypnea, and muscle tremors.	Recommended for use in dogs 6 weeks of age or older and in cats 8 weeks of age or older	Available in six separate dose strengths	6–12 mg/kg topically every 30 days

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Selegiline (Anipryl [also known as deprenyl and L-deprenyl]; human dose form is Eldepryl)	Action is to inhibit specific monoamine oxidase (MAO type B) to inhibit degradation of dopamine in CNS. In dogs, it is approved to control clinical signs of pituitary-dependent hyperadrenocorticism (Cushing's disease) and to treat cognitive dysfunction in geriatric dogs.	Adverse effects have not been reported in dogs. However, amphetamine-like signs can be produced in experimental animals. At high doses in dogs, hyperactivity has been observed (doses > 3 mg/kg). Do not use with other MAO-inhibitors or drugs that inhibit serotonin reuptake.	In the multicenter trial performed by Deprenyl Animal Health, Inc. selegiline controlled the clinical signs of > 70% of dogs with hyperadrenocorticism. However, other investigators have reported efficacy rates as low as 20%	2, 5, 10, 15, and 30 mg tablets; 5 mg capsules; 20, 30, and 40 cm ² transdermal patch	Dog: Treatment for Cushing's disease and cognitive dysfunction use the same dose. Begin with 1 mg/kg q24h PO. If there is no response within 2 months, increase dose to maximum of 2 mg/kg q24h PO. Cat: 0.25–0.5 mg/kg q12–24h PO
Senna (Senokot)	Laxative. Acts via local stimulation or via contact with intestinal mucosa	Adverse effects not reported for animals	Doses and indications are not well established for veterinary medicine. Use is strictly through anecdotal experience.	Granules in concentrate, or syrup	Dog (syrup): 5–10 mL/dog q24h PO; (granules): 1/2–1 tsp/dog q24h PO Cat (syrup): 5 mL/cat q24h; (granules) 1/2 teaspoon per cat q24h (with food)
Sevoflurane	Inhalant anesthetic	Action and adverse effects similar to other inhalant anesthetics.		100 mL bottle	Induction: 8% Maintenance: 3%–6% to effect
Sildenafil citrate (Viagra)	Phosphodiesterase 5 inhibiting vasodilator that preferentially vasodilates pulmonary circulation. Indicated for treatment of pulmonary hypertension	May cause hypotension especially if used in combination with nitrates; cutaneous flushing in inguinal area has been reported in dogs	Very expensive	25, 50, 100 mg tablets	Dog: 2 mg/kg q12h PO but dose interval may range from 8–24 hours. Cat: 1 mg/kg q8h PO
Silymarin (Silybin, Marin, "milk thistle")	Silymarin, contains silybin as the most active ingredient. It is also known as milk thistle, from which it is derived. Silymarin is a mixture of antihepatotoxic flavonolignans (derived from the plant <i>Silybum</i>).	No adverse reactions have been reported.	Silymarin is available in several dietary supplements. There may be variable content and absorption among products.	Silymarin tablets are widely available OTC. Commercial veterinary formulations (Marin) also contain zinc and Vitamin E in a phosphatidylcholine complex in tablets for dogs and cats.	5–15 mg/kg once daily, PO. Some sources recommend 30 mg/kg/day PO.

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Sodium bicarbonate (NaHCO ₃) (generic, baking soda, Soda Mint)	Alkalizing agent. Antacid. Used to treat systemic acidosis or to alkalize urine. Increases plasma and urinary concentrations of bicarbonate	Adverse effects attributed to alkalizing activity. <i>Drug interactions:</i> When administered orally, interaction may occur to decrease absorption of other drugs (partial list includes anticholinergic drugs, ketoconazole, fluoroquinolones, tetracyclines).	When used for systemic acidosis, doses should be adjusted on basis of blood gas measurements or assessment of acidosis. Doses vary depending on underlying condition (see dosage section). Note: 8.5% solution = 1 mEq/mL of NaHCO ₃ .	325, 520, 650 mg tablets; injection of various strengths (4.2% to 8.4%); 8.4% solution is equivalent to 1 mEq/mL.	Acidosis: 0.5–1 mEq/kg IV Renal failure: 10 mg/kg q8–12h PO Alkalization of urine: 50 mg/kg q8–12h PO (1 tsp is approximately 2 g) Antacid: 2–5 g mixed with food or water
Sodium chloride 0.9% (generic)	Sodium chloride is used for IV infusion as replacement fluid.	Not a balanced electrolyte solution. Long-term infusion may cause electrolyte imbalance.	Rate of infusion varies depending on patient needs.	500, 1000 mL infusion	15–30 mL/kg/h IV for moderate dehydration
Sodium chloride 7.2% (generic) Hypertonic saline	Concentrated sodium chloride used for acute treatment of hypovolemia	Not a balanced electrolyte solution. Long-term infusion may cause electrolyte imbalance.	Hypertonic saline is used for short-term infusion for rapid replacement of vascular volume.	7.2% solution	3–8 mL/kg IV (do not administer at a rate > 1 mL/kg/min)
Sotalol hydrochloride (Betapace)	Nonspecific β-(β ₁ and β ₂) adrenergic blocker (Class II antiarrhythmic). Action is similar to propranolol (1/3 potency); however, its beneficial effect may be caused more by the other antiarrhythmic effects. In addition to being a Class II antiarrhythmic drug, Sotalol may have some Class III (potassium channel-blocking) activity.	Adverse effects have not been reported for animals but are expected to be similar to propranolol. Like many antiarrhythmics, it may have some proarrhythmic activity. Negative inotropic effects may cause concern in some animals with poor contractility.	It may be a more effective maintenance agent than other drugs for controlling arrhythmias. Sotalol may have pro arrhythmic effect in German shepherds.	80, 160, 240 mg tablets	Dog: 1–2 mg/kg q12h PO (medium-size dogs, start with 40 mg per dog, then increase to 80 mg if needed) Cat: 2 mg/kg PO q12h
Spinosad (Comfortis)	Antiparasite drug used for flea control. Fleas are killed rapidly after administration.	Occasional vomiting has been observed, but otherwise safe.	Administer with food.	140, 270, 560, 810, and 1620 mg tablets. Also combined with milbemycin in some formulations.	Dogs: 30 mg/kg (13.5 mg/pound), PO, administered once per month Cats: 50–100 mg/kg, PO, once per month

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Spironolactone (Aldactone)	Potassium-sparing diuretic. Spironolactone competitively inhibits the action of aldosterone. Used for treating high blood pressure and congestion caused by heart failure.	Can produce hyperkalemia in some patients. Do not use in dehydrated patients. Severe ulcerative facial dermatitis may occur in cats. <i>Drug interactions:</i> Avoid supplements that are high in potassium.	Spironolactone usually is used with diuretic agent for CHF. It may decrease cardiac remodeling and improve patient survival; no effect though on cardiac remodeling in Maine Coon cats with cardiomyopathy. Spironolactone will cause slight false increase in plasma digoxin concentrations measured by some assays.	25, 50, 100 mg tablets	Dog: 2–4 mg/kg q24h PO (or 1–2 mg/kg q12h PO) (European approved label dose is 2mg/kg/day, PO.) Cat: avoid use in cats, but 1–2 mg/kg q12h PO has been used in some cases.
Stanozolol (Winstrol-V)	Anabolic steroid. Stanozolol has been used to decrease negative nitrogen balance in animals with chronic renal failure.	Stanozolol will produce anabolic effects with chronic use. There is increased risk of hepatic toxicity, with cats being at higher risk.	Monitor liver enzymes in treated animals.	50 mg/mL injection; 2 mg tablets, some commercial forms withdrawn from market.	Dog: 2 mg/dog (or range of 1–4 mg/dog) q12h PO; 25–50 mg/dog/week IM Cat: 1 mg/cat q12h PO; 25 mg/cat/week IM
Succimer (Chemet)	Used in treatment of lead toxicosis. Chelates lead and other heavy metals, such as mercury and arsenic.	No known adverse effects	Doses based on studies in dogs but evidence for use in cats is lacking.	100 mg capsules	Dog: 10 mg/kg q8h PO for 5 days, then 10 mg/kg q12h PO for 2 more weeks Cat: 10 mg/kg q8h PO for 2 weeks
Sucralfate (Carafate, [Sucrulate in Canada])	Gastric mucosa protectant. Antiulcer agent. Action of sucralfate is to bind to ulcerated tissue in GI tract to aid healing of ulcers.	Adverse effects have not been reported. Not absorbed systemically. <i>Drug interactions:</i> Sucralfate may decrease absorption of other orally administered drugs (e.g., fluoroquinolones and tetracyclines) via chelation with aluminum.	Dosing recommendations are based largely on empiricism. There have not been clinical trials of efficacy in animals.	1 g tablets; 200 mg/mL oral suspension	Dog: 0.5–1 g q8–12h PO Cat: 0.25 g q8–12h PO
Sufentanil citrate (Sufenta)	Opioid agonist. Action of fentanyl derivatives is via μ -receptor. Sufentanil is 5–7 \times more potent than fentanyl. 13–20 μ g of sufentanil produces analgesia equal to 10 mg of morphine.	Adverse effects similar to other opiates. High potency requires careful calculation of dose.	When used for anesthesia, often animals are premedicated with acepromazine or benzodiazepine.	50 μ g/mL injection	2 μ g/kg IV, up to a maximum dose of 5 μ g/kg (0.005 mg/kg)

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Sulfadiazine (generic, combined with trimethoprim in Tribriksen)	Sulfonamides compete with PABA for enzyme that synthesizes dihydrofolic acid in bacteria. Synergistic with trimethoprim. Broad spectrum of activity, including some protozoa. Bacteriostatic.	Adverse effects associated with sulfonamides include allergic reactions, type II and III hypersensitivity, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions.	Usually, sulfonamides are combined with trimethoprim or ormetoprim in 5:1 ratio to produce a synergistic effect.	500 mg tablets	100 mg/kg IV, PO (loading dose), followed by 50 mg/kg q12h IV, PO See Trimethoprim + sulfadiazine section for additional dosing.
Sulfasalazine (sulfapyridine + mesalamine) (Azulfidine [Salazopyrin in Canada])	Sulfonamide + anti-inflammatory drug. Used for treatment of colitis. Sulfonamide has little effect; salicylic acid (mesalamine) has anti-inflammatory effects.	Adverse effects are all attributed to sulfonamide component. Keratoconjunctivitis sicca has been reported.	Usually used for treatment of idiopathic colitis, often in combination with dietary therapy.	500 mg tablets	Dog: 10–30 mg/kg q8–12h PO (see also Mesalamine, Olsalazine) Cat: 20 mg/kg q12h PO
Tamoxifen citrate (Nolvadex)	Nonsteroid estrogen receptor blocker. Also has weak estrogenic effects. Tamoxifen may also increase release of gonadotropin-releasing hormone (Gn-RH). Used as adjunctive treatment for certain tumors	Adverse effects have not been thoroughly documented in animals. However, in people, tamoxifen causing increased tumor pain has been reported. Do not use in pregnant animals. <i>Drug interactions:</i> Reacts with antiulcer drugs	Consult specific anticancer protocols for doses and regimens.	10 and 20 mg tablets (tamoxifen citrate)	Veterinary dose not established. Human dose is 10 mg q12h PO.
Taurine (generic)	Nutritional supplement for cats. Used in prevention and treatment of ocular and cardiac disease (cardiomyopathy) caused by taurine deficiency	Adverse effects have not been reported.	Routine supplementation with taurine may not be necessary in cats that are receiving a balanced diet.	Available in powder	Dog: 500 mg q12h PO Cat: 250 mg/cat q12h PO
Telazol	See Tiletamine + zolazepam.				
Terbinafine hydrochloride (Lamisil)	Antifungal drug effective against dermatophytes and <i>Malassezia</i>	Vomiting and anorexia. Hepatotoxicity possible but not reported in animals	Doses used in dogs and cats much higher than those used in humans. Clinical results in dogs and cats for dermatophytes have been inconsistent.	250 mg tablets, 1% topical solution, 1% topical cream	Dog: 30–40 mg/kg PO (with food) q24h for 2–3 weeks Cats: 30–40 mg/kg/day PO for at least 2 weeks. Or, or 1/4 tablet for small cats (62.5 mg), 1/2 tablet for medium size cats (125 mg) and one tablet for large cats (250 mg), all administered once daily

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Terbutaline sulfate (Brethine, Bricanyl)	β -adrenergic agonist. β_2 -specific. Used primarily for bronchodilation.	Adverse effects related to excessive β -adrenergic stimulation. Tachycardia and tachyarrhythmias possible with high doses.	Used primarily for bronchodilation. May be administered orally, IM, or SC. Terbutaline (and other β_2 -agonists) have also been used in people to delay labor (dose in people is 2.5 mg q6h PO).	2.5, 5 mg tablets; 1 mg/mL injection (equivalent to 0.82 mg/mL)	Dog: 1.25–5 mg/dog q8h PO or 3–5 μ g/kg SC Cat: 0.1 mg/kg q8h, PO or 0.625 mg/cat (1/4 of 2.5 mg tablet) q12h PO For acute therapy in cats 5–10 μ g/kg (0.005–0.01 mg/kg) q4h SC, or IM
Testosterone cypionate ester (Andro-Cyp, Andronate, Depo-Testosterone, and other forms) and Testosterone propionate ester (Testex, [Malogen in Canada])	Testosterone ester. Similar effects as methyltestosterone. Testosterone esters are administered IM to avoid first-pass effects. Esters in oil are absorbed more slowly from IM injection. Esters are then hydrolyzed to free testosterone.	Adverse effects are attributed to androgenic and anabolic effects. Hepatic toxicity is also possible.	Clinical efficacy for chronic diseases has not been evaluated in small animals.	Testosterone cypionate: 100, 200 mg/mL injection Testosterone propionate: 100 mg/mL injection	Testosterone cypionate: 1–2 mg/kg every 2–4 weeks IM (see also Methyltestosterone). Testosterone propionate: 0.5–1 mg/kg 2–3 times/week IM
Tetracycline (Panmycin)	Tetracycline antibiotic. Mechanism of action of tetracyclines is to bind to 30S ribosomal subunit and inhibit protein synthesis. Usually bacteriostatic. Broad spectrum of activity, including bacteria, some protozoa, <i>Rickettsia</i> , <i>Ehrlichia</i> .	Tetracyclines can affect bone and teeth formation in young animals. Tetracyclines have been implicated in drug fever in cats. Hepatotoxicity may occur at high doses in susceptible individuals. <i>Drug interactions:</i> Tetracyclines bind to calcium-containing compounds, which decreases oral absorption.	Pharmacokinetic and experimental studies have been conducted in small animals, but no clinical studies. Do not use outdated solutions. For most indications, doxycycline can be substituted.	250, 500 mg capsules; 100 mg/mL suspension, 25 and 324 g/lb of powder	15–20 mg/kg q8h PO; or 4.4–11 mg/kg q8h IV, IM Rickettsial infection (dogs): 22 mg/kg for 14 days PO
Thenium closylate (Canopar)	Antiparasitic drug. Used to treat hookworms (<i>Ancylostoma</i> and <i>Uncinaria</i>).	Tablet is bitter if coating is broken. May cause occasional vomiting after oral administration.	Doses listed are based on recommendations from manufacturer.	500 mg tablets	Dogs > 4.5 kg: 500 mg PO once, repeat in 2–3 weeks; 2.5–4.5 kg: 250 mg PO q12h for 1 day, repeat in 2–3 weeks

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Theophylline	Methylxanthine bronchodilator. Mechanism of action is unknown, but may be related to increased cAMP or antagonism of adenosine. There is anti-inflammatory action as well as bronchodilating action.	Adverse effects: nausea, vomiting, diarrhea. With high doses, tachycardia, excitement, tremors, and seizures are possible. Cardiovascular and CNS adverse effects appear to be less frequent in dogs than in people.	Plasma concentrations of theophylline should be monitored in patients receiving chronic therapy to maintain plasma concentrations between 5 and 20 µg/mL. Many slow-release tablets are no longer available.	100, 125, 200, 250, 300 mg tablets; 27 mg/5 mL oral solution or elixir; injection in 5% dextrose. Extended-release forms are available as 100, 200, and 300 mg tablets. Availability of extended-release formulations may be variable.	Dog: 9 mg/kg q6–8h PO Extended-release formulations: 10 mg/kg q12h PO Cat: 4 mg/kg q8–12h PO Extended-release formulations: 20–25 mg/kg q24–48h PO
Thiamin (Vitamin B ₁ (Bewon and others)	Vitamin B ₁ used for treatment of vitamin deficiency	Adverse effects are rare because water-soluble vitamins are easily excreted. Riboflavin may discolor the urine.	Vitamin B supplements are administered often in combination.	250 µg/5 mL elixir; tablets of various size from 5 mg to 500 mg; 100 and 500 mg/mL injection	Dog: 10–100 mg/dog q24h PO 12.5–50 mg/dog IM, SC Cat: 5–30 mg/cat q24h PO (up to a maximum dose of 50 mg/cat q24h), 12.5–25 mg/cat IM or SC
Thioguanine (6-TG) (generic)	Anticancer agent. Antimetabolite of purine analog type. Inhibits DNA synthesis in cancer cells.	Adverse effects, as with any anticancer drugs, are expected (see 6-Mercaptopurine). Immunosuppression and leukopenia are common.	Thioguanine is often combined with other agents for treatment of cancer. Consult specific reference on cancer therapy for guidance.	40 mg tablets	Dog: 40 mg/m ² q24h PO Cat: 25 mg/m ² PO q24h × 1–5 days, then repeat every 30 days
Thiopental sodium (Pentothal)	Ultra-short-acting barbiturate. Used primarily for induction of anesthesia or for short duration of anesthesia (10–15 min procedures). Anesthesia is produced by CNS depression, without analgesia. Anesthesia is terminated by redistribution in the body.	Adverse effects are related to the anesthetic effects of the drug. Severe adverse effects are caused by respiratory and cardiovascular depression. Overdoses are caused by rapid or repeated injections. Avoid extravasation outside of vein.	Therapeutic index is low. Use only in patients in which it is possible to monitor cardiovascular and respiratory functions. Often administered with other anesthetic adjuncts.	Various size vials from 250 mg to 10 g (mix to desired concentration)	Dog: 10–25 mg/kg IV (to effect) Cat: 5–10 mg/kg IV (to effect)

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Thiotepa (generic)	Anticancer agent. Alkylating agent of the nitrogen mustard type (similar to cyclophosphamide). Used for various tumors, especially malignant effusions.	Adverse effects are similar to other anticancer agents and alkylating drugs (many of which are unavoidable). Bone marrow suppression is the most common effect.	One should consult specific cancer chemotherapy protocol for guidance on administration. Thiotepa usually is administered directly into body cavities.	15 mg injection (usually in solution of 10 mg/mL)	0.2–0.5 mg/m ² weekly, or daily for 5–10 days IM, intracavitory, or intratumor
Thyroid hormone	See Levothyroxine sodium and Liothyronine.				
Thyrotropin, Thyroid-stimulating hormone (TSH) (Thytopar, Thyrogen)	Thyroid-stimulating hormone is used for diagnostic testing. Stimulates normal secretion of thyroid hormone.	Adverse reactions rare. In people, allergic reactions have occurred.	For Thyrogen, reconstitute 1.1 mg vial with 6.0 mL sterile water, then divide into 12 aliquots. Administer 0.5 mL to each patient for testing. Remaining solution may be frozen for storage.	Old forms (Thytopar) are difficult to obtain. Human recombinant form (rh TSH) (Thyrogen) contains 1,000 µg/vial.	Dog: Collect baseline sample, followed by (human recombinant form) 50–100 µg per dog.
Ticarcillin disodium (Ticar, Ticillin)	β-lactam antibiotic. Action similar to ampicillin/amoxicillin. Spectrum similar to carbenicillin. Ticarcillin is primarily used for Gram-negative infections, especially those caused by <i>Pseudomonas</i> .	Adverse effects are uncommon. However, allergic reactions are possible. High doses can produce seizures and decreased platelet function. <i>Drug interactions:</i> Do not combine in same syringe or in vial with aminoglycosides.	Ticarcillin is synergistic and often combined with aminoglycosides (e.g., amikacin, gentamicin). 1% lidocaine may be used for reconstitution to decrease pain from IM injection.	Vials containing 1, 3, 6, 20, and 30 g for injection. 3 g vials with a final concentration of 384.6 mg/mL.	33–50 mg/kg q4–6h IV, IM
Tiletamine + zolazepam (Telazol, Zoletil)	Anesthetic. Combination of tiletamine (dissociative anesthetic agent similar in action to ketamine) and zolazepam (benzodiazepine similar in action to diazepam). Produces short duration (30 min) of anesthesia.	Wide margin of safety. Side effects include excessive salivation (may be antagonized with atropine), erratic recovery, and muscle twitching.	Administer by deep IM injection. (Consult manufacturer's package insert for dosing information for dogs and cats.)	50 mg of each component per mL	Dog (minor procedures): 6.6–10 mg/kg IM; (short-term anesthesia) 10–13 mg/kg IM Cat (minor procedures): 10–12 mg/kg IM; (surgery) 14–16 mg/kg IM
Tinidazole (Tindamax)	Antiprotozoal drug, similar to metronidazole, but considered a 2nd-generation drug. Used for <i>Trichomonas</i> , <i>Giardia</i> , and intestinal protozoa.	High doses can produce neurological adverse effects.	Dosing and use in dogs and cats are based on limited anecdotal information and extrapolation from human medicine.	250 and 500 mg tablets	Dog: 15 mg/kg q12h PO Cat: 15 mg/kg q24h PO

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Tobramycin sulfate (Nebcin)	Aminoglycoside antibacterial drug. Similar mechanism of action and spectrum as amikacin, gentamicin.	Adverse effects similar to those of amikacin, gentamicin.	Dosing requirements vary depending on bacterial susceptibility. See dose schedules for gentamicin and amikacin.	40 mg/mL injection	Dog: 9–14 mg/kg q24h IV, IM, SC Cat: 5–8 mg/kg q24h IV, IM, SC
Tocanide hydrochloride (Tonocard)	Antiarrhythmic drug. Considered an oral analogue of lidocaine. Class 1 antiarrhythmic.	In dogs, anorexia and GI toxicity have been reported. Arrhythmias, vomiting, ataxia also are possible. (In one study, 35% of dogs showed GI effects.)	Limited experience in animals. However, clinical studies demonstrate efficacy. Therapeutic concentrations are 6–10 µg/mL.	400, 600 mg tablets	Dog: 15–20 mg/kg q8h PO Cat: no dose established
Toceranib phosphate (Palladia)	Anticancer agent used for cutaneous mast cell tumors in dogs. It is a tyrosine kinase inhibitor that disrupts blood supply to tumors.	It has been associated with GI adverse effects, that include vomiting, decreased appetite, diarrhea, weight loss, and blood in feces.	Administer with antihistamines to decrease adverse effects. Proton pump inhibitors are also recommended. If adverse effects occur, discontinue for up to 2 weeks.	10, 15, and 50 mg tablets	Dog: 3.25 mg/kg PO every other day, or may be lowered to 2.5 mg/kg 3 days per week Cat: no dose established
Tramadol hydrochloride (Ultram, and generic)	Analgesic drug. Tramadol has some µ-opioid receptor action, and it may also inhibit the reuptake of norepinephrine (NE) and serotonin (5 HT). The metabolite (desmethyltramadol) may have greater opiate effects than the parent drug.	Sedation may occur in some animals, especially at high doses. In cats, some vomiting, behavior changes, and mydriasis may be observed at high doses. At very high doses in dogs, seizures may occur.	Tramadol has produced inconsistent results in both experimental studies and clinical studies in dogs. In most studies, it is a weak analgesic, or has effects not greater than a placebo. May be used with NSAIDs, other analgesics, and anesthetics.	Tramadol immediate release tablets are available in 50 mg tablets. Extended release tablets are 100, 200, and 300 mg.	Dog: 5 mg/kg q6–8h PO Cat: Start with 2 mg/kg, and increase up to 4 mg/kg q8–12h PO
Trandolapril (Mavik)	ACE inhibitor. Similar in mechanism to captopril and enalapril. Used for management of CHF. Converted to active trandolaprilat after administration.	Same adverse effects as for other ACE inhibitors	Not used extensively in veterinary patients	1, 2, 4 mg tablets	Not established for dogs. Dose in people is 1 mg/person/day to start, then increased to 2–4 mg/day.
Trazodone hydrochloride (Desyrel)	Antianxiety agent. Action is to alter serotonin action and reuptake at synapse. Used as a sedative, hypnotic, and antianxiety agent.	Causes sedation at high doses. High margin of safety.	Administer at least 1 hour prior to event that triggers anxiety. Trazodone has been used in dogs and cats to decrease anxiety associated with stressful events, or to facilitate confinement.	50, 100, 150, and 300 mg tablets	Dogs: 5 mg/kg, PO, as needed, but generally every 8 to 24 hours; or administer a single dose 1 hour prior to an anticipated event that may trigger anxiety. Cats: 50–100 mg per cat, PO (peak effect occurs in 2–2.5 hours).

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Triamcinolone and Triamcinolone acetonide (Vetalog, Triamtabs, Aristocort, generic)	Glucocorticoid anti-inflammatory drug. Triamcinolone has potency that is approximately equal to methylprednisolone (about 5× cortisol and 1.25× prednisolone), although some dermatologists suggest that potency is higher. Injectable suspension is slowly absorbed from IM or intralesional injection site. Used for intralesional therapy.	Adverse effects are similar to other corticosteroids. When used for ocular injections, there is some concern that granulomas may occur at injection site.	Note that cats may require higher doses than dogs (sometimes 2×).	Veterinary (Vetalog): 0.5 and 1.5 mg tablets. 2 or 6 mg/mL suspension injection; human form: 1, 2, 4, 8, 16 mg tablets; 10 mg/mL injection	Anti-inflammatory: 0.5–1 mg/kg q12–24h PO, then taper dose to 0.5–1 mg/kg q48h PO. (However, manufacturer recommends doses of 0.11 to 0.22 mg/kg/day.) Cat dose: start with 0.2 mg/kg per day, PO. Gradually taper to a dose of 0.1 mg/kg (0.5 mg per cat one tablet is a common dose), every other day. Triamcinolone acetonide injection: 0.1–0.2 mg/kg IM, SC, repeat in 7–10 days. Intralesional: 1.2–1.8 mg, or 1 mg for every cm diameter of tumor every 2 weeks
Triamterene (Dyrenium)	Potassium-sparing diuretic. Similar action as spironolactone, except that spironolactone has competitive inhibiting effect of aldosterone; triamterene does not.	Similar to spironolactone	Little clinical experience available for triamterene. There is no convincing evidence that triamterene is more effective than spironolactone.	50, 100 mg capsules	1–2 mg/kg q12h PO
Tribriissen	See Trimethoprim + sulfadiazine.				
Trentine hydrochloride (Syprine)	Chelating agent. Used to chelate copper when penicillamine cannot be tolerated in a patient.	Adverse effects have not been reported in animals.	Used only in patients that cannot tolerate penicillamine. Generally induces less cupruresis than penicillamine.	250 mg capsules	10–15 mg/kg q12h PO; 1–2h before feeding
Trifluoperazine (Stelazine)	Phenothiazine. Used for treatment of anxiety, to produce sedation, antiemetic. Action is believed to be via antagonism of dopamine (similar to acepromazine); antiemetic action may be via antimuscarinic action.	Adverse effects not reported in animals, but are expected to be similar to other phenothiazines.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.	10 mg/mL oral solution; 1, 2, 5, 10 mg tablets; 2 mg/mL injection	0.03 mg/kg IM q12h

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Triflupromazine hydrochloride (Vesprin)	Phenothiazine. Similar action as other phenothiazines, except triflupromazine may have stronger antimuscarinic activity than other phenothiazines. Used for antiemetic action.	Adverse effects have not been reported in animals. Adverse effects possible include anticholinergic effects.	Same as for other phenothiazines.	10, 20 mg/mL injection	0.1–0.3 mg/kg IM, PO q8–12h
Triiodothyronine	See Liothyronine.				
Trilostane (Vetoryl)	Used for treatment of hypercortisolemia (Cushing's syndrome) in dogs. 3-β-hydroxysteroid dehydrogenase inhibitor, in dogs, for treatment of pituitary-dependent hyperadrenocorticism (PDH).	Adverse effects include transient lethargy, anorexia, and vomiting. Otherwise, it has been well tolerated. One should check electrolyte levels in treated patients because trilostane may decrease aldosterone.	Trilostane is an efficacious and safe medication for treatment of dogs with PDH. Dose can be adjusted in individual patients based on cortisol measurements. In some patients, twice-daily dosing with lower doses is better tolerated than once-daily dose.	10, 30, 60, and 120 mg capsules	Dog: 3–6 mg/kg, once per day PO. Many dogs are controlled with a lower dose of 2–3 mg/kg q12h, PO. Adjust dose based on cortisol measurements. Large dogs (>30 kg) may require lower dose compared to small dogs (<15 kg). Cats: 3–6 mg/kg q24h PO, and gradually increase (as needed) to 10 mg/kg q24h. Some cats are better controlled with twice-daily administration. In these cats, start with low dose q12h, PO, then increase dose to 5 mg/kg q12h, PO as needed.
Trimeprazine tartrate (Temaril [Panectyl in Canada])	Phenothiazine with antihistamine activity (similar to promethazine). Used for treating allergies and motion sickness.	Adverse effects similar to those of promethazine.	There is evidence that trimeprazine is more effective when combined with prednisone for treatment of pruritus. Combination product is Temaril-P.	2.5 mg/5 mL syrup; 2.5 mg tablet. Temaril-P is available in tablets with 5 mg trimeprazine + 2 mg prednisolone.	0.5 mg/kg q12h PO or 0.5 mg/kg prednisolone + 1.25 mg/kg trimeprazine/day and gradually lower dose to 0.3 mg/kg prednisolone + 0.75 mg/kg trimeprazine every other day, PO.
Trimethobenzamide (Tigan, and others)	Antiemetic. Mechanism of action is not understood.	Adverse effects not reported in animals.	Efficacy as antiemetic not reported in animals.	100 mg/mL injection; 100, 250 mg capsules	Dog: 3 mg/kg q8h IM, PO Cat: not recommended

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Trimethoprim + sulfadiazine (Tribrissen, Tucoprim, and others)	Combines the antibacterial drug action of Trimethoprim and a sulfonamide. Together, the combination is synergistic, with a broad spectrum of activity.	Adverse effects primarily caused by sulfonamide component.	Dosage recommendations vary. There is evidence that 30 mg/kg/day is efficacious for pyoderma; for other infections, 30 mg/kg twice daily has been recommended.	30, 120, 240, 480, 960 mg tablet (all formulations have ratio of 5:1 sulfa:trimethoprim). Some trimethoprim-sulfadiazine tablets are less available.	15 mg/kg q12h PO, or 30 mg/kg q12–24h PO (for <i>Toxoplasma</i>). 30 mg/kg q12h PO
Trimethoprim + sulfamethoxazole (Bactrim, Septra, and generic forms)	Combines the antibacterial drug action of trimethoprim and a sulfonamide. Together, the combination is synergistic, with a broad spectrum of activity.	Adverse effects primarily caused by sulfonamide component.	Dosage recommendations vary. There is evidence that 30 mg/kg/day is efficacious for pyoderma; for other infections, 30 mg/kg twice daily has been recommended.	480, 960 mg tablet; 240 mg/5 ml oral suspension (all formulations have ratio of 5:1 sulfa:trimethoprim)	15 mg/kg q12h PO, or 30 mg/kg q12–24h PO; 30 mg/kg q12h IV
Tripeptenamine citrate (Pelamine, PBZ)	Histamine (H_1) blocker. Similar in action as other antihistamines. Used to treat allergic disease	Adverse effects similar to other antihistamines. Members of this class (ethanolamines) have greater antimuscarinic effects than other antihistamines.	There are no clinical reports of use in veterinary medicine. No evidence that it is more efficacious than other drugs in this class.	25, 50 mg tablets; 20 mg/mL injection	1 mg/kg q12h PO
Tylosin (Tylocine, Tylan, Tylosin tartrate)	Macrolide antibiotic. Tylosin is not used systemically, but has been administered to treat chronic diarrhea in dogs.	May cause diarrhea in some animals. Do not administer orally to rodents or rabbits.	Tylosin is rarely used in small animals. Powdered formulation (Tylosin tartrate) has been administered with food for control of signs of colitis in dogs. Tablets are approved in Canada for treatment of colitis.	Available as soluble powder 3 g per teaspoon 50 and 200 mg/mL injection	Dog and cat: 7–15 mg/kg q12–24h PO; 8–11 mg/kg q12h IM Dog (for colitis): 10–20 mg/kg q8h with food; if there is a response, increase the interval to q12–24h
Urofollitropin (FSH) (Metrodin)	Stimulates ovulation. Contains FSH. In people, it is used in combination with HCG to stimulate ovulation and induce pregnancy.	Side effects have not been reported in animals. In people, thromboembolism or severe ovarian hyperstimulation syndrome has been reported.	Results of clinical studies in animals have not been reported. Use in animals is based on experience in people.	75 U per vial for injection	Doses not established (human dose is 75 U/day IM for 7 days)

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Ursodiol (ursodeoxy-cholate) (Actigall)	Hydrophilic bile acid. Anticholelithic. Used for treatment of liver diseases. Increases bile flow. In dogs, may alter pool of circulating bile acids, displacing the more hydrophobic bile acids. In people, it is used to prevent or treat gallstones.	Adverse effects not reported in animals. May cause diarrhea.	Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. Administer with meals.	300 mg capsules and 250 or 500 mg tablets	10–15 mg/kg q24h PO
Valproic acid (Depakene [valproic acid]; Depakote [divalproex] [Epival is Canadian brand])	Anticonvulsant. Used, usually in combination with phenobarbital, to treat refractory epilepsy in animals. Action is not known, but it may increase GABA concentrations in the CNS.	Adverse effects have not been reported in animals, but hepatic failure has been reported in people. Sedation may be seen in some animals. Do not use in pregnant animals. <i>Drug interactions:</i> May cause bleeding if used with drugs that inhibit platelets.	Valproic acid is listed here with divalproex. Divalproex is composed of both valproic acid and sodium valproate. Equivalent oral doses of divalproex sodium and valproic acid deliver equivalent quantities of valproate ion.	125, 250, 500 mg tablets (Depakote); 250 mg capsules; 50 mg/mL syrup (Depakene); 100 mg/mL injection (Depacon)	Dog: 50–250 mg per dog (depending on size) q8h PO. For delayed-release forms, start with 250 mg per dog q12h PO, and increase to 500 mg per dog q12h, if needed. Cat: no dose established
Vancomycin (Vancocin, Vancoled)	Antibacterial drug. Mechanism of action is to inhibit cell wall and cause bacterial cell lysis (via mechanism different from that of β -lactams). Spectrum includes staphylococci, streptococci, and enterococci (but not Gram-negative bacteria). Used primarily for treatment of methicillin-resistant <i>Staphylococcus</i> spp. (e.g., MRSA, or MRSP).	Adverse effects have not been reported in animals. Administer IV; causes severe pain and tissue injury if administered IM or SC. Do not administer rapidly; use slow infusion, if possible (e.g., over 30 min).	Vancomycin can be used in animals for treatment of enterococci or staphylococci that are resistant to other antibiotics. Monitoring of trough plasma concentrations is recommended to ensure proper dose. Maintain trough concentration above 5–10 μ g/mL.	Vials for injection (0.5 to 10 g)	Dog: 15 mg/kg q6–8h IV infusion Cat: 12–15 mg/kg q8h IV infusion
Vasopressin (ADH) (Pitressin)	Antidiuretic hormone. Vasopressin is used for treatment of polyuria caused by central diabetes insipidus. Not effective for polyuria caused by renal disease. Also used as a vasopressor and during cardiac arrest (CPR).	Adverse effects have not been reported. Allergic reactions have been reported in people. Increase in blood pressure has been reported in people.	Doses are adjusted on the basis of monitoring of water intake and urine output. See also Desmopressin acetate. CPR: There is evidence that this drug may be equivalent to or even superior to epinephrine in some situations.	20 U/mL (aqueous)	Antidiuretic: 10 U IV, IM Vasopressor: 0.01–0.04 U/min CPR: 0.8 U/kg/IV. Dose may be repeated at 3- to 5-minute intervals.

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Verapamil hydrochloride (Calan, Isoptin)	Calcium channel blocking drug of the nondihydropyridine group. Blocks calcium entry into cells via blockade of slow channel. Produces vasodilation, negative chronotropic effects.	Hypotension, cardiac depression, bradycardia, AV block. May cause anorexia in some patients.	Diltiazem is preferred over verapamil in patients with heart failure because of less cardiac suppression. Oral formulation not absorbed sufficiently (of the active stereoisomer) for adequate effects.	40, 80, 120 mg tablet; 2.5 mg/mL injection	Dog: 0.05 mg/kg every 10–30 min IV (maximum cumulative dose is 0.15 mg/kg); oral dose is not established
Vinblastine sulfate (Velban)	Similar to vincristine. Sometimes used as an alternative to vincristine. Do not use to increase platelet numbers (may actually cause thrombocytopenia).	Does not produce neuropathy as vincristine does, but there may be a higher incidence of myelosuppression. Causes tissue necrosis if injected outside vein.	Vinblastine is used in cancer chemotherapy protocols for various tumors. Consult specific chemotherapy protocol for regimens.	1 mg/mL injection	2 mg/m ² IV (slow infusion) once/week
Vincristine sulfate (Oncovin, Vincasar, generic)	Anticancer agent. vincristine causes arrest of cancer cell division by binding to microtubules and inhibiting mitosis. Used in combination chemotherapy protocols. Vincristine also increases numbers of functional circulating platelets and is used for thrombocytopenia.	Generally well tolerated. Less myelosuppressive than other anticancer drugs. Neuropathy has been reported but is rare. Constipation can occur. Very irritating to tissues. Avoid extravasation outside vein during administration.	Vincristine is used in cancer chemotherapy protocols for various tumors. Consult specific chemotherapy protocol for regimens.	1 mg/mL injection	Antitumor: 0.5–0.7 mg/m ² IV (or 0.025–0.05 mg/kg) once/week Thrombocytopenia: 0.02 mg/kg IV once/week (with prednisolone)
Vitamin A (retinoids) (Aquasol A)	Vitamin A supplement. See also Isotretinoin for analogues used for other conditions.	Excessive doses can cause bone or joint pain, dermatitis.	Dosing of vitamin is expressed as U or retinol equivalents (RE), or μ g of retinol. 1 RE = 1 μ g of retinol. 1 RE of Vitamin A = 3.33 U of retinol.	Oral solution: 5000 U (1500 RE)/0.1 mL; 10,000, 25,000, and 50,000 U tablets	625–800 U/kg q24h PO (see dosing information section)
Vitamin B ₁	See Thiamin.				
Vitamin B ₂ (riboflavin)	Vitamin B ₂ supplement	Adverse effects are rare because water-soluble vitamins are easily excreted. Riboflavin may discolor the urine.	Not necessary to supplement in animals with well-balanced diets	Various size tablets in increments from 10–250 mg	Dog: 10–20 mg/day PO Cat: 5–10 mg/day PO

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Vitamin B ₁₂ (cyanocobalamin) and Cobalamin	Vitamin B ₁₂ supplement. Vitamin B ₁₂ has been used to treat some forms of anemia.	Adverse effects are rare because water-soluble vitamins are easily excreted.	Administered to animals with intestinal disease (e.g., IBD), or pancreatic insufficiency to prevent deficiency. Serum monitoring can determine optimum dose. Suggested range is 290–1, 500 ng/L for cats and 252–908 ng/L for dogs. Not necessary to supplement in animals with well-balanced diets	Various size tablets in increments from 25–1000 µg, and injection	Dog: 100–200 µg/day PO, SC or 250–500 µg/day IM or SC Cat: 50–100 µg/day PO, SC or 250 µg/cat IM or SC weekly and interval can be increased to every 2, 4, or 6 weeks.
Vitamin C (ascorbic acid) (see Ascorbic acid)	Used to treat Vitamin C deficiency and occasionally used as urine acidifier. Insufficient data to show that ascorbic acid is effective for preventing cancer or cardiovascular disease.	Adverse effects have not been reported in animals. High doses may increase risk of oxalate stones in bladder.	Not necessary to supplement in animals with well-balanced diets	Tablets of various sizes, and injection	100–500 mg/day
Vitamin D	See Dihydrotachysterol or Ergocalciferol.				
Vitamin E (alpha tocopherol) (Aquasol E and generic)	Vitamin considered as antioxidant. Used as supplement and as treatment of some immune-mediated dermatoses.	Side effects have not been reported.	Vitamin E has been proposed as treatment for a wide range of human illnesses, but evidence for efficacy in animals is lacking.	Wide variety of capsules, tablets, oral solution available (e.g., 1000 U/capsule)	100–400 U q12h PO (or 400–600 U q12h PO for immune-mediated skin disease)
Vitamin K ₁ (phytonadione, phytomenadione) (Aqua-MEPHYTON [injection], Mephylton [tablets]; Veta-K1 [capsules])	Vitamin K ₁ is used to treat coagulopathies caused by anticoagulant toxicosis (Warfarin or other rodenticides). (Anticoagulants deplete Vitamin K in the body, which is essential for synthesis of clotting factors.)	Do not administer IV.	Consult poison control center for specific protocol if specific rodenticide is identified. Use Vitamin K ₁ for acute therapy because it is more highly bioavailable. Administer with food to enhance absorption. Phytonadione and phytomenadione are synthetic lipid-soluble forms of Vitamin K ₁ . Menadiol is Vitamin K ₄ , which is converted in the body to Vitamin K ₃ (menadione).	2 or 10 mg/mL injection; Mephylton is 5 mg tablet; Veta-K1 is 25 mg capsule. Phytonadione is 2 mg/mL or 10 mg/mL injection.	Short-acting rodenticides: 1 mg/kg/day IM, SC, PO for 10–14 days Long-acting rodenticides: 2.5–5 mg/kg/day IM, SC, PO for 3–4 weeks, and up to 6 weeks

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Voriconazole (Vfend)	Azole (triazole) antifungal. Action is similar to other antifungal azole drugs, which inhibit ergosterol synthesis. Active against systemic fungi, dermatophytes, and Aspergillus.	In dogs, the clearance may increase with multiple dosing, thus diminishing the effectiveness. Liver enzyme elevations have been observed in dogs. Adverse effects in cats have been observed and include ocular problems and neurologic toxicity. May cause drug interactions by inhibiting cytochrome P 450 enzymes.	Clinical use is based on limited clinical experience, anecdotal use, and extrapolation from human medicine.	50 and 200 mg tablets, 10 mg/mL injection.	Dog: 5–6 mg/kg q12h PO Cat: A safe dose has not been established for cats. However, in some cats, a loading dose of 25 mg per cat PO, followed by 12.5 mg (2–2.3 mg/kg) every other day has been used. Observe for signs of adverse effects with multiple dosing.
Warfarin sodium (Coumadin, generic)	Anticoagulant. Depletes Vitamin K, which is responsible for generation of clotting factors. Used to treat hypercoagulable disease, prevent thromboembolism.	Adverse effects are attributable to decreased clotting. <i>Drug interactions:</i> Other drugs may potentiate warfarin's action (including aspirin, chloramphenicol, phenylbutazone, ketoconazole, cimetidine)	Warfarin response is individualistic. For optimum therapy, adjust dose by monitoring clotting time. For example, in some patients, dose is adjusted to maintain prothrombin time at 1.5–2 × to 2–2.5 × normal (or INR of 2–3).	1, 2, 2.5, 4, 5, 7.5, 10 mg tablets	Dog: 0.1–0.2 mg/kg q24h PO Cat (thromboembolism): Start with 0.25 or 0.5 mg/cat q24h PO and adjust dose based on clotting time assessment.
Xylazine hydrochloride (Rompun, and generic)	α_2 -adrenergic agonist. Used primarily for short-term anesthesia and analgesia.	Produces sedation and ataxia. Cardiac depression, heart block, and hypotension are possible with high doses. Produces emesis after IV injection, especially in cats.	Often used in combination with other drugs, e.g., ketamine	20 and 100 mg/mL injection	Dog: 1.1 mg/kg IV; 2.2 mg/kg IM Cat: 1.1 mg/kg IM (emetic [cats only] dose is 0.4–0.5 mg/kg IV)
Yohimbine (Yobine)	α_2 -adrenergic antagonist. Used primarily to reverse actions of xylazine or detomidine. Atipamezole is more specific as a reversing agent.	High doses can cause tremors and seizures.	Reverses signs of sedation and anesthesia caused by α_2 -agonists. Antipamezole may be more specific and is recommended for small animals.	2 mg/mL injection	0.11 mg/kg IV, or 0.25–0.5 mg/kg SC, IM

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Zidovudine (AZT) (Retrovir)	Antiviral drug. In people, used to treat AIDS. In animals, has been experimentally used for treatment of feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) viral infection in cats. AZT acts to inhibit the viral enzyme, reverse transcriptase, which prevents conversion of viral RNA into DNA.	Anemia and leukopenia are adverse effects. Monitor the packed cell volume in treated cats, and perform a complete blood count periodically.	At this time, experience with using AZT for treating viral disease in animals is largely experimental or anecdotal. It may have helped some experimental cats with FIV and may prevent persistent FeLV, but evidence for convincing efficacy is lacking.	10 mg/mL syrup; 10 mg/mL injection	Cat: 5–10 mg/kg PO, or SC, q12h. If administered SC, dilute in saline first to avoid injection site irritation.
Zolazepam	See Tiletamine + zolazepam.				
Zoledronate (Zometa, zoledronic acid)	Bisphosphonate drug. Inhibits bone resorption and decreases bone turnover by inhibiting osteoclasts. Used to treat malignancy of bone and pathologic bone disease. May provide pain relief with bone disease.	Use in dogs has not produced adverse effects.	Administer by IV infusion by diluting in fluids.	4 mg per 5 mL vial for injection	Dog: 0.2–0.25 mg/kg IV over 15 min diluted in 50–100 mL saline q28 days. Cat: 0.2 mg/kg IV over 15 min diluted in 25 mL every 21–28 days.
Zonisamide (Zonegran)	Anticonvulsant. Mechanism of action is uncertain, but it may potentiate the action of GABA, an inhibitory neurotransmitter, or it may stabilize membranes via changes in sodium and calcium conductance.	Adverse reactions can include lethargy, ataxia, and vomiting.	Zonisamide is used to treat refractory seizures in dogs when other drugs have not been effective.	100 mg capsule	Dog: 5–10 mg/kg q12h PO Cat: 10 mg/kg q12h PO

Key to Table Abbreviations:

ACE	angiotensin converting enzyme
CHF	congestive heart failure
CNS	central nervous system
COX	cyclooxygenase
CSF	cerebrospinal fluid
g	gram
GABA	gamma amino butyric acid
GI	gastrointestinal
IM	intramuscular
INR	international normalization ratio
IV	intravenous
μ g	micrograms
mg	milligram
MIC	minimum inhibitory concentration
mL	milliliter
NSAID	nonsteroidal anti-inflammatory drug
OTC	over the counter (without prescription)
PO	per os (oral)
PU/PD	polyuria and polydipsia
q	every, as in q8h = every 8 hours
Rx	prescription only
SC	subcutaneous
U	units

DISCLAIMER FOR DOSE TABLES:

Note: Doses listed are for dogs and cats, unless otherwise listed. Many of the doses listed are extra-label, or are human drugs not approved for animals administered in an extra-label manner. Doses listed are based on best available information at the time of table editing. The author cannot ensure efficacy or absolute safety of drugs used according to recommendations in this table. Adverse effects may be possible from drugs listed in this table of which authors were not aware at the time of table preparation. Veterinarians using this table are encouraged to consult current literature, product labels and inserts, and the manufacturer's disclosure information for additional information on adverse effects, interactions, and efficacy that were not identified at the time these tables were prepared.

APPENDIX X

CONVERSION TABLES

Table X-A

Conversion table of weight to body surface area (in square meters) for dogs			
kg	m^2	kg	m^2
0.5	0.06	26.0	0.88
1.0	0.10	27.0	0.90
2.0	0.15	28.0	0.92
3.0	0.20	29.0	0.94
4.0	0.25	30.0	0.96
5.0	0.29	31.0	0.99
6.0	0.33	32.0	1.01
7.0	0.36	33.0	1.03
8.0	0.40	34.0	1.05
9.0	0.43	35.0	1.07
10.0	0.46	36.0	1.09
11.0	0.49	37.0	1.11
12.0	0.52	38.0	1.13
13.0	0.55	39.0	1.15
14.0	0.58	40.0	1.17
15.0	0.60	41.0	1.19
16.0	0.63	42.0	1.21
17.0	0.66	43.0	1.23
18.0	0.69	44.0	1.25
19.0	0.71	45.0	1.26
20.0	0.74	46.0	1.28
21.0	0.76	47.0	1.30
22.0	0.78	48.0	1.32
23.0	0.81	49.0	1.34
24.0	0.83	50.0	1.36
25.0	0.85		

Although the above chart was compiled for dogs, it can also be used for cats. More precise values are represented in the formula $BSA \text{ in } m^2 = (K \times W^{2/3}) \times 10^{-4}$; where m^2 = square meters, BSA = body surface area, W = weight in g, and K = constant of 10.1 in dogs and 10.0 in cats.

Table X-B

Approximate equivalents for degrees Fahrenheit and Celsius*			
$^{\circ}F$	$^{\circ}C$	$^{\circ}F$	$^{\circ}C$
0	-17.8	98	36.7
32	0	99	37.2
85	29.4	100	37.8
86	30.0	101	38.3
87	30.6	102	38.9
88	31.1	103	39.4
89	31.7	104	40.0
90	32.2	105	40.6
91	32.7	106	41.1
92	33.3	107	41.7
93	33.9	108	42.2
94	34.4	109	42.8
95	35.0	110	43.3
96	35.5	212	100.0
97	36.1		

*Temperature conversion: $^{\circ}C$ Celsius to $^{\circ}F$ Fahrenheit, $(^{\circ}C)(9/5) + 32^{\circ}$; $^{\circ}F$ Fahrenheit to $^{\circ}C$ Celsius, $(^{\circ}F - 32^{\circ})(5/9)$.

CONVERSION TABLES (CONTINUED)

Table X-C

Weight-unit conversion factors		
Units Given	Units Wanted	For Conversion, Multiply by
lb	g	453.6
lb	kg	0.4536
oz	g	28.35
kg	lb	2.2046
kg	mg	1,000,000.
kg	g	1000.
g	mg	1000.
g	μ g	1,000,000.
mg	μ g	1000.
mg/g	mg/lb	453.6
mg/kg	mg/lb	0.4536
μ g/kg	μ g/lb	0.4536
Meal	kcal	1000.
kcal/kg	kcal/lb	0.4536
kcal/lb	kcal/kg	2.2046
ppm	μ g/g	1.
ppm	mg/kg	1.
ppm	mg/lb	0.4536
mg/kg	%	0.0001
ppm	%	0.0001
mg/g	%	0.1
g/kg	%	0.1

APPENDIX XI

IMPORTANT RESOURCES FOR VETERINARIANS

Accreditation

- National Veterinary Accreditation Program; www.aphis.usda.gov/nvap

Adverse event reporting

Submit reports of adverse events associated with animal foods or health products as well as suspected failures of animal health products to the manufacturer and one of the following:

- Drugs and devices: FDA CVM: 888-332-8387; www.fda.gov/AnimalVeterinary
- Pet foods and animal feeds: FDA consumer complaint coordinators; www.fda.gov/Safety/ReportaProblem/ConsumerComplaintCoordinators
- Topical insecticides: National Pesticide Information Center (sponsored by EPA): 800-858-7378; www.npic.orst.edu
- Vaccines/biologics: USDA Center for Veterinary Biologics: 800-752-6255; bit.ly/VetBiologics

Animal drugs

- FDA CVM: 240-276-9300; askcvm@fda.hhs.gov; www.fda.gov/drugs; *Report shortages of medically necessary veterinary drugs.*
- Food Animal Residue Databank: 888-873-2723; www.farad.org

Information on animal drugs and chemicals with the potential to cause foodborne residues (sponsored by the USDA Cooperative State Research, Education and Extension Service)

Blood banks, resources

- Animal Blood Resources International: 800-243-5759; www.abrint.net
A 24-hour hotline focusing on transfusion medicine (particularly blood component therapy), including recommended dosages and infusion rates for canines and felines; no cost to caller
- Blue Ridge Veterinary Blood Bank: 800-949-3822; www.evbb.com
A 24-hour commercial blood bank that focuses on transfusion medicine
- HEMOPET: 714-891-2022; www.hemopet.org
A 24-hour national, non-emergency, full service, nonprofit blood bank and educational network for animals
- Pet Blood Bank: Critical Care Specialist: 970-347-1017; www.pettransfusion.com
Provides transfusion products and training
- Plasvacc USA: 805-434-0321; www.plasvaccusa.com
A commercial blood bank for canines and equines
- Veterinarians Blood Bank: 877-838-8533; www.vetbloodbank.com
A commercial blood bank for canines and felines
- Association of Veterinary Hematology and Transfusion Medicine: www.avhtm.org
Additional resources and links

Controlled drugs

- DEA Office of Diversion Control; registration: 800-882-9539; www.deadiversion.usdoj.gov

Disaster and emergency response

- FEMA Disaster Assistance: 800-621-3362; www.fema.gov

Disease outbreaks

- USDA APHIS Emergency Operations Center: www.aphis.usda.gov/emergencyresponse
Report suspected animal disease outbreaks
- CDC Emergency Operations Center: 770-488-7100; www.cdc.gov/phpr/eoc.htm
24-hour hotline only for use by health care professionals or government officials
- State veterinarians: www.usaha.org/portals/6/StateAnimalHealthOfficials.pdf
- State public health veterinarians: <http://www.nasphv.org/Documents/StatePublicHealthVeterinariansByState.pdf>

Food safety

- FDA: 888-723-3366; www.fda.gov/food
- USDA FSIS: 202-720-9113; www.fsis.usda.gov
- USDA Meat and Poultry Hotline: 888-674-6854; bit.ly/USDAhotline

Impaired veterinarians and veterinary technicians

- Impaired Veterinarians Resources (sponsored by the AVMA): 800-248-2862, Ext. 6738; www.avma.org/ProfessionalDevelopment/Personal/PeerAndWellness

(Continued)

IMPORTANT RESOURCES FOR VETERINARIANS (CONTINUED)**Pet loss support – grief counseling**

- Chicago VMA: 630-325-1600; www.chicagovma.org
- Colorado State University, Argus Institute: 970-297-1242; www.argusinstitute.colostate.edu
- Cornell University: 607-253-3932; www.vet.cornell.edu
- University of Illinois: 217-244-2273 or 877-394-2273; www.vetmed.illinois.edu
- Michigan State University: 517-432-2696; www.cvm.msu.edu
- P&G Pet Care, Pet Loss Support Hotline: 888-332-7738
- University of Pennsylvania: 215-898-4556; www.vet.upenn.edu
- University of Tennessee: 865-755-8839; www.vet.utk.edu/socialwork
- Tufts University: 508-839-7966; www.tufts.edu/vet
- Virginia Tech/University of Maryland: 540-231-8038; www.vetmed.vt.edu
- Washington State University: 509-335-5704 or 866-266-8635; www.vetmed.wsu.edu

Poison control

- American Association of Poison Control Centers: 800-222-1222; www.aapcc.org
- ASPCA Animal Poison Control Center: 888-426-4435; www.aspca.org/apcc

Small fee per case for veterinarians enrolled in the Veterinary Life Line Partner Program; no charge for calls covered by ASPCA Animal Product Safety Service

- Pet Poison Helpline: 855-764-7661; www.petpoisonhelpline.com
A 24-hour, nationwide service offered by the Pet Poison Control Center, Small fee charged

Shipping

- Animals
 - Centers for Disease Control and Prevention: 800-232-4636; www.cdc.gov
For information about importing animals into the United States
 - USDA APHIS Veterinary Services: 301-851-3300; bit.ly/USDAVetServices
- Specimens
 - Department of Transportation, Office of Hazardous Materials: 800-467-4922; www.phmsa.dot.gov/hazmat

Workplace Safety

OSHA: 800-321-6742; www.osha.gov

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Text in boldface denotes chapter discussions. Prefixes are normally ignored in the alphabetical sequence; thus *S*-adenosylmethionine is listed after adenosine.

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